Abstract Book

Society of Surgical Oncology
SSO 2025 Annual Meeting

Tampa, FL
March 27 - 29, 2025

Electronic supplement to
Annals of Surgical Oncology
The Leading Resource in Surgical Oncology

SSO2025
ANNUAL MEETING

Annals of Surgical Oncology
The Leading Resource in Surgical Oncology
The Official Journal of the Society of Surgical Oncology

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CONTENTS

Volume 32, Supplement 1, March 2025

Pg. S4: 2025 Best Papers Abstracts
Pg. S70: 2025 E-Posters
Pg. S295: Abstracts Participating in the Global Partner Posters Program

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This supplement is not sponsored by outside commercial interests.

ABSTRACTS

2025 BEST PAPERS

SSO 2025 ANNUAL MEETING

Society of Surgical Oncology

March 27-29, 2025

Ann Surg Oncol (2025) 31:S1–S310
https://doi.org/10.1245/s10434-025-17184-1

Sarcoma

1. Single Cell Transcriptomics Identifies Distinct Gene Expression Programs in SDH-deficient GIST

Mark Antkowiak[1]; Ashwyn Sharma[2]; Chih-Min Tang[3]; Alex Wenzel[4]; Sara Rothschild[5]; Denisse Evans[6]; Christina Ochs[7]; Becky Owens[8]; Jill P. Mesirov[9]; Jason K. Sicklick[10]
[1]UC San Diego, San Diego, CA, US; [2]UC San Diego, La Jolla, CA, US; [3]UC San Diego, La Jolla, CA, US; [4]UC San Diego, La Jolla, CA, US; [5]Life Raft Group, Wayne, NJ, US; [6]Life Raft Group, Wayne, NJ, US; [7]Life Raft Group, Wayne, NJ, US; [8]Life Raft Group, Wayne, NJ, US; [9]UC San Diego, La Jolla, CA, US; [10]UC San Diego, La Jolla, CA, US

INTRODUCTION: Gastrointestinal stromal tumors (GIST) are driven by a variety of oncogene and tumor suppressor gene mutations. Succinate dehydrogenase deficient (SDH-deficient) GIST, often caused by germline mutations in the SDH genes, account for approximately 10% of all GIST and demonstrate heterogenous biology ranging from indolent tumors to aggressive metastatic disease. However, this variable biology of SDH-deficient GIST remains poorly understood. To examine the drivers of tumor behavior, we comprehensively characterized patient tumor samples using a single cell transcriptomics approach. **METHODS:** We performed single nucleus RNA-sequencing (snRNAseq) on tumor samples from 19 patients with SDH-deficient GIST. Following standard data processing and cell type annotation, we subset tumor cells and employed a machine learning approach (non-negative matrix factorization) to identify distinct transcriptional programs, which were characterized using gene set enrichment analysis (GSEA). We then excluded gene sets with a false discovery rate >0.01. Statistical analysis was performed to examine the association of tumor states with clinical, pathologic, and mutational profiles. **RESULTS:** Tumor samples were collected from 19 patients with SDH-deficient GIST including patients with *SDHA* (8, 42.1%), *SDHB* (8, and *SDHC* (3, 15.8%) mutant tumors. Patients with both primary (5, 26.3%) and metastatic (14, 73.7%) disease were included. Following data processing and normalization, a total of 143,206 cells were identified including 10 different cell types. Using a machine learning approach, four unique transcriptional programs were identified in the tumor cells (S1-S4) and were characterized using GSEA. The S1 state was associated with primary disease (S1 =44.5% *vs*. S2/3/4= 0% primary disease, P=0.02), while S3 was associated with multiple lines of therapy (S3 = 3.8 *vs*. S1/2/4 = 1.2 therapies, P<0.01) but a longer disease course (10.8 *vs*. 2.9 years, P< 0.01). **CONCLUSIONS:** For the first time, we comprehensively characterize SDH-deficient GIST using a single cell transcriptomic approach. We identify four transcriptional programs that each have unique pathways that correlate with tumor behavior and disease course. We show that S1 tumor cells are associated with localized disease, while S3 tumor cells represent late-stage tumors that are multi-drug resistant. These findings begin to elucidate the intra- and inter-tumoral heterogeneity of SDH-def GIST, as well as tumor evolution with therapy. These findings will be used to investigate unique cellular programs in each state that can be individually targeted therapeutically.

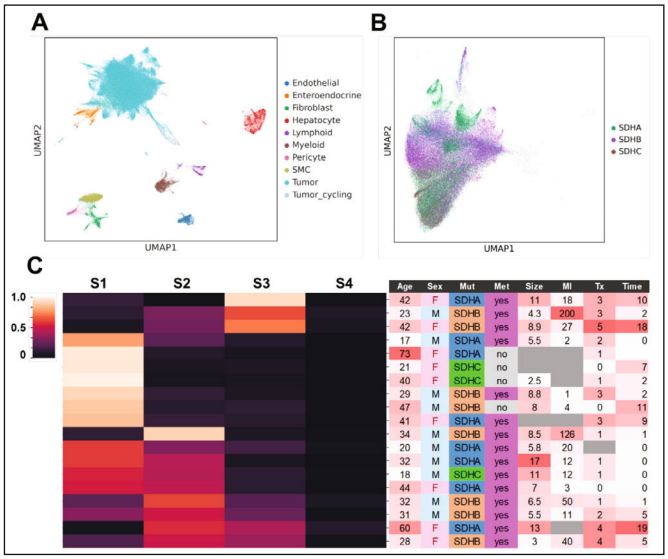


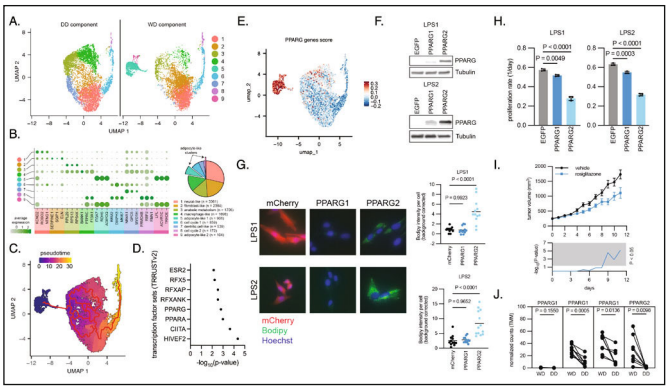
Figure 1. Discovery of Transcriptional Programs in SDH-deficient GIST. A. UMAP of all cell types in 19 SDH-deficient tumors. B. UMAP showing the tumor cell subset with SDHA, SDHB and SDHC mutations. C. Tumor transcriptional profiles discovered using a machine learning approach and the associated clinical characteristics: age, sex, mutation [Mut], metastatic disease [Met], size (cm), mitotic index (per 5 mm^2) [MI], lines of therapy [Tx], length of disease course (years) [Time].

2. PPARG2 Regulates Subtype Transitions in Well-Differentiated/Dedifferentiated Liposarcoma

Kyle D. Klingbeil, MD, PhD[1]; Blake Wilde, PhD[2]; Serena Lofftus, MD[3]; Tyler McCaw, MD PhD[4]; Manando Nakasaki, MD[5]; Chris Frias, BS MS[6]; Sarah Dry, MD[7]; Joseph Crompton, MD PhD[8]; Fritz Eilber, MD[9]; Claudio Villanueva, PhD[10]; Heather Christofk, PhD[11]; Brian Kadera, MD[12]
[1]UCLA Health, Los Angeles, CA, US; [2]UCLA Health, Los Angeles, CA, US; [3]UCLA Health, Los Angeles, CA, US; [4]UCLA Health, Los Angeles, CA, US; [5]UCLA Health, Los Angeles, CA, US; [6]University of Vermont College of Medicine, Burlington, VT, US; [7]UCLA Health, Los Angeles, CA, US; [8]UCLA Health, Los Angeles, CA, US; [9]UCLA Health, Los Angeles, CA, US; [10]UCLA Health, Los Angeles, CA, US; [11]UCLA Health, Los Angeles, CA, US; [12]UCLA Health, Los Angeles, CA, US

INTRODUCTION: It remains unclear whether tumor progression of well-differentiated/dedifferentiated liposarcoma (WD/DD LPS) is driven by mechanisms of trans-differentiation. We sought to understand whether trans-differentiation contributes to tumor evolution in WD/DD LPS. **METHODS:** Tumor tissue was harvested from patients with primary, untreated WD/DD LPS, and histology validated by expert pathology review. Single nuclei suspensions from each sample were used to construct cDNA libraries, followed by next-generation sequencing. The R package 'Seurat' was applied to integrate samples. LPS clusters were generated and analyzed by pseudo-time analysis to establish trajectory inferences between WD and DD subtypes. Genes that associated with pseudotime were assessed for overrepresentation in an expanded reference database (TRRUSTv2). The two splice isoforms of *PPARG* (*PPARG1* and *PPARG2*) were overexpressed using lentivirus in two human DD LPS cell lines, LPS1 and LPS2. Lipid droplet formation was assessed using bodipy staining. NSG mice harboring LPS2 xenografts were treated with rosiglitazone. Trimmed Mean of M-values (TMM) normalization was used to compare expression of *PPARG1* and *PPARG2* among human WD/DD LPS in the external dataset GSE221494. **RESULTS:** Six unique patient tumor samples, representing three WD/DD pairs and 27,333 nuclei, were included in the computational pipeline. Nine unique LPS clusters were identified, two of which were unique to WD LPS (Fig. 1A). Differential expression analysis revealed these two clusters expressed adipocyte-specific genes (Fig. 1B). Single-cell trajectory analysis was constructed and *PPARG* expression was among the top genes associated with pseudotime (Fig. 1C-D). Gene score analysis demonstrated high *PPARG* expression in WD clusters, suggesting PPARG suppression is part of the evolutionary trajectory from WD to DD LPS (Fig. 1E). Overexpression of the constitutively-active isoform *PPARG2* in DD LPS cell lines promoted protein

expression of PPARG, led to the accumulation of lipid droplets, and reduced proliferation rates, suggesting a terminal differentiation back to WD LPS (Fig. 1F-H). LPS2 xenografts treated with the PPARG-agonist rosiglitazone reduced tumor growth (Fig. 1I). Among available external datasets of WD/DD LPS, *PPARG2* expression was silenced in all samples of DD LPS. **CONCLUSIONS:** These findings suggest a model where WD LPS undergoes trans-differentiation towards DD LPS that includes suppression of *PPARG*. This study adds insight into the mechanisms of tumor evolution in WD/DD LPS and reveals key signaling pathways for therapeutic targeting.



3. Radiologic and Pathologic Response Evaluation After Neoadjuvant Chemotherapy for Retroperitoneal Sarcoma: A Transatlantic Australasian Retroperitoneal Sarcoma Working Group (TARPSWG) Collaboration

Stijn Van der Burg[1]; Piotr Rutkowski[2]; Markus Albertsmeier[3]; Sylvie Bonvalot[4]; Valerie Grignol, MD[5]; Chandrajit Raut[6]; Ferdinando Canazi[7]; John Mullinax, MD[8]; David E. Gyorki, MD, MBBS[9]; Elisabetta Pennacchioli[10]; Samual Ford[11]; Carolyn Nessim[12]; Kenneth Cardona, MD[13]; Alessandro Gronchi[14]; Winan J. van Houdt, MD, PhD[15]

[1]Netherlands cancer institute, Amsterdam, Noord-Holland, NL; [2]Maria-Sklodowska-Curie National Research Institute of Oncology, Warsaw, PL; [3]Ludwig-Maximilians-Universität, Munich, DE; [4]Institut Curie, Paris, FR; [5]The Ohio State University, Columbus, OH, US; [6]Division of Surgical Oncology, Department of Surgery, Brigham & Women's Hospital, Harvard Medical Sc, Boston, MA, US; [7]Istituto di Patologia Speciale Chirurgica, Università Cattolica del Sacro Cuore, Roma, Roma, IT; [8]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [9]: Division of Cancer Surgery, Peter MacCallum Cancer Centre, and Sir Peter MacCallum Department of O, Melbourne, Victoria, AU; [10]European Institute of Oncology, IRCCS, Milan, , IT; [11]University Hospitals Birmingham NHS Foundation Trust, Birmingham, GB; [12]University of Ottowa, Ottowa, ON, CA; [13]Emory University Hospital Midtown, Atlanta, GA, US; [14]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [15]Netherlands Cancer Institute, Amsterdam, NL

INTRODUCTION: Macroscopically complete resection is the primary treatment for retroperitoneal sarcomas (RPS). The role of neoadjuvant chemotherapy (NACT) in improving oncological outcomes remains uncertain. The aim of this study was to evaluate the association between radiologic and pathologic responses in predicting long-term oncological outcomes. **METHODS:** Data for this study were collected from the Retroperitoneal Sarcoma Registry (RESAR) and included patients with primary RPS treated with NACT between January 2017 and October 2020. The association between radiologic response, pathologic response and oncologic outcomes was evaluated. Radiologic response was determined based on RECIST 1.1. Pathological response was defined as <10% viable cells or >20% fibrosis/hyalinization. Kaplan-Meier curves with log-rank tests and Cox proportional hazards regression were used to compare oncologic outcomes, while a three-knot polynomial spline was employed to illustrate the association between changes in tumor size as a continuous variable and overall survival (OS). **RESULTS:** One hundred and forty-one patients from 16 sarcoma centers were included in this study. The most common histology was dedifferentiated liposarcoma (36.9%) followed by leiomyosarcoma (34.0%). After NACT, 14.5% of the patients had partial response (PR), 63.3% had stable disease, and 22.2% had progressive disease (PD) based on radiologic evaluation. PR was significantly associated with pathologic response based on fibrosis/hyalinization (OR 5.6; 95%CI 1.1-29.0, p=0.034), and not with viable cells. Differences in OS were not significant for patients with or without PD (HR 1.9; 95%CI 0.9-4.1; p= 0.113, Figure 1A). However, polynomial splined regression did indicate a linear function for increasing tumor size and worse survival (Figure 1C). If PD was seen on early radiologic evaluation, after a median of two cycles, the difference in OS was significant (HR 5.4; 95%CI 1.2-25.3; p= 0.032) (figure 1B). **CONCLUSIONS:** Radiologic progression during the first 2 cycles of NACT is associated with worse OS. Pathological response based on >20% fibrosis/hyalinization is significantly associated with radiological response. A larger cohort is necessary for statistical validation of these data and investigation of other trends noted.

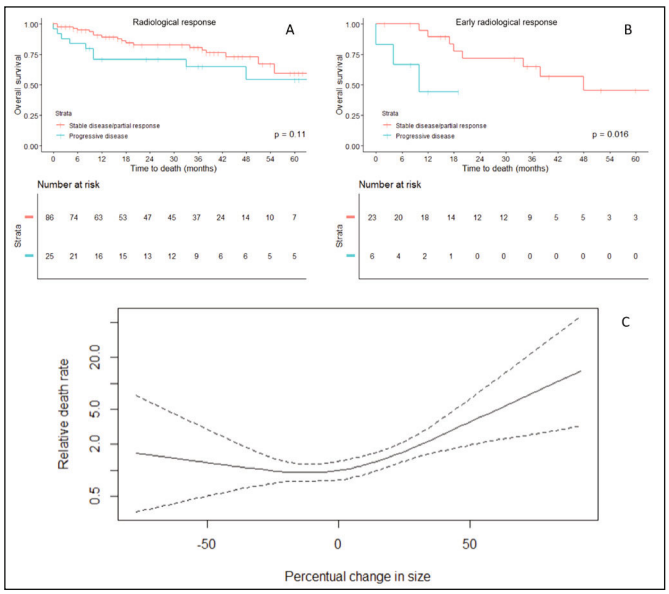


Figure 1. (A) Kaplan–Meier analysis of progressive disease versus stable disease/partial response on radiological evaluation; (B) Kaplan–Meier analysis of progressive disease versus stable disease/partial response on early radiological evaluation; (C) Polynomial spline with 95% confidence interval displaying the relative death rate per change in tumor size during neoadjuvant chemotherapy.

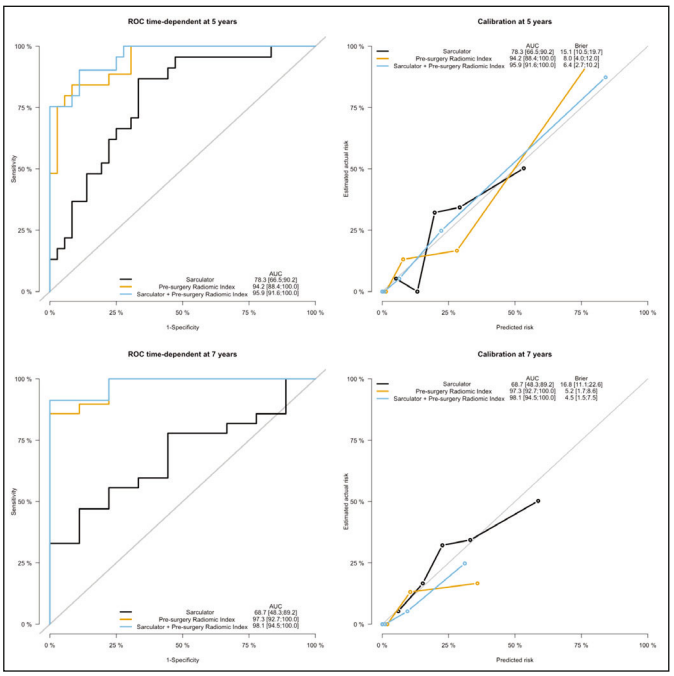
4. Development and Internal Validation of an MRI-Based Radiomic Signature for Prognostication of Patients With Extremity Soft Tissue Sarcoma

Andrea Vanzulli[1]; Gabriele Tinè[2]; Antonella Messina[3]; Raffaella Vigorito[4]; Carlo Morosi[5]; Paola Collini[6]; Elena Di Blasi[7]; Roberta Sanfilippo[8]; Elena Palassini[9]; Silvia Stacchiotti[10]; Marco Fiore[11]; Rosalba Miceli[12]; Alessandro Gronchi[13]; Sandro Pasquali[14]; Dario Callegaro, MD[15]

[1]Istituto Nazionale dei Tumori, Milan, IT; [2]Istituto Nazionale dei Tumori, Milan, IT; [3]Istituto Nazionale dei Tumori, Milan, IT; [4]Istituto Nazionale dei Tumori, Milan, IT; [5]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [6]Istituto Nazionale dei Tumori, Milan, IT; [7]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [8]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [9]Istituto Nazionale dei Tumori, Milan, IT; [10]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [11]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [12]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [13]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [14]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [15]Istituto Nazionale dei Tumori, Milano, IT

INTRODUCTION: The prognosis of patients with primary soft tissue sarcoma of the extremity and superficial trunk (eSTS) largely depends on tumor size, grade and histology. Nomograms like Sarculator combine these variables to provide precise estimates of individual patient prognosis. The aim of this study was to develop a radiomic signature (RS) to enhance the performance of Sarculator. **METHODS:** Patients with primary localized eSTS treated with surgery (2011-2015) at a single institution, who had preoperative MRI scans available, were included. Preoperative contrast-enhanced MRI scans were reviewed and segmented for the extraction of 2144 radiomic features. From these, 168 were used for the analysis. A Laplacian filter was applied to retain the features that explained ≥80% of the variance in the full dataset. The selected radiomic features were combined through a linear combination into

a prognostic RS applying an ad-hoc version of the Bayesian Least Absolute Shrinkage and Selector Operator (Lasso). Three Cox models were fitted: (1) Sarculator alone, (2) RS alone and (3) Sarculator+RS. Their performance was assessed in terms of discrimination (Harrell's C index) and calibration (calibration plots, Brier Score). **RESULTS:** The study included 91 patients: 8 with leiomyosarcoma (8.8%), 24 with undifferentiated pleomorphic sarcoma (26.4%), 8 with dedifferentiated/pleomorphic liposarcoma (8.8%), 17 with myxoid liposarcoma (18.7%), 3 with malignant peripheral nerve sheath tumor (3.3%), 20 with myxofibrosarcoma (22.0%), 4 with synovial sarcoma (4.4%), and 7 with other histologies (7.7%). The median follow-up was 55.8mo (IQR 44.8,72.9). The RS consisted of 8 radiomic features. Time-dependent ROC curves, calibration plots and Brier Scores at 5 and 7 years for the three Cox models (Sarculator, black line; RS, yellow line; and Sarculator+RS, light blue line) are presented in Figure 1. Both the RS alone model and the Sarculator+RS model had significantly higher AUC and significantly lower Brier Scores at both 5 and 7 years compared with the Sarculator-alone model. The C-index values after internal bootstrap cross-validation were 0.746 for Sarculator alone, 0.893 for RS alone and 0.914 for Sarculator+RS. **CONCLUSIONS:** The MRI-based radiomic signature developed in this study significantly improved the performance of the Sarculator in terms of both discrimination and calibration. The combination of the RS with Sarculator showed the best results, indicating potential for prognostication, pending external validation.



5. Uncovering the Conserved Biology of SDH-deficient Tumors Using Single Cell Transcriptomics

Mark Antkowiak[1]; Ashwyn Sharma[2]; Chih-Min Tang[3]; Alex Wenzel[4]; Jill P. Mesirov[5]; Jason K. Sicklick[6]

[1]UC San Diego, San Diego, CA, US; [2]UC San Diego, San Diego, CA, US; [3]UC San Diego, San Diego, CA, US; [4]UC San Diego, San Diego, CA, US; [5]UC San Diego, San Diego, CA, US; [6]UC San Diego, San Diego, CA, US

INTRODUCTION: Succinate dehydrogenase (SDH) is a key enzyme in the citric acid cycle. Mutations causing SDH deficiency have been associated with tumorigenesis, most notably in Carney-Stratakis syndrome, a hereditary disorder linked to the development of gastrointestinal stromal tumors (GIST) and paragangliomas/pheochromocytomas (PPGL). While SDH plays a key role in energy homeostasis, the role of SDH-deficiency in tumorigenesis remains poorly characterized. To uncover the molecular underpinnings of SDH-deficiency on tumor biology, we analyzed single cell transcriptomic data from patients with GIST and PPGL with or without genetic SDH deficiency. **METHODS:** We performed single nucleus RNA-sequencing (snRNAseq) on 34 GIST and combined our data with single cell RNA-sequencing (scRNAseq) of 30 PPGL. Following standard data processing and cell type annotation, we subset tumor cells and performed differential gene expression analysis on aggregated gene expression. To identify overexpressed pathways in SDH-deficient tumors, we performed single sample Gene Set Enrichment Analysis (ssGSEA) and compared pathway enrichment between SDH-deficient and non-SDH-deficient tumors. **RESULTS:** Of 64 patient samples, 29 (45%) harbored SDH gene mutations including 20 GIST (59%) and 9 PPGL (30%). Differential gene expression demonstrated 1,733 genes significantly enriched in SDH-deficient GIST, 273 in SDH-deficient PPGL, and 224 in both. GSEA identified 129 pathways significantly upregulated in both SDH-deficient GIST and PPGL. Pathway characterization showed enrichment of pathways related to mitochondrial function and epigenetic regulation as expected, but also glutamate metabolism and neuronal or smooth muscle development. Interestingly, SDH-deficient tumors also demonstrated enrichment in several conserved oncogenic pathways including EGFR, PIK3CA/AKT/mTOR, and Notch pathways. **CONCLUSIONS:** Using a single cell transcriptomic approach, we discover a set of pathways enriched in both SDH-deficient GIST and PPGL, including metabolic and oncogenic signaling pathways. These findings highlight the complex molecular processes underlying tumorigenesis in the setting of SDH-deficiency and present new avenues for research into the underlying biology and therapeutic targeting of SDH-deficient tumors.

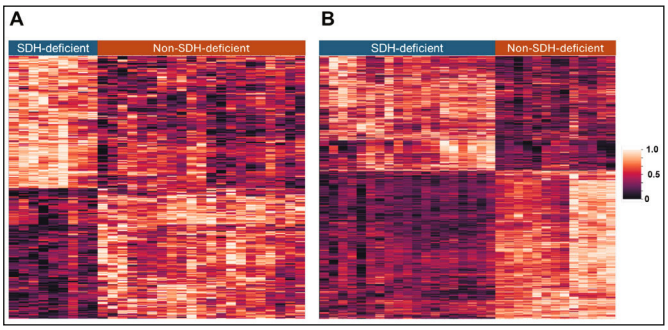


Figure 1. Pathway enrichment in SDH-deficient tumors. A. Single sample gene set enrichment analysis (ssGSEA) was performed on SDH-deficient PPGL vs. non-SDHdeficient PPGL, showing the top upregulated and downregulated pathways. B.ssGSEA in SDH-deficient GIST vs. non-SDH-deficient GIST.

6. Pathologic tumor viability after neoadjuvant chemotherapy is not an associated outcome in undifferentiated pleomorphic sarcoma (UPS) and myxofibrosarcoma (MFS)

Nichita J. Kulkarni, MD[1]; David Mahvi, MD[2]; Kenneth Seier, MS[3]; Narasimhan Agaram, MBBS[4]; Cristina Antonescu, MD[5]; Evan Rosenbaum, MD[6]; Ciara Kelly, MBBCh BAO[7]; Aimee Crago, MD/PhD[8]; Li-Xuan Qin, PhD[9]; Samuel Singer, MD[10]; Edmund K. Bartlett, MD[11]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US; [11]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Neoadjuvant chemotherapy is considered in patients with UPS or MFS at high risk for metastasis. Prior studies reporting pathologic response have all included patients treated with preoperative radiation. We sought to assess the prognostic significance of pathologic tumor viability in patients treated with neoadjuvant chemotherapy without preoperative radiation. **METHODS:** We analyzed data from a single-institution prospectively maintained sarcoma database for patients with UPS or MFS treated with neoadjuvant chemotherapy and curative intent surgery from 1995 to 2024. Pathologic response was defined as the percent tumor viability in the surgical specimen. Cumulative incidence curves and Fine and Gray models were used for disease specific survival (DSS) and recurrence free survival (RFS). Multivariate analysis was performed for DSS including variables significant in the univariate model and percent tumor viability as the primary outcome of interest. **RESULTS:** A total of 76 patients were included, 56 with UPS and 20 with MFS. The median tumor size was 11.7 cm, and 80% were in the lower extremity. Median follow up was 7.25 years for survivors. The most common chemotherapy regimen was doxorubicin/ifosfamide in 52 patients, followed

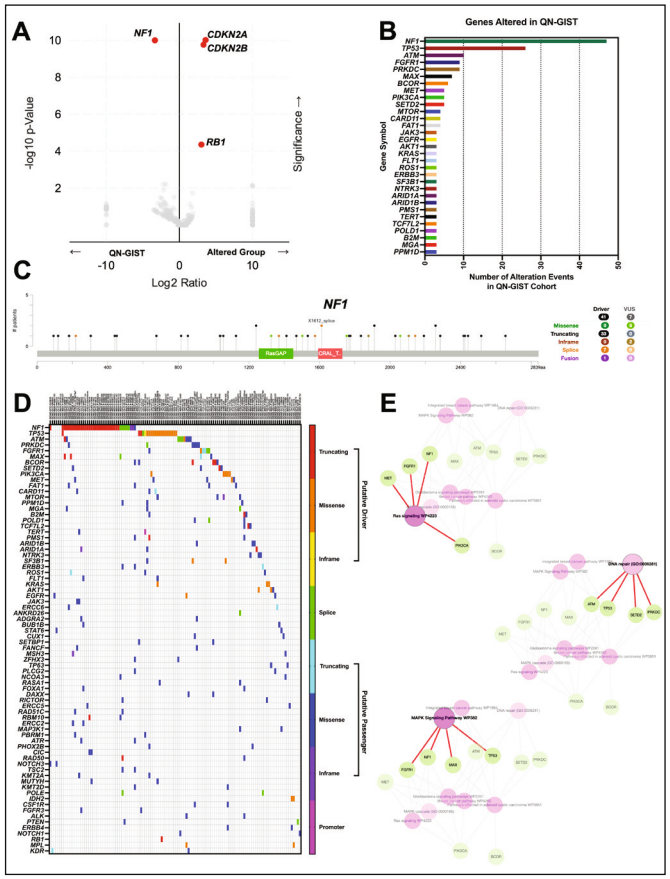
by gemcitabine/docetaxel in 12 patients. Following neoadjuvant therapy, the median percent tumor viability in the surgical specimen was 30% (range 0-95%). 5-year DSS was 65%, and 5-year RFS was 52%. Variant type (UPS vs. MFS) and radiographic response as measured by RECIST criteria were not significantly associated with DSS on univariate analysis. Percent tumor viability as a continuous variable was not associated with DSS (HR 1.001, p=0.88) or RFS (HR 1.007, p=0.21). After controlling for variables independently associated with DSS, percent tumor viability was not significantly associated with DSS (HR 0.988, p=0.10). Even in the 9 (12%) patients with exceptionally good response (< 5% viability), there was no significant association with DSS (HR 3.883, p=0.21) or RFS (HR 6.184, p=0.08). **CONCLUSIONS:** Percent tumor viability following neoadjuvant chemotherapy without preoperative radiation is not associated with and does not appear to be a prognostic biomarker for survival outcomes in patients with UPS or MFS. Future studies should assess specific components of response such as tumor necrosis or hyalinization as well as investigate other novel biomarkers to assess for predictive surrogate endpoints for clinical trial design.

7. Quadruple negative gastrointestinal stromal tumor demonstrates heterogenous dysregulation of RAS-MAPK signaling and DNA repair

Andrew M. Fleming, MD[1]; Daniel B Gehle, MD[2]; Julia Pedo Freitas, MD[3]; Ian B Solsky, MD[4]; Jeremiah L Deneve, DO[5]; Paxton V. Dickson, MD[6]; Evan S Glazer, MD, PhD[7]; David Shibata, MD[8]; Andrew J Murphy, MD[9]

[1]The University of Tennessee Health Science Center / St. Jude Children's Research Hospital, Memphis, TN, US; [2]The University of Tennessee Health Science Center / St. Jude Children's Research Hospital, Memphis, TN, US; [3]The University of Tennessee Health Science Center, Memphis, TN, US; [4]The University of Tennessee Health Science Center, Memphis, TN, US; [5]University of North Carolina, Chapel Hill, NC, US; [6]University of Tennessee Health Science Center / St. Jude Children's Research Hospital, Memphis, TN, US; [7]The University of Tennessee Health Science Center / St. Jude Children's Research Hospital, Memphis, TN, US; [8]The University of Tennessee Health Science Center / St. Jude Children's Research Hospital, Memphis, TN, US; [9]The University of Tennessee Health Science Center / St. Jude Children's Research Hospital, Memphis, TN, US

INTRODUCTION: Gastrointestinal stromal tumors (GIST) lacking hallmark *KIT, PDGFRA, BRAF,* and/or *SDHA-D* driver mutations—so called "quadruple negative" GISTs (QN-GIST)—respond poorly to conventional therapy. This analysis identifies candidate therapeutic targets for patients with QN-GIST using the world's largest publicly accessible clinicogenomics dataset. **METHODS:** All GIST samples were identified within the American Association for Cancer Research (AACR) Project Genomics Evidence Neoplasia Information Exchange (GENIE) dataset "GENIE Cohort v16.0-public," released June 2024. Sample-level clinical and genomic alterations were analyzed and stratified by *KIT/PDGFRA/BRAF/SDHA-D* mutational status via cBioPortal for Cancer Genomics. Individual mutations were characterized in the QN-GIST cohort, and pathway analysis was performed via the "Gene Ontology Biological Process 2021" dataset. **RESULTS:** Among 1,893 GIST samples analyzed, 259/1,893 were QN-GIST (14%). Patients with QN-GIST were younger (median age: 58 years vs. 63 years, q<.0001) and more often female (53.8% vs. 43.1%, q<.01). Patients with QN-GIST had higher rates of *NF1* mutations (28.1% vs. 2.57%, q<.0001) and lower rates of mutations in cell cycle regulators *CDKN2A* (1.6% vs. 18.6% q<.0001), *CDKN2B* (2.0% vs. 20.1%, q<.0001), and *RB1* (0.82% vs. 6.6%, q<.01) (Figure 1A). The most frequent genetic alterations in QN-GIST were *NF1* (n=47), *TP53* (n=26), *ATM* (n=10), *PRKDC* (n=9), *FGFR1* (n=9), *MAX* (n=7), *BCOR* (n=6), *SETD2* (n=5), *PIK3CA* (n=5), and *MET* (n=5) (Figure 1B). *NF1* mutations demonstrated mutual exclusivity with mutations in *KIT* (Log2 Odds Ratio (OR) <-3, *CDKN2A* (Log2 OR <.0001), and *CDKN2B* (Log2 OR <-2, q=.01). Among 41 *NF1* putative driver mutations analyzed, there were 33/41 truncating mutations (80.5%), 7/41 splice events (17.1%), and 1 fusion (2.4%) (Figure 1C). All 41/41 NF1 mutations were reported as somatic (100.0%). Heatmapping of recurrent genetic events highlighted mutations in DNA repair genes (Figure 1D). Mutation pathway analysis demonstrated enrichment for genes involved in RAS signaling (q<.0001), MAPK signaling (q<.0001), and DNA repair (q<.001) (Figure 1E). **CONCLUSIONS:** QN-GIST demonstrate recurrent truncating mutations in *NF1* and multiple mutations implicated in RAS-MAPK signaling and DNA repair. These signaling pathways warrant analysis as alternative therapeutic targets for QN-GIST patients refractory to conventional treatments.



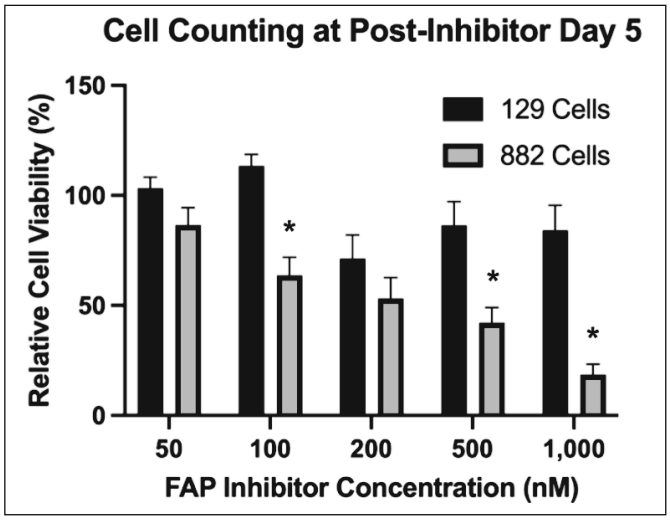
8. Fibroblast Activation Protein in Gastrointestinal Stromal Tumor

Iulia Barbur, MD[1]; Ferdinando Rossi, PhD[2]; Susan Zeng, PhD[3]; Juan Esteban Perez, MD[4]; Richard J. Straker, MD[5]; Taylor E Hartlein, M.D[6]; Ronald DeMatteo, MD[7]

[1]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [2]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [3]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [4]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [5]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [6]University of Pennsylvania, Philadelphia, PA, US; [7]Hospital of the University of Pennsylvania, Philadelphia, PA, US

INTRODUCTION: Gastrointestinal stromal tumor (GIST) is the most common human sarcoma and commonly driven either by a KIT or PDGFR mutation. Fibroblast activation protein (FAP) expression is a poor prognostic indicator for some cancers and is associated with metastasis. However, the role of FAP in GIST has not been defined. **METHODS:** A tissue microarray of 69 primary GISTs with 3 cores/patient was created and clinical data were collected; the threshold for positive FAP staining by immunohistochemistry was set as 15% of cells based on negative controls (kidney, testis, liver) and measured by QuPath positive cell detection software. The human GIST cell lines 129 (exon 11 heterozygous KIT mutation) and 882 (exon 13 homozygous KIT mutation) were studied in vitro. FAP inhibition was achieved with either a small molecule FAP inhibitor (UAMC-1110) or siRNA knockdown (smartpool siRNA). Proliferation assays utilized a 24 well plate over a 5 day course with 4 replicates per condition, whereas viability assays utilized a 72 hour 96 well plate with Dojindo reagent and 10 replicates per condition. **RESULTS:** FAP expression was higher in PDGFRA (n = 16) versus KIT (n = 23) mutant GIST (median 1,270 vs. 211; p = 0.01) by RNA sequencing. Within the tissue microarray, 67% of stomach GISTs stained positive for FAP versus only 27% of small bowel primaries (p < 0.001). For the FAP+ patients, the mean percentage of stained cells was similar at 46% versus 44% and median at 42% versus 41% for stomach versus small bowel GISTs, respectively. FAP positive tumors correlated inversely with mitoses (p < 0.001), but did not correlate with sex, age, or tumor size. By quantitative PCR, 882 cells had higher RNA expression of FAP than 129 cells, and only 882 cells demonstrated FAP protein by western blot. Consistent with

this, the FAP inhibitor altered cell proliferation of 882 cells, but not 129 cells ($p < 0.001$, Fig.), and decreased 882 cell viability at 1 hour ($p < 0.05$). FAP knockdown via smartpool siRNA did not alter KIT or PDGFR RNA expression. **CONCLUSIONS:** FAP expression in human GIST is heterogenous and depends on tumor location (stomach versus small bowel), primary mutation (KIT versus PDGFRA), and even type of KIT mutation present. FAP inhibition reduced proliferation and viability of a human GIST cell line in a dose-response manner. Therefore, FAP may be a therapeutic target in GIST.



9. Single-cell transcriptomic analysis reveals effects of amputation and inhaled cytokine on myeloid-derived suppressor cells in dogs undergoing treatment for naturally occurring osteosarcoma

Cyrus Sholevar[1]; Aryana Razmara[2]; Marshall Lammers[3]; Natalie Liu[4]; Megan Purl[5]; Sean Judge[6]; William Culp[7]; Michael Kent[8]; William Murphy[9]; Robert Rebhun[10]; Titus Brown[11]; Robert Canter[12]

[1]University of California Davis Medical Center, Sacramento, CA, US; [2]University of California Davis, Sacramento, CA, US; [3]University of California Davis Medical Center, Sacramento, CA, US; [4]University of California Davis Medical Center, Sacramento, CA, US; [5]University of California Davis Medical Center, Sacramento, CA, US; [6]University of California Davis Medical Center, Sacramento, CA, US; [7]University of California Davis School of Veterinary Medicine, Davis, CA, US; [8]University of California Davis School of Veterinary Medicine, Davis, CA, US; [9]University of California Davis Medical Center, Sacramento, CA, US; [10]University of California Davis School of Veterinary Medicine, Davis, CA, US; [11]University of California Davis School of Veterinary Medicine, Davis, CA, US; [12]University of California Davis Medical Center, Sacramento, CA, US

INTRODUCTION: Dogs are outbred animals that develop naturally occurring malignancies and provide valuable insight into tumor immunology and cancer immunotherapy. Using samples from a novel canine clinical trial, we set out to investigate the effects of inhaled interleukin 15 (inhIL-15) on myeloid-derived suppressor cells (MDSCs), a heterogeneous population of myeloid cells with potent immunosuppressive effects. We hypothesized that changes in MDSC quantity and function following amputation and inhIL-15 are associated with earlier disease recurrence. **METHODS:** We conducted a phase II first-in-dog clinical trial of adjuvant inhIL-15 and chemotherapy in dogs undergoing amputation for extremity osteosarcoma (OSA). Blood samples were collected pre-operatively, 1-3 days post-operatively, after completing a two-week course of inhIL-15, and after initiating chemotherapy. Peripheral blood mononuclear cells from dogs with short (87 days) and long (368 days) disease-free intervals (DFI) were analyzed with single-cell sequencing using the 10X platform. **RESULTS:** Sharing some similarity with human MDSC gene signatures, dog MDSC clusters were identified with high fidelity based on IL-18, IL-1B, KCNJ2, and STEAP4 expression. Pre-operative MDSC populations showed marked variability between short DFI (8.2%) and long DFI (1.6%) dogs. MDSC populations were increased 1-3 days post-operatively in both dogs and remained higher in the short DFI dog (8.9% vs. 6.9%). The ratio of MDSCs to natural killer cells, implicated in antitumor responses in OSA, increased from an average of 1.5 at baseline to 26.8 post-amputation consistent with the immunosuppressive effects of surgery. Monocytic MDSCs were the predominant subtype of MDSCs post-operatively (78.2%), while polymorphonuclear (PMN) MDSCs predominated in the post-inhIL-15 (81.8%) and post-chemotherapy (83.5%) timepoints. The high affinity IL-15 receptor alpha was highly expressed on monocytes and monocytic MDSCs, and expression increased in both post-operatively. MDSCs also showed differential expression of CYP4F22 (cytochrome P450 family), CD4, and LTF (lactotransferrin) genes compared to monocytes. Expression of LOXL1 and LOXL3, genes associated with human MDSC immunosuppressive function, were elevated in canine MDSCs. **CONCLUSIONS:** MDSCs were increased after amputation in dogs with OSA, and higher frequencies at baseline and after amputation were observed in the setting of short DFI compared to long DFI. IL-15Ra was expressed on monocytic MDSCs after amputation, suggesting this may be an actionable pathway to target MDSCs, alter the immunosuppressive environment, and prolong disease-free survival in this devastating disease.

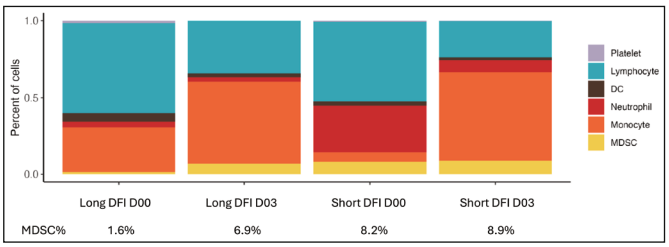


Figure 1. Peripheral blood immune populations in dogs with long versus short disease-free intervals before and after amputation for osteosarcoma

10. Circulating Cell-Free DNA Concentrations Predict Poor Survival in Soft Tissue Sarcoma

Samuel A. Yellin[1]; Rebecca Marcus, MD[2]; Lisa Ercolano, MD[3]; Patricia Petrosko[4]; Phillip Gallo[5]; Louis Gil Acevedo[6]; Harmeet Kharoud, MD[7]; Robin Barr[8]; Tong Lam[9]; Ali Zaidi[10]; William Laframboise[11]; David Bartlett[12]; Patrick Wagner[13]

[1]Allegheny Health Network, Pittsburgh, PA, US; [2]Allegheny Health Network, Pittsburgh, PA, US; [3]Allegheny Health Network, Pittsburgh, PA, US; [4]Allegheny Health Network, Pittsburgh, PA, US; [5]Allegheny Health Network, Pittsburgh, PA, US; [6]Allegheny Health Network, Pittsburgh, PA, US; [7]Allegheny Health Network, Pittsburgh, PA, US; [8]Allegheny Health Network, Pittsburgh, PA, US; [9]Allegheny Health Network, Pittsburgh, PA, US; [10]Allegheny Health Network, Pittsburgh, PA, US; [11]Allegheny Health Network, Pittsburgh, PA, US; [12]Allegheny Health Network, Pittsburgh, PA, US; [13]Allegheny Health Network, Pittsburgh, PA, US

INTRODUCTION: Soft tissue sarcomas (STS) are a heterogeneous group of uncommon malignancies, for which surgical resection forms the cornerstone of curative treatment. Liquid biomarkers are increasingly used to guide decision-making in clinical oncology, but their sensitivity and specificity rely on the yield of peripheral circulating cell-free DNA (cfDNA). We studied the association of patient and tumor factors with cfDNA yield in STS, as these tumors are poorly understood and cfDNA yield could influence the interpretation of biomarker testing in clinical practice. **METHODS:** We investigated baseline cfDNA concentration in a series of STS patients undergoing treatment at Allegheny Health Network. Baseline characteristics including patient demographics, tumor size, disease site & extent, and histologic grade & oncologic outcome were analyzed for association with log-transformed cfDNA concentration using linear regression and Cox regression. **RESULTS:** In total, 81 patients with STS were analyzed. The median (IQR) and mean (+/-SD) circulating concentration of cfDNA were 5.9 (3.63-11.8) ng/mL and 9.35 +/- 10.23 ng/mL. cfDNA concentration was associated with advanced patient age ($p=0.03$) and tumor size in patients with unifocal disease ($p<0.05$). cfDNA did not differ with respect to AJCC stage, histologic grade, or site of tumor origin (extremity vs. retroperitoneal vs. visceral). cfDNA concentration was associated with poor overall and disease survival, this difference was stage-independent (HR 2.26 [1.24-4.12], $p=0.008$) on multivariable analysis. **CONCLUSIONS:** cfDNA concentration in patients with STS is associated with patient age and tumor size, factors which may contribute to sensitivity and specificity of commercial assays relying on cfDNA and impact the interpretations of results. cfDNA concentration is a stage-independent biomarker of poor survival irrespective of the outcome of downstream cfDNA-based assays, and may have additive prognostic utility in tandem with established risk factors for poor outcome in STS.

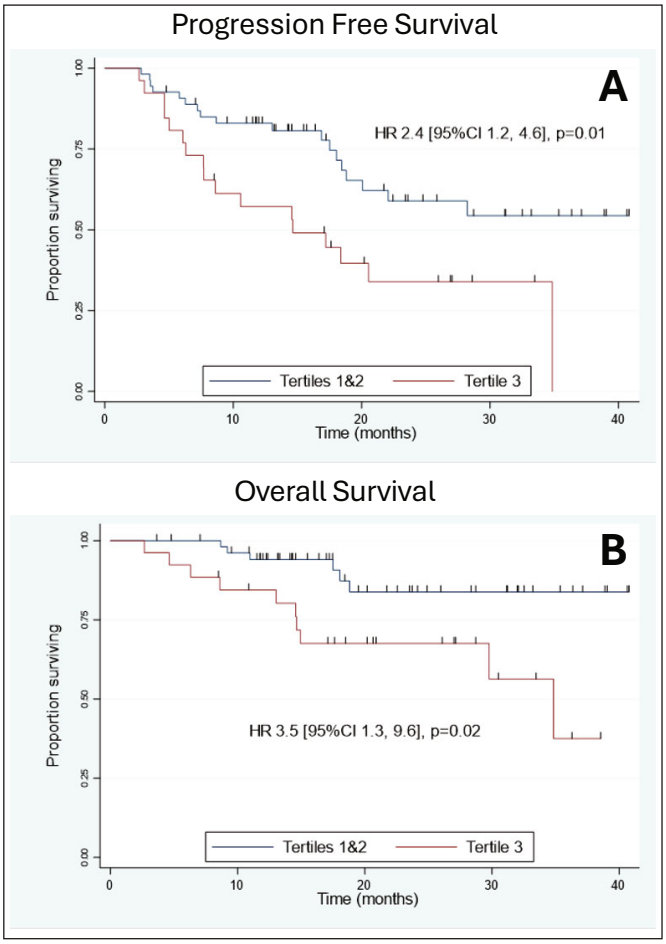


Figure 1. Influence of peripheral cfDNA concentration on progression-free survival and overall survival in soft tissue sarcoma. Increased cfDNA concentrations, as divided by tertiles, were significantly associated with worse progressionfree (panel A) and overall (panel B) survival.

Breast I

11. Clinical Management and Oncological Outcomes of Pure Pleomorphic and Florid Lobular Carcinoma in Situ of the Breast: Results from the MultiLCIS Study

Massimo Ferrucci, MD, PhD[1]; Daniele Passeri, MD[2]; Francesco Milardi, MD[3]; Rocco Cappellesso, MD, PhD[4]; Paola Del Bianco, MD[5]; Gian Luca De Salvo, MD[6]; Angelo Paolo Dei Tos, MD, PhD[7]; Gianluca Franceschini, MD, PhD[8]; Pietro Maria Ferrando, MD, PhD[9]; Lucio Fortunato, MD[10]; Matteo Ghilli, MD[11]; Adele Sgarella, MD[12]; Carla Cedolini, MD, PhD[13]; Francesca Catalano, MD[14]; Serena Scomersi, MD[15]; Simone Mele, MD[16]; Francesca Muscara, MD[17]; Graziano Meneghini, MD[18]; Eugenia Raffaeli, MD[19]; Donato Casella, MD, PhD[20]; Lazaros Papadopoulos, MD[21]; Laura Frias, MD, PhD[22]; Martin Fernando Rivas Ibarra, MD[23]; Hasan Karanlik, MD[24]; Maggie Banys Papulowsky, MD, PhD[25]; Christian Rizzetto, MD[26]; Francesca Pellini, MD[27]; Guido Papaccio, MD[28]; Eleonora Meduri, MD[29]; Michela Stumpo, MD[30]; Simona Grossi, MD[31]; Leonardo Barellini, MD[32]; Alba Di Leone, MD, PhD[33]; John Benson, MD, PhD[34]; Angela Santoro, MD, PhD[35]; Virginia Castagnetta, MD[36]; Isabella Castellano, MD, PhD[37]; Jacobo Cumbo, MD[38]; Ada Ala, MD[39]; Gianmarco Piccolino, MD[40]; Chiara Anghelone, MD[41]; Serenca Bertozzi, MD, PhD[42]; Martina Rapisarda, MD[43]; Margherita Fezzi, MD[44]; Moira Ragazzi, MD[45]; Filippo Cappello, MD[46]; Nicola Rocco, MD, PhD[47]; Giacomo Montagna, MD, MPH[48]; Alberto Marchet, MD[49]; Walter Paul Weber, MD[50]

[1]Veneto Institute of Oncology IRCCS, Padova, Veneto, IT; [2]Department of Surgery, Oncology and Gastroenterology, University of Padova, IT; [3]Department of Surgery, Oncology and Gastroenterology, University of Padova, IT; [4]Surgical Pathology and Cytopathology Unit, Department of Medicine-DIMED, University of Padova, IT; [5]Veneto Institute of Oncology IRCCS, Padova, IT; [6]Veneto Institute of Oncology IRCCS, Padova; [7]Surgical Pathology and Cytopathology Unit, Department of Medicine-DIMED, University of Padova, Padova; [8]Multidisciplinary Breast Centre, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome; [9]Department of General and Specialized Surgeries, AOU Città della Salute e della Scienza, Turin; [10]Breast Center, Department of Surgery, San Giovanni Addolorata Hospital, Rome; [11]Breast Cancer Centre, University Hospital of Pisa; [12]Breast Surgery, General Surgery 3, Department of Surgical Sciences, IRCCS San Matteo Hospital Founda, Pavia; [13]Breast Unit, University Hospital of Udine, Udine; [14]Multidisciplinary Breast Unit, Cannizzaro Hospital of Catania; [15]Department of General Surgery, Azienda Sanitaria Universitaria Giuliano-Isontina, University Hospita; [16]Breast Surgery Unit, AUSL-IRCCS Reggio Emilia; [17]Breast Unit, University Hospitals NHS Foundation Trust, Cambridge, GB; [18]Functional Department Transmural Breast Surgery, AULSS, Vicenza, IT; [19]Department of General Surgery, Azienda Ospedaliero Universitaria delle Marche, Ancona; [20]Department of Breast Cancer Surgery, University of Siena; [21]IASO General Clinic, Athens; [22]University Hospital La Paz, Madrid; [23]Universidad de Santiago de Chile; [24]Istambul University Institute of Oncology; [25]Universitätsklinikum Schleswig-Holstein Campus Lübeck; [26]Breast Surgery Unit, "Ca' Foncello" Regional Hospital,Treviso; [27]Breast Unit, Oncologic Surgery Department, AOUI Verona, Verona; [28]Breast Care Center, Ospedale dell'Angelo, Mestre; [29]Division of Breast Surgical Oncology, Cancer Institute FPO IRCCS, Candiolo, Turin; [30]Department of Pathology, Misericordia Hospital, Grosseto; [31]Eusoma Breast Centre, "G. Bernabeo" Hospital, Ortona; [32]UOC Oncologia Chirurgica Ricostruttiva della Mammella, Azienda USL Toscana Nord Ovest - Spedali Riun, Livorno; [33]Multidisciplinary Breast Centre, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, IT; [34]Breast Unit, University Hospitals NHS Foundation Trust, Cambridge, GB; [35]Multidisciplinary Breast Centre, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, IT; [36]Multidisciplinary Breast Centre, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, IT; [37]Department of General and Specialized Surgeries, AOU Città della Salute e della Scienza, Turin, IT; [38]Department of General and Specialized Surgeries, AOU Città della Salute e della Scienza, Turin, IT; [39]Department of General and Specialized Surgeries, AOU Città della Salute e della Scienza, Turin, IT; [40]Breast Center, Department of Surgery, San Giovanni Addolorata Hospital, Rome, IT; [41]Breast Surgery, General Surgery 3, Department of Surgical Sciences, IRCCS San Matteo Hospital Founda, Pavia, IT; [42]Breast Unit, University Hospital of Udine, IT; [43]Multidisciplinary Breast Unit, Cannizzaro Hospital of Catania, IT; [44]Department of General Surgery, Azienda Sanitaria Universitaria Giuliano-Isontina, University Hospita, IT; [45]Breast Surgery Unit, AUSL-IRCCS Reggio Emilia, IT; [46]Surgical Pathology and Cytopathology Unit, Department of Medicine-DIMED, University of Padova, IT; [47]Department of Advanced Biomedical Sciences, University "Federico II" of Naples, IT; [48]Memorial Sloan Kettering Cancer Center, New York, NY, US; [49]Veneto Institute of Oncology IRCCS, Padova, IT; [50]University Hospital Basel, US

INTRODUCTION: Pure pleomorphic (PLCIS) and florid (FLCIS) lobular carcinoma in situ without concurrent invasive carcinoma (IC) or ductal carcinoma in situ (DCIS) are rare, and their treatment is not standardized due to limited evidence. We gathered the first large multicentric cohort of cases to identify the optimal therapeutic approach. **METHODS:** This international study (NCT06133465) collected data from 32 centers in 8 countries. Cases of pure PLCIS and/or FLCIS on core biopsy and/or final specimen were included. Slides review by dedicated pathologists and a minimum follow-up of 2 years were required. **RESULTS:** We collected 374 patients with pure P-/FLCIS on core biopsy and/or on surgical specimen between 01/2004-06/2022. 64 showed P-/FLCIS only upon final histology. Upgrades on surgical specimen were observed in 101/310 cases with a preoperative diagnosis of pure P-/FLCIS: 80/101 (79.2%) upgraded to IC and 21/101 (20.8%) to DCIS. The upgrade rate to IC was 29.8% for PLCIS and 14.1% for FLCIS (p=0.003). Factors significantly associated with upgrade included radiological mass-like aspect, lesion size, multicentric distribution, irregular margins, and necrosis on core biopsy. Our analysis focused on the 273 pure PLCIS (168/273, 61.5%) or FLCIS (105/273, 38.5%) cases confirmed on surgical specimen. Median age was 58 years; median lesion size was 13 mm. 244 lumpectomies and 29 mastectomies were performed. Margin involvement (P-/FLCIS on ink) occurred in 59/244 cases (24.2%), leading to 31 re-operations and no further excisions in 28 cases. Sentinel lymph node biopsy was performed in 69/273 (25.3%) cases, with no metastases found. Adjuvant radiotherapy was administered to 40/273 (14.7%) patients, and endocrine therapy to 63/273 (23.1%). After a median follow-up of 74 months (IQR 35-91), local recurrence (LR) occurred in 35/273 cases (12.8%): 16 IC, 2 DCIS and 17 P-/

FLCIS. Margin involvement (p<0.001) and multicentric distribution (p=0.001) were associated with LR. Adjuvant therapies did not affect recurrence rates (RR) in patients with clear (p=0.37) or involved (p=0.08) margins. LR was significantly higher in patients with positive margins who did not undergo a re-excision (22/31, 71%), compared to who did (2/28, 7.1%) (p<0.001). RR were similar between pure PLCIS and FLCIS cases (13.7% vs. 11.4%, p=0.583). **CONCLUSIONS:** The P-/FLCIS upgrade rate to IC/DCIS was 32.6%, indicating the need for surgery. Surgery with clear margins, rather than adjuvant therapies, should be the mainstay of treatment for this disease.

Clinicopathological Features, Surgical and Oncological Outcomes of Pure P-/FLCIS

	PLCIS (N = 168)	FLCIS (N = 105)	Overall (N = 273)	p-value
Patients' characteristics [n/N (%)]				
Age (years)				
Median (IQR)	60 (54 - 66)	53 (48 - 59)	58 (51 - 64)	0.483
Range	40 - 75	30 - 88	30 - 88	
Previous Cancer				0.376
No	122/168 (72.6)	96/105 (91.4)	218/273 (79.9)	
Yes, ipsilateral	32/168 (19.0)	4/105 (3.8)	36/273 (13.2)	
Yes, contralateral	14/168 (8.3)	5/105 (4.8)	19/273 (7.0)	
Fertility				0.638
Pre-menopausal	25/168 (14.9)	27/105 (25.7)	52/273 (19.0)	
Post-menopausal	143/168 (85.1)	78/105 (74.3)	221/273 (81)	
Family history				0.486
No	122/168 (72.6)	75/105 (71.4)	197/273 (72.2)	
Yes, first degree	32/168 (19.0)	16/105 (15.2)	48/273 (17.6)	
Yes, other	14/168 (8.3)	14/105 (13.3)	28/273 (10.3)	
Radiologic characteristics [n/N (%)]				
Mammography				0.273
Performed	165/168 (98.2)	103/105 (98.1)	268/273 (98.2)	
Not evidence of disease	5/165 (3.0)	7/105 (6.7)	12/268 (4.5)	
Calcifications	139/165 (84.2)	76/105 (72.4)	215/268 (80.2)	
Architectural distortion	47/165 (28.5)	35/105 (33.3)	82/268 (30.6)	
Ultrasound				0.741
Performed	131/168 (78.0)	94/105 (89.5)	225/273 (82.4)	
Not evidence of disease	29/131 (22.1)	23/94 (24.5)	52/225 (23.1)	
Echogenicity				
Hypoechogenic	93/131 (71.0)	63/94 (67.0)	156/225 (69.3)	
Hyperechogenic	9/131 (6.9)	8/94 (8.5)	17/225 (7.6)	
Margins				
Irregular	66/131 (50.4)	58/94 (61.7)	124/225 (55.1)	
Regular	36/131 (27.5)	13/94 (13.8)	49/225 (21.8)	
Magnetic Resonance Imaging				0.349
Performed	76/168 (45.2)	49/105 (46.7)	125/273 (45.8)	
Not evidence of disease	0/76 (0.0)	0/49 (0.0)	0/125 (0.0)	
Enhancement				
Mass like	36/76 (47.4)	18/49 (36.7)	54/125 (43.2)	
Non-mass like	40/76 (52.6)	31/49 (63.3)	71/125 (56.8)	
Size				0.193
Median (IQR)	14 (7-23)	12 (7-21)	13 (7-22)	
Histopathological characteristics [n/N (%)]				
Calcifications				0.742
Yes	94/168 (56.0)	59/105 (56.2)	153/273 (56.0)	
No	74/168 (44.0)	46/105 (43.8)	120/273 (44.0)	
Necrosis				0.182
Yes	73/168 (43.5)	29/105 (27.6)	102/273 (37.4)	
No	95/168 (56.5)	76/105 (72.4)	171/273 (62.6)	
Associated classic LCIS				0.687
Yes	67/168 (39.9)	39/105 (37.1)	106/273 (38.8)	
No	101/168 (60.1)	66/105 (62.9)	167/273 (61.2)	
Estrogen receptors				0.264
Performed	113/168 (67.3)	46/105 (43.8)	159/273 (58.2)	
Positive	97/113 (85.8)	45/46 (97.8)	142/159 (89.3)	
Negative	16/113 (14.2)	1/46 (2.2)	17/159 (10.7)	
Progesteron receptors				0.719
Performed	108/168 (64.3)	43/105 (41.0)	151/273 (55.3)	
Positive	58/108 (53.7)	30/43 (69.8)	88/151 (58.3)	
Negative	50/108 (46.3)	13/43 (30.2)	63/151 (41.7)	
Treatment and outcomes [n/N (%)]				
Surgical treatment				0.087
Lumpectomy	142/168 (84.5)	102/105 (97.1)	244/273 (89.4)	
Unilateral mastectomy	22/168 (13.1)	2/105 (1.9)	24/273 (8.8)	
Bilateral mastectomy	4/168 (2.4)	1/105 (1.0)	5/273 (1.8)	
Additional surgical approach				0.109
Sentinel lymph node biopsy	53/168 (31.6)	16/105 (15.2)	69/273 (25.3)	
Re-excision	22/168 (13.1)	9/105 (8.6)	31/273 (11.4)	
Final margin status				0.371
On ink	25/168 (14.9)	10/105 (9.5)	35/273 (12.8)	
≤ 1 mm	17/168 (10.1)	14/105 (13.3)	31/273 (11.4)	
> 1 mm	126/168 (75.0)	81/105 (77.1)	207/273 (75.8)	
Adjuvant therapies				0.538
Endocrine therapy	47/168 (28.0)	16/105 (15.2)	63/273 (23.1)	
Radiation therapy	28/168 (16.7)	12/105 (11.4)	40/273 (14.7)	
Chemotherapy	0/168 (0.0)	0/105 (0.0)	0/273 (0.0)	
Recurrences				0.093
Local	23/168 (13.7)	12/105 (11.4)	35/273 (12.8)	
Loco-regional	0/168 (0.0)	0/105 (0.0)	0/273 (0.0)	
Distant	0/168 (0.0)	0/105 (0.0)	0/273 (0.0)	
Vital status				0.913
Alive	167/168 (99.4)	105/105 (100)	272/273 (99.6)	
Dead	1/168 (0.6)	0/105 (0.0)	1/273 (0.4)	

PLCIS, pleomorphic lobular carcinoma in situ; FLCIS, florid lobular carcinoma in situ; IQR, interquartile range

12. Sentinel Lymph Node Biopsy for cN1 HR+/HER2- Breast Cancer Patients with Palpable Adenopathy: Results of a Multicenter, Single-Arm Clinical Trial

Anita Mamtani[1]; Andrea V. Barrio[2]; George Plitas[3]; Melissa Pliewskie[4]; Niamey Wilson[5]; Heiwon Chung Whang[6]; Hiram S. Cody[7]; Stephanie Downs-Canner[8]; Giacomo Montagna[9]; Minna K. Lee[10]; Kimberly J. Van Zee[11]; Deborah Capko[12]; Daniel X. Choi[13]; Mahmoud El-Tamer[14]; Laurie Kirstein[15]; Tracy-Ann Moo[16]; Virgilio Sacchini[17]; Audree Tadros[18]; Varadan Sevilimedu[19]; Monica Morrow[20]
[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]University of Michigan, Ann Arbor, MI, US; [5]Hartford HealthCare, Hartford, CT, US; [6]Lehigh Valley Health Network, Allentown, PA, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New-York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New-York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US; [11]Memorial Sloan Kettering Cancer Center, New York, NY, US; [12]Memorial Sloan Kettering Cancer Center, New York, NY, US; [13]Memorial Sloan Kettering Cancer Center, New York, NY, US; [14]Memorial Sloan Kettering Cancer Center, New York, NY, US; [15]Memorial Sloan Kettering Cancer Center, New York, NY, US; [16]Memorial Sloan Kettering Cancer Center, New-York, NY, US; [17]Memorial Sloan Kettering Cancer Center, New York, NY, US; [18]Memorial Sloan Kettering Cancer Center, New York, NY, US; [19]Memorial Sloan Kettering Cancer Center, New York, NY, US; [20]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Randomized trials established the safety of omitting axillary lymph node dissection (ALND) among early-stage, clinically node-negative (cN0) breast cancer patients with < 3 positive sentinel lymph nodes (+SLNs) having upfront surgery and adjuvant radiation. Patients with palpable mobile level I/II axillary adenopathy (cN1) were not eligible for these studies. Presently, > 80% of HR+/HER2- cN1 patients undergo ALND either at upfront surgery or after neoadjuvant therapy, despite evidence that 50-60% will have only 1-2 positive nodes. We prospectively evaluated the use of upfront SLNB and rates of ALND in this single-arm clinical trial. **METHODS:** Patients with cTx/cT1-2 cN1 HR+/HER2- breast cancer with palpable, biopsy-proven nodal metastases, with axillary ultrasound (AUS) demonstrating ≤ 3 morphologically abnormal nodes, were accrued at 4 centers. Patients underwent upfront lumpectomy or mastectomy and SLNB, performed with single or dual tracer mapping (blue dye and/or Tc-99m sulfur colloid). Completion ALND (cALND) was indicated for ≥ 3 positive SLNs. **RESULTS:** From 4/2021 to 8/2024, 78 patients were enrolled on study. Median age was 58 years (range 24-83), 1 (1.3%) had an occult (cTx) tumor, 37 (47%) were cT1, and 40 (51%) were cT2. 56 (72%) had ductal histology, and 59 (76%) were moderately differentiated. On AUS, 39 (50%) had 1 abnormal-appearing node, 33 (42%) had 2, and 6 (8%) had 3. The median pathologic tumor size was 2.3 cm (IQR 1.6, 3.4), 50 (64%) had lymphovascular invasion, and 54 (69%) had extracapsular extension. SLNB was performed with dual tracer in 87%, and ≥ 3 SLNs were retrieved in 96% of cases. The palpable diseased node(s) were blue and/or radioactive in 68% of patients. Overall, 24 (31%) had 1 +SLN, 30 (38%) had 2 +SLNs, and 24 (31%) had ≥ 3 +SLNs. SLNB alone was performed in 59 (76%) of patients, while 19 (24%) had cALND; an indicated cALND was deferred in N = 5 cases (Figure). Axillary radiotherapy was given to 81% of patients, and systemic therapy was received when indicated. Among those with ≥ 12 months of follow-up (n = 39, median 19 months), there have been no isolated axillary recurrences or locoregional recurrences to date; 1 patient has developed distant disease. **CONCLUSIONS:** SLNB is feasible among cN1 HR+/HER2- patients, with ≥ 3 SLNs retrieved in 96% of cases. Nearly 70% of patients had only 1 or 2 positive SLNs and met accepted criteria for avoidance of ALND. This approach affords the opportunity to omit unnecessary ALND and minimize morbidity among cN1 patients with limited nodal disease burden.

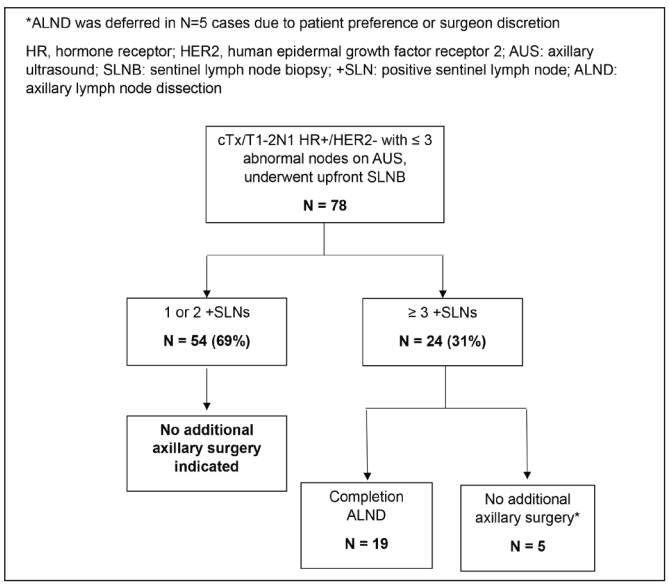


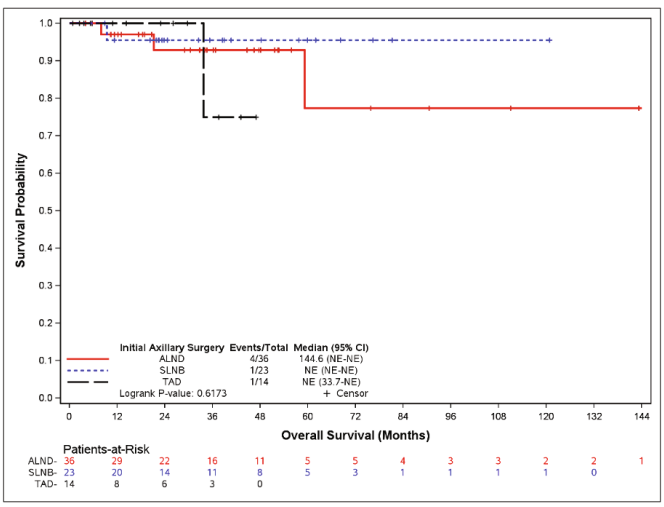
Figure. Nodal positivity and rate of axillary lymph node dissection

13. The Significance of Micrometastatic Axillary Disease after Neoadjuvant Chemotherapy in Breast Cancer

Paige Aiello, MD[1]; Nicole Harris[2]; Syeda Mahrukh Hussnain Naqvi, MD, MPH[3]; Weihong Sun, MD[4]; David Detz[5]; Susan Hoover, MD[6]; Nazanin Khakpour, MD[7]; John Kiluk, MD[8]; Laura Kruper, MD, MSCE[9]; Christine Laronga[10]; Melissa Mallory, MD[11]; Brian Czerniecki, MD, PhD[12]; Marie C Lee, MD[13]
[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4]Moffitt Cancer Center, Tampa, FL, US; [5]Moffitt Cancer Center, Tampa, FL, US; [6]Moffitt Cancer Center, Tampa, FL, US; [7]Moffitt Cancer Center, Tampa, FL, US; [8]Moffitt Cancer Center, Tampa, FL, US;

[9]Moffitt Cancer Center, Tampa, FL, US; [10]Moffitt Cancer Center, Tampa, FL, US; [11]Moffitt Cancer Center, Tampa, FL, US; [12]Moffitt Cancer Center, Tampa, FL, US; [13]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Clinical relevance of minimal residual axillary disease after neoadjuvant chemotherapy (NAC) is a topic of debate. Our study sought to evaluate outcomes of micro-metastatic axillary disease in NAC breast cancer patients. **METHODS:** This is a retrospective single institution review of a prospective NAC breast cancer database from 2013-2024. Data points include clinical stage, receptor status, original axillary surgery: sentinel lymph node biopsy (SLNB), targeted axillary dissection (TAD), axillary lymph node dissection (ALND) and subsequent completion ALND (cALND). Descriptive statistics summarized characteristics of the entire sample. Chi-square tests and ANOVA were used for categorical variables. Kaplan-Meier survival curves log-rank test expressed impact of various axillary surgery types on overall survival (OS) and recurrence-free survival (RFS). Univariate Cox proportional hazards models estimated hazard ratios (HR) and 95% confidence intervals (CI) for OS and RFS. **RESULTS:** Of 1878 NAC patients, 73 patients (3.9%) had axillary nodal micrometastatic or isolated tumor cells (ITC) on final pathology. Mean follow up was 36 months (range 0-143); most patients were clinical T2 (66%), ER+ (70%), PR + (62%), HER2+ (45%). Most patients had initial ALND (49%); 32% had SLNB and 19% had TAD. 30% had cALND after SLNB or TAD. Among cALND, 64% had no additional positive nodes found. Distant recurrence occurred in 16% of patients at mean follow-up time of 24 months; <1% died from breast cancer. There was no difference in OS between all types of original axillary surgical management (p<0.6173) or between the group that had SLNB or TAD alone vs cALND (p<0.6714). There was no difference in RFS between all axillary operations (p<0.1488) and no difference in recurrence when patients had ALND or SLNB/TAD alone or ALND after SLNB/TAD. **CONCLUSIONS:** There is limited evidence on surgical management of axillary micro metastatic disease after NAC; our series demonstrated that the incidence is low and found no difference in OS based on surgical management. More prospective research is warranted in de-escalation of axillary surgery in breast cancer.



14. Machine Learning Models for Optimal Selection of the 21-gene Recurrence Score Assay in Breast Cancer

Javier I. J. Orozco, MD[1]; Douglas A Hanes, PhD[2]; Crystal Fancher, MD[3]; Melanie Goldbarb, MD[4]; Janie Weng Grumley, MD[5]
[1]Saint John's Cancer Institute at Providence Saint John's Health Center, Santa Monica, CA, US; [2]Center for Cardiovascular Analytics, Research and Data Science, Providence Research Network, Portland, OR, US; [3]Saint John's Cancer Institute at Providence Saint John's Health Center, Santa Monica, CA, US; [4]Saint John's Cancer Institute at Providence Saint John's Health Center, Santa Monica, CA, US; [5]Saint John's Cancer Institute at Providence Saint John's Health Center, Santa Monica, CA, US

INTRODUCTION: The 21-gene recurrence score (21-RS), a prospectively validated multi-gene assay, is widely used to predict the benefit of adjuvant chemotherapy in patients with estrogen-receptor (ER)-positive, HER2-negative early-stage breast cancer. However, RS assay accessibility may be limited by cost and availability. Developing a predictive model may help select patients needing testing and reduce unnecessary costs. This study aims to compare several machine-learning models (ML) to identify patients >50 years old who may not need 21-RS testing. **METHODS:** We selected a cohort of 38,734 female patients >50 years old diagnosed with invasive breast carcinoma (pT1-T2, pN0-N1) from the National Cancer Database (2018-2020). Variables included patient age, pathologic tumor size, histology, grade, lymph-vascular invasion, nodal status, ER (%), PR (%), HER2 (0 vs low), and Ki67. Patients were randomly split into training (n=18,413), testing (n=7,846), and validation cohorts (n=24,855). Six ML models were developed to predict RS categories (low risk: RS<26 vs. high risk: RS ≥26). The area under the receiver operating curve (AUC) sensitivity, specificity, and positive predictive value (PPV) were calculated. **RESULTS:** The median (IQR) age at diagnosis was 64 years (58-70). The median (IQR) tumor size was 1.5 cm (1.1-2.1), and most tumors were invasive ductal (81.2%), grade 2 (58 %), pN0 (83 %), PR-positive (90 %), and 21-gene low-risk RS (87%). Variable selection showed that grade, PR, and Ki67 were the most influential features in predicting patients with low risk. All the models performed similarly in the testing cohort (AUC=0.88). Notably, a minimal logistic regression model, only using PR, grade, and Ki67, showed similar accuracy (AUC=0.88, 95%CI 0.87-0.88), sensitivity (61%), specificity (91%), and PPV (98%) to more complex ML models (Table). Using this simple model, 53% of low-RS cases were predicted to be low, and only 1.2% of high-RS were predicted to be low by the model. **CONCLUSIONS:** Machine learning models, particularly a minimal logistic regression model, accurately predicted low-risk RS in patients >50 years old. Based on this model, 53% of patients could safely omit 21-gene RS testing, reducing unnecessary molecular testing. These findings highlight the potential of machine learning for personalized decision-making while minimizing healthcare costs.

15. Transgender and gender-diverse patients with breast cancer: A matched NCDB cohort analysis

Kelley Chan, MD, MS[1]; Joseph H Cotler, PhD[2]; Alexandra C. Istl, MD, MPH[3]; Andrew E Petroll, MD, MS[4]; Sailaja E Kamaraju, MD, MS[5]; Melinda E Stolley, PhD[6]; Chandler S. Cortina, MD, MS[7]
[1]Loyola University Medical Center, Maywood, IL, US; [2]American College of Surgeons, Chicago, IL, US; [3]Medical College of Wisconsin, Milwaukee, WI, US; [4]Medical College of Wisconsin, Milwaukee, WI, US; [5]Medical College of Wisconsin, Milwaukee, WI, US; [6]Medical College of Wisconsin, Milwaukee, WI, US; [7]Medical College of Wisconsin, Milwaukee, WI, US

INTRODUCTION: Breast cancer (BC) disparities in transgender/gender-diverse (TGD) populations have been described in small retrospective cohorts and case series. Using the NCDB, this study aimed to compare treatment characteristics and overall survival (OS) between TGD patients with BC vs a matched cisgender cohort. **METHODS:** This retrospective cohort study included TGD patients, age ≥18, with a BC diagnosis from 2004–2022 in the NCDB. Self-identified gender identity was made available after limited-use access approval by the NCDB. A matched 1:1 cisgender cohort was developed, matching on year of diagnosis, age, sex assigned at birth (SAB), race, Hispanic ethnicity, AJCC disease stage, and tumor receptor status. TGD patients with an unknown SAB were matched to cisgender females. Chi-squared tests with Bonferroni corrections and multivariable logistic regression models examined treatment associations with gender identity. Kaplan-Meier analysis determined five-year OS by gender identity. **RESULTS:** Of 4,376,089 patients with BC, 252 (0.006%) were TGD. TGD patients had a median age of 51 years (IQR 42–61), 65.1% were non-Hispanic (NH) White, 15.5% were NH Black, and 8.7% were Hispanic. Half (55.6%) were female SAB, 20.2% were male SAB, and 24.2% had unknown SAB. Most had DCIS (22.2%) or stage I (36.5%) disease, 60.7% were node-negative, and 52.5% had hormone receptor-positive (HR+) disease. Nearly all underwent surgery (90.5%), and a higher proportion of those assigned female SAB underwent mastectomy compared to those assigned male SAB (85.9% vs 51.2%, $p<0.001$). The majority (87.7%) of TGD patients did not undergo post-mastectomy breast reconstruction (PMBR). Compared to the matched cisgender cohort (n=211), TGD patients with HR+ disease received endocrine therapy (ET) less often (58.5% vs 67.6%, $p=0.04$) and underwent PMBR less often (9.7% vs 34.4%, $p=0.001$). On regression analysis, TGD patients were less likely to receive ET for HR+ disease (OR 0.50; 95% CI 0.30–0.82, $p=0.032$) or undergo PMBR (OR 0.21; 95% CI 0.11–0.40, $p<0.001$). TGD patients had a lower five-year OS compared to matched cisgender patients (84.6% *vs* 91.7% $p=0.041$, Figure). This difference persisted after excluding TGD patients with an unknown SAB (n=154, 84.1% vs 93.9%, $p=0.026$). **CONCLUSIONS:** In this cohort study, TGD patients were less likely to receive ET for HR+ BC, less likely to receive PMBR, and had inferior five-year OS compared to matched cisgender patients. Strategic research is needed

to elucidate the etiology of these differences to eliminate disparities and ensure equitable BC care for TGD patients that aligns with their gender identity.

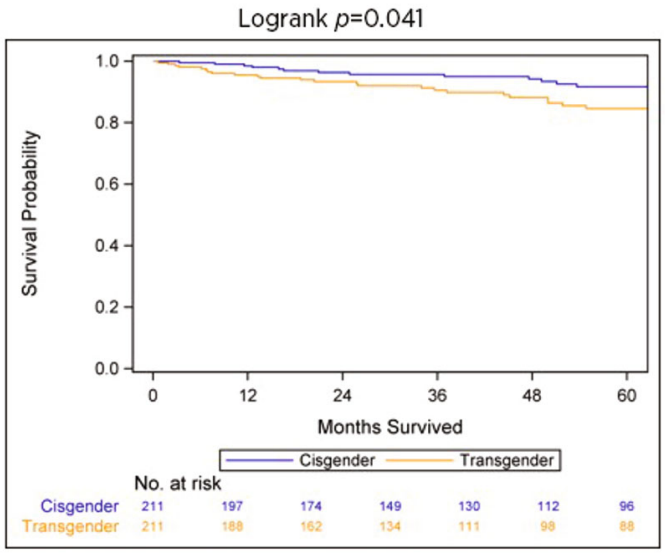


Figure. 5-year overall survival of matched TGD and cisgender patients with breast cancer stratified bt gender identity, N=211. Overall Survival: Cisgender 91.7% vs TGD 84.6%.

16. Management and Outcomes in Breast Cancer Patients With 1-of-1 and 2-of-2 Positive Sentinel Nodes

Walker Lyons, MD[1]; Elizabeth M Fish, DO[2]; Richard Bleicher, MD[3]; Cecilia Chang, MS[4]; Alycia So, MD[5]; Andrea Porpiglia, MD[6]; Allison Aggon, DO[7]; Austin DP Williams, MD[8]

[1]Fox Chase Cancer Center, Philadelphia, PA, US; [2]Fox Chase Cancer Center, Philadelphia, PA, US; [3]Fox Chase Cancer Center, Philadelphia, PA, US; [4]North Shore University Health System, Evanston, IL, US; [5]Fox Chase Cancer Center, Philadelphia, PA, US; [6]Fox Chase Cancer Center, Philadelphia, PA, US; [7]Fox Chase Cancer Center, Philadelphia, PA, US; [8]Fox Chase Cancer Center, Philadelphia, PA, US

INTRODUCTION: ACOSOG Z0011 and AMAROS found that axillary lymph node dissection (ALND) conferred no benefit to patients with 1-2 positive sentinel nodes (+SLNs). There is apprehension to omit ALND for patients in whom only 1 or 2 SLNs are retrieved and all are positive due to concern of missing more significant disease that would impact adjuvant therapies and outcomes. This study assesses current practice patterns and pathologic findings when ALND is pursued. **METHODS:** From the National Cancer Database, we identified female patients with cT1-3N0 breast cancer who underwent upfront surgery with sentinel lymphadenectomy (SLNB) from 2018-2021. Patients with ≤2 SLNs were included and stratified based on the number positive/removed: 0/1, 1/1, 1/2, 2/2. We analyzed rates, results and factors associated with ALND. **RESULTS:** A total of 102,802 patients met inclusion criteria, distributed into analysis groups as follows: 0/1 – 79,106 (77%), 1/1 – 10,549 (10%), 1/2 – 10,068 (10%), 2/2 – 3,079 (3%). Completion ALND was most commonly performed for patients with 2/2 +SLNs (41%); 26% of those with 1/1+SLNs, 19% of 1/2 +SLNs and 6% of 0/1 +SLNs underwent ALND. On multivariable analysis, adjusting for pertinent clinicopathologic features, the strongest independent predictor of ALND was SLN status (Table). Among patients who underwent ALND, 24% had additional positive nodes with the highest rate being among those with 2/2 +SLNs (56%) followed by 1/1 (40%), 1/2 (27%) and 0/1 (7%). The mean number of additional +LNs identified differed among SLN groups: 0/1 – 0.15, 1/1 - 1.6, 1/2 – 0.63, 2/2 – 2.6 (p<0.001). Among SLN+ patients with triple negative breast cancer or HER2+ cancer, ALND was not associated with differences in the rates of adjuvant chemotherapy or radiation. Among the 16,288 SLN+, HR+HER2- patients older than 50, ALND was associated with higher rates of adjuvant chemotherapy (43% vs. 24%, p<0.001) despite no difference in 21-gene recurrence scores (ALND: 16.3 vs. no ALND: 16.1, p=0.43). With a median follow up of 35.4 months, ALND was not associated with improved overall survival in all nodal groups. **CONCLUSIONS:** ALND is currently being performed at higher-than-expected rates for many patients with ≤2 +SLNs and may be associated with medical overtreatment in HR+HER2- patients. Multidisciplinary discussion of cases in which all SLNs are positive and ongoing provider education are needed to reduce the rates of axillary overtreatment.

Table. Multivariable analysis of factors associated with undergoing completion axillary lymph node dissection.

	OR	95% CI	p
SLN status			
0/1 (ref)	-	-	-
1/1	3.802	3.542-4.081	**<.0001**
1/2	2.562	2.374-2.765	**<.0001**
2/2	6.762	6.094-7.502	**<.0001**
Breast surgery			
Partial mastectomy (ref)	-	-	-
Mastectomy	3.487	3.300-3.684	**<.0001**
Clinical Tumor Stage			
cT1 (ref)	-	-	-
cT2	1.174	1.104-1.249	**<.0001**
cT3	1.496	1.288-1.738	**<.0001**
Lymphovascular Invasion	1.227	1.148-1.312	**<.0001**
Tumor Grade			
Low (ref)	-	-	-
Intermediate	1.091	1.020-1.166	**0.0111**
High	1.199	1.101-1.306	**<.0001**
Receptor Subtype			
HR+/HER2- (ref)	-	-	-
HER2+	1.083	0.954-1.230	0.2196
TNBC	1.156	1.030-1.297	**0.0140**

17. Nodal Treatment Effect in Patients with Nodal Pathologic Complete Response is Not Associated with Differences in Outcomes

Claire Miller[1]; Varadan Sevilimedu, MBBS, DrPH[2]; Andrea V Barrio, MD[3]; Atif J Khan, MD[4]; Monica Morrow, MD[5]; Daniel X. Choi, MD[6]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Previous studies established the safety and accuracy of sentinel lymph node biopsy (SLNB) after neoadjuvant chemotherapy (NAC) in patients presenting with clinically positive nodes. After NAC, lymph nodes are routinely evaluated for evidence of treatment effect (TE), but the clinical significance of the presence or absence of TE remains unknown. We evaluated outcomes based on the presence or absence of treatment effect in clinically node positive patients who had nodal pathologic complete response (pCR) after NAC. **METHODS:** Biopsy-proven node-positive patients treated between 6/2008-6/2021 with nodal pCR after NAC were identified from a prospectively maintained database. Nodes were evaluated for TE, and patients with TE identified were compared to those in whom TE was not identified. Primary outcomes included axillary recurrence (AR), breast cancer specific survival (BCSS), and overall survival (OS). **RESULTS:** Overall, 1119 eligible patients were identified; 616 (55%) had nodal pCR. Median follow up was 7 years. Median age was 49 years; 21% were hormone receptor positive (HR+/HER2-), 54% were HER2+, and 24% were triple negative. 222 (36%) patients underwent an ALND and 394 (64%) had a SLNB. Nodal TE was identified in 494 (80%) patients, and observed in 96% (n= 214) of ALND patients and 71% (n= 281) of SLNB patients. Patients with nodal TE identified had higher clinical T stage (p<0.001) and were more likely to have a breast pCR (<0.001). Overall, there were no differences in OS (p=0.3) or BCSS (p=0.22) between patients with and without TE. In SLNB patients, where TE was identified less frequently, there were no differences in OS (p=0.4) or BCSS (p=0.77) between those who had TE identified and those in whom TE was not identified. There were no axillary recurrences in patients who did not have treatment effect identified. **CONCLUSIONS:** In patients with nodal pCR after NAC, there are no differences in OS or BCSS between those who had nodal TE identified and those who did not. Additionally, for patients who underwent SLNB, axillary failure was infrequent; and OS and BCSS

were similar regardless of nodal TE, indicating that absence of nodal TE after SLNB is not an indication for completion ALND.

Table 1. Recurrence rates in patients with treatment effect (TE) identified vs. not identified

Recurrence	Total Cohort	TE Identified	TE Not-Identified	*p value*
n	616	495	123	
Breast Recurrence	6 (0.9%)	6 (1.2%)	0	*
Axillary Recurrence	4 (0.6%)	4 (0.8%)	0	*
Distant Recurrence	55 (8.9%)	49 (9.8%)	6 (4.8%)	0.12
Breast Cancer Death	40 (6.5%)	36 (7.3%)	4 (3.2%)	0.22
Any Cause Death	54 (8.7%)	48 (9.6%)	6 (4.8%)	0.3

*Rates too small to report p values

18. The Importance of Sentinel Lymph Node Biopsy in Early-Stage Breast Cancer Patients Under 50

Cara L. Berkowitz, MD, MSTR[1]; Elizabeth M De Jesus, MD[2]; Stephany Perez-Rojas, MSc[3]; Jiarui Yan, MPH[4]; Sara P Ginzberg, MD, MSHP[5]; Peter R Eby, MD[6]; Christine E Edmonds, MD[7]; Leisha C Elmore, MD, MPHS[8]; Rachel C Jankowitz, MD[9]; Neil K Taunk, MD, MSCTS[10]; Julia Tchou, MD, PhD[11]; Jennifer Q Zhang, MD[12]; Anne Marie McCarthy, PhD[13]; Oluwadamilola M. Fayanju, MD, MA, MPHS, FACS[14]

[1]University of Pennsylvania, Philadelphia, PA, US; [2]University of Pennsylvania, Philadelphia, PA, US; [3]University of Pennsylvania, Philadelphia, PA, US; [4]University of Pennsylvania, Philadelphia, PA, US; [5]University of Pennsylvania, Philadelphia, PA, US; [6]University of Pennsylvania, Philadelphia, PA, US; [7]University of Pennsylvania, Philadelphia, PA, US; [8]University of Pennsylvania, Philadelphia, PA, US; [9]University of Pennsylvania, Philadelphia, PA, US; [10]University of Pennsylvania, Philadelphia, PA, US; [11]University of Pennsylvania, Philadelphia, PA, US; [12]University of Pennsylvania, Philadelphia, PA, US; [13]University of Pennsylvania, Philadelphia, PA, US; [14]University of Pennsylvania Health System, Philadelphia, PA, US

INTRODUCTION: The Sentinel Node vs Observation After Axillary Ultrasound (SOUND) trial suggested that sentinel lymph node biopsy (SLNB) could be safely omitted in patients with early-stage (cT1) breast cancer with negative preoperative axillary ultrasound (cN0). However, uncertainty remains regarding rates of occult nodal disease outside of a trial setting and concomitant risk of undertreatment. Importantly, the results of Oncotype DX trials for patients with absent (TAILORx) and limited (RxPONDER) nodal involvement suggest caution in eliminating SLNB for patients <50, as accurate nodal staging could impact decisions about adjuvant chemotherapy. This study aims to examine rates of pathologic nodal involvement (pLN+) and chemotherapy administration in a national sample of SOUND-eligible patients. **METHODS:** We identified women ≥18 who underwent upfront partial mastectomy for cT1N0M0 HR+/HER2- invasive breast cancer in the National Cancer Database from 2010-2021. Patients missing survival/clinical stage data or who received neoadjuvant therapy were excluded. Chi-square tests and multivariate logistic regression were used to evaluate associations between patient/disease characteristics, pLN+, and chemotherapy administration. **RESULTS:** A total of 353,491 patients met inclusion criteria. Median follow-up was 84.1m (95% CI 83.96-84.19). Of the total, 36,971 (10.4%) patients were age <50, 204,255 patients (57.8%) were 50-70 and 112,265 patients (31.8%) were >70. Most patients in all three groups were Non-Hispanic White (76.6% vs 84.5% vs 88.8%, p<0.001) with ductal histology (80.2% vs 76.3% vs 72.4%, p<0.001). In patients <50, 15.8% had pLN+ (1.1% ≥4 pLN+) vs 11.6% (0.8% ≥4 pLN+) in those 50-70 and 7.8% (0.5% ≥4 pLN+) in those >70 (p<0.001). Chemotherapy was administered in 28.7% of patients <50 compared to 15.5% in those 50-70 and 3.7% in those >0.001). After adjustment, older patients 50-70 (OR 0.51, 95% CI 0.49-0.52, p<0.001) and >70 (OR 0.12, 95% CI 0.12-0.13, p<0.001) were significantly less likely to receive chemotherapy compared to those <50. In addition, patients with 1-3 pLN+ (OR 7.96, 95% CI 7.74-8.18, p<0.001) and ≥4 pLN+ (OR 58.37, 95% CI 52.33-65.24, p<0.001) were significantly more likely to receive chemotherapy vs pLN negative patients. **CONCLUSIONS:** Our study suggests that patients <50 are more likely to be pLN+ and receive chemotherapy compared to older patients. These findings highlight the importance of nodal staging in younger patients to accurately inform treatment strategies, as omitting SLNB could impact recommendations for chemotherapy.

19. Receptor status discordance following neoadjuvant systemic therapy for breast cancer

Fatemeh P. Parvin-Nejad, MD[1]; Paula L Garcia, MHA[2]; Giacomo Montagna, MD, MPH[3]; Stephanie Downs-Canner, MD[4]; Monica Morrow, MD[5]; George Plitas, MD[6]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New-York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New-York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Preoperative systemic therapy (PST) of breast cancer is directed by diagnostic core biopsy receptor subtyping. Residual disease subtype may be discordant with initial classification either by therapy induced selection or tumor heterogeneity. The frequency and clinical significance of subtype discordance is poorly understood. We sought to characterize the clinicopathologic features of receptor discordance in a large cohort of consecutive patients treated with PST. **METHODS:** A retrospective review of a prospectively maintained database was performed to identify patients with residual invasive disease found at surgery following neoadjuvant systemic therapy from 2010-2021. Estrogen receptor (ER) and HER2 receptor positivity were compared on pre-treatment core biopsy and post-treatment surgical pathology specimens. **RESULTS:** A total of 1198 patients were identified who had received neoadjuvant treatment, had residual tumor at the time of surgery, and had available ER and HER2 status on both pre-treatment biopsy and post-treatment surgical specimens. Patients had pathologic T stage of 1.8% ypT0/Tis, 63.8% ypT1, 25.6% ypT2, 6.8% ypT3, 1.4% ypT4, and 0.7% ypTx. Pathologic N stage was 47.3% ypN0/N0(i+), 32.4% ypN1, 12.5% ypN2, 6.8% ypN3, and 0.9% ypNx. PST regimens included chemotherapy only (NAC) (847, 70.7%), chemo-immunotherapy (NACI) (140, 11.7%), and HER2-directed therapy with chemotherapy (NACH) (211, 17.6%). In total, 15.3% of patients (183/1198) had receptor discordance (Table 1). Among discordant cases, systemic therapy included NAC (96, 52.5% of discordances), NACI (16, 8.7%), and NACH (71, 38.8%). The most common change was from HER2+ to HER2- in 64 patients (35.0% of discordances); all of these patients had received NACH (30.3% of NACH-treated cohort). A change from ER- to ER+ occurred in 57 patients (31.1% of discordances); of the ER- to ER+ group, 39 patients received NAC (4.6% of NAC-treated cohort), 12 received NACI (8.6% of NACI-treated cohort), and 6 received NACH (2.8% of NACH-treated cohort). **CONCLUSIONS:** Over one in seven patients receiving neoadjuvant systemic therapy exhibit receptor status discordance, most commonly from HER2+ to HER2- following NACH. Further study is needed to examine how receptor status changes impact decisions in adjuvant therapy and outcome.

Table 1. Receptor status changes between diagnostic core biopsy and surgical pathology specimens

	Post-surgery			
Pre-neoadjuvant	ER+/HER2-	ER-/HER2+	ER+/HER2+	ER-/HER2-
ER+/HER2- (n=368)	307 (83.4%)	1 (0.3%)	24 (6.5%)	36 (9.8%)
ER-/HER2+ (n=33)	5 (15.2%)	20 (60.6%)	0 (0%)	8 (24.2%)
ER+/HER2+ (n=167)	50 (29.9%)	3 (1.8%)	113 (67.7%)	1 (0.6%)
ER-/HER2- (n=630)	52 (8.3%)	3 (0.5%)	0 (0%)	575 (91.3%)

N=1198, total discordances = 183. Percentages listed are of pre-neoadjuvant receptor subtype.

20. Patterns and Predictors of Recurrence After Neoadjuvant Chemo-Immunotherapy in Early-Stage Triple-Negative Breast Cancer

Lauren Perry[1]; Varadan Sevilimedu[2]; Natalia Polidorio[3]; Marisa Lazarus[4]; Giacomo Montagna[5]; Nour Abuhadra[6]; Ellen Yang[7]; Rachel Han[8]; Hannah Y. Wen[9]; Lior Braunstein[10]; Monica Morrow[11]; George Plitas[12]; Stephanie Downs-Canner[13]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center,

New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US; [11]Memorial Sloan Kettering Cancer Center, New York, NY, US; [12]Memorial Sloan Kettering Cancer Center, New York, NY, US; [13]Memorial Sloan Kettering Cancer Center, New-York, NY, US

INTRODUCTION: Adding pembrolizumab to neoadjuvant chemotherapy (NAC+P) for stage II-III triple-negative breast cancer (TNBC) improves rates of pathologic complete response (pCR), and event-free and overall survival compared to neoadjuvant chemotherapy (NAC) alone. Recurrence patterns in a real-world cohort are not known. We compared recurrence rates and assessed factors associated with DFS in patients receiving NAC+P versus NAC for early TNBC. **METHODS:** Two cohorts of patients with stage II-III TNBC were compared: 344 treated with NAC+P from 6/21-4/24 based on the KEYNOTE-522 regimen, and 513 treated with NAC from 7/09-3/19. Clinical and recurrence data were collected. Primary outcomes were local recurrence (LR), locoregional recurrence (LRR), and distant recurrence (DR). Secondary outcomes were DFS and factors associated with DFS. Kaplan-Meier time-to-event analyses were assessed for DFS. Univariate and multivariable Cox regression models assessed for factors associated with DFS. **RESULTS:** In NAC+P, most presented with cT2 (70%), cN0 (53%) disease at a median age of 52 years (IQR 41, 62); in NAC, presenting disease burden was slightly higher (cT2 [48%] or cT3/4 [28%], cN1 [52%], median 51 years [IQR 41, 60]). Rates of breast, nodal, and overall pCR (58% vs 36%, $p < 0.001$) were higher in NAC+P. One-year crude LR rates were not different between NAC+P and NAC: 2.3% vs 4.3%, $p = 0.13$. One-year LRR and DR rates were lower with NAC+P: LRR (0.6% vs 4%, $p = 0.01$) and DR (8% vs 12%, $p = 0.03$). Thirty-one NAC+P patients had DR, and the most common sites of first progression were liver (29%), lung (29%), or brain (26%). Among 121 NAC patients with DR, the sites of first progression were multiorgan (50%), lung (19%), or liver (12%). Of 61 patients with multiorgan DR, 36 (59%) had brain metastases. At a median follow-up of 1.2 years (IQR 0.8, 1.6), the 1-year disease recurrence rate in NAC+P was 10% (95% CI 6-13%). With a median follow-up of 6 years (IQR 3.3, 7.7), the 5-year disease recurrence rate in NAC was 24% (95% CI 20-28%). Factors associated with improved DFS in NAC+P were lower cT stage, immune-related adverse events, breast pCR, nodal pCR, and overall pCR; in NAC, lower cT stage, ACT-based regimen, and overall pCR were associated with improved DFS. **CONCLUSIONS:** Compared to NAC, NAC+P resulted in improved crude 1-year rates of LRR and DR, along with improved DFS with shorter follow-up. Factors associated with DFS (including pCR) differed, and isolated brain metastases as a site of first progression were more common in patients treated with NAC+P who developed DR**.**

Endocrine/Head & Neck and Thoracic

21. Validation of lymph node thresholds as prognostic factors in medullary thyroid cancer staging

Christina V. Lindsay, BS[1]; *Samantha M Thomas, MS[2]; Frances Wang, MS[3]; Alberto Monreal, MD[4]; Randall P Scheri, MD[5]; Hadiza S Kazaure, MD[6]*

[1]Duke University School of Medicine, Durham, NC, US; [2]Duke University, Durham, NC, US; [3]Duke University, Durham, NC, US; [4]Division of Surgical Oncology, Department of Surgery, Duke University, Durham, NC, US; [5]Division of Surgical Oncology, Department of Surgery, Duke University, Durham, NC, US; [6]Division of Surgical Oncology, Department of Surgery, Duke University, Durham, NC, US

INTRODUCTION: The current AJCC medullary thyroid cancer (MTC) staging system qualitatively stratifies lymph node (LN) status based on involved cervical compartments. Based on emerging evidence, the American Thyroid Association guidelines suggest that the AJCC system should incorporate a quantitative assessment of LN metastases. Our past work used restrictive cubic splines, Markov Chain Monte Carlo, and bootstrap simulation to identify 8 positive LNs and a LN ratio (LNR) of 14% as thresholds in the SEER database significantly associated with an increase in MTC-specific mortality. Here, we a) validate these thresholds using the NCDB, and b) compare our thresholds to the current AJCC staging system. **METHODS:** Patients with MTC were abstracted from the NCDB (2004-20) and categorized as having <8 versus ≥8 positive LNs and a LNR of <14% versus ≥14%. Chi-square and Fisher's exact tests were used to compare categorical variables, and t-tests for continuous variables. Overall survival (OS) was estimated using the Kaplan-Meier method and log-rank test. Cox Proportional hazards models were used to estimate the association of LN thresholds with OS after adjustment for select covariates. **RESULTS:** There were 5685 patients. Median age was 55 years; 56.4% were female, 74.3% were non-Hispanic white, and 58.3% received care at an academic/research program. Median tumor size was 2 cm (interquartile range (IQR) 1.2-3.4). Approximately 53.5% had positive LNs; 21.2% were AJCC stage N1a and 32.3% N1b; 26.3% had ≥8 nodes, 44.3% had LNR ≥14%. The 5-year OS for LNR ≥14% was 78.2% (95% confidence interval (CI) 76.4-79.9), while it was 93.9% (95% CI 92.9-94.8) for LNR <14%. The 5-year OS for ≥8 positive LNs was 77.2% (95% CI 74.8-79.4) and 90.4% (95% CI 89.4-91.4) for <8. After multivariate adjustment, patients with a LNR of ≥14% had a 44% increased mortality risk compared to LNR of <14% (hazard ratio (HR) 1.44, 95% CI 1.10-1.88, p=0.008). Those with ≥8 positive LNs had a 37% increased mortality risk vs those with <8 positive LNs (HR 1.37, 95% CI 1.13-1.66, p=0.001). Upon adjusted analysis, the current AJCC N-stage was not associated with OS (N1a vs. N0: HR 1.16, 95% CI 0.60-2.23, p=0.66; N1b vs. N0: HR 0.80, 95% CI 0.41-1.57, p=0.51). Indeed, there was no significant adjusted mortality difference when N0 was compared to N1 (HR 0.98, 95% CI 0.47-2.03, p=0.96). **CONCLUSIONS:** Prognostic LN thresholds for MTC previously identified in the SEER database were also valid in the NCDB. A LNR ≥14% and ≥8 positive LNs provide better prognostic discrimination than the current AJCC system. These validated LN thresholds could be used to refine the current MTC staging system**.**

22. A Novel Approach to the Molecular Classification of Paragangliomas and Pheochromocytomas using Single Cell Transcriptomics

Mark Antkowiak[1]; *Ashwyn Sharma[2]; Chih-Min Tang[3]; Alex Wenzel[4]; Jill P. Mesirov[5]; Jason K. Sicklick[6]*

[1]UC San Diego, San Diego, CA, US; [2]UC San Diego, San Diego, CA, US; [3]UC San Diego, San Diego, CA, US; [4]UC San Diego, San Diego, CA, US; [5]UC San Diego, San Diego, CA, US; [6]UC San Diego, San Diego, CA, US

INTRODUCTION: Paragangliomas and pheochromocytomas (PPGL) are rare neuroendocrine tumors that are genetically and transcriptionally diverse. The molecular classification of PPGL dates back to microarray analysis, which demonstrated two major clusters of tumor: a pseudohypoxia cluster (C1) and a WNT/kinase signaling cluster (C2). We sought to utilize a novel approach using single cell transcriptomics from developing human fetal adrenal glands to refine the molecular classification of PPGL. By reference mapping tumor cells to developing adrenal cells (in which neural crest cells differentiate into sympathoblasts [S], medullary bridge cells [Br], Schwann cell precursors [SCP], or mature chromaffin cells [C]), we investigated the transcriptional programs driving tumor behavior. **METHODS:** We analyzed single cell transcriptomic data from 30 patients with PPGLs. To identify patterns in the tumor gene expression profiles, we created a fetal adrenal atlas consisting of 3 publicly available datasets and performed reference mapping of the tumor cells to this cell atlas. We then performed differential gene expression analysis and pathway analysis using single sample gene set enrichment analysis (ssGSEA) to characterize pathway activity. **RESULTS:** A total of 81,213 tumor cells were identified. Reference mapping of tumor cells to the fetal adrenal cell atlas (22,358 cells) identified 3 unique subtypes of PPGL tumor cells, including S-like, Br-like, and C-like. Differential gene expression analysis identified a unique set of transcripts in each group and pathway enrichment analysis demonstrated enrichment of neuronal and extracellular matrix pathways in sympathoblast-like tumor cells that were enriched for *MAML3* fusions (Notch signaling), WNT signaling in medullary bridge-like tumor cells which were enriched for *SDHx* mutations, and ERBB/EGFR pathways in chromaffin-like tumor cells that were enriched in *NF1*, *VHL*, *MAX*, and *EPAS1* mutant tumors. **CONCLUSIONS:** Using a single cell transcriptomic approach, we identify and characterize three unique clusters of PPGL, including sympathoblast-like, medullary bridge-like and chromaffin-like tumor cells. Using this classification, we develop a more granular approach for tumor classification that uncovered unique molecular drivers that may be utilized for exploring novel therapeutic approaches**.**

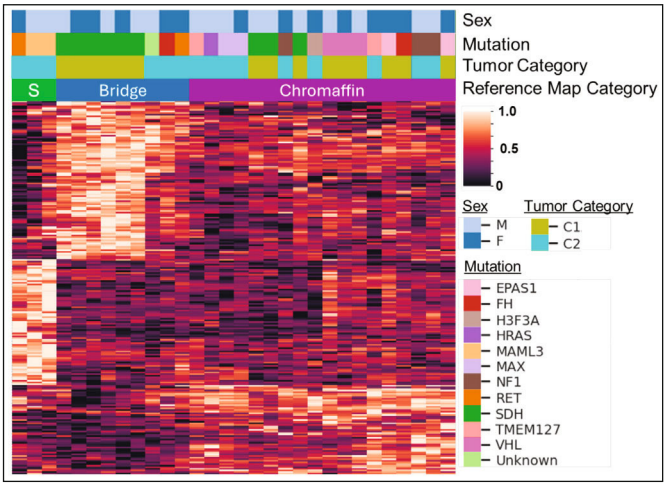
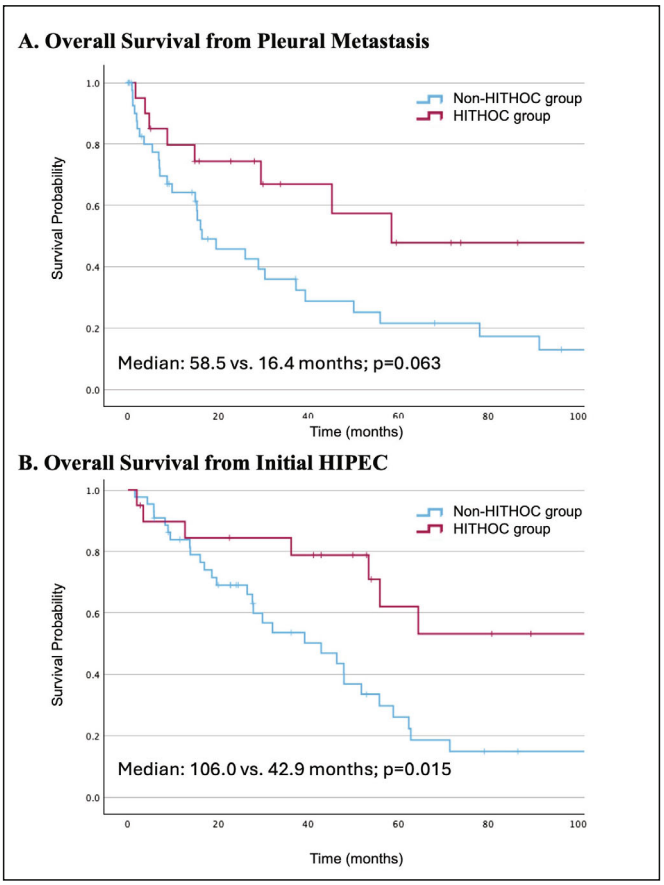


Figure 1. Pathway enrichment in PPGL by reference map category. Single sample gene set enrichment analysis was performed on PPGL tumor cells that were reference mapped to the adrenal atlas. Three distinct clusters of tumors can be seen (Sympathoblast-like [S], Medullary Bridge-like, and Chromaffin-like).

23. Outcome Analysis of Cytoreductive Surgery and Hyperthermic Intrathoracic Chemoperfusion (HITHOC) for Pseudomyxoma Peritonei with Pleural Metastasis

Edra Ha[1]; Inderpal Sarkaria[2]; Yota Suzuki[3]; Victor Crentsil[4]; Olugbenga Okusanya[5]; James D Luketich[6]; M. Haroon A Choudry, MD[7]; Neil Christie[8]
[1]University of Pittsburgh, Pittsburgh, PA, US; [2]University of Texas Southwestern Medical Center, Dallas, TX, US; [3]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [4]University of Pittsburgh Medical Center Mercy, Pittsburgh, PA, US; [5]Thomas Jefferson University, Philadelphia, PA, US; [6]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [7]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [8]University of Pittsburgh Medical Center, Pittsburgh, PA, US

INTRODUCTION: Although cytoreductive surgery (CRS) and hyperthermic intrathoracic chemoperfusion (HITHOC) have been applied in the treatment of primary pleural malignancies, its role in managing pleural metastases from pseudomyxoma peritonei (PMP) remains underexplored. This study aims to evaluate the outcomes of PMP with pleural involvement, focusing specifically on the role of CRS/HITHOC. **METHODS:** We conducted a single-institution, retrospective analysis of patients with PMP who underwent CRS/hyperthermic intraperitoneal chemotherapy (HIPEC) between 2008 and 2022. Patients with metachronous or synchronous pleural metastases were included, and outcomes were compared between those treated with or without CRS/HITHOC. Following thoracic disease debulking, chest tubes were inserted, and a heated chemotherapy solution (40–42°C) was circulated for one hour. The administered chemotherapy doses were 175–200 mg/m² of cisplatin or 30 mg of mitomycin. We evaluated perioperative and oncologic outcomes. **RESULTS:** A total of 814 patients with PMP underwent CRS/HIPEC during the study period. Sixty-four patients (7.9%) developed pleural metastases (7 synchronous and 57 metachronous), with a median pleural recurrence interval of 15.6 (Interquartile range: 6.8-26.6 months) months. Of these, 20 patients (31.3%; 4 synchronous and 16 metachronous) received CRS/HITHOC as part of multimodal management. There was no significant difference in median age between groups (52 vs. 58 years; p=0.417), though the CRS/HITHOC group showed a trend towards fewer preceding recurrences at other sites (40.0% vs. 68.2%; p=0.054). All 20 patients undergoing HITHOC had pleurectomy and decortication, with concomitant lung resection (14 patients), diaphragm resection (13 patients), and pericardium resection (3 patients). The median length of hospital stay was seven days, and there was no 30-day mortality (0%). The HITHOC group demonstrated a trend towards improved OS after pleural recurrence (58.5 vs. 16.4 months; p=0.063; Figure 1A). Survival from the time of initial HIPEC was significantly longer in the HITHOC group (106.0 vs. 42.9 months; p=0.015; Figure 1B). **CONCLUSIONS:** Despite some differences in baseline characteristics, the incorporation of HITHOC into the management of PMP with pleural involvement was associated with significantly improved survival. HITHOC may represent an effective strategy for both the treatment and palliation of pleural metastases in PMP patients. However, given the rarity of this disease, conclusions regarding the survival benefit from these interventions are difficult to prove.



24. Visualization of primary and metastatic medullary thyroid cancer in an orthotopic mouse model using a fluorescent humanized anti-CEA antibody

Javier Bravo[1]; Sohee Lee[2]; Sunidhi Jaiswal[3]; Kristin E. Cox[4]; Siamak Amirfakhri[5]; Thinzar Lwin[6]; Grace Lin[7]; Robert M. Hoffman[8]; Hak Soo Choi[9]; Paul Yazaki[10]; Michael Bouvet, MD, FACS, Professor of Surgery, Director of Endocrine Surgery[11]
[1]UC San Diego Health, San Diego, CA, US; [2]UC San Diego Health, San Diego, CA, US; [3]UC San Diego Health, San Diego, CA, US; [4]UC San Diego Health, San Diego, CA, US; [5]UC San Diego Health, San Diego, CA, US; [6]City of Hope National Medical Center, Duarte, CA, US; [7]UC San Diego Health, San Diego, CA, US; [8]UC San Diego Health, San Diego, CA, US; [9]Gordon Center for Medical Imaging, Department of Radiology, Massachusetts General Hospital and Harva, Boston, MA, US; [10]Department of Immunology & Theranostics, Beckman Research Institute, Duarte, CA, US; [11]University of california san diego, San Diego, CA, US

INTRODUCTION: Medullary thyroid cancer (MTC) is distinct from other types of thyroid cancers since it arises from thyroid parafollicular cells (C-cells) and expresses carcinoembryonic antigen (CEA). The standard treatment for MTC is surgical resection plus cervical lymph node dissection. Total thyroidectomy has been shown to significantly improve survival rates in patients with localized disease. In this study, a patient-like mouse model of MTC with primary and metastatic tumors was used to assess an anti-CEA antibody as a potential probe for fluorescence guided surgery (FGS). **METHODS:** The MTC cell-line TT was obtained from the American Type Culture Collection. Subcutaneous tumor models were established by injecting TT cells in the flanks of athymic mice. Orthotopic MTC models were created by injecting TT cells ($1x10^7$) into the thyroid gland of athymic mice. The humanized anti-CEA monoclonal antibody M5A was conjugated with the near-infrared (NIR) dye NHS-IRDye800CW to generate M5A-IR800. Mice with subcutaneous (n = 3) or orthotopic tumors (n = 7) received 50 µg of M5A-IR800 intravenously prior to imaging. Subcutaneous models were imaged daily and orthotopic models were imaged at 96 hr. The LI-COR Pearl Imaging System was used for imaging. Tumor-to-background ratios (TBRs) were calculated by dividing the mean fluorescence intensity

of thyroid tumors versus surrounding tissues. Necropsies were performed and organs were imaged for fluorescence biodistribution data. Pathology and immunohistochemistry were performed on the primary and metastatic tumors. **RESULTS:** The mean TBR of subcutaneous MTC tumors was 1.47 at 24 hrs, 2.06 at 48 hrs, 2.41 at 72 hrs, and 3.70 at 96 hrs following M5A-IR800 injection, respectively. The mean TBR for orthotopic MTC tumors labeled with M5A-IR800 was 6.85 (± 3.75) at 96 hrs (Figure 1). Tumors and metastases exhibited the greatest fluorescence signal followed by the liver, with little to no expression in other organs. Hematoxylin and eosin staining confirmed the presence of MTC tumor cells. CEA overexpression was confirmed with immunohistochemical staining. **CONCLUSIONS:** M5A-IR800 brightly targeted MTC cells in subcutaneous and orthotopic mouse models with TBRs > 3 when compared to adjacent organs. This tumor-specific fluorescent antibody is a promising clinical tool that can be used to identify MTC and potentially improve surgical outcomes for patients with MTC**.**

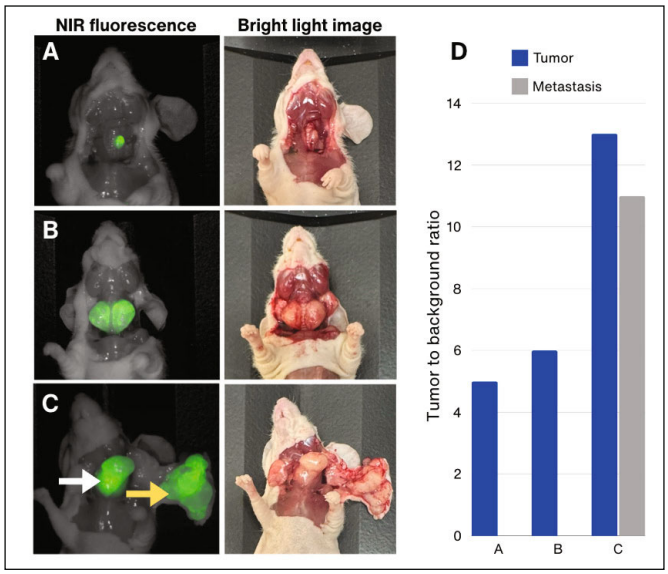


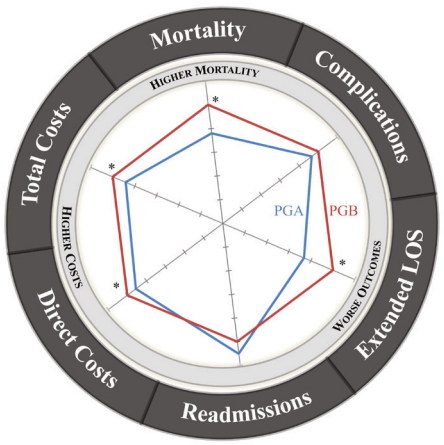
Figure 1. A) NIR and bright light imaging of a small unilateral thyroid tumor. B) NIR and bright light imaging of bilateral thyroid tumors. C) NIR and bright light imaging of a large thyroid tumor (white arrow) and local metastasis (yellow arrow). D) TBRs of tumors in panels A, B and C at 96 hr post-injection of M5A-IR800. Mean TBR = 8.79 ±3.96 (95% CI: 2.49 - 15.08).

25. Lung Cancer Surgery at Community-Based versus Specialized Care Facilities: A Value-Based Care Assessment

Edward A. Joseph, MBBS[1]; Muhammad Muntazir Mehdi Khan, MBBS[2]; Philip Schumacher[3]; Brandon Weiss[4]; Casey J. Allen, MD[5]
[1]Allegheny Health Network, Pittsburgh, PA, US; [2]Allegheny Health Network, Pittsburgh, PA, US; [3]Allegheny General Hospital, Pittsburgh, PA, US; [4]Allegheny Health Network, Pittsburgh, PA, US; [5]Allegheny Health Network, Pittsburgh, PA, US

INTRODUCTION: Value-based care focuses on improving patient outcomes while reducing costs. Conducting specific procedures at designated facilities may offer opportunities to save costs without compromising quality of care. We aimed to evaluate the outcomes and costs of lung cancer surgery at community-based versus academic/specialized care facilities. **METHODS:** Specific ICD-10 diagnosis and procedure codes were used to identify patients who underwent lobectomy for malignant neoplasm of the lung from 2021 to 2023, using data from the Vizient® Clinical Data Base. Perioperative outcomes and costs were compared between Peer Group A (PGA) facilities, which include comprehensive academic medical centers, large specialized complex care centers, and the Alliance of Dedicated Cancer Centers, and Peer Group B (PGB) facilities, consisting of complex care medical centers, community hospitals, and critical access/small community hospitals. **RESULTS:** Among 48,300 patients, the mean age was 68.1 ± 8.9 years; 56.5% (n=27,307) were female, and 81.1% (n=38,838) were White/Caucasian. Overall, the median length of stay (LOS) was 4.0 (2.0–6.0) days, the complication rate was 2.3%, the 30-day readmission rate was 6.1%, and the in-hospital mortality rate was 0.8%. Of these patients, 85.0% (n=41,052) received care at PGA facilities, while 15.0% (n=7,248) were treated at PGB facilities. There were no significant differences in complication and readmission rates between the two groups (both p>0.05). However, both direct costs ($14,164 [$10,670–$18,164] vs. $15,521 [$11,676–$21,293]) and total costs ($22,881 [$17,604–$30,379] vs. $26,165 [$19,987–$35,525]) were lower at PGA facilities (both p<0.05). Multivariate analysis revealed that care at PGB facilities was an independent predictor of in-hospital mortality (OR: 1.32, 95% CI: 1.02–1.70), extended LOS (OR: 1.34, 95% CI: 1.27–1.43), and higher direct (OR: 1.10, 95% CI: 1.06–1.15) and total (OR: 1.14, 95% CI: 1.11–1.18) costs (all p<0.05). **CONCLUSIONS:** Care at academic/specialized care (PGA) facilities is associated with lower costs and improved outcomes for patients undergoing lung cancer surgery. This suggests that designating specific procedures to high-volume or specialized centers may improve the value of care delivery for lung cancer patients**.**

Radar Chart Demonstrating the Value Implications of Care Facility in Surgically Managed Lung Cancer Patients



PGA: Peer group A facilities
PGB: Peer group B facilities
LOS: Length of Stay
* Statistically significant; p<0.05

26. NRF2 and SMARCA4 predict the transformation from lung adenocarcinoma to squamous cell carcinoma post chemotherapy

T Hess, MD[1]; Hansa Joshi, MD[2]; Nasrine Bendjilali, PhD[3]; Gord Zhu, MD[4]; Tina B. Edmonston, MD[5]; Francis Spitz, MD[6]; David Shersher, MD[7]; Samera Hamad, PhD[8]
[1]Cooper University Hospital, Camden, NJ, US; [2]Cooper University Hospital, Camden, NJ, US; [3]College of Science and Mathematics, Rowan University, Glassboro, NJ, US; [4]Cooper University Hospital, Camden, NJ, US; [5]Cooper University Hospital, Camden, NJ, US; [6]Cooper University Hospital, Camden, NJ, US; [7]Cooper University Hospital, Camden, NJ, US; [8]Cooper University Hospital, Camden, NJ, US

INTRODUCTION: Lung cancer remains the leading cause of cancer-related mortality in the United States, with lung adenocarcinoma (LUAD) as the most prevalent subtype. Transformation from LUAD to the more aggressive type of lung cancer, squamous cell carcinoma (SCC), is a resistance mechanism to chemotherapy and targeted therapy in non-small cell lung cancer (NSCLC). This has been controversial in clinical practice. NRF2, an antioxidant gene, is altered in about 45% of NSCLC. We aimed to elucidate whether NRF2 is a key factor in this transformation after treatment by using the molecular fingerprint of the NRF2 signaling pathway and LUAD or SCC differentiation. **METHODS:** RNA-seq data of 508 tumor samples from the adenocarcinoma (LUAD) (TCGA, PanCancer Atlas) study were downloaded from cBioPortal for Cancer Genomics (https://www.cbioportal.org/). All LUAD samples are chemo-treated tumors. Single-sample Gene Set Enrichment Analysis (ssGSEA) was used to generate molecular fingerprinting for NRF2, LUAD, and SCC. **RESULTS:** A total of 398 upregulated genes were observed in the tumors that transformed to squamous cell carcinoma. About 50% of those tumors are enriched with $NRF2^{High}$ signature and were SMARCA4 altered tumors. SMARCA4 alteration was not observed in non-transformed LUAD tumors. This combination of mutations leads to a

lower probability of patient survival. **CONCLUSIONS:** This proof-of-concept study demonstrated that transformation from LUAD to SCC post-chemotherapy could be NRF2 and SMARCA4 -alteration dependent. This phenomenon is under-recognized and IHC- NRF2 and SMARCA4 should be considered in addition to NRF2 and SMARCA4 genomic evaluation to predict the risk of SCC transformation.

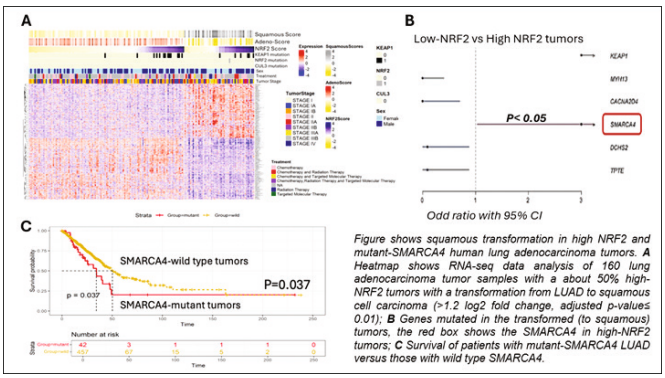


*Figure shows squamous transformation in high NRF2 and mutant-SMARCA4 human lung adenocarcinoma tumors. **A** Heatmap shows RNA-seq data analysis of 160 lung adenocarcinoma tumor samples with a about 50% high-NRF2 tumors with a transformation from LUAD to squamous cell carcinoma (>1.2 log2 fold change, adjusted p-values 0.01); **B** Genes mutated in the transformed (to squamous) tumors, the red box shows the SMARCA4 in high-NRF2 tumors; **C** Survival of patients with mutant-SMARCA4 LUAD versus those with wild type SMARCA4.*

27. Molecular Quantification and Tumor Reactivity Assessment of Tumor-infiltrating Lymphocytes Using Multiplexed Digital PCR

Fadi Rami[1]; Joe Yglesias[2]; Kranthi Kunkalla[3]; Joe Dean[4]; Hequn Yin[5]; Brian Gastman[6]; Peter Prieto[7]; Rongsu Qi[8]
[1]Iovance Biotherapeutics, Inc., San Carlos, CA, US; [2]Iovance Biotherapeutics, Inc., San Carlos, CA, US; [3]Iovance Biotherapeutics, Inc., San Carlos, CA, US; [4]Iovance Biotherapeutics, Inc., San Carlos, CA, US; [5]Iovance Biotherapeutics, Inc., San Carlos, CA, US; [6]Iovance Biotherapeutics, Inc., San Carlos, CA, US; [7]Iovance Biotherapeutics, Inc., San Carlos, CA, US; [8]Iovance Biotherapeutics, Inc., San Carlos, CA, US

INTRODUCTION: Lifileucel is an autologous, tumor-infiltrating lymphocytes (TIL) cell therapy approved by the FDA for treatment of unresectable or metastatic melanoma in adults. To manufacture lifileucel, TIL are expanded *ex vivo* from resected tumors for reinfusion into the patient. We sought to develop a method to assess T-cell quantity and potential tumor reactivity to guide selection of tumor material with more tumor-reactive TIL and fewer bystanders for TIL manufacturing. Flow cytometry and immunohistochemistry are gold-standard methods for T-cell assessments, but are time consuming, laborious, and use much of the sample. **METHODS:** We selected a multiplex digital PCR (dPCR) method for accurate and time-efficient T-cell quantification using minimal tumor tissue. This method allows absolute nucleic acid quantification and hence cell number quantification. Our experimental design involves detection of the following DNA targets: 1) *TRBC ΔB* as a unique non–T-cell DNA marker that is biallelically absent in mature T cells due to VDJ rearrangements, 2) *TRBC* as a regional corrector that allows correction of possible copy number (CN) alterations at the T-cell marker locus in cancer cells, and 3) *RPP30* as a reference DNA marker existing as a diploid in all cells. We integrate measurements of the 3 markers to identify T-cell percentage per this equation:

$$\text{T-cell percentage} = \frac{(TRBC\ \text{CN} - \Delta B\ \text{CN}) \times 100}{RPP30\ \text{CN}}$$

To assess tumor reactivity potential of TIL within resected tumor, we developed a multiplex dPCR method measuring expression levels of genes overexpressed in tumor-reactive TIL based on our in-house single-cell transcriptomic data and literature. The panel consists of *CXCL13*, *CD200*, *TRBC*, and *CD19* aimed at estimating the presence of exhausted T cells and tertiary lymphoid structures. Copies of RNA transcripts are extracted from tumor fragments and reverse transcribed to cDNA. Taqman probes are tested and validated. **RESULTS:** We show a proof-of-concept experiment for the measurement of T-cell fraction from 10 fragments dissected from 1 lung tumor sample. Samples were run in triplicates and T-cell fractions ranged from 13.5%-42.2% (Figure 1). **CONCLUSIONS:** The 2 multiplex dPCR-based quantification strategies demonstrated the cellular infiltration and tumor reactivity of TIL. These robust, easy to use, and reproducible methods will aid in selection of starting tumor material for TIL manufacturing.

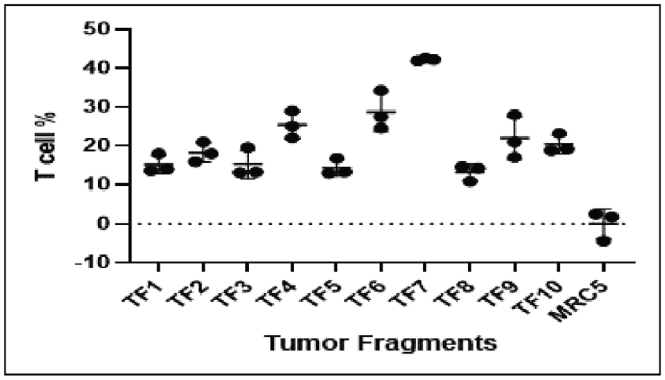


Figure1. T-cell percentage in lung tumor fragments

28. Sex-Based Differences in Medullary Thyroid Cancer Mortality: Nature or Nurture?

Nathan G. Sattah, BA[1]; Vincent M D'Anniballe, MS[2]; Samantha M Thomas, MS[3]; Randall P Scheri, MD[4]; Hadiza S Kazaure, MD[5]
[1]Duke University School of Medicine, Durham, NC, US; [2]Duke University School of Medicine, Durham, NC, US; [3]Duke University, Durham, NC, US; [4]Duke University, Durham, NC, US; [5]Duke University, Durham, NC, US

INTRODUCTION: Studies have suggested that medullary thyroid cancer (MTC) is inherently more aggressive in males compared to females, with resultant survival differences. After matching by cancer stage, this study explored whether differences in survival between male and female MTC patients are better explained by inherent tumor behavior ("nature") or care characteristics such as timing of diagnosis and treatment variations ("nurture"). This study hypothesizes that sex-based differences will persist following patient matching and adjusted analyses if " is the primary driver of survival. **METHODS:** Patients with stage I-IV MTC were identified in the National Cancer Database (2004-20). Male and female patients were matched one-to-one using a greedy nearest-neighbor propensity score based on pathologic stage. Overall survival (OS) was defined as the time from diagnosis to death due to any cause. Unadjusted survival was estimated using the Kaplan-Meier method and log-rank tests were used to compare groups. A Cox Proportional hazards model was used to estimate the association of biological sex with OS after adjustment for available covariates. Individual baseline hazard estimates were incorporated into the model for each matched pair. OS rates and hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated. **RESULTS:** A total of 4,062 patients were matched (2,031 female, 2,031 male). Distribution by stage was 24.7%, 15.3%, 18.9%, 35.5%, 0.5%, and 5.2% for MTC stage I, II, III, IVA-C. Baseline characteristics (notably age, race/ethnicity, income, insurance, treatment facility type, and comorbidity score) did not differ by sex. Median tumor size was 2.0 cm vs. 2.2 cm for female vs. male patients ($p < 0.001$); there were no differences in time from diagnosis to treatment, surgical approach, lymph node dissection and chemotherapy rates, or follow-up time. Overall, female patients experienced longer unadjusted OS compared to male patients (10-year OS 81.1% (95% CI 78.7 – 83.2) vs. 69.6% (95% CI 66.8 – 72.3), log-rank $p < 0.001$). Survival differed for all stages, and were statistically significant for stage II, and IVA disease. After multivariable adjustment, male patients had an 81% higher mortality risk compared to female patients (HR 1.81 (95% CI 1.50 – 2.20, $p < 0.001$)). **CONCLUSIONS:** Male patients with MTC have worse survival compared to female patients, even after matching and multivariable adjustment. Sex-based differences were most evident in stage II, III, and IVA MTC, which comprise almost 70% of the study sample. These findings raise the possibility that "nature," i.e., MTC behavior, differs by sex.

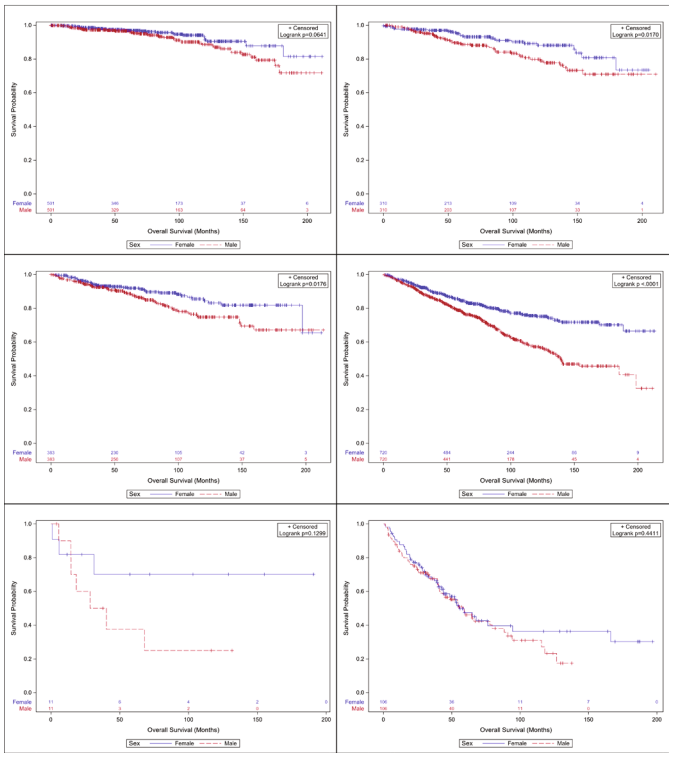


Figure 1. Unadjusted Overall Survival – by Biologic Sex and Stage: I (top left), II (top right), III (middle left), IVA (middle right), IVB (bottom left), IVC (bottom right)

29. Peptide Receptor Radionuclide Therapy Is Associated With a Reduced Risk of Primary Tumor Obstruction and Surgery in Widely Metastatic Small Bowel Neuroendocrine Tumor Patients

Aradhya Nigam[1]; Michael Mederos[2]; Courtney Porfido[3]; Nitya Raj[4]; Lisa Bodei[5]; Diane Reidy-Lagunes[6]; Brian R Untch[7]

[1]Memorial Sloan Kettering, New York, NY, US; [2]Memorial Sloan Kettering, New York, NY, US; [3]Memorial Sloan Kettering, New York, NY, US; [4]Memorial Sloan Kettering, New York, NY, US; [5]Memorial Sloan Kettering, New York, NY, US; [6]Memorial Sloan Kettering, New York, NY, US; [7]Memorial Sloan Kettering, New York, NY, US

INTRODUCTION: The management of the primary tumor for patients with widely metastatic small bowel neuroendocrine tumors is controversial with some centers performing resection of asymptomatic, nonobstructing tumors at presentation. Peptide receptor radionuclide therapy (PRRT) is used to treat patients with metastatic SBNET and can result in clinically relevant temporary inflammation and swelling (pseudoprogression). It is unknown whether patients with a primary tumor in place are at higher risk of pseudoprogression-induced bowel obstruction. We aimed to determine the incidence of small bowel obstruction, pseudoprogression, and morbidity in SBNET patients with an unresected primary tumor who were treated with PRRT and compare the results to those who were not treated with PRRT. **METHODS:** A retrospective cohort study was performed of patients treated with well-differentiated, distant metastatic jejunal/ileal SBNETs at a single referral tertiary care center (Memorial Sloan Kettering Cancer Center) between 1980 and 2023. Patients who had their primary tumor in place and had at least two years of follow-up were stratified according to upfront medical therapy into PRRT and non-PRRT systemic therapy cohorts. PRRT patients were followed prospectively after approval in 2018. Outcomes evaluated included the incidence of pseudoprogression, small bowel obstruction (SBO), progression-free survival (PFS) and overall survival (OS). Progression-free survival (PFS) was defined as clinical or radiographic progression due to disease progression, recurrence, or death. **RESULTS:** Amongst 120 patients with metastatic well-differentiated and a primary tumor in place, 49 (41%) underwent PRRT therapy and 71 (59%) underwent non-PRRT systemic therapies. Median follow-up for the PRRT group was 42mo and for the non-PRRT systemic therapy group was 61mo after initiation of therapy. The number of patients who developed an SBO requiring surgical intervention within two years was 11 (15%) in the non-PRRT systemic therapy cohort and 3 (6%) in the PRRT cohort ($p<0.05$) with a median time to obstruction of 9.9 ± 7.3mo and 6.0 3.4mo, respectively ($p=0.51$). All patients were able to be salvaged with surgery. In the PRRT cohort, an additional 3 (6%) patients presented with SBO and had radiographic evidence of pseudoprogression but were managed nonoperatively. Amongst all patients, those who developed an SBO had worse 2- and 5-year PFS ($p<0.001$ for both) compared to those who did not develop an SBO. Patients who developed an SBO also demonstrated worse 5-year OS ($p<0.001$) (Figure 1). **CONCLUSIONS:** In patients with widely metastatic SBNET and unresected primary tumors, surgically managed SBO within two years of PRRT was infrequent and of lower incidence than those not receiving PRRT. No patients required operation for pseudoprogression. Any patient who developed primary-tumor related SBO within two years demonstrated worse disease-specific outcomes – representing a patient cohort with worse tumor biology.

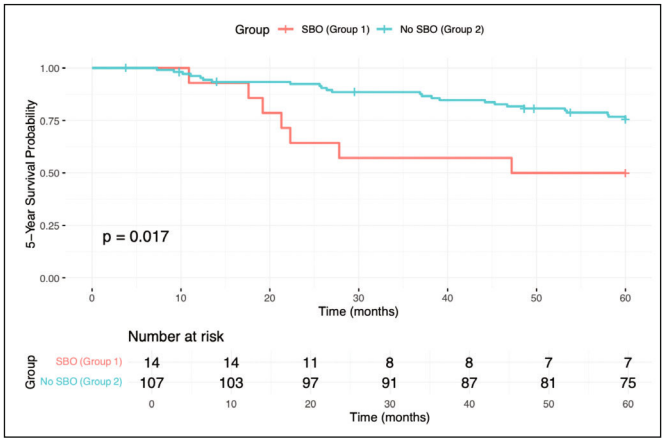


Figure 1. Competing Risk Analysis of Five-Year Overall Survival Comparing Patients Who Developed an SBO Compared to No SBO Developed

30. Impact of induction chemotherapy on dysphagia in patients with esophageal cancer

Huy Pham[1]; Elliott Yee[2]; Benedetto Mungo[3]; Sunnie Kim[4]; John D Mitchell[5]; Robert Meguid[6]; Elizabeth David[7]; Simran Randhawa[8]; David Binder[9]; Megan Marsh[10]; Martin D McCarter, MD[11]

[1]University of Colorado School of Medicine, Aurora, CO, US; [2]University of Colorado School of Medicine, Aurora, CO, US; [3]University of Colorado School of Medicine, Aurora, CO, US; [4]University of Colorado School of Medicine, Aurora, CO, US; [5]University of Colorado School of Medicine, Aurora, CO, US; [6]University of Colorado School of Medicine, Aurora, CO, US; [7]University of Colorado School of Medicine, Aurora, CO, US; [8]University of Colorado School of Medicine, Aurora, CO, US; [9]University of Colorado School of Medicine, Aurora, CO, US; [10]University of Colorado School of Medicine, Aurora, CO, US; [11]University of Colorado School of Medicine, Aurora, CO, US

INTRODUCTION: Dysphagia is a hallmark symptom in patients with esophageal and gastroesophageal junction cancers and can negatively impact nutritional status, psychological well-being, and overall prognosis. While some studies suggest neoadjuvant therapy (NAT) in the form of systemic chemotherapy or chemoradiation (CRT) can relieve dysphagia, others report worsened symptoms post treatment. We aimed to investigate the comparative efficacy of induction chemotherapy (IC) followed by CRT versus CRT alone in alleviating dysphagia and the need for additional nutrition-centric interventions such as esophageal stents and feeding jejunostomies. **METHODS:** We performed an IRB approved retrospective cohort study of adult patients with biopsy-proven esophageal cancer who underwent NAT followed by definitive esophagectomy at the University of Colorado Cancer Center between 2007 and 2023. Dysphagia symptoms were assigned a score (0 (no dysphagia), 1 (dysphagia to solids), 2 (dysphagia to soft solids), 3 (dysphagia to solids and liquids), and 4 (inability to swallow saliva)) according to the standardized Mellow and Pinkas (M&P) scale. Dysphagia was assessed after IC for those receiving IC+CRT and after CRT for those receiving CRT alone. Statistical analysis included Wilcoxon signed-ranked test. **RESULTS:** A total of 234 patients met inclusion criteria. Among the 76 patients who received IC+CRT, 60 (79%) reported dysphagia prior to any preoperative treatment with a mean M&P score of 1.38, which significantly decreased to 0.70 following IC ($p < 0.001$). This reduction in M&P score for the IC+CRT group was not significantly different from the CRT alone group

(p = 0.26). FOLFOX and FLOT were the primary chemotherapy regimens in the IC+CRT cohort and resulted in comparable reductions in M&P scores (p = 0.076). No esophageal stents were placed during the preoperative period and the rates of feeding tube placement due to dysphagia prior to esophagectomy were similar between the two groups, with 7.9% in the IC+CRT group and 6.3% in the CRT only group (p = 0.8685) **CONCLUSIONS:** Dysphagia improves substantially following IC in patients with resectable esophageal cancer, but not significantly more than with CRT alone. Similar rates of feeding tube placement and improvement in M&P scores after NAT suggest IC confers a similar advantage in attenuating dysphagia as CRT**.**

Table 1. Mellow and Pinkas score reductions based on treatment arm, histologic diagnosis, and tumor location

	# of patients	Mellow and Pinkas score reduction	p-value
Treatment arm			
IC + CRT	60	-0.68	0.26
CRT	110	-0.48	
Histologic diagnosis (all 3 treatment arms of IC+CRT, CRT only, & chemo only)			
Adenocarcinoma	167	-0.59	0.14
Squamous cell carcinoma	12	0.00	
Tumor location (all 3 treatment arms of IC+CRT, CRT only, & chemo only)			
True esophagus	28	-0.54	0.30
GEJ	151	-0.55	

HPB I

31. DNA/RNA-Based Next-Generation Sequencing (NGS) Improves the Early Diagnosis and Management of Malignant Bile Duct Strictures: A Five-Year, Prospective, Multi-Institutional Study

Geoffrey R. Nunns, MD[1]; Brian A. Boone, MD[2]; Ibrahim Nassour, MD[3]; Patricio M. Polanco, MD[4]; Herbert J Zeh, MD[5]; James Wallis Marsh[6]; Melissa Hogg, MD, FSSO[7]; Kenneth K Lee[8]; James Pingpank[9]; M. Haroon A Choudry, MD[10]; Abhinav Humar, MD[11]; Carl Schmidt, MD[12]; John C Mansour, MD[13]; Melanie Ongchin, MD[14]; Alessandro Paniccia[15]; Amer H. Zureikat, MD[16]; Aatur D Singhi, [17]

[1]University of Pittsburgh, Pittsburgh, PA, US; [2]West Virginia University, Morgantown, WV, US; [3]University of Florida, Gainesville, FL, US; [4]University of Texas Southwestern Medical Center, Dallas, TX, US; [5]UT Southwestern Medical Center, Dallas, TX, US; [6]West Virginia University, Morgantown, WV, US; [7]Northshore University Health System, Evanston, IL, US; [8]UPMC Medical Center, Pittsburgh, PA, US; [9]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [10]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [11]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [12]West Virginia University, Morgantown, WV, US; [13]UT Southwestern Medical Center, Dallas, TX, US; [14]University of Pittsburgh, Pittsburgh, PA, US; [15]UPMC Medical Center, Pittsburgh, PA, US; [16]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [17]UPMC Medical Center, Pittsburgh, PA, US

INTRODUCTION: Accurate diagnosis of biliary strictures is challenging, as ERCP with pathologic assessment of bile duct specimens suffers from low sensitivity. Recently, DNA-based next generation sequencing (NGS) of biliary specimens was reported to be a promising adjunct for the detection of malignant strictures; however, it has not been evaluated prospectively and across multiple institutions. Furthermore, with the advent of RNA testing, RNA-based NGS has not been fully explored in the evaluation of biliary strictures. We therefore performed a prospective, multi-institutional study of DNA/RNA-based NGS of ERCP-obtained biliary specimens. **METHODS:** We conducted a prospective, 5-year study using a DNA/RNA-based NGS panel of 161 cancer-associated genes and 763 fusion genes across 1237 patients at 19 institutions. Sequencing was performed with a minimum coverage of 500x for each genomic region and ≥100,000 RNA reads (Ion GeneStudio System). Molecular findings were correlated with patient demographics (e.g., race/ethnicity, germline data, history of primary sclerosing cholangitis [PSC]), CA19-9, preoperative findings, and clinical follow-up. A stricture was designated as benign or malignant based on surgical pathology and/or follow up of >1 year. **RESULTS:** Molecular testing was successful for 1657 (99%) biliary specimens from 1225 (99%) patients. Based on follow-up from 1159 (95%) patients, DNA/RNA-based NGS demonstrated 81% sensitivity and 97% specificity for a malignant bile duct stricture. In comparison, pathologic assessment had a sensitivity of 45% and a specificity of 99%. Combining molecular testing with pathologic assessment improved detection of malignant strictures with a sensitivity of 88% and a high specificity of 96%. High-risk populations, such as Hispanic patients, germline carriers, and PSC patients, also showed improved sensitivity with DNA/RNA-based NGS (70% to 85%) compared to cytopathologic assessment (24% to 47%). Additionally, actionable molecular alterations were identified in 23% of molecularly positive neoplasms, altering cancer directed treatment in 46% of these cases. **CONCLUSIONS:** Combined DNA/RNA-based NGS of biliary specimens has a high technical success rate and improves the evaluation of bile duct strictures, especially among high-risk patients. This study highlights the importance of NGS testing in bile duct strictures to optimize surgical decision making as well as preoperative therapy.

Table. Diagnostic performance of Combined DNA/RNA NGS among various patient populations.

Parameter	Sensitivity (95% CI)	Specificity (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
All patients (*n = 1159*)				
CA19-9 ≥44 U/mL (n = *592*)	69% (0.64 - 0.73)	55% (0.48 - 0.63)	79% (0.74 - 0.83)	42% (0.35 - 0.49)
Pathologic assessment	45% (0.42 - 0.48)	99% (0.98 - 1.00)	98% (0.96 - 0.99)	57% (0.54 - 0.61)
NGS testing	81% (0.78 - 0.84)	97% (0.95 - 0.98)	97% (0.95 - 0.98)	80% (0.76 - 0.83)
Pathologic assessment & NGS testing	88% (0.85 - 0.90)	96% (0.94 - 0.98)	97% (0.95 - 0.98)	86% (0.83 - 0.89)
PSC patients (*n = 198*)				
CA19-9 ≥44 U/mL (n = *103*)	63% (0.46 - 0.78)	68% (0.55 - 0.79)	53% (0.38 - 0.68)	76% (0.63 - 0.86)
Pathologic assessment	24% (0.14 - 0.37)	100% (0.97 - 1.00)	100% (0.73 - 1.00)	76% (0.69 - 0.82)
NGS testing	78% (0.64 - 0.88)	97% (0.92 - 0.99)	88% (0.92 - 0.80)	91% (0.85 - 0.95)
Pathologic assessment & NGS testing	83% (0.70 - 0.91)	97% (0.92 - 0.99)	92% (0.81 - 0.98)	93% (0.87 - 0.97)
Hispanic (*n = 55*)				
CA19-9 ≥44 U/mL (n = *3*)	100% (0.06 - 1.00)	50% (0.03 - 0.97)	50% (0.03 - 0.97)	100% (0.06 - 1.00)
Pathologic assessment	40% (0.20 - 0.64)	100% (0.87 - 1.00)	100% (0.60 - 1.00)	74% (0.59 - 0.85)
NGS testing	70% (0.46 - 0.87)	100% (0.88 - 1.00)	100% (0.73 - 1.00)	85% (0.70 - 0.94)
Pathologic assessment & NGS testing	90% (0.67 - 0.98)	100% (0.88 - 1.00)	100% (0.78 - 1.00)	95% (0.81 - 0.99)
Asian (*n = 36*)				
CA19-9 ≥44 U/mL (n = *10*)	67% (0.31 - 0.91)	100% (0.06 - 1.00)	100% (0.52 - 1.00)	25% (0.01 - 0.78)
Pathologic assessment	32% (0.15 - 0.55)	100% (0.72 - 1.00)	100% (0.56 - 1.00)	46% (0.28 - 0.66)
NGS testing	73% (0.50 - 0.88)	93% (0.64 - 0.99)	94% (0.69 - 0.99)	68% (0.44 - 0.86)
Pathologic assessment & NGS testing	77% (0.54 - 0.91)	93% (0.64 - 1.00)	94% (0.71 - 1.00)	72% (0.46 - 0.89)
Germline carrier (*n = 48*)				
CA19-9 ≥44 U/mL (n = *30*)	74% (0.51 - 0.89)	57% (0.20 - 0.88)	85% (0.61 - 0.96)	40% (0.14 - 0.73)
Pathologic assessment	47% (0.30 - 0.65)	100% (0.73 - 1.00)	100% (0.76 - 1.00)	44% (0.27 - 0.62)
NGS testing	85% (0.68 - 0.95)	100% (0.73 - 1.00)	100% (0.85 - 1.00)	74% (0.49 - 0.90)
Pathologic assessment & NGS testing	91% (0.75 - 0.98)	100% (0.73 - 1.00)	100% (0.86 - 1.00)	82% (0.56 - 0.95)

Abbreviations: CA19-9, carbohydrate antigen 19-9; NSG, next generation sequencing; PSC, primary sclerosing cholangitis

32. Focal Adhesion Kinase Inhibitor and Radiation Therapy Lead to Depletion of Senescent CAF Population in PDAC.

Usman Y. Panni, MD[1]; Varintra Lander, MD, PhD[2]; John Baer, PhD[3]; Alice Kao, BS[4]; Faiz Ahmed, BS[5]; Brett Knolhoff, BS[6]; Patrick Grierson, MD, PhD[7]; Ryan C Fields, MD[8]; Hyun Kim, MD[9]; David G DeNardo, PhD[10]

[1]Washington University in St. Louis, St. Louis, MO, US; [2]Washington University in St. Louis, St. Louis, MO, US; [3]Washington University in St. Louis, St. Louis, MO, US; [4]Washington University in St. Louis, St. Louis, MO, US; [5]Washington University in St. Louis, St. Louis, MO, US; [6]Washington University in St. Louis, St. Louis, MO, US; [7]Washington University in St. Louis, St. Louis, MO, US; [8]Washington University in St. Louis, St. Louis, MO, US; [9]Washington University in St. Louis, St. Louis, MO, US; [10]Washington University in St. Louis, St. Louis, MO, US

INTRODUCTION: Pancreatic ductal adenocarcinoma (PDAC) is a lethal malignancy with a poor 5-year survival rate. The intractable nature of PDAC is largely attributed to its predominantly immunosuppressive microenvironment. PDAC's fibrotic stroma contributes to poor drug delivery, limited infiltration of antitumor immune cells, and a heterogeneous population of cancer-associated fibroblasts (CAFs). This fibrotic stroma drives RT resistance and is attributed to a senescent myofibroblast subset of CAFs that promotes tumor progression and immune cell dysfunction. Our prior work showed that a combination of focal adhesion kinase inhibitor (FAKi) and RT can lead to enhanced immune priming and antitumor T cell responses in mouse models and early biomarker studies. Given these intriguing findings, we sought to determine the role of stereotactic body RT (SBRT) combined with a FAKi, VS6063, in our Phase II trial (NCT04331041) of locally advanced PDAC patients. We hypothesize that patients with PDAC who receive SBRT + FAKi will show changes in the CAFs subsets that improve outcomes. **METHODS:** In this study, we performed single-cell RNA sequencing (scRNASeq) on endoscopic ultrasound-guided fine-needle matched biopsy samples from patients treated with SBRT and VS6063. Patients received SBRT 50 Gy in 5 daily fractions. On the second day of radiation, patients began treatment with VS-6063, dosed at 400 mg twice daily for up to one year. Biopsy samples were collected before treatment and 12-14 weeks post-treatment. Generated libraries were sequenced for scRNASeq using BD Rhapsody, and sequencing was done on a NovaSeq 6000 sequencing system (Illumina), yielding an average of 50,000 mean reads per cell. FASTQ files were processed and aligned, and data was analyzed using Seurat v5.0.0. **RESULTS:** Between August 2021 and September 2024, 24 patients have been

enrolled in our trial. Of these, matched pre- and post-SBRT plus VS6063 PDAC biopsy samples were available for 10 patients and subsequently analyzed using scRNASeq. We identified the CAF population across all these PDAC samples. We classified them into antigen presenting CAFs (ApCAFs), inflammatory CAFs (iCAFs), and three subsets of myofibroblasts (MyCAFs) (Figure 1. a), and we showed that the pre-treatment CAF populations were enriched for MyCAF1 and MyCAF3 (senescent CAFs) subsets. Following SBRT plus VS6063 treatment, there was an increase in ApCAFs, iCAFs, and MyCAF1 populations and depletion of MyCAF3, suggesting an upregulated antitumor immune response posttherapy (Figure 1b). Additionally, when stratified based on patients' overall survival, a significant decrease in MyCAF3 and iCAFs population was observed in patients with longer survival. **CONCLUSIONS:** SBRT/FAKi treatment in patients with advanced PDAC leads to improved clinical outcomes, possibly due to dynamic effects related to CAF populations. These findings underscore the role of CAFs in therapeutic response to RT response and potential prognostic implications for PDAC treatment.

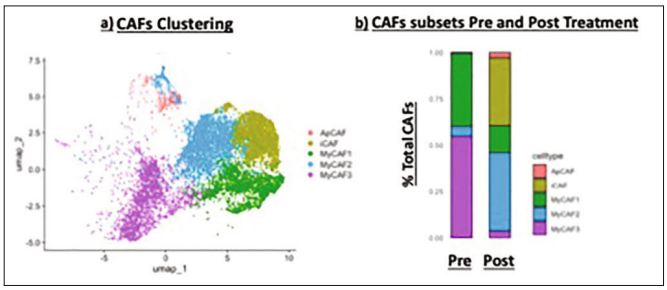


Figure 1. a) UMAP clustering of CAF subpopulations. b) Barplot of CAFs subpopulations stratified before and after FAKi/SBRT

33. Sustained Antitumor Activity of iCas9.B7-H3 CAR T Cells Against Primary Intrahepatic Cholangiocarcinoma

Shahrzad Arya[1]; Marco Ventin[2]; Giulia Cattaneo[3]; Seyed Amir Sanatkar[4]; Cristina Martin[5]; Liti Zhang, MD[6]; Jingyu Jia[7]; Nabeel M. Bardeesy[8]; Xinhui Wang[9]; Sandra Ryeom[10]; Cristina R. Ferrone, MD, MS, FSSO[11]
[1]Cedars-Sinai Medical Center, Los Angeles, CA, US; [2]Cedars-Sinai Medical Center, Los Angeles, CA, US; [3]Cedars-Sinai Medical Center, Los Angeles, CA, US; [4]Massachussets General Hospital, Boston, MA, US; [5]Massachussets General Hospital, Boston, MA, US; [6]Cedars-Sinai Medical Center, Los Angeles, CA, US; [7]Massachussets General Hospital, Boston, MA, US; [8]Massachussets General Hospital, Boston, MA, US; [9]Massachussets General Hospital, Boston, MA, US; [10]Columbia University Irving Medical Center, New York, NY, US; [11]Cedars-Sinai Medical Center, Los Angeles, CA, US

INTRODUCTION: Intrahepatic cholangiocarcinoma (ICC) is the second most common primary liver tumor, with rising incidence rates over the past two decades. Most patients present with unresectable or advanced metastatic disease, making current therapeutic options ineffective. B7-H3, an immune checkpoint molecule, is overexpressed in ICC, positioning it as a promising therapeutic target. This study investigates the persistence and efficacy of iCas9.B7-H3 CAR T cells against primary ICC tumors. Our CAR T construct includes an inducible caspase 9 (iCas9) suicide gene for controlled elimination in cases of cytokine release syndrome. **METHODS:** An orthotopic ICC xenograft model was established in NSG mice engrafted with 5x10^5 ICC3-GFP.Luc cells. Mice received systemic treatment with iCas9.B7-H3 CAR T cells (5x10^6) seven days after tumor implantation. To assess persistence, mice were rechallenged with 2.5x10^5 ICC3-GFP.Luc cells through tail vein systemic injection. Tumor burden was assessed using bioluminescence imaging (BLI), and overall survival (OS) was analyzed using Kaplan-Meier methods. **RESULTS:** iCas9.B7-H3 CAR T cells effectively eradicated primary ICC tumors throughout the 180-day study, significantly enhancing survival (P=0.0007) without adverse effects. After the rechallenge, these CAR T cells successfully rejected systemic ICC implantation for an additional 150 days, contributing to the overall survival benefit observed during the entire study period (P=0.0014). Notably, CAR T cell levels significantly increased following rechallenge (P=0.0003), along with a rise in memory stem cell population (P=0.00005); however, no differences in exhaustion markers were observed. All mice in the iCas9.B7-H3 group survived without tumor recurrence, confirmed by BLI and immunohistochemistry (IHC). **CONCLUSIONS:** These findings demonstrate the potential of iCas9.B7-H3 CAR T cells as a durable therapeutic option for ICC. The sustained response to primary ICC tumors and tumor rechallenge supports the initiation of clinical trials for advanced ICC patients.

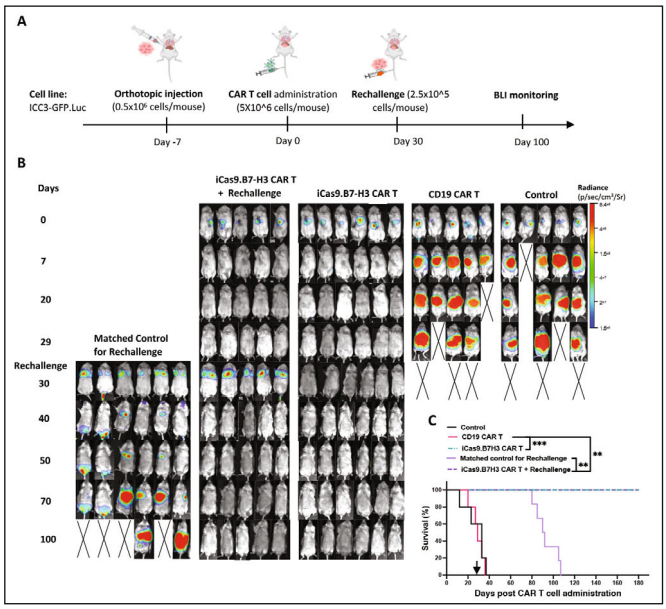


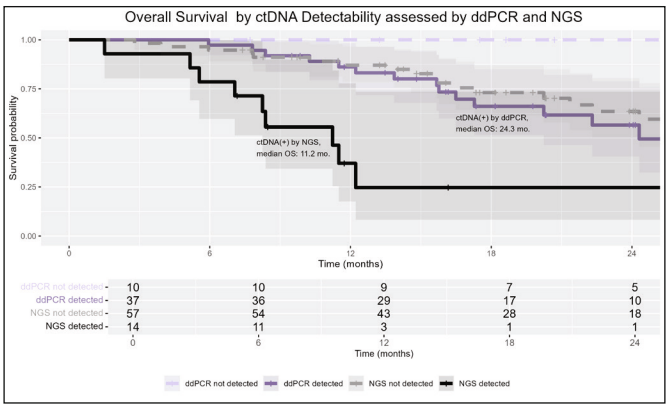
Figure 1. Sustained Antitumor Activity of iCas9.B7-H3 CAR T Cells Against Primary ICC Tumors and Their Response to Tumor Rechallenge. (A) Schema of primary ICC xenograft model (ICC3.GFP-Luc) infused with CAR T cells. (B) Primary ICC tumor burden measured by BLI in each group treated as indicated (n = 5 mice/group), (X denotes mice dead of disease). (C) Kaplan–Meier survival curve of mice (n=5-6 mice/group). Statistical comparisons were performed using log-rank test (C) **p-value≤0.01, ***p-value≤0.001.

34. The Assay Matters: ctDNA detection by NGS vs ddPCR lead to distinct outcomes in localized pancreatic cancer

Dominic Vitello, MD[1]; Dhavan Shah[2]; Amy Wells, MD[3]; Madison Cox[4]; Larissa Masnyk[5]; Lauren Janczewski, MD[6]; John Abad, MD[7]; Kevin Dawravoo[8]; Alex Liu[9]; Hui Zhang[10]; Massimo Cristofanilli[11]; Lawrence Jennings[12]; Lucas Santana-Santos[13]; David Bentrem[14]; Qiang Zhang[15]; Akhil Chawla, MD[16]
[1]Northwestern Medicine, Chicago, IL, US; [2]Northwestern University, Chicago, IL, US; [3]Northwestern Medicine, Chicago, IL, US; [4]Northwestern Medicine, Chicago, IL, US; [5]Northwestern University, Chicago, IL, US; [6]Northwestern Medicine, Chicago, IL, US; [7]Northwester Medicine, Chicago, IL, US; [8]Northwestern Medicine, Chicago, IL, US; [9]Northwestern University, Chicago, IL, US; [10]Northwestern Univrsity, Chicago, IL, US; [11]Weill Cornell Medical College, New York, NY, US; [12]Northwestern Medicine, Chicago, IL, US; [13]Northwestern Medicine, Chicago, IL, US; [14]Northwestern Medicine, Chicago, IL, US; [15]Northwestern University, Chicago, IL, US; [16]Northwestern University, Chicago, IL, US

INTRODUCTION: We have previously identified that KRAS circulating tumor DNA (ctDNA) is prognostic in patients undergoing neoadjuvant chemotherapy (NAC). We sought to understand the significance of increasing sensitivity to mutant *KRAS* ctDNA detection with digital droplet PCR (ddPCR) by 1) comparing the sensitivity of mutant *KRAS* ctDNA detection by NGS and ddPCR and 2) understanding the prognostic implication of enhanced sensitivity for *KRAS* ctDNA detection throughout treatment with NAC. **METHODS:** Patients with newly diagnosed, localized PDAC were enrolled in a prospective cohort study and treated under the standard of care. Peripheral blood samples were collected at diagnosis, after NAC, and after local therapy. Samples were analyzed using NGS and ddPCR probing for KRAS G12D, G12V, G12R mutations. Kaplan-Meier with log-rank tests were performed. **RESULTS:** 99 patients were enrolled. The median (IQR) follow-up time was 27.1 (15.8-68.9) months. At diagnosis, mutant *KRAS* ctDNA detection by ddPCR was seen in 37 of 48 patients (77.1%) and in only 15 of 75 (20.0%) by NGS, all of whom were detectable by ddPCR. Detection of mutant *KRAS* ctDNA by ddPCR or NGS at diagnosis were both associated with worse OS, yet with prognostically distinct outcomes (ddPCR ctDNA+ 24.3 months vs. not reached, p<0.05; NGS ctDNA+ 11.2 vs. 27.2 months, p<0.001, Figure 1). Over the course of NAC and local therapy, 10 of 53 patients (18.9%) gained ctDNA *KRAS* mutations as

assessed by ddPCR compared to 3 of 75 patients (3.9%) for NGS. 15 patients cleared a ctDNA *KRAS* mutation as assessed by ddPCR, compared to only 6 as assessed by NGS. Patients who cleared a mutation by ddPCR had longer OS compared to those that did not (NR vs. 18.0 months, p=0.034). NGS was unable to provide similar predictive discrimination (p=0.13). **CONCLUSIONS:** In localized pancreatic cancer, ddPCR is far more sensitive in the detection of mutant *KRAS* ctDNA than NGS and has greater prognostic value as a dynamic biomarker throughout treatment. Patients with KRAS ctDNA detected by NGS have far worse outcomes than those detected by ddPCR, likely due to high ctDNA load required for detection by NGS**.**



35. Validation of molecular subtyping in the PANCREAS clinical trial

Jaewon Lee[1]; Mohammed Aldakkak[2]; Yan Li[3]; Margaret Gulley[4]; Naim Rashid[5]; Erkut Borazanci[6]; Susan Tsai, MD[7]; Jen Jen Yeh, MD[8]

[1]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [2]Medical College of Wisconsin, Milwaukee, WI, US; [3]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [4]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [5]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [6]HonorHealth Research Institute, Scottsdale, AZ, US; [7]The Ohio State University, Columbus, OH, US; [8]University of North Carolina at Chapel Hill, Chapel Hill, NC, US

INTRODUCTION: Molecular profiling classifies pancreatic ductal adenocarcinoma (PDAC) into two tumor-intrinsic subtypes, classical and basal-like, that have treatment implications. We previously developed PurIST, a single-sample classifier that defines PDAC subtypes using 8 gene pairs, which has been translated into a CLIA-certified array-based assay (NanoString nCounter) with rapid turnaround, making it feasible in the clinical setting. The PANCREAS trial (NCT04683315) is an open-label Phase II trial that matches the molecular subtype of a patient's cancer using NanoString platform in a CLIA-certified laboratory to different neoadjuvant systemic therapies in resectable and borderline resectable PDAC. We sought to evaluate the performance of PurIST subtyping in the clinical trial. **METHODS:** Molecular subtyping of samples was performed in the CLIA-certified laboratory for the PANCREAS trial per protocol. We then performed RNA-seq on matched RNA samples available from the PANCREAS trial. Concordance was measured using Cohen's kappa and F-score. As the PANCREAS trial is still ongoing, for outcome comparisons, we used an independent retrospective cohort of 99 patients with PurIST subtypes by RNA-seq and NanoString as well as survival data available. Overall survival (OS) was analyzed using log-rank test and hazard ratios (HR) were calculated using Cox proportional hazards model. **RESULTS:** 40 samples were available from the PANCREAS trial and 99 samples from the retrospective cohort. Turnaround time of NanoString assay and molecular subtyping for the PANCREAS trial was less than 5 business days. In the PANCREAS trial, 4 patients (10%) were basal-like by NanoString and 4 patients (10%) were basal-like by RNA-seq with one discrepancy between each method, leading to an overall accuracy of 95% and Cohen's kappa of 0.722, indicating substantial agreement, as well as F1 score of 0.972, indicating excellent performance. In the retrospective cohort, 13 tumors (13%) classified as basal-like by RNA-seq and 14 (14%) by NanoString, with overall accuracy of 93% and Cohen's kappa of 0.700, with F1 score of 0.959. In the combined cohort, Cohen's kappa was 0.706 and F1 score was 0.963, indicating an overall excellent performance of NanoString platform compared to RNA-seq. Stage I-III patients (n = 89) with basal-like tumors had significantly shorter OS, although the difference was more pronounced in RNA-seq subtype (log-rank P < 0.0001 for RNA-seq and 0.027 for NanoString; HR 5.21 for RNA-seq and 2.19 for NanoString). **CONCLUSIONS:** The CLIA-certified array-based NanoString assay accurately predicted PurIST subtypes with excellent precision, recall, and performance compared to RNA-seq. It will be important to evaluate the performance of PurIST subtyping by RNA-seq and NanoString in larger cohorts using CLIA-certified laboratories and for treatment response prediction**.**

36. Circulating Neoplastic-Immune Hybrid Cells are Biomarkers of Occult Metastasis and Treatment Response in Pancreatic Cancer

Ranish K. Patel[1]; Michael Parappilly[2]; Hannah C Farley[3]; Emile J Latour[4]; Lei G. Wang[5]; Ashvin Nair[6]; Ethan S Lu[7]; Zachary Sims[8]; Byung Park[9]; Katherine Nelson[10]; Skye C Mayo[11]; Gordon B Mills[12]; Brett C Sheppard[13]; Young Hwan Chang[14]; Summer L Gibbs[15]; Adel Kardosh[16]; Charles D. Lopez[17]; Melissa H Wong[18]

[1]Oregon Health and Science University, Portland, OR, US; [2]Oregon Health and Science University, Portland, OR, US; [3]Oregon Health & Science University, Portland, OR, US; [4]Oregon Health & Science University, Portland, OR, US; [5]Oregon Health and Science University, Portland, OR, US; [6]Oregon Health and Science University, Portland, OR, US; [7]Oregon Health and Science University, Portland, OR, US; [8]Oregon Health and Science University, Portland, OR, US; [9]Oregon Health and Science University, Portland, OR, US; [10]Oregon Health and Science University, Portland, OR, US; [11]Oregon Health and Science University, Portland, OR, US; [12]Oregon Health and Science University, Portland, OR, US; [13]Oregon Health and Science University, Portland, OR, US; [14]Oregon Health and Science University, Portland, OR, US; [15]Oregon Health and Science University, Portland, OR, US; [16]Oregon Health and Science University, Portland, OR, US; [17]Oregon Health and Science University, Portland, OR, US; [18]Oregon Health and Science University, Portland, OR, US

INTRODUCTION: Pancreatic ductal adenocarcinoma (PDAC) poses several diagnostic and prognostic challenges, as existing blood and radiographic biomarkers fail to reliably stage disease, predict rapid metastatic recurrence (rPDAC), or assess response to neoadjuvant therapy (NAT). We investigated the potential for circulating neoplastic-immune hybrid cells (CHCs) to serve as a non-invasive multi-functional biomarker for PDAC. **METHODS:** Peripheral blood specimens were obtained from patients with PDAC. Peripheral blood mononuclear cells (PBMCs) were isolated, processed onto slides, and stained with antibodies to detect CHCs by co-expression of pan-cytokeratin and CD45. CHC numbers were normalized to 50,000 PBMCs, and correlated with clinical, surgical, and tumor-pathological characteristics. rPDAC was defined as metastatic recurrence within 6-months of margin-negative pancreatectomy. Cyclic immunofluorescence analyses were utilized to compare hybrid phenotypes in peripheral blood and tumors. **RESULTS:** Peripheral blood specimens were collected immediately prior to resection (n=42); 8 patients had radiographically occult metastatic disease at surgical exploration and 6 developed rPDAC. Those with occult metastatic disease and rPDAC had higher preoperative CHCs compared to patients who did not (65.0 and 74.4 CHCs, vs. 11.52 CHCs; $p<0.001$). Preoperative CA 19-9 levels did not differ between groups. Patients receiving NAT with complete or near-complete pathologic responses had lower preoperative CHCs than partial and/or non-responders (1.7 vs. 13.1 CHCs; $p=0.008$). CHCs were longitudinally evaluated in 8 patients treated with NAT. In patients who experienced partial pathologic response (n=4), CHCs decreased to undetectable levels during treatment and increased in the interval between NAT completion and surgical resection. Patients with poor or no pathologic response (n=3) had persistent CHCs detection while on-therapy. A single patient who developed metastatic disease while on-therapy had rising CHC levels prior to radiographic evidence of metastases. Additionally, in a cohort of patients with metastatic PDAC, treatment-induced phenotypic changes were observed in CHCs and mirrored paired metastatic-tumor samples. **CONCLUSIONS:** CHC enumeration and phenotyping display promise as a real-time indicator of disease burden, recurrence risk, and treatment response in PDAC. CHCs have great potential as tumor-derived biomarkers, which could provide valuable information to optimize therapeutic strategies and improve survival in patients with PDAC**.**

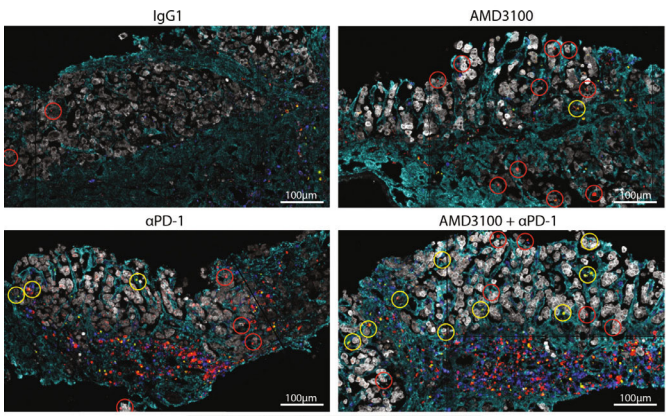
37. Overcoming CXCR4-mediated T cell exclusion potentiates antitumor cytotoxicity in fibrolamellar carcinoma

Lindsay K. Dickerson, MD[1]; Jason A Carter, MD, PhD[2]; Sara K Daniel, MD[3]; Alaa R Farghli[4]; Xiuyun Jiang, PhD[5]; Kevin M Sullivan, MD[6]; Kevin P Labadie, MD[7]; Emily Beirne[8]; Heidi L Kenerson[9]; Raymond S Yeung, MD, PhD[10]; Shreeram Akilesh[11]; Ian N Crispe, MBBS, PhD[12]; Praveen Sethupathy, PhD[13]; Venu G Pillarisetty, MD[14]

[1]University of Washington, Seattle, WA, US; [2]University of Washington, Seattle, WA, US; [3]Mayo Clinic, Rochester, MN, US; [4]Cornell University College of

Veterinary Medicine, Ithica, NY, US; [5]University of Washington, Seattle, WA, US; [6]Louisiana State University Health Sciences Center, New Orleans, LA, US; [7]City of Hope Comprehensive Cancer Center, Duarte, CA, US; [8]University of Washington, Seattle, WA, US; [9]University of Washington, Seattle, WA, US; [10]University of Washington, Seattle, WA, US; [11]University of Washington, Seattle, WA, US; [12]University of Washington, Seattle, WA, US; [13]Cornell University College of Veterinary Medicine, Ithica, NY, US; [14]University of Washington, Seattle, WA, US

INTRODUCTION: Fibrolamellar carcinoma (FLC) has a poor prognosis, due in part to high rates of recurrence after surgery and the absence of effective systemic therapies. We hypothesized that combination blockade of chemokine receptor CXCR4 and immune checkpoint PD-1 would overcome T cell stromal sequestration and immune suppression in FLC, leading to tumor cell death. **METHODS:** FLC and non-tumor liver (NTL) were analyzed using immunohistochemistry (IHC) and single-nuclear RNA sequencing (snRNAseq) to determine expression of CXCR4 and its ligands; unsupervised tensor decomposition analysis was used to map intercellular chemokine signaling. FLC tumor slice cultures (TSCs; n=11) were treated with control (IgG1), a CXCR4 inhibitor (AMD3100), anti-PD-1 blocking antibody αPD-1), or combination blockade (AMD3100/αPD-1). Single-cell RNAseq (scRNAseq), IHC, and a novel spatial proteomics analysis were used to assess T cell mobilization and function. **RESULTS:** Expression of CXCR4 was significantly upregulated in FLC compared with NTL, with CXCR4 expressed primarily in lymphocytes and macrophages. Stellate cells, which make up stroma, were the dominant source of CXCL12, the primary ligand of CXCR4. Intercellular chemokine signaling was altered in FLC compared with NTL: signaling was received primarily by epithelial cells, lymphocytes, and macrophages, and most frequently involved the CXCR4 receptor/ligand family. $CD3^+$ T cells colocalized with CXCL12 in the FLC stroma on IHC. Gene set enrichment analysis using scRNAseq data found that TSC treatment with AMD3100/αPD-1 resulted in increased markers of T cell proliferation (normalized enrichment score [NES] 1.9, FDR 5.9 x 10^{-3}) and positive regulation of chemotaxis (NES 1.8, FDR 1.1 x 10^{-2}) in $CD8^+$ cytotoxic T cells. Spatial proteomics analysis showed that AMD3100/αPD-1 increased T cell activation and infiltration into the carcinoma compartment (Figure). Cleaved caspase-3 (CC3) IHC demonstrated increased tumor apoptosis after AMD3100/αPD-1 compared with IgG1 and monotherapy (52% vs 30% (IgG1), 37% (AMD3100), 41% (αPD-1) $CC3^+$ cells, p=3x10^{-5}, p=0.001, p=0.002). **CONCLUSIONS:** CXCR4 chemokine signaling mediates T cell exclusion in FLC. CXCR4 and PD-1 blockade work through independent mechanisms — promoting T cell infiltration and activation, respectively — to cooperatively increase tumor cell death. These findings support consideration of clinical trials testing drugs targeting CXCR4 and PD-1 in FLC and other T cell-excluded cancers.

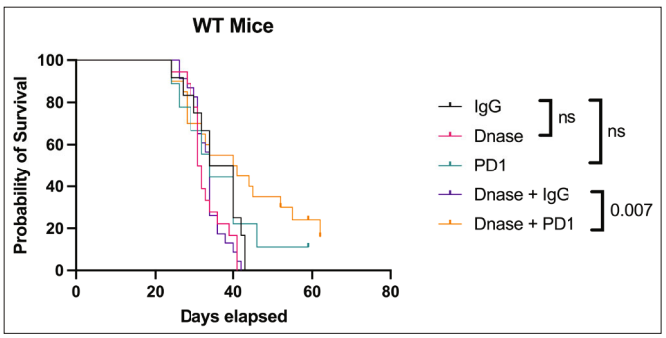


The first-ever application of high-resolution spatial proteomics to fibrolamellar carcinoma tumor slice cultures found that treatment with AMD3100/αPD-1 increased T cell infiltration and activation. Dark gray - panCK, light gray - panRAS (tumor cells), cyan - fibronectin (stroma), blue - $CD4^+$ T cells, red - $CD8^+$ Tcells, yellow - GZMA (marker of activation). Red and yellow circles highlight tumor-adjacent $CD8^+GZMA^-$ and $GZMA^+$ cells.

38. Neutrophil extracellular trap inhibition revitalizes PDAC responsiveness to immunotherapy via reduced fibrosis and the expansion of TCF1+CD8+ progenitor T cells

Britney Niemann[1]
[1]West Virginia University, Morgantown, WV, US

INTRODUCTION: Pancreatic adenocarcinoma (PDAC) is an aggressive disease with a 5-year survival of 13%. This poor prognosis is due to the unique and complex immunosuppressive tumor microenvironment (TME) that provides resistance to therapy, including immunotherapy. Identifying new targets and therapeutic combinations to enhance response to immunotherapy is a critical goal. Neutrophil extracellular traps (NETs) are one target of interest. Activated neutrophils release their intracellular contents to form NETs, a process largely mediated by the enzyme peptidyl arginine deiminase 4 (PAD4). NETs are elevated in PDAC and associated with tumor progression, modulating the TME resulting in immunosuppression and fibrosis, metastasis, and decreased survival. Given the expansive role of NETs in the pathogenesis of PDAC, we investigated the influence of NETs on the PDAC TME and immunotherapy response. **METHODS:** An orthotopic murine PDAC model was utilized in C57BJ6 (WT) or $PAD4^{-/-}$ mice. Tumor burden and survival were assessed after treatment with PBS, IgG control, DNase, PD1 therapy, or a combination of DNase and PD1. Circulating and intra-tumoral NET markers were evaluated as well as the degree of fibrosis and the immune profile of the TME. Blood and tumor tissue from human PDAC patients were also evaluated for levels of NETs and tumor infiltrating T cells. **RESULTS:** In human PDAC patients there was a correlation between intra-tumoral $CD8^+$ cells and circulating NET markers, pointing to a potential link between NETs and cytotoxic T cell infiltration. Patients with high NET levels also experienced more major post-operative complications. In the murine model, removal of NETs from the PDAC TME, either genetically ($PAD4^{-/-}$) or via DNase treatment, reduced tumor growth and enhanced survival compared to controls. Decreased expression of collagen and matrix metalloproteinase (MMP) genes, as well as reduced intra-tumoral collagen deposition were found in NET deficient mice. Additionally, an increase in $TCF1^+PD1^+CD44^+CD8^+$ progenitor T cells, a subpopulation of T cells responsive to immunotherapy, were identified after DNase treatment. These changes resulted in a further tumor burden reduction and prolonged survival when anti-PD1 therapy was given in conjunction with NET inhibition. **CONCLUSIONS:** NETs influence extracellular matrix (ECM) remodeling and the T cell response to PDAC, allowing for a significant response to anti-PD1 therapy. These findings support the combination therapy of immune checkpoint blockade and NET inhibition in patients with PDAC.

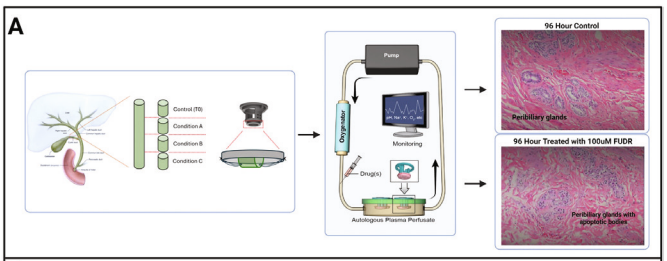


39. Mitigation of a Floxuridine-Induced Bile Duct Injury for Patients Undergoing HAIP Therapy

Alyssa Eade[1]; Yuri Lin[2]; Carrie Ryan[3]; Xiaohu Zhang[4]; Ashley Rainey[5]; Kirsten Remmert[6]; Hannah Stepp[7]; Emily Smith[8]; Priyanka Desai[9]; Surajit Sinha[10]; Lindsay R Friedman[11]; Tracey Pu, MD[12]; Carolina Larrain[13]; Andrew M Blakely[14]; Jeremy L. Davis, MD[15]; David Kleiner[16]; Craig Thomas[17]; Jonathan M Hernandez[18]
[1]National Institutes of Health, Bethesda, MD, US; [2]National Institutes of Health, Bethesda, MD, US; [3]National Institutes of Health, Bethesda, MD, US; [4]National Institutes of Health, Bethesda, MD, US; [5]National Institutes of Health, Bethesda, MD, US; [6]National Institutes of Health, Bethesda, MD, US; [7]National Institutes of Health, Bethesda, MD, US; [8]National Institutes of Health, Bethesda, MD, US; [9]National Institutes of Health, Bethesda, MD, US; [10]National Institutes of Health, Bethesda, MD, US; [11]National Institutes of Health, National Cancer Institute, Surgical Oncology Program, Bethesda, MD, US; [12]National Cancer Institutes/National Institutes of Health, Bethesda, MD, US; [13]National Institutes

of Health, Bethesda, MD, US; [14]National Institutes of Health, Bethesda, MD, US; [15]National Institutes of Health, Bethesda, MD, US; [16]National Institutes of Health, Bethesda, MD, US; [17]National Institutes of Health, Bethesda, MD, US; [18]National Institutes of Health, Bethesda, MD, US

INTRODUCTION: Hepatic artery infusion pumps (HAIPs) are increasingly employed in the management of liver malignancies although patients receiving HAIP therapy frequently undergo floxuridine (FUDR) dose-reductions and dose-holds to avoid a secondary sclerosing cholangitis. Dexamethasone is utilized in conjunction with floxuridine (FUDR) to limit this adverse event, but little is known about the mechanism(s) of toxicity including avenues for prevention. **METHODS:** Cystic ducts were obtained from patients at the time of HAIP placement. Standard histopathologic techniques were used to compare cystic ducts to archival hepatic duct samples. Cystic ducts were perfused for 96 hours *ex vivo* using oxygenated autologous plasma in a custom perfusion circuit (Figure 1). FUDR was added to the cystic duct perfusate to determine susceptible cell population(s). A 1+ combination drug screen was run with FUDR and 3000 compounds using the Highest Single Agent (HSA) model on cholangiocytes. A second, prioritized 1+ screen was then run on cholangiocytes and cancer cell lines. **RESULTS:** Compared to hepatic duct samples, cystic ducts had a similar density of stromal cells, lymphocytes, endothelium, and matrix composition, establishing suitability as a surrogate. Cystic ducts (n=29) were examined after 96 hours of perfusion, and histologic analysis confirmed preservation of all cell populations as compared to immediate removal from the patient. Cystic ducts (n=26) were then perfused with the addition of FUDR (range 15uM-200uM). Histologic examination revealed nuclear alterations and apoptotic body formation isolated to the biliary epithelium and peribiliary gland cell populations (Figure). IHC for DNA damage (γH2AX) revealed positive staining in the SOX9-positive biliary epithelium and peribiliary glands (<1% of cells/um^2 vs. 8% of cells/um^2, p=<0.0001). Next, cholangiocyte lines expressing SOX9, CK7 and CK19 were screened with FUDR and 3,000 drug candidates to evaluate for agents that increased IC50 values. We then performed a second 1+ screen with 114 selected agents using the cholangiocytes and cancer cell lines to avoid agents that my compromise FUDR efficacy. We have selected GDC-0152, methotrexate, and nicotinamide riboside for further interrogation (Figure). Validation and mechanistic investigation is ongoing. **CONCLUSIONS:** Using an *ex vivo* human perfusion system and patient cystic ducts, we identified damage to the biliary epithelium and peribiliary glands as potentially the earliest insult from HAI of FUDR. Using large 1+ drug screens, we have identified 3 agents that may hold promise to mitigate FUDR toxicity.



B

Agent Name	Primary Cholangiocytes	Stem Cholangiocytes	Cholangiocarcinoma	Colorectal Carcinoma
GDC-0152	374	191	-62	-520
Methotrexate	1355	838	248	223
Nicotinamide Riboside	288	275	50	-37

Figure 1. A. Sectioning and fixation of cystic duct samples for perfusion with autologous plasma, +/- drug, in an ex vivo circuit and resultant histopathologic examination. B. FUDR 1+ HSA excess in primary cholangiocytes, stem cholangiocytes, cholangiocarcinoma and colorectal carcinoma. Positive values indicate increased viability whereas negative values indicate decreased viability.

40. Patients with Postoperative Complications or Worse Quality of Life Have More Decisional Regret After Resection of Pancreatic Ductal Adenocarcinoma

Judy Li, MD[1]; Thomas M Li, MD[2]; Adam Geffner, BA[3]; Sophie Neugarten, BA[4]; Camilo Correa-Gallego, MD[5]; Umut Sarpel, MD, MSc[6]; Daniel Labow, MD[7]; Ganesh Gunasekaran, MD[8]; Myron Schwartz, MD[9]; Parissa Tabrizian, MD[10]; Spiros Hiotis, MD, PhD[11]; James O Park, MD[12]; Noah A. Cohen, MD[13]
[1]Icahn School of Medicine at Mount Sinai, New York, NY, US; [2]Icahn School of Medicine at Mount Sinai, New York, NY, US; [3]Icahn School of Medicine at Mount Sinai, New York, NY, US; [4]Icahn School of Medicine at Mount Sinai, New York, NY, US; [5]Icahn School of Medicine at Mount Sinai, New York, NY, US; [6]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, US; [7]Nuvance Health, Danbury, CT, US; [8]Icahn School of Medicine at Mount Sinai, New York, NY, US; [9]Icahn School of Medicine at Mount Sinai, New York, NY, US; [10]Icahn School of Medicine at Mount Sinai, New York, NY, US; [11]Icahn School of Medicine at Mount Sinai, New York, NY, US; [12]Icahn School of Medicine at Mount Sinai, New York, NY, US; [13]Icahn School of Medicine at Mount Sinai, New York, NY, US

INTRODUCTION: Surgery is potentially curative for patients with localized pancreatic ductal adenocarcinoma (PDAC). Given the high rate of complications, decline in quality of life (QoL) postoperatively, and high rates of recurrence, clear preoperative communication and expectation setting is critical. This study investigates clinical outcomes that affect postoperative decisional regret (DR) in patients with PDAC. **METHODS:** This mixed-methods study investigates the impact of clinical outcomes and QoL on the degree of DR in patients with PDAC who have undergone curative-intent resection at least 6 months prior to study recruitment. Patients completed validated surveys assessing DR and QoL by the European Organization for Research and Treatment of Cancer (EORTC). Groups are stratified by presence or absence of DR, assessed by the Decisional Regret Scale (DRS). Characteristics and survey scores were compared by chi-square, independent t-test, and Mann-Whitney U-test. Narrative responses were thematically analyzed. **RESULTS:** 45 patients met inclusion criteria and completed all questionnaires. 19 (42.2%) patients expressed regret about their decision to pursue curative-intent surgery, with 5 patients expressing moderate to severe regret (DRS $\geq$ 25). There was no significant difference in median postoperative timing of survey completion between groups (56 months in DR group vs 34 months, P=0.908). Baseline characteristics, medical treatments, and operative approaches were similar. Both groups had similar recurrence rates at time of survey completion. While 30 and 90 day readmission rates were similar, a greater proportion of the DR group had 30 day complications (42.1% vs 15.4%, P=0.045). Those expressing regret reported poorer physical functional status (mean score 79.30 $\pm$ 18.84 vs 92.31 $\pm$ 10.27, P=0.011) and greater impact on social activities (mean score 67.54 $\pm$ 33.55 vs 84.67 $\pm$ 19.19, P=0.038). Thematic analysis of narrative responses revealed that a majority of patients expressed a strong desire to have a greater focus on potential QoL changes during preoperative discussions. **CONCLUSIONS:** Patients expressing postoperative DR experienced more 30 day complications, and still report lasting effects on their current physical status and social activities. This emphasizes the importance of thorough preoperative counseling on surgical risks and potential changes in postoperative QoL so that patients may make the best informed decision.

Table 1. Clinical Outcomes and Quality of Life Affect Postoperative Decisional Regret After Resection of Pancreatic Ductal Adenocarcinoma

	DR Absent N=26 (%)	DR Present N=19 (%)	Overall N=45 (%)	P-value
Gender				
Male	12 (46.2)	9 (47.4)	21 (46.7)	0.936
Female	14 (53.8)	10 (52.6)	24 (53.3)	
Race				
White	20 (76.9)	13 (68.4)	33 (73.3)	0.483
African American/Black	5 (19.2)	5 (26.3)	10 (22.2)	
Asian	0 (0)	1 (5.3)	1 (2.2)	
Other/unknown	1 (3.8)	0 (0)	1 (2.2)	
Ethnicity				
Hispanic/Latino	1 (3.8)	4 (21.1)	5 (11.1)	0.144
Age at diagnosis (mean, SD)	64.38 $\pm$ 8.23	64.68 $\pm$ 9.60	64.51 $\pm$ 8.73	0.911
Preoperative treatment				
Neoadjuvant chemotherapy	17 (65.4)	13 (68.4)	30 (66.7)	0.831
Upfront surgery	9 (34.6)	6 (31.6)	15 (33.3)	
Surgical Procedure				
Pancreaticoduodenectomy	18 (69.2)	14 (73.7)	32 (71.1)	0.502
Distal pancreatectomy	7 (26.9)	3 (15.8)	10 (22.2)	
Other	1 (3.8)	2 (10.5)	3 (6.7)	
Adjuvant chemotherapy received?	20 (76.9)	17 (89.5)	37 (82.2)	0.435
Readmission Rates				
Within 30 days	4 (15.4)	3 (15.8)	7 (15.6)	0.970
Within 90 days	1 (3.8)	0 (0)	1 (2.2)	0.387
Complications (Any Grade) [A]				
Within 30 days	4 (15.4)	8 (42.1)	12 (26.7)	**0.045**
Within 90 days	2 (7.7)	0 (0)	2 (4.4)	0.216
Time since surgery to survey completion (months, median, range)	34 [6, 137]	56 [6, 131]	41 [6, 137]	0.908
Has the patient had a recurrence at time of survey completion?	10 (38.5)	5 (26.3)	15 (33.3)	0.526
EORTC Physical Function score (mean, SD) [B]	92.31 $\pm$ 10.27	79.30 $\pm$ 18.84	86.81 $\pm$ 15.73	**0.011**
EORTC Social Functioning score (mean, SD) [C]	84.67 $\pm$ 19.19	67.54 $\pm$ 33.55	77.27 $\pm$ 27.40	**0.038**

[A] Complications graded by Clavien-Dindo classification.

[B] Physical symptoms assessed by the European Organization for Research and Treatment of Cancer (EORTC) QoL survey on a scale of 0-100.

[C] Social functioning assessed by the European Organization for Research and Treatment of Cancer (EORTC) QoL survey on a scale of 0-100.

Colorectal

41. Targeting neutrophil extracellular traps to overcome therapeutic resistance in colorectal cancer

Sepideh Gholami, MD[1]
[1]*Northwell Health, New York, NY, US*

INTRODUCTION: Presence of necrosis is a predictor of poor prognosis in colorectal cancer (CRC) and thought to occur passively as the tumor outgrows its blood supply. Neutrophil extracellular traps (NETs) have been recently shown to actively induce necrosis in mouse models of breast and lung cancer. We evaluated the role of NETs in mediating necrosis, metastasis, and resistance to therapy in CRC. **METHODS:** Presence of NETs in blood (n=22) and extend of necrosis in tumor samples (n=64) from patients with resected primary CRC and CRC liver metastasis were scored and correlated with clinical outcomes and immunophenotypic properties. Single cell RNA sequencing and spatial transcriptomics were performed on tumors with or without necrotic regions. The functional role of NETs in tumor necrosis, metastatic spread, and chemotherapy response was interrogated using an orthotopic CRC mouse model with implanted syngeneic AKPS (ApcKD; KrasG12D; Trp53KO; Smad4KO) organoids via two. **METHODS:** 1) pharmacologically with disulfiram (a drug that blocks NET formation) and 2) genetically using neutrophil-specific Protein Arginine Deaminase 4 deficient mice (which don't form citrullinated NETs). **RESULTS:** Compared to healthy controls, CRC patients displayed elevated levels of NET-primed neutrophils ($p< 0.01$) in circulation. NETs also accumulated within the tumor vasculature adjacent to necrotic regions. Necrotic tumor regions had 15-fold higher NETs compared to non-necrotic regions. The extent of necrosis correlated with stage ($p=0.007$), but not tumor size ($p=0.99$). Spatial transcriptomics of cancer cells in necrotic regions of human primary CRC tumors showed enrichment in pathways related to migration and epithelial-to-mesenchymal transition compared to non-necrotic tumors. AKPS tumor-bearing mice had a myeloid bias in the hematopoietic compartment early after tumor organoid transplantation and subsequent expansion of circulating neutrophils during tumor progression. Genetic or pharmacological treatment to block NET formation decreased necrosis in colon tumors ($p< 0.01$), and reduced liver metastasis ($p< 0.05$) compared to control mice. Disulfiram in combination with chemotherapy reduced tumor size by over 50% compared to controls ($p< 0.01$). **CONCLUSIONS:** We demonstrate that neutrophils, through NET formation, induce CRC tumor necrosis and drive cancer cells to gain pro-metastatic traits. Genetic or pharmacological targeting of NETs decreases tumor necrosis and liver metastasis and acts synergistically with chemotherapy to reduce tumor burden.

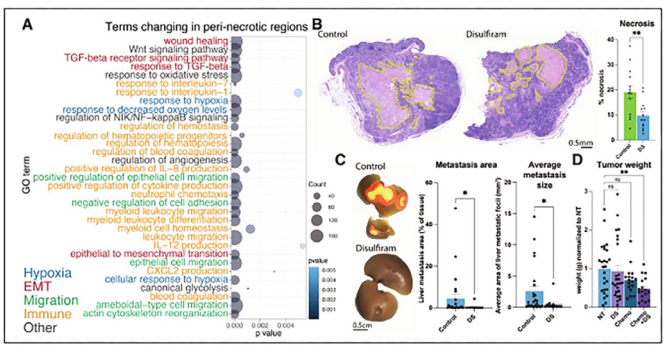


Figure. A) Necrotic tumors demonstrate pro-metastatic traits. GO terms of the genes upregulated specifically in peri-necrotic tumor regions compared to non-necrotic regions of human colorectal primary tumor specimens used for single cell RNA sequencing. B-D) NET-inhibition reduces tumor necrosis, size, and metastasis. B) Representative H&E-stained images and quantification of necrosis within the colon tumors of mice treated with disulfiram compared to control mice. N=13 disulfiram-treated mice and N=14 control mice. C) Representative brightfield images with overlying tumoral mScarlet fluorescence and quantification of the percentage of liver metastasis area and the average area of metastatic foci from AKPS-bearing mice treated with disulfiram compared to control mice. N=10 control mice and N=7 disulfiram-treated mice. D) Tumor weight at endpoint of treatment mice normalized to vehicle treated control mice. Control (NT; N=26), disulfiram-treated (DS; N=25), chemotherapy-treated (Chemo; N=17), combination therapy-treated (Chemo+DS; N=17). Bars show mean ± s.e.m., *$p<0.05$, **$p<0.01$, n.s., non-significant, as determined by unpaired two-tailed t-test (B), Mann-Whitney test (C), one-way ANOVA with Dunnett's multiple comparison test (D).

42. Fusobacterium nucleatum Tissue Density is Associated with Patient, Tumor, and Immune Microenvironment Features and Overall Survival in Appendix Cancer

Christopher Sherry, DO[1]*; Hyun Park*[2]*; Neda Dadgar*[3]*; Chelsea Knotts, MD*[4]*; Rosie Blodgett*[5]*; Ali Zaidi*[6]*; Kunhong Xiao*[7]*; Ashten Omstead*[8]*; Erin Grayhack*[9]*; Vera Donnenberg*[10]*; Albert Donnenberg*[11]*; David Bartlett, MD*[12]*; Patrick Wagner, MD*[13]
[1]*Allegheny Health Network, Pittsburgh, PA, US;* [2]*Allegheny Health Network, Pittsburgh, PA, US;* [3]*Cleveland Clinic Foundation, Cleveland, OH, US;* [4]*Allegheny Health Network, Pittsburgh, PA, US;* [5]*Allegheny Health Network, Pittsburgh, PA, US;* [6]*Allegheny Health Network, Pittsburgh, PA, US;* [7]*Allegheny Health Network, Pittsburgh, PA, US;* [8]*Allegheny Health Network, Pittsburgh, PA, US;* [9]*Allegheny Health Network, Pittsburgh, PA, US;* [10]*Allegheny Health Network, Pittsburgh, PA, US;* [11]*Allegheny Health Network, Pittsburgh, PA, US;* [12]*Allegheny Health Network, Pittsburgh, PA, US;* [13]*Allegheny Health Network, Pittsburgh, PA, US*

INTRODUCTION: Fusobacterium nucleatum (Fn) is a gram-negative bacterium strongly suspected to play a causative or tumor-promoting role in colorectal cancer. We have previously reported a high prevalence of Fn in appendiceal cancer (AC) as well, with levels comparable to acute appendicitis and higher than those seen in the healthy appendix. The present study assessed Fn density in a series of AC specimens for association with patient and tumor characteristics and oncologic outcomes in AC. **METHODS:** Fn density was assessed in a set of 41 primary tumors and 13 sites of peritoneal metastasis using a semi-quantitative RNA-in situ hybridization assay in FFPE tissue (RNAscope). The density of Fn in each sample was visually scored, then log-transformed and tested for association with patient (age, sex) and tumor (grade, PCI, primary vs metastatic) variables, immune cell densities (CD3/CD8 lymphocytes and tumor-associated M1-like/M2-like macrophages), and oncologic outcome (progression-free and overall survival, PFS/OS). Subgroup comparisons were carried out using non-parametric tests of association (Spearman's rank correlation test) and linear regression, and survival analysis was performed using Cox regression. **RESULTS:** Fn density was found to be associated with intermediate grade tumors ($p=0.04$ G2 vs. G3; and $p=0.05$ G2 vs. G1); as well as with tumor extent (peritoneal carcinomatosis index, rho=0.35, $p=0.02$). Fusobacterium density was associated with increasing age ($p=0.01$), but not sex. We saw no variation on the base of primary vs. peritoneal metastatic tumors. Fn density was negatively associated with CD8 lymphocyte density within high grade tumors (rho=-0.6, $p=0.02$) and positively association with M2-like macrophages (rho=0.3, $p=0.03$). A survival advantage was seen in patients with high Fn density (>40th percentile; HR 0.19 [95%CI 0.05, 0.7], $p=0.02$), which was independent of grade on multivariable analysis (HR 0.12 [95%CI 0.02, 0.8], $p=0.02$). **CONCLUSIONS:** Fn is prevalent in AC primary tumors and peritoneal metastases. We detected associations of Fn density with intermediate grade and increasing patient age, as well as M2-like macrophage density, the latter indicating a potential role for Fn in modulating the immune response to AC. Fn density was associated with improved overall survival independent of grade. Future studies are planned to validate and these findings in larger series and further define the potential influence of Fn within the AC tumor microenvironment.

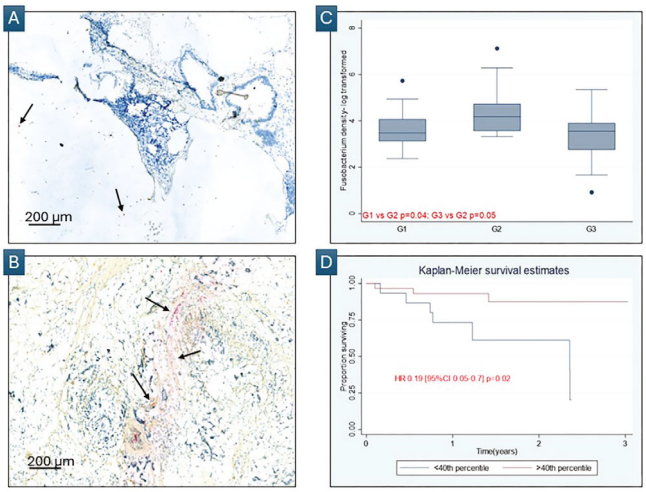


Figure 1. Fusobacterium nucleatum (Fn) infiltration of a low-grade tumor and associated mucin (panel A), and an infiltrative high-grade tumor with adjacent

inflamed stroma (panel B) visualized with RNA in-situ with arrows indicating Fn infiltration. Fn density was associated with intermediate grade (panel C, G1 vs G2 p=0.04, G2 vs G3 p=0.05) and improved overall survival (panel D, HR 0.19 [95% CI 0.05-0.7] p-0.02).

43. Local Recurrence after Full Thickness Local Excision versus Radical Resection after chemoradiation therapy for rectal cancer with ypT2 residual disease

Avihai Moscovici[1]
[1]*Lankenau Medical Center, Wynnewood, PA, US*

INTRODUCTION: Interest in organ preservation for rectal cancer patients has resulted in advances in treatment but raised questions regarding adequacy of care if residual cancer remains in the rectal wall. Some have advocated the need for radical resection in any patient with a ypT2 cancer on local excision. Purpose: To evaluate the local recurrence rates of FTLE versus radical resection in patients with ypT2 rectal cancer. **METHODS:** We reviewed a prospectively maintained database of rectal cancer operations that took place between April 2000 and July 2024, in a high-volume tertiary referral center, to identify all pathological T2 patients who received neoadjuvant therapy (YpT2). Patients were then divided into Full Thickness Local Excision (FTLE) and Radical Resection (RR) groups. These groups were further analyzed and compared regarding initial pre-operative data, morbidity, and outcomes. **RESULTS:** From April 2000 to July 2024, we performed 273 colorectal procedures on patients with YpT2. Of these, 227 underwent radical intra-abdominal resection (RR), and 46 full-thickness local excisions (FTLE). There were 150 males and 77 females on the RR group comparing to 31 males and 15 females in the FTLE group. Average patient age was 58.19 for RR and 58.94 for FTLE. BMI was similar in both groups – 27.5 for RR patients versus 27.9 in FTLE. The average estimated blood loss (EBL) was 272 ml for the RR group and 86 ml for the FTLE group. Forty-four patients (19.38%) in the RR group experienced 30-day morbidity compared to five patients (10.86%) in the FTLE group. Re-operation rates were 1.76% (4/227) versus 0% in the FTLE group. Diverting ostomy was performed in 81.49% of the RR group, while none of the FTLE required diversion. Local recurrence rates were similar: two patients (4.35%) in the FTLE group and 10 patients (4.41%) in the RR group. **CONCLUSIONS:** This data supports the strategy of FTLE and organ preservation as definitive therapy for rectal cancer that remains but is confined to the bowel wall, after neoadjuvant therapy. These findings refute the strategy of follow-up radical surgery for ypT2 cancers after FTLE. Not unexpectedly all of the secondary measures of EBL, OR time, morbidity, avoidance of a stoma are all better with FTLE compared to radical surgery. We must remain mindful of the fact that while this is provocative data, additional experiences and randomized trials will help better define the exact role of organ preservation with FTLE after downstaging of rectal cancer.

44. PIK3CA Mutations are More Frequent in Early-Onset Appendiceal Cancer and Associated with Poorer Survival

Princy Gupta, MBBS[1]*; Rushabh Gujarathi, MBBS*[2]*; Lu Qiao*[3]*; Elizabeth L Godfrey, MD*[4]*; Kurt Schultz, MD*[5]*; Samuel Butensky, MD*[6]*; Justin Bader, MD*[7]*; Ardaman Shergill, MD*[8]*; Jason Sheltzer, PhD*[9]*; Kiran Turaga, MD, MPH*[10]
[1]*Yale School of Medicine, New Haven, CT, US;* [2]*University of Chicago, Chicago, IL, US;* [3]*Yale School of Medicine, New Haven, CT, US;* [4]*Yale New Haven Health/ Yale School of Medicine, New Haven, CT, US;* [5]*Yale School of Medicine, New Haven, CT, US;* [6]*Yale School of Medicine, New Haven, CT, US;* [7]*Yale School of Medicine, New Haven, CT, US;* [8]*University of Chicago Medical Center, Chicago, IL, US;* [9]*Yale School of Medicine, New Haven, CT, US;* [10]*Yale School of Medicine, New Haven, CT, US*

INTRODUCTION: The incidence of appendiceal cancer (AC) is rising in the US, with a steep rise of 251.89% in early-onset AC (age <50 years) between 2010-2019. Certain mutations like PIK3CA have been reported at a higher frequency in early-onset AC, but data regarding their implications on survival is lacking. This study aims to compare the mutational profiles of early-onset and late-onset AC and assess their impact on survival outcomes. **METHODS:** A retrospective analysis of AC patients from the Memorial Sloan Kettering – Metastatic Events and Tropisms (MSK-MET) database was conducted. Patients were stratified into two groups: early-onset (<50 years) and late-onset (≥50 years) AC based on age at surgery. Pearson's Chi-squared test was used to compare categorical variables, while logistic regression was used to evaluate the mutational profile differences. Kaplan-Meier survival analysis and Cox proportional hazards regression were performed for survival associations. **RESULTS:** Of 200 patients analyzed (median age: 55.4 years, IQR: 47.22-67.75), 35% (70) were early-onset AC. No significant differences in sex, race, histological subtypes, or survival (log rank p = 0.86) were found between early-onset and late-onset AC. Early-onset AC patients had significantly higher odds of harboring PIK3CA mutations compared to late-onset AC (17.6% vs 8.1%, odds ratio [OR] 3.99, p = 0.01) after adjusting for sex, histology, and sample type. PIK3CA mutations were exclusively seen in patients with metastatic AC (12.36%) and were more common in non-mucinous than mucinous AC (17.7% vs 7.1%, p=0.04). Among metastatic AC patients, those with PIK3CA mutations had worse overall survival (OS) from surgery (3-year survival probability of 41% vs 70%; hazard ratio = 2.65, 95% CI 1.33-5.30, p-value = 0.006). **CONCLUSIONS:** Early-onset AC patients showed a higher likelihood of having PIK3CA mutations, which negatively impacted survival after surgery. These alterations are targetable, and their prognostic impact should be considered when designing clinical trials involving patients with AC, especially studies focused on early-onset AC**.**

Table – Multivariable cox analysis for survival

Cox Proportional Hazards Analysis

Variable		N	Hazard Ratio	p
KRAS		177	0.35 (0.20, 0.63)	<0.001
GNAS		177	0.83 (0.40, 1.72)	0.618
TP53		177	3.04 (1.70, 5.43)	<0.001
PIK3CA		177	2.65 (1.33, 5.30)	0.006
Sex	Female	94	Reference	
	Male	83	1.67 (0.97, 2.87)	0.063
Histology	Non-mucinous	73	Reference	
	Mucinous	104	0.65 (0.36, 1.19)	0.160
Race	non-White	23	Reference	
	White	154	2.02 (0.77, 5.30)	0.156
Onset	Late-onset	113	Reference	
	Early-onset	64	0.89 (0.50, 1.59)	0.703

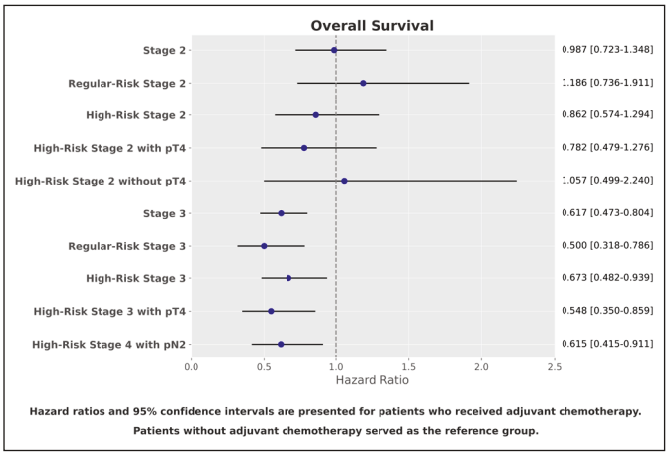


45. Impact of adjuvant chemotherapy on overall survival in early-onset stage II-III mucinous adenocarcinoma of the colon

Usama Waqar[1]*; Courtney L Devin*[2]*; Terrah J Paul Olson*[3]*; Patrick Sullivan, MD*[4]*; Seth A Rosen*[5]
[1]*Emory University, Atlanta, GA, US;* [2]*Emory University, Atlanta, GA, US;* [3]*Emory University, Atlanta, GA, US;* [4]*Emory University Hospital Midtown, Atlanta, GA, US;* [5]*Emory University, Atlanta, GA, US*

INTRODUCTION: Mucinous adenocarcinoma is an aggressive subtype of colon cancer. Adjuvant chemotherapy (AC) has been shown to improve overall survival (OS) in stage II-III mucinous adenocarcinoma. Its benefit in patients with early-onset cancer, a population that may respond differently to AC, remains uncertain. This study evaluates the impact of AC on OS in early-onset stage II-III mucinous adenocarcinoma of the colon. **METHODS:** We analyzed data from the 2006-2020 National Cancer Database. Patients aged ≤49 with pathologically confirmed stage II-III mucinous adenocarcinoma who underwent definitive surgery were included. Exclusion criteria included neoadjuvant chemotherapy, radiation, palliative care, or rectosigmoid/appendix tumors. Patients were categorized into AC and non-AC groups. High-risk stage II was defined by ≥1 of the following: <12 lymph nodes retrieved, pT4 disease, lymphovascular or perineural invasion, and poor diferentiation histology. High-risk stage III included pT4 or pN2 disease. Kaplan-Meier, log-rank tests, and multivariable regression analyses were used to assess OS by AC status. **RESULTS:** Of 3,854 patients, 1,624 (42.1%) had stage II and 2230 (57.9%) had stage III disease. AC was administered to 71.8% patients, more commonly in stage III (91.8%) vs. stage II (44.3%) patients (p<0.001). Among stage II patients, 41.3% were high-risk; these patients were more likely to receive AC (high-risk: 58.2% vs. standard risk: 34.6%, p<0.001), particularly patients with pT4 disease (pT4: 68.9% vs. non-pT4 high-risk: 43.2%, p<0.001). No difference in AC use was observed between standard- and high-risk stage III patients (p=0.997). On regression analyses, factors associated with AC use included young age (OR 0.979 [95% CI 0.965-0.993]), Medicare insurance (0.513 [0.313-0.840]), left colon tumors (1.405 [1.125-1.754]), stage III disease (12.013 [9.811-14.709]), high-risk stage II features (1.415 [1.080-1.855]), and high-risk stage III features (2.025 [1.562-2.627]). Survival analyses showed no improvement in OS with AC in stage II patients, including those with pT4 disease. For all stage III patients, AC was associated with better OS. On

multivariable cox regression, AC was associated with survival benefit in stage III, but not in stage II (Figure). **CONCLUSIONS:** Patients with early-onset stage II mucinous adenocarcinoma of the colon often receive AC. Based on our analyses, it may not confer any survival benefit, even with pT4 disease. In contrast, AC is associated with significantly better OS in stage III patients.



46. Role of Neo-Adjuvant PIPAC to downstage Colorectal Cancer with Peritoneal Carcinomatosis

Ashwin KR[1]; Somashekhar SP[2]; Rohit Kumar[3]; Kushal Aggarwal[4]; Esha Shanbag[5]
[1]Aster hospital Whitefield, Bangalore, Karnataka, IN; [2]Aster hospital, Bangalore, Karnataka, IN; [3]Aster hospital, Bangalore, Karnataka, IN; [4]Aster hospital, Bangalore, Karnataka, IN; [5]Aster hospital, Bangalore, Karnataka, IN

INTRODUCTION: Bidirectional Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) has emerged as a promising treatment option for patients with colorectal cancer with peritoneal carcinomatosis. Recent studies suggest that PIPAC, particularly in conjunction with systemic intravenous (IV) chemotherapy, may enhance the objective response rate and improve quality of life compared to IV chemotherapy alone in salvage scenarios. **METHODS:** This study included patients diagnosed with primarily inoperable colorectal cancer with peritoneal carcinomatosis who were not candidates for Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC). Following multidisciplinary team (MDT) discussions, these patients underwent a regimen of bidirectional PIPAC combined with IV chemotherapy. The PIPAC treatment involved Oxaloplatin, administered every 4 weeks, with IV chemotherapy delivered within one week post-PIPAC. Clinical characteristics, disease extent, and perioperative outcomes were analyzed for patients who subsequently underwent CRS-HIPEC. **RESULTS:** A total of 120 PIPAC applications were performed on 45 patients, with 30 of these patients receiving three cycles of PIPAC and accompanying IV chemotherapy. Of the 45 patients, 28 eventually underwent CRS-HIPEC. The cohort had a mean age of 54.5 years (±10.74), a Peritoneal Carcinomatosis Index (PCI) of 15 (±5), and an average surgical duration of 9.6 hours (±1.2). Patients completing three cycles of PIPAC showed a mean reduction in PCI of 5 (±0.8). The observed clinical responses were categorized as follows: 60% with PRGS 1, 25% with PRGS 2, and 15% with PRGS 3. Surgical outcomes revealed that 52.4% underwent total peritonectomy, while 12.7% required multivisceral resection, and 55.8% had bowel resections. The stoma rate was recorded at 3.5%. Overall, the grade 3 to 5 morbidity rate was 25.4%, with significant complications including postoperative intra-abdominal collections (21.8%), electrolyte imbalances (16.4%), and pulmonary issues (16.4%). The 30-day mortality rate was 3.8%. **CONCLUSIONS:** The combination of neo-adjuvant PIPAC with IV chemotherapy appears to be a promising strategy for achieving favorable response rates. Moreover, CRS-HIPEC following neo-adjuvant PIPAC and IV chemotherapy is shown to be safe, feasible, and well-tolerated, potentially offering a valuable treatment pathway for this challenging patient population. Further studies are warranted to solidify these findings and explore long-term outcomes.

47. A cohort study of factors associated with survival and chronic aspirin use in colorectal cancer

Michael Schell, PhD[1]; Anastasia Murphy, PhD[2]; Junmin Whiting[3]; Leah Hendrick[4]; Vonetta Williams, PhD[5]; Seth Felder, MD[6]; Julian Sanchez, MD[7]; Sophie Dessureault[8]; Amalia Stefanou[9]; Sean P Dineen[10]; Iman Imanirad[11]; Tiago Biachi[12]; Jessica Frakes[13]; Sarah Hoffe[14]; Kavita Ghia, MPH[15]; Alicia Chin, APRN[16]; Surinder Batra, PhD[17]; Lee Green, PhD[18]; Mokenge Malafa[19]
[1]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [2]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [5]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [6]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [7]Moffitt Cancer Center, Tampa, FL, US; [8]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [9]Moffitt Cancer Center, Tampa, FL, US; [10]Moffitt Cancer Center, Tampa, FL, US; [11]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [12]Moffitt Cancer Center, Tampa, FL, US; [13]Moffitt Cancer Center, Tampa, FL, US; [14]Moffitt Cancer Center, Tampa, FL, US; [15]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [16]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [17]Department of Biochemistry and Molecular Biology, University of Nebraska Medical Center, Omaha, NE, US; [18]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [19]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US

INTRODUCTION: The impact of aspirin (ASA) use on colorectal cancer (CRC) outcomes is of great interest to patients and investigators. While there is level 1 evidence to show the possibility of decreased CRC incidence with long term pre-diagnostic ASA use, its potential role in CRC mortality outcomes is poorly understood. Our study sought to evaluate factors associated with survival, pre-diagnosis ASA use, and its interaction with race in patients with CRC. **METHODS:** A retrospective cross-sectional study was performed with a complete cohort treated at an NCI-designated Comprehensive Cancer Center over a 15-year period. Key factors related to pre-diagnosis ASA use and CRC outcomes were abstracted. Chronic ASA use was self-reported at the patient level. Multivariable logistic regression was performed to ascertain key factors associated with ASA use. Multivariable survival analysis was performed using Cox proportional hazards modeling with backward elimination. Significance was set at p=0.05. **RESULTS:** We identified 3,238 patients with CRC diagnosed and treated between January 2006 and December 2020. One quarter of cohort patients used ASA 81mg. Non-ASA use was strikingly associated with increasing stage of disease: stage II (OR=1.36, 95% CI 1.06-1.76, p=.016), stage III (OR=1.48, 95% CI 1.17-1.88, p=.001), and stage IV (OR=2.70, 95% CI 2.09-3.49, P<.0001) compared to stage I patients. Adjusted for ethnicity, marital status, and health insurance, ASA users were more likely to be older (aOR 4.03, 95% CI 2.96-5.49, p<0.001), male (aOR 1.45, 95%CI 1.22-1.73, p<0.001), white (aOR 1.81, 95% CI 1.16-2.83, p=0.009), and have a Charlson Comorbidity Index (CCI) score >0 (aOR 1.38, 95%CI 1.11-1.71, p=0.004) compared with non-ASA users. Black patients were less likely to use pre-diagnosis ASA compared to white patients (13% vs 25.3%, presented with higher stage of disease (aOR 1.63, 95% CI 1.25-2.13, p=0.031). **CONCLUSIONS:** This study demonstrates a clear association between pre-diagnosis ASA use and earlier stage at diagnosis, as well as improved OS from CRC. Furthermore, these data demonstrate that racial disparities in CRC outcomes and ASA use exist even in patients that are treated at an NCI Comprehensive Cancer Center, and suggests that pre-diagnosis ASA use may be an unexplored strategy for not only attaining risk-but for also improving disparities in CRC outcomes.

48. Neutrophil Extracellular Traps Form Barriers to 5-FU in Colorectal Cancer Liver Metastases

Susan J Kim[1]; Yunwei Zhang[2]; Kaelyn C Cummins[3]; Hongji Zhang[4]; Allan Tsung[5]
[1]University of Virginia Health, Charlottesville, VA, US; [2]University of Virginia Health, Charlottesville, VA, US; [3]University of Virginia Health, Charlottesville, VA, US; [4]University of Virginia Health, Charlottesville, VA, US; [5]University of Virginia Health, Charlottesville, VA, US

INTRODUCTION: Metastatic spread to the liver is the leading cause of colorectal cancer related death. While 5-fluorouracil (5-FU) based therapies are the standard of care for treatment, they have limited efficacy. Chemotherapy induces neutrophil recruitment and neutrophil extracellular trap (NET) formation, which may be responsible for conferring treatment resistance. We reveal that DNase treatment can improve 5-FU therapy in CRC liver metastasis (CRCLM) by targeting NETs that prevent 5-FU penetration and action. **METHODS:**

Eight-weeks-old male C57BL/6 mice were inoculated with $5*10^5$ GFP-labeled MC38 colorectal cancer cells through the portal vein to mimic metastatic spread. Mice were then treated with weekly intraperitoneal injections of PBS control, 5-FU (25mg/kg), DNase I (20mg/kg), or a combination of both agents for three weeks. *In vivo* tumor progression was monitored using bioluminescent imaging until euthanasia at 25 days. Tumors from the differing treatment groups were immunohistochemically examined, staining for myeloperoxidase (MPO) as well as endothelial marker CD31. **RESULTS:** DNase I significantly augment the efficacy of 5-FU chemotherapy in the treatment of CRCLM at different time points as revealed by bioluminescent imaging and gross measures upon sacrifice. Additionally, tumor bearing *Pad4$^{fl/fl}$GRP8^{Cre}* (neutrophil-specific PAD4 KO) mice exhibited improved efficacy of 5-FU in CRCLM. Furthermore, the effects were negated upon the addition of NETs. When evaluating tumoral specimens from each group, we demonstrated that NETs co-localized with CD31 within the vascular lumen, effectively creating a physical barrier. This barrier effect was diminished among groups with DNase I administration. **CONCLUSIONS:** These data demonstrate NETs form a barrier along vascular lumen, preventing effective penetration of 5-FU during treatment. This offers a rationale that NETs may serve as a targetable biomarker to improve response to chemotherapy in CRCLM**.**

49. Incidence of and Risk Factors for Radiographically Occult Nodal Metastases in Colon Cancer: Is It Time for a New Lymphadenectomy Standard?

Praveen Dilip Chatani, MD[1]; Jordan Fredette, MPH[2]; Andrea Porpiglia, MD[3]; Stephanie Greco, MD, FACS[4]; Sanjay S Reddy, MD, FACS[5]; Jeffrey M. Farma, MD, FACS[6]; Anthony M Villano, MD[7]

[1]Fox Chase Cancer Center, Philadelphia, PA, US; [2]Fox Chase Cancer Center, Philadelphia, PA, US; [3]Fox Chase Cancer Center, Philadelphia, PA, US; [4]Fox Chase Cancer Center, Philadelphia, PA, US; [5]Fox Chase Cancer Center, Philadelphia, PA, US; [6]Fox Chase Cancer Center, Philadelphia, PA, US; [7]Fox Chase Cancer Center, Philadelphia, PA, US

INTRODUCTION: Adequate lymphadenectomy in non-metastatic colon cancer is a critical component of oncologic colectomy. Proper identification of clinically-occult positive nodes after resection is essential for best oncologic outcomes as it informs adjuvant chemotherapy use. Inadequate lymphadenectomy thus risks undertreatment. The incidence of and risk factors for node-positivity, as well as the optimal lymph node yield to accurately stage patients, are poorly characterized. **METHODS:** The National Cancer Database was queried for patients with clinically node-negative colon adenocarcinoma undergoing curative-intent resection between 2010 and 2021. Patient demographic, clinical, and pathologic variables were analyzed using descriptive statistics; multivariate logistic regression analysis was employed to identify variables independently associated with pathologic upgrade to nodal-positivity. **RESULTS:** Over the 11-year study period, clinically node-negative patients who underwent curative resection of colon adenocarcinoma (n = 195,213) were upstaged to node-positive in 26.3% of cases (n = 51,333). Patient and tumor characteristics most strongly associated with upgrade to nodal positivity on multivariate logistic regression (Table 1) were age <50 (OR 1.68; p<0.05), Black or Asian race (OR 1.25 and 1.30;0.05), sigmoid primary (OR 1.28;0.05), poorly-differentiated histology (OR 1.92;0.05), lymphovascular (OR 7.33;0.05) or perineural invasion (OR 1.94;0.05), microsatellite-stability (OR 1.70 p<0.05), and KRAS mutation (OR 1.18;0.05). With every 1cm increase in tumor size, risk of pathologic upgrade increased by 1.2%. Nodal harvest also correlated with increased risk of pathologic upgrade at a rate of 0.6% per node excised; patients with ≥18 nodes excised were more likely to demonstrate nodal-positivity than those with 12-17 (OR 1.12;0.05). Robotic approach resulted in greater median nodal harvest (20 nodes, p<0.05) compared to laparoscopic (19 nodes) or open (18 nodes). **CONCLUSIONS:** Our study demonstrates that young, non-white patients, those with left-sided cancers, and lesions demonstrating poor differentiation, lymphovascular/perineural invasion, KRAS mutation, or microsatellite-stability are significantly more likely to harbor radiographically occult nodal metastases. Furthermore, resection of at least 18 nodes increases the risk of pathologic upgrade, suggesting modification of operative standards in colon surgery. A risk nomogram for use in the preoperative setting is forthcoming.

Table 1. Multivariate logistic regression predictive of pathologic nodal positivity.

Variable	Est.	Std. Error	Wald	P-value	Odds	(Low)	(High)
Surgical Approach							
Open	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Robotic	-0.058	0.021	8.078	**0.004**	**0.943**	0.906	0.982
Robotic to Open	0.044	0.064	0.466	0.495	1.045	0.921	1.185
Laparoscopic	-0.075	0.014	30.020	**0.000**	**0.928**	0.903	0.953
Laparoscopic to Open	-0.032	0.026	1.521	0.217	0.968	0.920	1.019
Age (yrs)							
<50	0.519	0.027	359.011	**0.000**	**1.681**	1.593	1.774
51 – 60	0.371	0.023	268.684	**0.000**	**1.450**	1.387	1.516
61 – 70	0.224	0.018	151.004	**0.000**	**1.251**	1.207	1.296
71 – 80	0.090	0.017	27.292	**0.000**	**1.094**	1.058	1.132
81 - 90	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Sex							
Male	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Female	-0.038	0.012	10.524	**0.001**	**0.962**	0.940	0.985
Race							
Caucasian	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Black	0.223	0.019	136.673	**0.000**	**1.250**	1.204	1.298
Asian	0.264	0.031	71.851	**0.000**	**1.303**	1.225	1.385
Other	-0.040	0.055	0.548	0.459	0.960	0.863	1.069
Unknown	0.034	0.075	0.207	0.649	1.035	0.894	1.198
CDCC							
0	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
1	-0.009	0.015	0.415	0.520	0.991	0.962	1.020
2	-0.024	0.022	1.163	0.281	0.976	0.934	1.020
3+	-0.049	0.025	3.880	**0.049**	**0.952**	0.907	1.000
Grade							
Well-differentiated	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Moderately-differentiated	0.300	0.021	196.831	**0.000**	**1.350**	1.295	1.408
Poorly-differentiated	0.654	0.026	634.171	**0.000**	**1.923**	1.828	2.023
Undifferentiated	0.611	0.047	166.036	**0.000**	**1.843**	1.679	2.023
Unknown	-0.219	0.053	17.300	**0.000**	**0.803**	0.724	0.891
Primary Site							
Cecum	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Appendix	-0.550	0.110	24.861	**0.000**	**0.577**	0.465	0.716
Ascending Colon	-0.147	0.018	69.198	**0.000**	**0.864**	0.834	0.894
Hepatic Flexure	-0.195	0.029	45.996	**0.000**	**0.822**	0.777	0.870
Transverse	-0.149	0.022	46.545	**0.000**	**0.861**	0.825	0.899
Splenic	0.063	0.034	3.392	0.066	1.065	0.996	1.139
Descending Colon	0.057	0.027	4.500	**0.034**	**1.059**	1.004	1.116
Sigmoid	0.250	0.017	209.344	**0.000**	**1.284**	1.241	1.328
Overlapping	0.036	0.051	0.491	0.491	1.037	0.938	1.146
NOS	-0.005	0.066	0.005	0.941	0.955	0.874	1.133
Nodes Examined							
12-17	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
≥18	0.110	0.013	75.425	**0.000**	**1.117**	1.089	1.145
Nodes Examined (num)	0.006	0.001	124.006	**0.000**	**1.006**	1.005	1.007
Tumor Size (cm)	0.011	0.003	47.899	**0.000**	**1.011**	1.008	1.015
Lymphovascular Invasion							
Absent	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Present	1.992	0.013	22357.871	**0.000**	**7.328**	7.139	7.521
Unknown	1.082	0.021	2639.531	**0.000**	**2.952**	2.832	3.076
Perineural Invasion*							
Absent	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Present	0.663	0.035	368.740	**0.000**	**1.940**	1.813	2.076
Unknown	-0.540	0.068	62.897	**0.000**	**0.583**	0.510	0.666
KRAS Mutation*							
Wild-type	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Mutant	0.169	0.070	5.819	**0.016**	**1.184**	1.032	1.357
Unknown	-0.280	0.043	41.807	**0.000**	**0.756**	0.694	0.823
MSI-Stability*							
Unstable	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)	(ref)
Stable	0.529	0.033	250.342	**0.000**	**1.697**	1.589	1.181
Unknown	0.299	0.038	61.786	**0.000**	**1.349**	1.252	1.453

*Variable only available from 2018 onwards

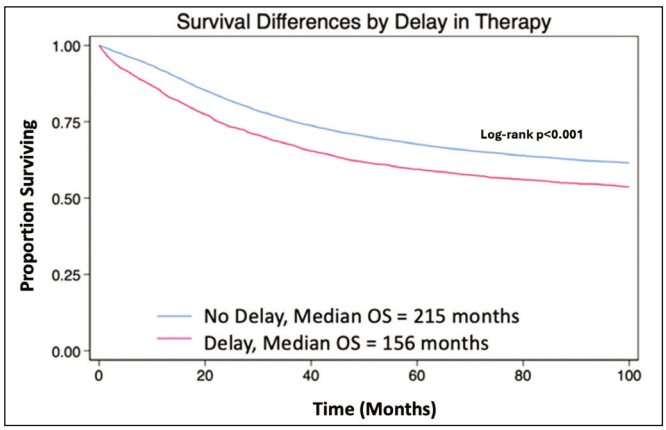
50. Treatment Delay and Survival in Early Onset Colorectal Cancer: What Matters?

Ryan T Heslin, MD[1]; Zachary Whitham, MD[2]; Jennie Meier, [3]; Morgan F Pettigrew, MD[4]; Natalie Williams, MD[5]; Matthew Porembka, MD[6]; Amanda Dann, MD[7]; Patricio M. Polanco, MD[8]; John C Mansour, MD[9]; Herbert J Zeh, MD[10]; Adam Yopp, MD[11]; Sam Wang, MD[12]; Cecilia G Ethun, MD[13]; Alex Kim, MD, Ph.D[14]

[1]UT Southwestern, Dallas, TX, US; [2]UT Southwestern, Dallas, TX, US; [3]UT Southwestern, dallas, TX, US; [4]UT Southwestern, Dallas, TX, US; [5]UT Southwestern, Dallas, TX, US; [6]UT Southwestern, Dallas, TX, US; [7]UT Southwestern, Dallas, TX, US; [8]UT Southwestern, Dallas, TX, US; [9]UT Southwestern, Dallas, TX, US; [10]UT Southwestern, Dallas, TX, US; [11]UT Southwestern, Dallas, TX, US; [12]UT Southwestern, Dallas, TX, US; [13]UT Southwestern, Dallas, TX, US; [14]UT Southwestern Medical Center, Dallas, TX, US

INTRODUCTION: The incidence of early-onset colorectal cancer (EOCRC, < 50 years of age) is increasing globally and is associated with poor patient-related outcomes. Single-institution studies demonstrated high frequency of left-side/rectal tumors, poorly differentiated histology, and advanced stage cancer in EOCRC. Lack of screening for EOCRC likely contributes to delay in diagnosis and therapy, which contributes to patient outcomes. This study represents a "real-world" examination of EOCRC in Texas and to further assess the impact of delay in treatment, factors associated with delay and the subsequent impact on overall survival. **METHODS:** We included 135,328 patients with colorectal cancer from the Texas Cancer Registry from 2004-2017. We analyzed demographics, clinicopathologic variables and social vulnerability (SVI) and assessed factors impacting treatment delay and overall survival. We utilized unadjusted and covariable-adjusted cox proportional hazards for survival analysis and used Kaplan-Meier curves for overall survival analysis. Finally, we used logistic regression to evaluate factors associated with treatment

delay greater than 6 weeks. **RESULTS:** Of 135,328 patients with CRC in TCR, 14,082 were identified as EOCRC. When compared to average-onset colorectal cancer (50 years of age or older), predilection for left-sided (38%) and rectal (29%) cancer was demonstrated in EOCRC. Among EOCRC patients, 75% underwent surgery, 10% underwent radiation and 54% received chemotherapy. Among patients with EOCRC, maximum SV (HR 1.22, 95%CI 1.12-1.34), male sex (HR1.13, 95%CI 1.09-1.20) and delay in therapy > 6 weeks (HR 1.48, 95%CI 1.45-1.50) were associated with worse survival. In EOCRC, factors associated with delay in treatment were rectal cancers (HR 3.94, 95%CI 3.46-4.49), left-sided (HR 1.26, 95%CI 1.26-1.66), Medicaid (HR1.55, 95%CI 1.31-1.84) and uninsured status (HR 1.69, 95%CI 1.49-1.92). Notably, neither race nor SV quartile were associated with delay in treatment for EORC, while minority status/language barriers revealed significant association (HR 1.39, 95%CI 1.15-1.67). **CONCLUSIONS:** The study represents a "real-world" clinicopathologic profile of EOCRC patients. Our analysis revealed that delay in treatment past 6 weeks is associated with worse overall survival. Notable factors associated with delay in treatment include left-sided/rectal cancer, lack of private insurance, minority status and language barriers. These findings note the importance of timely diagnosis and treatment in EOCRC patient.



Best Papers I

51. Eliminating breast surgery for invasive cancer after neoadjuvant systemic therapy: 5-year outcomes on an inaugural multicenter phase 2 clinical trial

Henry Kuerer, MD[1]; Ben Smith[2]; Vicente Valero, MD[3]; Savitri Krishnamurthy[4]; Emilia Diego[5]; Wei Yang[6]; Yu Shen[7]; Anthony Lucci, MD[8]; Heather Lin[9]; Helen Johnson[10]; Tanya Moseley[11]; Judy C. Boughey, MD[12]; Simona Shaitelman[13]; Richard White[14]; Melissa Mitchell[15]; Mediget Teshome, MD, MPH, FACS[16]; Makesha Miggins[17]; Kelly K. Hunt, MD, FSSO[18]; Gaine M Rauch[19]; for the Exceptional Responders Study Group, [20]

[1]MD Anderson Cancer Center, Houston, TX, US; [2]MD Anderson Cancer Center, Houston, TX, US; [3]MD Anderson Cancer Center, Houston, TX, US; [4]MD Anderson Cancer Center, Houston, TX, US; [5]University of Pittsburgh, Pittsburgh, TX, US; [6]MD Anderson Cancer Center, Houston, TX, US; [7]MD Anderson Cancer Center, Houston, TX, US; [8]UT-MD Anderson Cancer Center, Houston, TX, US; [9]MD Anderson Cancer Center, Houston, TX, US; [10]University of Texas MD Anderson Cancer Center, Houston, TX, US; [11]MD Anderson Cancer Center, Houston, TX, US; [12]Mayo Clinic, Rochester, MN, US; [13]MD Anderson Cancer Cneter, Houston, TX, US; [14]Atrium Health Levine Cancer Center, Charlotte, NC, US; [15]MD Anderson Cancer Center, Houston, TX, US; [16]UCLA Medical Center, Los Angeles, CA, US; [17]MD Anderson Cancer Center, Houston, TX, US; [18]MD Anderson Cancer Center, Houston, TX, US; [19]MD Anderson Cancer Center, Houston, TX, US; [20]MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: A 60% pathologic complete response (pCR) in triple receptor negative breast cancer (TNBC) and HER2+ breast cancer with neoadjuvant systemic therapy (NST) suggests that breast surgery may not be necessary in these patients. A pCR can be accurately identified through percutaneous image-guided vacuum-assisted core biopsy (VACB). The trial was conducted to investigate the outcome of radiotherapy alone, without breast surgery, in patients who had a VACB-determined pCR. The preplanned outcomes of this trial over 5 years are detailed in this report. **METHODS:** Consented patients were aged 40 years or older with unicentric cT1-2N0-1M0 TNBC or HER2+BC and a residual breast lesion smaller than 2 cm on imaging after NST. Biopsy was performed using a 9G image guided VACB, containing at least 12 cores from the tumor bed. If no invasive or in situ disease was detected, breast surgery was not performed. Patients received hypofractionated whole-breast radiotherapy +boost. The primary outcome measured was the rate of ipsilateral breast tumor recurrence (IBTR), with secondary outcomes focusing on safety and baseline and longitudinal circulating tumor cells (CTCs), along with circulating tumor DNA (ctDNA) and validated patient-reported outcomes (Decisional Regret Scale, Breast Cancer Treatment Outcome Scale, and FACT-B+4). **RESULTS:** During 2017-2021, 50 total patients were enrolled and underwent VACB following NST. Mean age was 60.4 years (SD 7.8); 21 patients had TNBC and 29 HER2+BC. VACB was well tolerated with 2 (4%) grade 1 complications and identified a pCR in 31 patients (62%). Among patients without breast surgery, median follow-up was 51.7 months (IQR: 38.3-63.1), 5-year IBTR rate was 0% (primary endpoint), and DFS and OS rates were each 100%. Two patients were CTC-positive at baseline, 2 were positive at 6-months, and 1 at 12-months. Two patients were positive for TP53 at baseline with one clearing at 6 and 12 months and the other had persistence. Patients reported high comfort with the decision to participate in the trial, only slight asymmetry was noted between breasts, and quality of life was high and increased over time. **CONCLUSIONS:** In the first clinical trial in the field to eliminate breast surgery based on image-guided VACB–determined pCR after NST, patients who did not undergo breast surgery had no recurrences. This new treatment approach was safe and effective. These 5-year oncologic outcomes were durable and suggest that this novel method could shift the paradigm of surgical management of breast cancer after NST with further clinical trials**.**

52. Appendiceal Cohort analysis from the Intraperitoneal Chemotherapy After Cytoreductive Surgery for Peritoneal Metastasis (ICARuS) clinical trial

Garrett M. Nash, MD[1]; Nicole Aguirre, MD[2]; Georgios Karagkounis, MD[3]; Tina Gowda, MD[4]; Karri Hester, MD[5]; Julio Garcia-Aguilar, MD, PhD[6]; Philip B. Paty, MD[7]; Mithat Gonen, PhD[8]; Mostafa Mohamed, BA[9]; Martin R. Weiser, MD[10]; Rachel Rassam, NP[11]; Jesse Joshua Smith, MD, PhD[12]; Emmanouil P. Pappou, MD, PhD[13]; Iris H. Wei, MD[14]; Marc J Gollub, MD[15]; Efsevia Vakiani, MD[16]; Jinru Shia, MD[17]; Michael Foote, MD[18]; Leonard B Saltz, MD[19]; Andrea Cercek, MD[20]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloane Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US; [11]Memorial Sloan Kettering Cancer Canter, New York, NY, US; [12]Memorial Sloan Kettering Cancer Center, New York, NY, US; [13]Memorial Sloan Kettering Cancer Center, New York, NY, US; [14]Memorial Sloan Kettering Cancer Center, New York, NY, US; [15]Memorial Sloan Kettering Cancer Center, New York, NY, US; [16]Memorial Sloan Kettering Cancer Center, New York, NY, US; [17]Memorial Sloan Kettering Cancer Center, New York, NY, US; [18]Memorial Sloan Kettering Cancer Center, New York, NY, US; [19]Memorial Sloan Kettering Cancer Center, New York, NY, US; [20]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Appendiceal cancer (AC) is characterized by peritoneal dissemination early in the course of disease. Cytoreductive surgery (CRS) is a treatment option for peritoneal metastasis (PM) and is associated with long-term survival. However, peritoneal recurrence after CRS is common, and intraperitoneal chemotherapy (IPC) has been used to prevent this. The efficacy of IPC in AC PM remains unclear. **METHODS:** ICARuS is a randomized, phase II, multicenter trial conducted to evaluate the 3-year PFS of Hyperthermic Intraperitoneal Chemotherapy (HIPEC) with mitomycin C vs. Early Postoperative Intraperitoneal Chemotherapy (EPIC) with floxuridine after CRS, for PM of colorectal (CRC) or AC. Systemic chemotherapy was used preoperatively, when indicated. Patients with resectable PM were eligible for 1:1 randomization after complete CRS. Patients were stratified by recent systemic chemotherapy and disease origin (AC vs. CRC). CRC outcomes were reported previously. **RESULTS:** 206 AC patients were randomized between 4/2013 and 6/2023 (HIPEC, N=105; EPIC, N=104). Median follow up was 37.5 months. The median PCI was 14 in both arms. Three-year progression-free

survival (PFS) was 39% in both arm, p=0.86. The median overall survival (OS) was 79 months in the HIPEC arm and 96 months in the EPIC arm (p=0.85). No differences between the groups were found in peritoneal or extra-peritoneal PFS. When stratifying for differentiation, there were no difference in OS or PFS between the two arms. (Figure 1). **CONCLUSIONS:** Three-year PFS did not significantly differ between HIPEC/EPIC arms. Durable survival can be achieved after CRS for well and moderately differentiated appendix cancer, though it appears that IPC may not contribute to those outcomes, given the probability that they are equally ineffective.

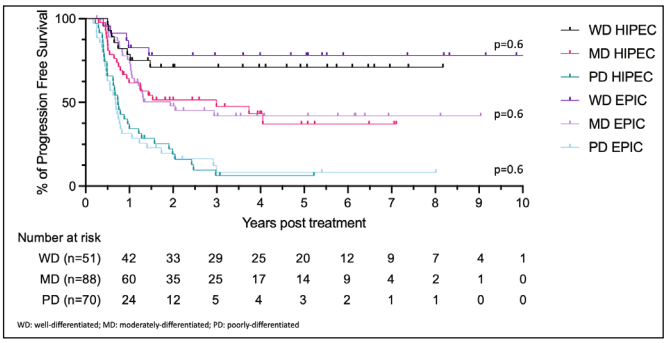


Figure 1. Progression Free Survival by Grade ICARuS Appendiceal Cohort

53. Association of Axillary Lymph Node Dissection With Oncological Outcomes in Patients With Residual Micrometastases After Neoadjuvant Chemotherapy: The OPBC-07/microNAC Study

Giacomo Montagna, MD, MPH[1]; Michael Alvarado, MD[2]; Sara Myers, MD, PhD[3]; Mary M. Mrdutt[4]; Susie X. Sun, MD[5]; Varadan Sevilimedu, MBBS, DrPH[6]; Marissa K. Boyle, MD[7]; Susan B. Kesmodel, MD[8]; Natalia Polidorio, MD, PhD[9]; Margit Riis, MD[10]; Viviana Galimberti, MD[11]; Sung Gwe Ahn, MD, PhD[12]; Han-Byoel Lee, MD, PhD[13]; Neslihan Cabioglu, MD[14]; Mahmut Muslumanoglu, MD[15]; Jai Min Ryu, MD[16]; Tae-Kyung Robyn Yoo, MD[17]; Massimo Ferrucci, MD, PhD[18]; Monica Morrow, MD[19]; Walter Paul Weber, MD[20]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]University of California, San Francisco, San Francisco, CA, US; [3]Brigham and Women's Hospital, Boston, MA, US; [4]Mayo Clinic, Rochester, MN, US; [5]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, NY, US; [7]Cedars-Sinai Medical Center, Los Angeles, CA, US; [8]University of Miami Health System, Miami, FL, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Oslo University Hospital, Oslo, NO; [11]Insituto Europeo di Oncologia (IEO) IRCCS, Milano, IT; [12]Gangnam Severance Hospital, Seoul, KR; [13]Seoul National University Hospital, Seoul,KR; [14]Istanbul University, Istanbul, TR; [15]Istanbul University, Istanbul, TR; [16]Samsung Medical Center, Seoul, KR; [17]ASAN Medical Center, Seoul, KR; [18]Veneto Institute of Oncology IRCCS, Padova, IT; [19]Memorial Sloan Kettering Cancer Center, New York, NY, US; [20]University Hospital Basel, Basel, CH

INTRODUCTION: Axillary lymph node dissection (ALND) is standard of care for patients with residual micro- and macro-metastases after neoadjuvant chemotherapy (NAC). However, studies suggest that ALND is increasingly being omitted in favor of nodal radiation (RT); particularly in ypN1mic patients. We sought to compare oncological outcomes in ypN1mic patients treated with and without ALND. **METHODS:** Data were collected from 63 centers: 45 in the Oncoplastic Breast Consortium (OPBC) network, and 18 in North and South America. We included cT1-4 N0-3 breast cancer patients who underwent NAC followed by axillary staging with either sentinel lymph node biopsy (SLNB) or targeted axillary dissection (TAD) and were found to be ypN1mic. Further axillary treatment included completion ALND and/or nodal RT or observation. Competing risk analysis was performed to assess the cumulative incidence rates of any axillary recurrence (AR, isolated or combined with local or distant recurrence), and any invasive (locoregional or distant) recurrence. Five-year cumulative incidence rates were compared using the Gray's test. **RESULTS:** We included 1216 patients treated between 01/2009-05/2023. Median patient age was 48 years. 60% had cT2 tumors and 63.8% had biopsy-proven N+ disease. 51% had HR+/HER2- tumors and 72% received anthracycline and taxane-based NAC regimens. 80% had nodal RT. The mean number of SLNs removed was 3.2 (SD 1.8) with a mean of 1.2 containing micrometastases. 663 (54.5%) had completion ALND, of whom 539/663 (82%) also had nodal RT. Among 553 (45.5%) without ALND, 429 (78%) received nodal RT and 124 (22%) had no further axillary treatment. Patients treated with ALND were more likely to be non-Caucasian, to be cN+, to have more SLNs with micrometastases, to have micrometastases detected on frozen section and to have postmastectomy RT (Table). In the ALND group, additional positive nodes were found in 197/663 (29.7%) of cases, and consisted of macrometastases in 82/663 (12.4%), micrometastases in 98/663 (14.8%) and ITCs in 17/663 (2.6%). 5-year rates of any AR and any invasive recurrence in the entire cohort were 2.1% (95% CI 1.2-3.3%) and 21% (95% CI 17-25%), respectively. There was no statistical difference between patients who underwent ALND and those who did not in either endpoint (2.2% vs 1.9%, p = 0.7 and 21% vs 21%, p > 0.9, respectively). **CONCLUSIONS:** Rates of axillary and any invasive recurrence did not significantly differ based on the use of ALND. Overall, these results do not support ALND for all ypN1mic patients treated with nodal RT.

Table 1. Clinicopathological Features of the Study Cohort, Stratified by Type of Axillary Surgery

	Full cohort n = 1216	SLNB/TAD only n = 553	SLNB/TAD + ALND n = 663	p-value
Age, median, years (IQR)	48 (41,58)	48 (41, 58)	48 (41, 57)	> 0.9
Race/ethnicity				**<0.001**
Asian	222 (18)	82 (15)	140 (21)	
Black	46 (3.8)	16 (2.9)	30 (4.5)	
Hispanic	186 (15)	74 (13)	112 (17)	
White	683 (56)	332 (60)	351 (53)	
Other/unknown	79 (6.5)	49 (8.9)	30 (4.5)	
Clinical T category				0.13
1	168 (14)	76 (14)	92 (14)	
2	730 (60)	349 (63)	381 (57)	
3	260 (21)	106 (19)	154 (23)	
4	54 (4.4)	20 (3.6)	34 (5.1)	
X	2 (0.2)	0 (0)	2 (0.3)	
Unknown	2	2	0	
Clinical N category				**<0.001**
0	440 (36)	257 (47)	183 (28)	
1	666 (55)	266 (48)	400 (61)	
2	88 (7.3)	21 (3.8)	67 (10)	
3	18 (1.5)	7 (1.3)	11 (1.7)	
Unknown	4	2	2	
Staging technique				
SLNB	960 (79)	444 (80)	516 (78)	0.5
MARI	4 (0.3)	1 (0.2)	3 (0.5)	
TAD	251 (21)	108 (20)	143 (22)	
Unknown	1	0	1	
Number of SLNs removed, mean (SD)	3.2 (1.8)	3.2 (1.7)	3.2 (1.9)	0.2
Micrometastases detected on frozen section	518 (43)	97 (18)	421 (63)	**<0.001**
Number of SLNs with micrometastases, mean (SD)	1.2 (0.5)	1.1 (0.4)	1.2 (0.5)	**<0.001**
Number of concomitant SLNs, TAD or MARI nodes with ITCs, mean (SD)	0.13 (0.53)	0.11 (0.41)	0.15 (0.62)	0.7
Total number of LNs removed, mean (SD)	11 (8)	4 (2)	16 (7)	**<0.001**
Breast pCR (ypT0/is)				0.6
Yes	223 (18)	99 (18)	124 (19)	
NAC regimens HER2- tumors^				0.065
ACT	599 (72)	253 (68)	346 (76)	
ACT + Platinum	67 (8.1)	35 (9.4)	32 (7)	
AC-T + Platinum with Pembrolizumab	29 (3.5)	16 (4.3)	13 (2.8)	
AC free regimen	34 (4.1)	12 (3.2)	22 (4.8)	
Other	100 (12)	55 (14.8)	45 (9.8)	
NAC regimens HER2+ tumors^^				0.6
ACT-H	77 (20)	38 (21)	39 (19)	
ACT-HP	103 (27)	50 (27)	53 (26)	
TC-HP	121 (31)	52 (29)	69 (34)	
TC-H	5 (1.3)	1 (0.5)	4 (2)	
Other	81 (21)	41 (23)	40 (20)	
Histology				0.6
Ductal	1,106 (91)	509 (92)	597 (90)	
Lobular or mixed	76 (6.3)	31 (5.6)	45 (6.8)	
Occult	4 (0.3)	1 (0.2)	3 (0.5)	
Other	29 (2.4)	11(2)	18 (2.7)	
Unknown	1	1	0	
Tumor differentiation				0.1
Well	59 (5.1)	32 (6.2)	27 (4.3)	
Moderately	524 (46)	247 (48)	277 (44)	
Poorly	563 (49)	238 (46)	325 (52)	
Unknown	70	36	34	
Subtype				0.6
HR+/HER2-	620 (51)	283 (51)	337 (51)	
HR+/HER2+	268 (22)	129 (23)	139 (21)	
HR-/HER2+	119 (9.8)	53 (9.6)	66 (10)	
HR-/HER2-	209 (17)	88 (16)	121 (18)	

table continued

LVI#				> 0.9
Yes	371 (31)	166 (30)	205 (31)	
Type of breast surgery				0.1
BCS	593 (49)	284 (51)	309 (47)	
Mastectomy	621 (51)	269 (49)	352 (53)	
No breast surgery##	2 (0.2)	0 (0)	2 (0.3)	
Whole breast radiotherapy*				0.058
Yes	586 (99)	276 (98)	310 (100)	
Postmastectomy radiotherapy **				**0.001**
Yes	514 (83)	208 (77)	306 (87)	
Nodal radiotherapy				0.1
Yes	968 (80)	429 (78)	539 (82)	

Frequency (row percent) reported for categorical variables, and mean (SD) reported for continuous variables.

SLNB sentinel lymph node biopsy; TAD targeted axillary dissection; MARI marking axillary lymph nodes with radioactive iodine seeds; SLNs sentinel lymph nodes; LNs lymph nodes; pCR pathologic complete response; ACT anthracycline and taxane; AC anthracycline; H Herceptin, HP, Herceptin and Perjeta; TC taxol (or Taxotere) and carboplatinum; LVI lymphovascular invasion; BCS breast-conserving surgery

^ Applied to HER2- tumors only (n=829)

^^ Applies to HER2+ tumors only (n=387)

LVI was present on core biopsy or final pathology

Occult carcinoma

* Applies to BCS patients only (n=593)

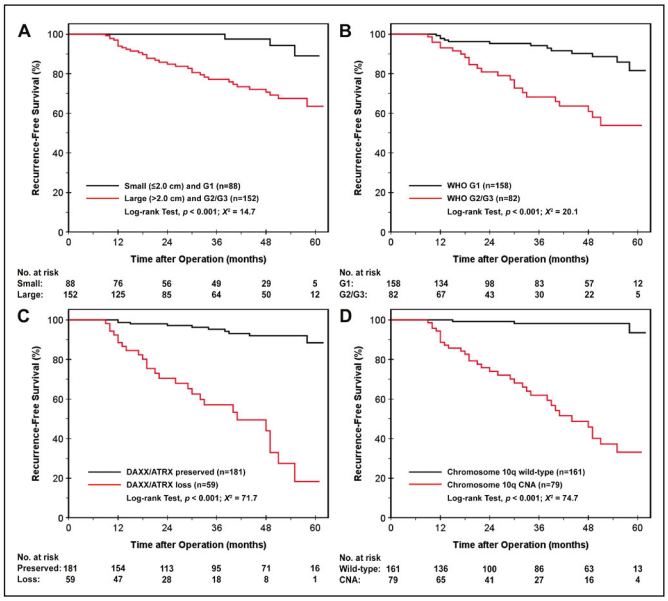
** Applies to mastectomy patients only (n=621

54. Chromosomal Abnormalities Involving 10q are a Prognostic Biomarker of Poor Outcome for Patients with Pancreatic Neuroendocrine Tumors (PanNETs)

Gregor Werba[1]; Abigail I Wald[2]; Brian A. Boone, MD[3]; Patricio M. Polanco, MD[4]; Melissa Hogg, MD, FSSO[5]; Herbert J Zeh, MD[6]; Kenneth K Lee[7]; Alessandro Paniccia[8]; Amer H. Zureikat, MD[9]; Aatur D Singhi[10]

[1]UPMC Medical Center, Pittsburgh, PA, US; [2]UPMC Medical Center, Pittsburgh, PA, US; [3]West Virginia University, Morgantown, WV, US; [4]University of Texas Southwestern Medical Center, Dallas, TX, US; [5]Northshore University Health System, Evanston, IL, US; [6]UT Southwestern Medical Center, Dallas, TX, US; [7]UPMC Medical Center, Pittsburgh, PA, US; [8]UPMC Medical Center, Pittsburgh, PA, US; [9]UPMC Medical Center, Pittsburgh, PA, US; [10]UPMC Medical Center, Pittsburgh, PA, US

INTRODUCTION: The genomic landscape of PanNETs is characterized by multiple chromosomal abnormalities that may have prognostic and surgical implications. PanNETs with *MEN1* alterations and few chromosomal abnormalities rarely develop distant metastases. In comparison, patients with PanNETs that have multiple chromosomal abnormalities, regardless of alterations, frequently develop metastatic disease. However, previous studies have been limited in determining if molecular findings could inform surgical decision-making. **METHODS:** A multi-institutional cohort of 248 resected PanNETs was evaluated using a 74-gene DNA/RNA-targeted sequencing panel (PancreaSeq GC) that evaluates *MEN1* and copy number alterations (CNAs) involving 13 chromosomal regions. Molecular findings were correlated with patient demographics, pathologic features, DAXX/ATRX status, and follow-up. **RESULTS:** At least one CNA was identified in 150 of 248 (61%) PanNETs, ranging from 1 to 12 (median, 7 CNAs). The most prevalent CNAs involved chromosomes 3p (n=107, 43%), 2p (n=90, 36%), 22q (n=88, 10q (n=85, 34%), 2q (n=85, 18q (n=69, 28%), and 17p (n=61, 25%). The presence of a CNA correlated with several, poor prognostic features, but the most adverse findings were associated with chromosome 10q. PanNETs with 10q CNAs were characterized by larger size (3.7 cm vs 2.4 cm, p<0.001), higher WHO grade (57% vs 24%, lymphovascular invasion (75% vs 31%, perineural invasion (60% vs 18%, advanced pT stage (31% vs 9%, lymph node metastases (53% vs 15%, DAXX/ATRX loss (67% vs 5%, and synchronous (7% vs 1%, p=0.021), and metachronous (42% vs 2%, p<0.001) distant metastasis. The 3- and 5-year recurrence-free survival (RFS) rates for patients with a 10q CNA were 62% and 33%, respectively, compared to 98% and 94%, respectively (p<0.001). Among patients with a small (≤2.0 cm), low WHO grade PanNET, 15 (18%) had a 10q CNA and 3 of the 4 patients that developed distant metastases had a 10q CNA. By multivariate analysis, a 10q CNA was a negative prognostic factor for RFS (p<0.001), independent of tumor size, WHO grade, and DAXX/ATRX status. **CONCLUSIONS:** Chromosome 10q abnormalities were associated with several adverse prognostic features, distant metastasis, and shorter RFS. Moreover, a 10q CNA was a negative, independent prognostic factor for RFS. These findings suggest that 10q abnormalities play a pivotal role in the metastatic progression of PanNETs, and its identification warrants surgical intervention independent of tumor size.



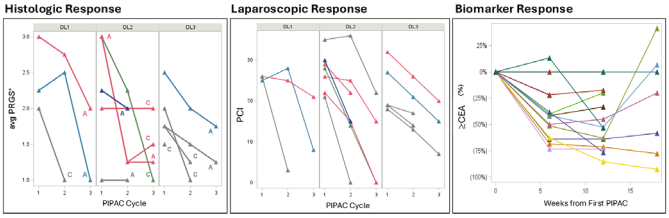
55. Dose escalation Phase 1 trial of Mitomycin C Pressurized Intraperitoneal Aerosolized Chemotherapy in Combination with Systemic Chemotherapy for Unresectable Appendiceal and Colorectal Carcinomatosis

Mustafa Raoof, MD[1]; Marwan Fakih[2]; Kevin Sullivan, MD[3]; Paul Frankel[4]; Timothy Synold[5]; Isaac B Paz[6]; Yuman Fong[7]; Sue Chang[8]; Sarah Cole[9]; Susan Yost[10]; Melissa Eng[11]; Raechelle Tinsley[12]; Larry Hernandez[13]; Jeremy Jones[14]; Richard Whelan[15]; Danielle DePeralta, MD[16]; Amit Merchea[17]; Thanh H Dellinger[18]

[1]City of Hope Medical Center, Duarte, CA, US; [2]City of Hope Cancer Center, Duarte, CA, US; [3]LSU HSC, New Orleans, LA, US; [4]City of Hope Cancer Center, Duarte, CA, US; [5]City of Hope Cancer Center, Duarte, CA, US; [6]City of Hope National Medical Center, Duarte, CA, US; [7]City of Hope National Medical Center, Duarte, CA, US; [8]City of Hope Cancer Center, Duarte, CA, US; [9]City of Hope Cancer Center, Duarte, CA, US; [10]City of Hope Cancer Center, Duarte, CA, US; [11]City of Hope Cancer Center, Duarte, CA, US; [12]City of Hope Cancer Center, Duarte, CA, US; [13]City of Hope Cancer Center, Duarte, CA, US; [14]Mayo Clinic, Jacksonville, FL, US; [15]Northwell Health, New York, NY, US; [16]Northwell Health, Hofstra School of Medicine, New York, NY, US; [17]Mayo Clinic, Jacksonville, FL, US; [18]City of Hope Cancer Center, Duarte, CA, US

INTRODUCTION: Peritoneal carcinomatosis (PC) from appendiceal or colorectal cancer has significant morbidity and limited survival. Pressurized intraperitoneal aerosolized chemotherapy (PIPAC) is a promising minimally invasive approach to treat unresectable PC. Mitomycin C (MMC)-PIPAC in combination with systemic chemotherapy has not been investigated. **METHODS:** In this US multicenter phase I study of MMC-PIPAC, patients who were ineligible for cytoreduction after at least 4 months of first- or second-line systemic chemotherapy were included. MMC-PIPAC was given every 6 weeks and systemic FOLFIRI was given every 2 weeks except the week of PIPAC. Dose escalation was performed using a 3+3 design (planned dose levels: DL1-7, DL2-12.5, DL3-19 and DL4-25 mg/m^2). The primary endpoint was to assess the safety of MMC-PIPAC in combination with FOLFIRI and to establish the recommended Phase 2 dose. Secondary outcomes were to evaluate: Radiographic response (RECIST criteria), Histologic response (decline in peritoneal regression grading score), laparoscopic response (decline in peritoneal carcinomatosis index), and biochemical response (decline in CEA). **RESULTS:** A total of 18 patients (11 males: 7 females) have been enrolled with a median age of 58y (range 31-79y). Half of the patients were appendiceal (non-low grade) and the other half were colorectal. Most (71%) completed all three protocol treatments (100% for DL1 and DL2, 56% for DL3). Overall grade 3 severe adverse event (SAE) rate was 28% (0% for DL1, 12% for DL2, and 57% for DL3). One patient had a dose-limiting toxicity on DL3 (Small bowel obstruction). Other grade 3 SAEs included thrombocytopenia, anemia, abdominal pain and skin infection. Further dose escalation was not pursued due to concern for peritoneal sclerosis. One patient had complete radiographic response, 2 had partial response, 15 had stable or unmeasurable

disease. Histologic, laparoscopic, and biomarker responses were observed in almost all patients (Fig 1). **CONCLUSIONS:** Administration of MMC-PIPAC every 6 weeks is safe up to DL3 (19 mg/m^2) in combination with FOLFIRI. Histologic, laparoscopic, and biomarker responses were observed in most patients. The findings provide a strong rationale for a randomized phase 2 trial.



56. Multicenter Randomized Clinical Trial of CRT vs DCF as Initial Treatment for Subsequent Conversion Surgery for Clinical T4b Esophageal Cancer

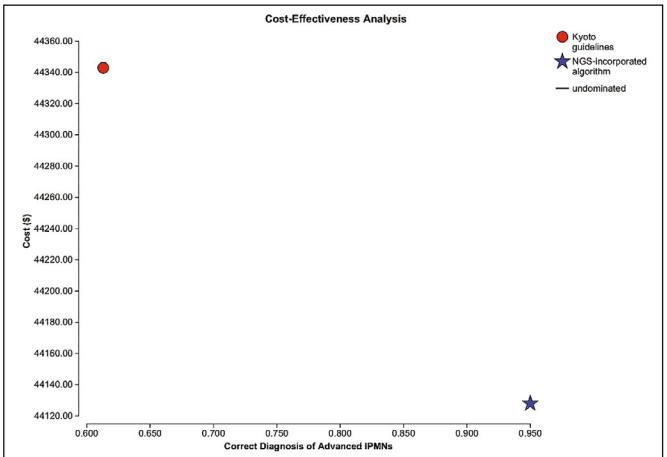
Keijiro Sugimura[1]; Hiroshi Miyata[2]; Koji Tanaka[3]; Tomoki Makino[4]; Atsushi Takeno[5]; Osamu Shiraishi[6]; Makoto Yamasaki[7]; Takushi Yasuda[8]; Yuichiro Doki[9]
[1]Department of Surgery, Kansai Rosai Hospital, Amagasaki, Hyogo, JP; [2]Osaka Internationa Cancer Institute, Osaka, JP; [3]Departments of Gastroenterological Surgery, Graduate School of Medicine, Osaka University, Suita, Os, Osaka, JP; [4]Departments of Gastroenterological Surgery, Graduate School of Medicine, Osaka University, Suita, Os, Osaka, JP; [5]Department of Surgery, National Hospital Organization, Osaka National Hospital, Osaka, JP; [6]Department of Surgery, Kindai University Faculty of Medicine, Osaka, JP; [7]Departments of Gastroenterological Surgery, Graduate School of Medicine, Osaka University, Osaka, JP; [8]Department of Surgery, Kindai University Faculty of Medicine,, Osaka, JP; [9]Departments of Gastroenterological Surgery, Graduate School of Medicine, Osaka University, Osaka, JP

INTRODUCTION: Although induction followed by conversion surgery (CS) is potentially curative for T4b esophageal cancer, the optimal initial induction treatment is unclear. We conducted a multicenter randomized prospective phase 2 trial of chemoradiotherapy (CRT) versus chemotherapy (CT) as initial induction therapy for CS in clinical T4b esophageal cancer. We compared treatment effects, adverse events and survival. **METHODS:** Ninety-nine patients with T4b esophageal cancer were randomly allocated to chemoradiotherapy (Group A, n=49) or CT (Group B, n=50) as initial induction treatment. CRT consisted of radiation (50.4 Gy) with cisplatin and 5-fluorouracil. CT consisted of 2 cycles of docetaxel plus cisplatin and 5-fluorouracil (DCF). CRT or CT was followed by CS if resectable. If unresectable, the patient received the other treatment as secondary treatment. CS was performed if resectable after secondary treatment. The primary end point was 2-year overall survival. The Japan Registry of Clinical Trials (s051180164). **RESULTS:** In Group A, CS was performed in 34 (69%) and 7 patients (14%) after initial and secondary treatment. In Group B, CS was performed in 25 (50%) and 17 patients (34%) after initial and secondary treatment. The R0 resection rate after initial and secondary treatment was similar (78% vs 76%, *P*=1.000). Adverse events including leukopenia, neutropenia, febrile neutropenia, and diarrhea were significantly more frequent in Group B. Group A had better histological complete response of the primary tumor (40% vs 17%, *P*=0.028) and histological nodal status (*P*=0.038). The 2-year survival rate was 55.1% (95% CI 41.1-68.3%) in the CRT group and 34.7% (95% CI 22.8-48.9%) in the CT group, although the difference was not significant (p=0.11). Local and regional lymph node recurrence in patients undergoing R0 resection was significantly higher in CT than CRT (30% versus 8%, p=0.03 and 37% versus 8%, p=0.002, respectively). **CONCLUSIONS:** The results of the present trial showed that upfront CRT was superior to upfront CT in terms of adverse effects, pathological effects and 2 year-overall survival as initial induction therapy for CS in clinical T4b esophageal cancer.

57. Incorporating Cyst Fluid Next-Generation Sequencing (NGS) into the Management Algorithm is the More Cost-Effective Strategy Compared to the Kyoto Guidelines in Predicting Advanced IPMNs in Patients with Worrisome Features

Amudhan Kannan, MD[1]; Gilbert Z Murimwa, M.D[2]; John C Mansour, MD[3]; Alex Jones, MD[4]; Ali Abbas, [5]; Tarek Sawas, MD[6]; Daniel Ellis, MD[7]; Hendrikus Vanderveldt, MD[8]; Veronica Coleman, PA-C[9]; Samantha Foley, PA-C[10]; Naveen Rajamohan, MD[11]; Randall E. Brand, MD[12]; Amer H. Zureikat, MD[13]; Kenneth K Lee[14]; Gaurav Khatri, MD[15]; Jason Fleming, MD[16]; Herbert J Zeh, MD[17]; Aatur D Singhi, MD[18]; Nisa M Kubiliun, MD[19]; Patricio M. Polanco, MD[20]
[1]University of Texas Southwestern Medical Center, Dallas, TX, US; [2]UTSouthwestern Medical Center, Dallas, TX, US; [3]UT Southwestern Medical Center, Dallas, TX, US; [4]University of Texas Southwestern Medical Center, Dallas, TX, US; [5]University of Texas Southwestern Medical Center, Dallas, TX, US; [6]University of Texas Southwestern Medical Center, Dallas, TX, US; [7]University of Texas Southwestern Medical Center, Dallas, TX, US; [8]University of Texas Southwestern Medical Center, Dallas, TX, US; [9]University of Texas Southwestern Medical Center, Dallas, TX, US; [10]University of Texas Southwestern Medical Center, Dallas, TX, US; [11]University of Texas Southwestern Medical Center, Dallas, TX, US; [12]UPMC, Pittsburgh, PA, US; [13]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [14]UPMC Medical Center, Pittsburgh, PA, US; [15]University of Texas Southwestern Medical Center, Dallas, TX, US; [16]UT Southwestern, Dallas, TX, US; [17]UT Southwestern Medical Center, Dallas, TX, US; [18]UPMC Medical Center, Pittsburgh, PA, US; [19]University of Texas Southwestern Medical Center, Dallas, TX, US; [20]University of Texas Southwestern Medical Center, Dallas, TX, US

INTRODUCTION: The presence of high-risk mutations (HRMs) in cyst fluid detected by next-generation sequencing (NGS) has proven to be highly sensitive and specific in predicting advanced IPMNs (IPMNs with high-grade dysplasia [HGD] or invasive carcinoma [IC]) compared to existing guideline parameters. Consequently, our institution incorporated NGS testing for patients presenting with worrisome features. This study aimed to evaluate the cost-effectiveness of an NGS-incorporated algorithm compared to the Kyoto guideline in predicting advanced neoplasia in patients with worrisome features. **METHODS:** We compared the Kyoto guideline (pancreaticoduodenectomy [PD] for patients with multiple worrisome features following five MRCPs) with the NGS-incorporated protocol (PD for patients who underwent four MRCPs and one EUS with NGS showing HRMs, along with single or multiple worrisome features) using a decision tree model. The analysis was based on data from 167 patients who underwent prospective NGS testing with available final surgical pathology (considered the gold standard). Costs were calculated based on data from our institution, and effectiveness was measured by the accuracy of diagnosing advanced IPMNs. The primary outcome was the cost-effectiveness comparison, focusing on the cost per correct diagnosis of advanced IPMNs between the two guidelines. A willingness-to-pay threshold of $100,000 per correct diagnosis of advanced IPMNs was set and probabilistic sensitivity analysis was performed to assess the robustness of the conclusions. **RESULTS:** Of the 167 patients included, 90 (54%) had advanced IPMNs. A total of 93 patients had multiple worrisome features, of whom 57 (61.3%) had advanced IPMNs based on final surgical pathology. Eighty patients had at least one worrisome feature and tested positive for one of the HRMs on NGS, with 76 (95%) of these patients having advanced IPMNs on final surgical pathology. The average costs for MRCP, EUS, NGS, and PD at our institution were $2,657, $1,742, $700, and $31,058, respectively. The NGS-incorporated algorithm correctly diagnosed 95% of advanced IPMNs at a cost of $44,343, while the Kyoto guideline correctly diagnosed 61.3% of advanced IPMNs at a cost of $44,128. These results yielded a negative incremental cost-effectiveness ratio of -$638 per correct diagnosis of advanced IPMNs, indicating that the NGS-incorporated protocol is the more cost-effective strategy. Sensitivity analyses confirmed the robustness of these findings. **CONCLUSIONS:** The accurate prediction of advanced IPMNs, leading to appropriate surgical resection, drives the cost-effectiveness of the strategy. Given its accuracy in predicting advanced IPMNs, the NGS-incorporated algorithm is the more cost-effective approach for managing IPMN patients with worrisome features.



Algorithm	Cost	Effectiveness (Correct diagnosis of advanced IPMNs)	ICER	Net Monetary Benefit (NMB)
Kyoto Guidelines	$44,343	95%	- $638 per correct diagnosis of advanced IPMNs	$16,957
NGS-incorporated protocol	$44,128	61.3%	NA	$50,872

Figure 1. Cost-Effectiveness Analysis Graph

58. Ac-225 delivered by self-assembling dis-assembling (SADA) bispecific antibodies ablates colorectal and appendiceal peritoneal xenografts with minimal toxicity

Nicole Aguirre, MD[1]; Karina Leung, BS[2]; Hong-Fen Guo, MS[3]; Michelle Kim, MS[4]; Sebastian Carrasco, PhD[5]; Edward K Fung, PhD[6]; Irene Cheung, PhD[7]; Andrea Cercek, MD[8]; Michael Foote, MD[9]; Steven M Larson, MD[10]; Sarah M Cheal, PhD[11]; Darren Veach, PhD[12]; Georgios Karagkounis, MD[13]; Garrett M. Nash, MD[14]; Nai-Kong Cheung, MD, PhD[15]

[1]Memorial Sloane Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Weill Cornell Medicine, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US; [11]Weill Cornell Medicine, New York, NY, US; [12]Memorial Sloan Kettering Cancer Center, New York, NY, US; [13]Memorial Sloan Kettering Cancer Center, New York, NY, US; [14]Memorial Sloan Kettering Cancer Center, New York, NY, US; [15]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Peritoneal carcinomatosis is deadly and highly morbid. The standard of care, cytoreductive surgery, often leaves behind microscopic or clinically occult disease, where intraperitoneal chemotherapy and systemic chemotherapy have shown limited success. Systemically administered targeted radionuclide therapy using highly potent ?-particle emitters may improve prognosis, but can be limited by suboptimal therapeutic indices (TI). The two step α-SADA-PRIT-approach exploits initial long plasma half-life of SADA tetramers for increased tumor uptake and the rapid renal clearance of their monomer, to maximize TI before administering α-emitting radioisotope payloads. **METHODS:** To determine most beneficial treatment regimen nude mice with or without established subcutaneous (sq) GPA33(+) human SW1222 CRC xenografts were given two cycles anti-GPA33-SADA followed by escalating doses of [^{225}Ac]Ac-Proteus ([^{225}Ac]Ac-Pr; where Pr-ligand facilitates the binding to SADA). Treatment cycles were given 7 days apart. Dosimetry against sq SW1222 was calculated based on serial tissue biodistribution The newly determined α-SADA-PRIT regimen was then tested against intraperitoneal (IP) GPA33-expressing human CRC SW1222 xenografts and AC patient derived xenograft (PDX), where toxicity, tumor response and survival were followed up to 180 days. Log rank Mantel Cox statistics was used for survival comparison. **RESULTS:** α-SADA-PRIT treatment dose of 2 x 74kBq was chosen based on cures in the sq model during the dose escalation study. In the IP SW1222 model MS was 39d and 40d in the antibody-only and [^{225}Ac]Pr-only control groups, and 134d in the α-SADA-PRIT treatment group (n=10, p <0.0001). In the IP Appendiceal PDX MS was 42d in both antibody-only and [^{225}Ac]Pr-only control groups, and at 100 days the α-SADA-PRIT treatment group (n=10/10) is healthy and tumor free. (p <0.0001). [^{225}Ac]Pr did not cause dose-limiting acute (<30 days) or long term (to 6 months) toxicities. Transient weight loss and leukopenia were reversible. Salient histopathological findings showed renal tubular simplification and degeneration. In sq SW1222 xenografted mice, estimated radiation dose to tumor, blood and kidney were 30, 0.1 and 2.6 Gy (Gy/37kBq, relative biological effectiveness= 1), TI = 301 blood; 12.1 kidney. **CONCLUSIONS:** α-SADA-PRIT induced major tumor response and significantly prolonged survival in an IP CRC model and for the first time in an IP AC tumor. Minimal myeloid, renal, hepatic, or neural toxicities were seen.

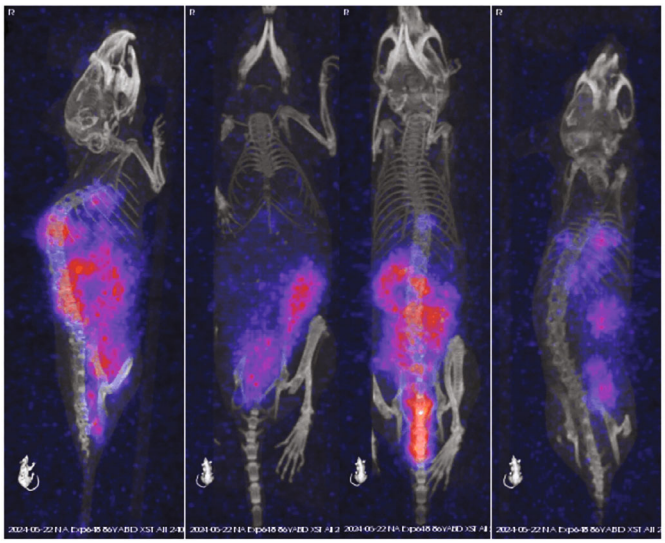


Figure 1. PET CT with [^{86}Y]Pr exhibiting widespread peritoneal metastasis in an IP model of AC.

59. Using Circulating Tumor DNA to Monitor Sarcoma Treatment and Recurrence

Beatrice J Sun, MD[1]; Tiffany M Yue, BS[2]; Dong Hur, BS[3]; Joseph Allen, BS[4]; Daniel Delitto, MD, PhD[5]; George Poultsides, MD[6]; Byrne Lee, MD[7]

[1]Stanford University School of Medicine, Stanford, CA, US; [2]Stanford University School of Medicine, Stanford, CA, US; [3]Stanford University School of Medicine, Stanford, CA, US; [4]Stanford University School of Medicine, Stanford, CA, US; [5]Stanford University School of Medicine, Stanford, CA, US; [6]Stanford University School of Medicine, Stanford, CA, US; [7]Stanford University School of Medicine, Stanford, CA, US

INTRODUCTION: Soft tissue sarcomas (STS) exhibit high rates of relapse despite standard systemic and locoregional therapies and early detection of recurrence is currently limited to periodic imaging. Circulating tumor DNA (ctDNA) is a promising tool used to detect tumor cells in the blood before disease is radiographically detectable and exhibits applications in lung, breast, and colorectal cancer, although its role in sarcoma has not been defined. This study evaluates the use of tumor-informed ctDNA profiling as a potential adjunct for disease surveillance in STS. **METHODS:** Patients with various soft-tissue sarcoma diagnoses who were treated at a tertiary cancer center between 2019 and 2024 and had at least 3 tumor-informed ctDNA assays were reviewed. ctDNA levels and cross-sectional imaging were compared to determine whether ctDNA trends correlated with disease recurrence and/or treatment response. Changes to medical or surgical treatment strategies were evaluated. **RESULTS:** 210 patients with soft-tissue sarcomas were included: median age was 53 years and 67% were female. While over 20 sarcoma subtypes were identified, the most common were leiomyosarcoma (44%), undifferentiated pleomorphic sarcoma (9%), liposarcoma (8%), and angiosarcoma (5%). Primary tumors were located in the abdomen/retroperitoneum (33%), extremity (22%), trunk (13%), and gynecologic organs (32%). In total, 2,134 ctDNA levels were obtained for the cohort (median 9 per patient). During a median ctDNA surveillance of 22 months, 46% of patients had surgery, 72% were treated with chemotherapy, and 33% underwent radiation. ctDNA correlated with imaging findings in 90%. 129 of 149 patients (87% sensitivity) with disease progression or recurrence on imaging had corresponding rise in ctDNA levels, and all underwent changes in treatment plan. All 61 patients (100% specificity) with no known recurrence during surveillance had negative ctDNA levels. 62 patients

underwent surgical resection during ctDNA monitoring. In 81%, postsurgical ctDNA assays converted to negative. **CONCLUSIONS:** Tumor-informed ctDNA demonstrates high sensitivity and specificity in detecting sarcoma recurrence and may be a valuable adjunct for sarcoma disease surveillance. This noninvasive tool may lead to quicker treatment changes with potential for better outcomes and less surveillance imaging needed. Future larger-scale, prospective studies are warranted to validate these findings and determine which sarcoma subtypes will benefit from ctDNA monitoring.

60. Phase II Preoperative pembrolizumab for MSI high or MSS/PD-L1 gastric cancer followed by surgery and adjuvant therapy with pembrolizumab (NCT03257163): Final Results of a Multicenter Study

Timothy J. Kennedy, MD[1]
[1]Rutgers Cancer Institute, New Brunswick, NJ, US

INTRODUCTION: Despite advances in therapy, outcomes of patients with gastric cancer in the US leave room for improvement. Preliminary data suggest that patients with microsatellite unstable tumors (MSI-H), EBV expressing tumors, and tumors with positive PD-L1 expression may benefit from immunotherapy. This trial evaluated the benefit of PD-1 checkpoint immunotherapy in this subset of patients with operable gastric cancer. **METHODS:** We present results of a phase 2 multi-institutional clinical trial (*NCT03257163*). Patients with clinically staged T2-T4, N0-N3, M0 gastric adenocarcinoma with MSI-H, PDL1 CPS ≥ 1%, or EBV positivity were included. Patients received 2 cycles of neoadjuvant pembrolizumab 200 mg IV q3 weeks followed by surgical resection. Pembrolizumab was given for 16 additional cycles post-op, concurrently with adjuvant chemoradiation (45 Gy) and 5 cycles of capecitabine (825 mg/m2 days 1-14 during cycles 3, 6 and 7 and 625 mg /m2 BID days 1-14 (cycles 4 and 5 with RT)). Patients were included in the analysis if they received at least one cycle of postoperative pembrolizumab. The primary endpoint is DFS, powered to detect 3-yr DFS of 70% with 89% power. **RESULTS:** All enrolled patients received two cycles of pembrolizumab preoperatively (n=45). Eight patients did not undergo surgery (1 refused secondary to frailty, 2 with distant progression on pre-operative imaging, 2 with finding of peritoneal disease on surgical exploration and 3 with locally advanced tumors deemed unresectable on surgical exploration). Six patients did not receive adjuvant therapy (2 due to surgical complications delaying adjuvant therapy, 2 for failure to thrive after surgery, 1 refused adjuvant therapy and 1 scheduled to start adjuvant therapy). Overall, 31 patients went on to receive adjuvant therapy and are included in the predetermined, evaluable analytic cohort. These 31 patients had a median age of 67 years (range 44 – 85) and represented an ethnically diverse population with 22.6% Hispanic, 29.0% Asian, 25.8% Black and 25.8% White. Median follow-up was 31.1 months (range 3.45-63.8). In these 31 patients, 14 (45.2%) patients had MSI-H, 2 (6.5%) EBV (+), and 29 (93.5%) had PDL1 expression ≥ 1% tumors. Most tumors had advanced clinical stage with 81% ≥ cT3 and 58% cN+. In the 31 evaluable patients, the 3-year DFS was 79.4%, and 3-year overall survival (OS) was 78.9%. For patients with MSI-H tumors, 3-year DFS was 81.8%. For patients with MSS/PD-L1+ tumors, 3-year DFS was 77.8%. For the 45-patient cohort, 3-year DFS was 70% and 3-year OS was 65%. Three patients had complete pathologic response, two with MSI-H tumors and one with PD-L1 CPS of 4%. Downstaging occurred in 62.2% of patients who underwent surgery and 40% of surgical specimens had a T0/T1 primary tumor consistent with significant pathologic response. **CONCLUSIONS:** A biomarker-driven preoperative treatment strategy for MSI-H, EBV+, and MSS/PDL1+ operable gastric adenocarcinoma patients is promising and warrants additional evaluation. This study, which met its primary endpoint of 3-year DFS >70%, suggests that this is a novel and effective approach. The treatment strategy incorporates immune checkpoint immunotherapy, low dose chemotherapy, and radiation thus avoiding more intensive combination chemotherapy regimens for patients with these biomarkers.

Melanoma

61. Single-dose Neoadjuvant Pembrolizumab in Resectable Metastatic Melanoma

Neha Shafique, MD[1]; Mohammad S. Farooq, MD, MS[2]; Valentina Mattfeld, BA[3]; Gracia M Vargas, MD[4]; Xiaowei Xu, Md, PhD[5]; John T Miura, MD[6]; Tara C Mitchell[7]; Giorgos C Karakousis, MD[8]
[1]Hospital of University of Pennsylvania, Philadelphia, PA, US; [2]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [3]University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, US; [4]Hospital of University of Pennsylvania, Philadelphia, PA, US; [5]Hospital of University of Pennsylvania, Philadelphia, PA, US; [6]University of Pennsylvania, Philadelphia, PA, US; [7]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [8]University of Pennsylvania, Philadelphia, PA, US

INTRODUCTION: Neoadjuvant immune checkpoint blockade therapy for resectable oligometastatic melanoma has shown promising results in clinical trials, however data on the optimal dose and schedule remain largely lacking. We report on the largest case series of patients with oligometastatic melanoma treated with a single dose of neoadjuvant programmed cell death receptor 1 (PD-1) inhibition. **METHODS:** We identified PD-1 naive patients with resectable Stage III/IV melanoma who received one dose of pembrolizumab (200 mg intravenous) prior to surgical resection at a single high volume melanoma center. Outcomes studied included time to surgery, 30-day surgical complications, time to initiation of adjuvant therapy, major pathologic response (MPR) defined as <10% viable tumor, patterns and treatment of first recurrence, and 5-year overall survival (OS). **RESULTS:** 48 patients met inclusion criteria (47 Stage III/1 patient Stage IV). The cohort was 66.6% male and median age was 64 years (interquartile range [IQR] 56-70). Median time from neoadjuvant dose to surgery was 21 days (IQR 16-24), with all patients undergoing surgical resection. One patient experienced a grade II immune adverse event prior to surgery with fatigue and liver enzyme elevation and did not go on to adjuvant therapy. All other patients (47; 97.9%) started adjuvant therapy with a median time from surgery of 24 days (IQR 20-30). There was one major postoperative complication in one patient (2.1%), who developed a deep surgical site infection requiring an admission for intravenous antibiotics. Another patient required reoperation for a positive deep margin. MPR in the cohort was 22.9%. With a median follow-up time of 67.7 months, the 5-year OS for the entire cohort was 82.7% (100% among patients with MPR and 76.5% for less than MPR). 22 patients (45%) developed a recurrence of which 9 patients (40.1%) developed distant metastases and the remainder locoregional recurrences. Of patients who recurred, 13 (59.1%) underwent salvage surgery with a 5-yr OS of 59.3%. **CONCLUSIONS:** Single dose of neoadjuvant pembrolizumab is a safe and feasible approach with no delays in surgery or initiation of adjuvant therapy. Optimal selection of patients for surgical salvage for recurrence after PD-1 failure remains to be well defined**.**

62. Prospective multicenter evaluation (MERLIN_001 trial, NCT04759781) of a clinicopathologic and gene expression profile test to predict sentinel node status in T1-T3 cN0 melanoma

Tina J. Hieken, MD[1]; Michael E. Egger, MD, MPH[2]; Christina V. Angeles, MD[3]; John R. Hyngstrom, MD[4]; Erin E. Burke, MD[5]; Michael C. Lowe, MD, M.A.[6]; Georgia M. Beasley, MD, MHSc[7]; Edmund K. Bartlett, MD[8]; Scott C. Bresler, MD, PhD[9]; Kelly L. Harms, MD[10]; Jonathan Zager, MD[11]; Nabil Wasif, MD, MPH[12]; Sanjay Bagaria, MD[13]; Kelly M. McMasters, MD, PhD[14]; David A. Wada, MD[15]; Prakash K. Pandalai, MD[16]; Keith A. Delman, MD[17]; Jay S. Lee, MD[18]; Klaus J. Busam, MD[19]; Vernon K Sondak, MD[20]
[1]Mayo Clinic, Rochester, MN, US; [2]University of Louisville Department of Surgery, Louisville, KY, US; [3]University of Michigan Medical School, Ann Arbor, MI, US; [4]University of Utah, Huntsman Cancer Institute - Cancer Hospital South, Salt Lake City, UT, US; [5]UK HealthCare, Lexington, KY, US; [6]Emory Winship Cancer Institute, Atlanta, GA, US; [7]Duke University, Durham, NC, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]University of Michigan Health Pathology, Ann Arbor, MI, US; [10]University of Michigan, Department of Dermatology, Ann Arbor, MI, US; [11]Moffitt Cancer Center, Tampa, FL, US; [12]Mayo Clinic Arizona, Phoenix, AZ, US; [13]Mayo Clinic Florida, Jacksonville, FL, US; [14]University of Louisville, Department of Surgery, Louisville, KY, US; [15]University of Utah, Huntsman Cancer Institute - Cancer Hospital South, Salt Lake City, UT, US; [16]University of Kentucky, Lexington, KY, US; [17]Emory University School of Medicine, Department of Surgery, Atlanta, GA, US; [18]Duke University, Department of Surgery, Durham, NC, US; [19]Memorial Sloan Kettering Cancer Center, New York, NY, US; [20]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Guidelines recommend sentinel lymph node biopsy (SLNB) for cN0 melanoma patients (pts) with a predicted risk of SLN metastasis ≥10% and considering SLNB for a 5-10% risk. A gene expression profile (GEP)-based test that accurately identifies pts with a low risk of SLN metastasis could refine pt selection for SLNB, but current guidelines advise against using GEP for SLN risk prediction absent prospective trial data. This blinded prospective study across nine US centers evaluated the performance of the CP-GEPtest, combining clinicopathologic factors (age, Breslow thickness) with gene expression (GEP) of 8 genes for predicting SLN status in pT1-T3 cN0M0 cutaneous melanoma

pts undergoing clinically indicated SLNB. **METHODS:** GEP was performed on formalin-fixed, paraffin-embedded tissue from the primary tumor diagnostic biopsy. CP-GEP test results were reported in binary fashion as Low or High Risk. The primary outcome measure was negative predictive value (NPV) in Low Risk pts. Preplanned analyses included NPV assessment by T substage and age. **RESULTS:** GEP was performed successfully in 97.4% of samples. 1,686 T1-T3 pts with a successful CP-GEP test underwent SLNB (17.6% SLN-positive [SLN+]); 37% were classified as Low Risk by CP-GEP. Among all pts classified as Low Risk, 7.1% were SLN+ for an NPV of 92.9% (95% CI 90.6-94.8%). High Risk classification carried a 23.8% SLN+ rate. Most T1b pts (66.6%) were Low Risk, with a SLN+ rate of 5.1% (95% CI 3.0-9.2%) whereas High Risk T1b patients had a SLN+ rate 17.3% (11.7-24.2%). Fewer T2a pts were Low Risk (37.6%), with a SLN+ rate of 7.9% (95% CI 4.8-12.1%). In the pre-specified clinical stage IB subgroup (T1b-T2a), the SLN+ rate in Low Risk patients was 6.4% (95% CI 4.5-8.7%) and 18.7% (15.6-22.2%) for High Risk patients (Table). Model performance was consistent across age subgroups, with the SLN+ rate in Low Risk patients being 0% (95% CI 0-13.7%) for age <40 (n=145), 8.2% (95% CI 5.6-12.9%) for age 40-64 (n=744), and 6.2% (95% CI 3.9-9.4%) for age >64 (n=797). **CONCLUSIONS:** In the first prospective multicenter blinded trial of a GEP prediction tool for SLN status, the CP-GEP test reliably identified pts with a <10% risk of SLN metastasis. For Stage IB patients the SLN+ rate was 3-fold greater for a High Risk vs Low Risk CP-GEP test. This approach has potential to more precisely estimate individual pt risk of harboring a SLN metastasis than by clinical stage alone, and thus inform shared surgeon-patient decision-making for SLNB.

Clinical Group	% SLN-Positive	% SLN-Positive in Low Risk (95% CIs)	% SLN-Positive in High Risk (95% CIs)	Percent Low Risk by CP-GEP
All Patients T1-T3 (n=1,686)	17.6%	7.1% (5.2-9.4)	23.8% (21.3-26.5)	37.0%
T1a (n=29)	3.4%	0 (0-14.8)	16.7% (0.4-64.1)	79.3%
T1b (n = 467)	9.2%	5.1% (3.0-8.2)	17.3% (11.7-24.2)	66.6%
T2a (n = 639)	15.0%	7.9% (4.8-12.1)	19.3% (15.5-23.5)	37.6%
Stage IB Subgroup (T1b-T2a) (n = 1,106)	12.6%	6.4% (4.5-8.7)	18.7% (15.6-22.2)	49.8%
T2b (n=177)	18.6%	18.2% (7.0-35.5%)	18.8% (12.7-26.1%)	18.6%
T3a (n=187)	34.8%	14.3% (0.4-57.1%)	35.6% (28.6-43.0%)	3.7%
T3b (n=150)	36.7%	50.0% (1.3-98.7%)	36.5% (28.7-44.8%)	1.3%

63. Surrogate Endpoints for Clinical Trial Design in Early-Stage Primary Cutaneous Melanoma Staged with Sentinel Node Biopsy: an International, Multicenter Cohort Study

Sophie E Orme, MB BS[1]; Serigne Lo[2]; Robyn P.M. Saw, MBBS, MS[3]; Kerwin Shannon[4]; Andrew Spillane[5]; John F Thompson[6]; Jonathan Stretch[7]; Omgo Nieweg[8]; Sydney Ch'ng[9]; Danielle K. DePalo, MD[10]; Helana Ghali, BS[11]; Michelle M Dugan, MD[12]; Jonathan S Zager, MD[13]; Martin J Heaton, MD FCRS(Plast.)[14]; Andrew P Snelling, FRCS(Plast.)[15]; Roger Olofsson Bagge, MD PhD[16]; Iva Johansson[17]; Carolyn Nessim, MD, MSc[18]; Marc D Moncrieff, MD FRCS(Plast.)[19]

[1]Norfolk and Norwich University Hospitals Trust, Norwich, GB; [2]Melanoma Institute Australia, Sydney, AU; [3]Melanoma Institute Australia, Sydney, AU; [4]Melanoma Institute Australia, Sydney, AU; [5]Melanoma Institute Australia, Sydney, AU; [6]Melanoma Institute Australia, Sydney, AU; [7]Melanoma Institute Australia, Sydney, AU; [8]Melanoma Institute Australia, Sydney, AU; [9]Melanoma Institute Australia, Sydney, AU; [10]Moffitt Cancer Center, Tampa, FL, US; [11]University of South Florida Morsani College of Medicine, Tampa, FL, US; [12]Moffitt Cancer Center, Tampa, FL, US; [13]Moffitt Cancer Center, Tampa, FL, US; [14]Department of Plastic & Reconstructive Surgery, Norfolk and Norwich University Hospitals NHS Foundat, Norwich, GB; [15]Department of Plastic & Reconstructive Surgery, Norfolk and Norwich University Hospitals NHS Foundat, Norwich, GB; [16]Sahlgrenska University Hospital, Gothenburg, SE; [17]Sahlgrenska University Hospital, Gothenburg, SE; [18]The Ottawa Hospital (General Campus), Ottawa, ON, CA; [19]Department of Plastic & Reconstructive Surgery, Norfolk and Norwich University Hospitals NHS Foundat, Norwich, GB

INTRODUCTION: Adjuvant systemic therapy (AST) for resected AJCC stage IIB-C and III melanoma following sentinel node (SN) biopsy became standard of care based on analyses showing improvements in relapse-free survival (RFS) and distant metastasis-free survival (DMFS), despite the FDA recognizing overall survival (OS) as the gold-standard endpoint, and the AJCC classification system emphasizing disease-specific survival (DSS). Historic trials for melanoma and other solid tumors have demonstrated that early gains in RFS may not translate into meaningful improvements in OS/DSS. The validity of RFS/DMFS as surrogate endpoints is debatable pending OS and DSS data from current phase III checkpoint inhibitor trials in resected melanoma, raising concerns regarding the long-term benefit of AST for these patients, many of whom may be treated with surgery alone. **METHODS:** We analyzed 10,379 patients with resected melanoma (AJCC stages I-III, 2000–20) from 5 academic centers in Australia, North America, and Europe, staged with SNB. For RFS or DMFS to be valid surrogates, rigorous assessments are necessary at the individual patient and trial levels. Individual-level validation examined correlations between RFS, DMFS, and OS/DSS, while trial-level validation assessed stratified log hazard ratios by center, AJCC stage, and SN status, weighted by sample size. **RESULTS:** With median follow-up of 54 months (IQR 27-92), 5-year RFS was 80.7% for SN-ve and 49.3% for SN+ve patients (HR=3.4, p<0.001). DMFS rates were 86.3% and 60.3%, respectively (HR=3.4, p<0.001); DSS were 91.4% and 71.2%, respectively (HR=3.7, p<0.001) and OS was 85.5% and 66.8% (HR=2.4, p<0.001). Individual-level correlations between RFS and OS/DSS were insufficient to support surrogacy of RFS for OS/DSS across 1 to 10 years (R^2=0.31–0.66). DMFS significantly correlated with DSS only after the 5 years (R^2=0.79). RFS was strongly correlated with DMFS starting from 2 years (R^2>0.75). Trial-level analysis demonstrated strong correlations between RFS and DMFS (R^2=0.97, p<0.001) and DSS (R^2=0.84, p<0.001), indicating good evidence for surrogacy between these endpoints. However, correlation with OS remained unconfirmed (R^2=0.59). **CONCLUSIONS:** Our analysis shows that RFS is a valid surrogate for DMFS in adjuvant trials for resected melanoma at individual and trial levels. However, improvements in RFS and DMFS offer limited predictive value for OS. Results reported before 5-years should be interpreted cautiously when predicting DSS outcomes for patients with AJCC stage I-III melanoma.

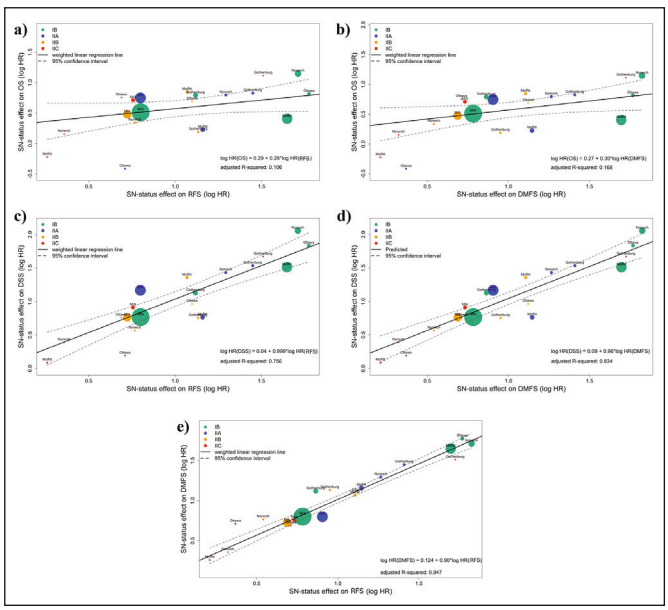


Figure 1. Correlation between sentinel node status effects on a) RFS and OS; b)DMFS and OS; c) RFS and DSS; d) DMFS and DSS; e) RFS and DMFS, in early-stage primary cutaneous melanoma. Symbol size is proportional to the number of patients per center. SN = sentinel node; RFS = relapse free survival; DMFS = distant metastasis free survival; OS = overall survival; DSS = disease specific survival; log HR = log hazard ratio

64. Adoptive Cell Transfer of Tumor Infiltrating Lymphocytes for Metastatic Acral Lentiginous Melanoma

Alexandra Gustafson[1]; Paul H McClelland[2]; Shirley K Nah[3]; Aaron Dinerman[4]; Bradley S White[5]; Billel Gasmi[6]; Donald White[7]; Sivasish Sindiri[8]; Jared J Gartner[9]; Todd Prickett[10]; Paul Robbins[11]; Maria Parkhurst[12]; Hyunmi Halas[13]; Mei Li Kwong[14]; Stephanie Goff[15]; James Yang[16]; Steven A. Rosenberg[17]; Nicholas Klemen[18]

[1]National Cancer Institute, Bethesda, MD, US; [2]NCI, Bethesda, MD, US; [3]NCI, Bethesda, MD, US; [4]NCI, Bethesda, MD, US; [5]NCI, Bethesda, MD, US; [6]NCI, Bethesda, MD, US; [7]NCI, Bethesda, MD, US; [8]NCI, Bethesda, MD, US; [9]NCI, Bethesda, MD, US; [10]NCI, Bethesda, MD, US; [11]NCI, Bethesda, MD, US; [12]NCI, Bethesda, MD, US; [13]NCI, Bethesda, MD, US; [14]NCI, Bethesda, MD, US; [15]NCI, Bethesda, MD, US; [16]NCI, Bethesda, MD, US; [17]NCI, Bethesda, MD, US; [18]NCI, Bethesda, MD, US

INTRODUCTION: Adoptive cell transfer (ACT) of tumor infiltrating lymphocytes (TIL) can mediate durable regression of metastatic melanoma and is an FDA-approved treatment. Acral lentiginous melanoma (ALM) is a rare subtype of melanoma arising from palmar, plantar, or subungual skin that is associated with aggressive biology. Acral melanomas are genomically distinct from cutaneous melanomas in that they largely lack ultraviolet (UV) radiation signatures and have a low tumor mutational burden (TMB). Consequently, patients with acral melanoma treated with immune checkpoint blockade (ICB) have worse survival than patients with non-acral cutaneous melanomas. The efficacy of TIL therapy for acral melanoma is unknown. **METHODS:** We reviewed data from 438 patients with metastatic melanoma who were treated on prospective trials at our institution from 1999 until 2018. We included TIL protocols utilizing a preparative lymphodepleting chemotherapy regimen, autologous TIL, and cytokine support with high dose interleukin-2. We retrospectively reviewed clinical and pathologic reports, while blinded to clinical outcomes and genomic data, to determine whether patients' primary tumors were acral or non-acral cutaneous melanoma. We then compared prospectively recorded outcomes of TIL therapy for cutaneous or acral melanoma including objective response (RECIST v1.0), progression free survival (PFS) and overall survival (OS). **RESULTS:** We determined that 29 (7%) of 438 patients had acral melanomas while 409 (93%) had cutaneous melanomas. There were no statistically significant differences in demographic or pretreatment variables. Objective responses to TIL were observed in 13 (44.8%) of 29 patients with acral melanoma and in 163 (39.9%) of 409 patients with cutaneous melanoma (P = 0.70), with 1 (3.4%) and 65 (15.9%) complete responses respectively (P = 0.10). Median PFS was 3.5 and 4.1 months (P = 0.50) respectively for patients with acral and cutaneous melanoma, while median OS was 16.0 and 16.7 months (P = 0.94, Figure 1). Acral melanomas had a lower TMB than cutaneous melanomas (median 2.5 vs 13.8 mutations per megabase, P < 0.0001). **CONCLUSIONS:** In this single institution retrospective cohort study, patients with acral and cutaneous melanoma had similar outcomes following TIL therapy. This was an unexpected finding given the difference in TMB and in the context of other literature showing worse outcomes in acral melanomas. This is the first study to report outcomes of TIL therapy for an acral melanoma cohort, and it demonstrates better-than-expected efficacy for this rare but lethal malignancy.

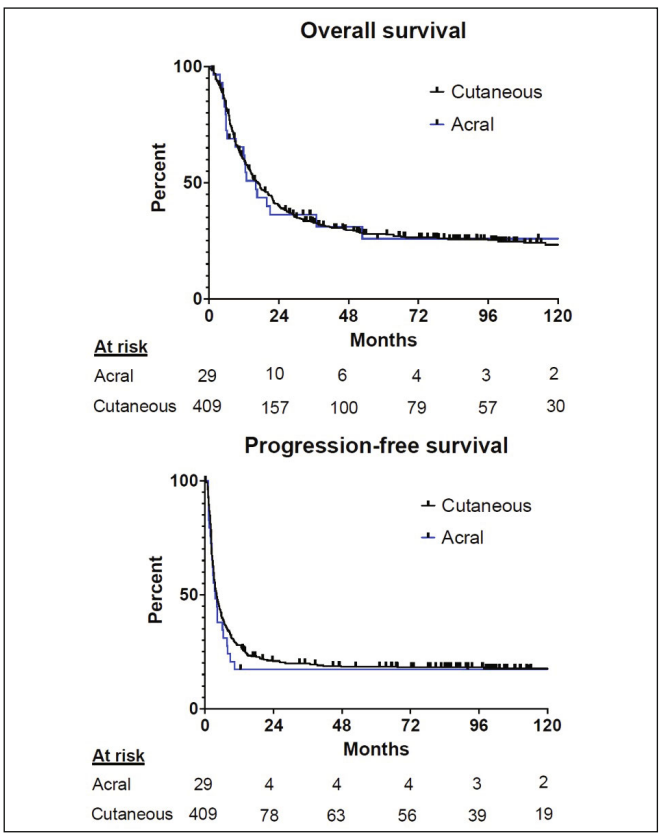


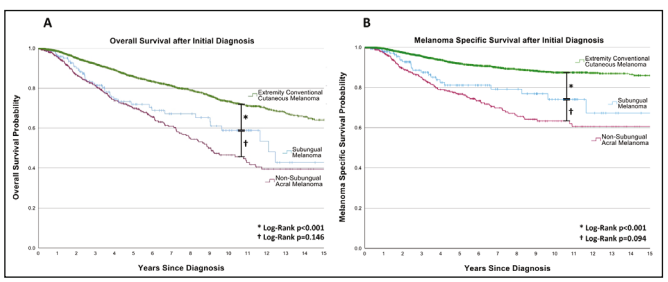
Figure 1. Overall survival and progression-free survival of acral and cutaneous melanoma patients after adoptive cell transfer.

65. Long-term outcomes and prognostic risk factors in subungual melanoma: An international series from the Sentinel Lymph Node Working Group

Cristian D Valenzuela, MD[1]; Kaiya Kozuma, BS[2]; Heidi E Kosiorek, MS[3]; Adrienne B Shannon, MD[4]; Matthew C Perez, MD[5]; Una Milovanovic, BS[6]; J Harrison Howard[7]; Cristina O'Donoghue, MD, MPH[8]; Schlomo Schneebaum, MD[9]; Barbara A Pockaj, MD[10]; Roger Olofsson Bagge, MD, PhD[11]; Richard L White[12]; Mohammed Kashani-Sabet, MD[13]; Stanley P Leong, MD[14]; Jonathan S Zager, MD[15]; John T Vetto, MD[16]

[1]Oregon Health & Science University, Portland, OR, US; [2]Oregon Health & Science University, Portland, OR, US; [3]Mayo Clinic, Rochester, MN, US; [4]Moffitt Cancer Center, Tampa, FL, US; [5]Moffitt Cancer Center, Tampa, FL, US; [6]Moffitt Cancer Center, Tampa, FL, US; [7]University of South Alabama, Mobile, AL, US; [8]Rush University Medical Center, Chicago, IL, US; [9]Tel Aviv Sourasky Medical Center, Tel Aviv, , IL; [10]Mayo Clinic Arizona, Phoenix, AZ, US; [11]Department of Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden, Gothenburg, , SE; [12]Atrium Health Levine Cancer Center, Charlotte, NC, US; [13]California Pacific Medical Center, San Francisco, CA, US; [14]California Pacific Medical Center, San Francisco, CA, US; [15]Moffitt Cancer Center, Tampa, FL, US; [16]Oregon Health and Science University, Portland, OR, US

INTRODUCTION: Subungual melanoma (SUM) is a rare subtype that historically has worse outcomes than conventional cutaneous melanoma. However, SUM remains poorly understood, as data has been limited to small case series. We report the largest case series of SUM, measuring outcomes and risk factors relative to anatomically-adjacent melanoma types: non-subungual acral melanoma (NSAM), and non-acral extremity conventional cutaneous melanoma (ECCM). **METHODS:** A retrospective review of an international collaborative database, the Sentinel Lymph Node Working Group, compared cases of SUM (n=184), NSAM (n=668), and ECCM (n=5308), that received surgical treatment including sentinel lymph node biopsy. Clinicopathologic variables and long-term outcomes were analyzed. Overall survival (OS), melanoma specific survival (MSS), and recurrence free survival (RFS) were estimated with the Kaplan-Meier method. Student's t-test, Chi-square, and Mann-Whitney U analyses compared appropriate variables. Multivariable Cox regression survival analysis was performed on relevant clinicopathologic variables in SUM. **RESULTS:** Median age for SUM (64.1 years) was similar to NSAM (62.3), but significantly higher than ECCM (59.5, p<0.001). Median Breslow thickness was comparable between SUM (2.4mm) and NSAM (2.4), but significantly thicker than ECCM (1.5, p<0.001). Ulceration was present in 49.2% of SUM, comparable to NSAM (45.5%), but significantly higher than ECCM (24.3%, p<0.001). Median OS was comparable between SUM and NSAM (145.1 vs 107.1 months, p=0.146), but was significantly worse than ECCM (236.5, p<0.001; Fig. 1A). MSS trended better for SUM compared to NSAM (p=0.094), but was significantly worse than ECCM (p<Fig. 1B). RFS was comparable between all three groups: 11.8-18.5 months (p>0.05). Multivariable analysis found increasing age, sentinel lymph node positivity, and absence of tumor infiltrating lymphocytes, were independently associated with increased hazard of death in SUM cases (p<0.05). Other factors including Breslow thickness, race, ulceration, microsatellitosis, and regression, were not independently associated with increased hazard of death in SUM (p>0.1). **CONCLUSIONS:** In terms of OS and MSS, SUM resembles NSAM more closely than ECCM. Age, tumor infiltrating lymphocytes, and sentinel node positivity are important factors for SUM long-term prognosis. With the largest SUM series to date, we further define long-term outcomes and prognostic risk factors in this rare melanoma.



66. Immunosuppressive macrophages generate a tolerogenic immune microenvironment in the sentinel lymph nodes in melanoma

Shankar Suman[1]; Wendy K Nevala[2]; Alexey A Leontovich[3]; James W. Jakub, MD[4]; Liyi Geng[5]; John A. Copland, PhD[6]; Sarah A McLaughlin[7]; Svetomir N Markovic[8]
[1]Mayo Clinic, Rochester, MN, US; [2]Mayo Clinic, Rochester, MN, US; [3]Mayo Clinic, Rochester, MN, US; [4]US; [5]Mayo Clinic, Rochester, MN, US; [6]Department of Cancer Biology, Mayo CLinic, Jacksonville, FL, US; [7]Mayo Clinic, Jacksonville, FL, US; [8]Mayo Clinic, Rochester, MN, US

INTRODUCTION: Cytokines are pivotal in facilitating cell communication within the tumor microenvironment (TME). Tumor-associated macrophages significantly influence the regulation of immunosuppressive cytokines, thereby promoting tumor metastasis. The elevation of Th2 cytokines in cancers is well-documented for suppressing anticancer immunity. However, the relationship between these cytokines and tumor-secreted extracellular vesicles (EVs) in generating immunosuppressive macrophages remains unknown. **METHODS:** Lymphatic fluid from a portion of the cutaneous melanoma draining lymphatic channels entering the sentinel lymph node (SLN) was collected along with a section of the SLN. Control lymphatic fluid was collected from post-operative lymphocele following breast surgery. We analyzed the altered cytokine profile using a cytokine array kit after treating EVs from THP1 monocytic cells-derived naïve macrophages and further validated with human blood-derived macrophages. We also compared the levels of cytokines in the blood of patients with metastatic melanoma (n=30) and healthy subjects (n=33) using the Luminex multiplex assay. The expression of cytokines and macrophage markers in normal and cancer tissues were evaluated in The Cancer Genome Atlas (TCGA) dataset. **RESULTS:** Our research revealed that EVs from lymphatic channels draining from a cutaneous melanoma into its SLN stimulate an increase in Th2 cytokines in naive macrophages, thereby reinforcing their tumor-supporting function. Remarkably, several of these cytokines were also elevated in the blood of patients with metastatic melanoma compared to healthy controls. Moreover, the TCGA dataset strongly correlates upregulated cytokines (CCL2, CCL4, IP10, IL8, and CXCL13) and the generation of immunosuppressive macrophages (CD209, CD163) in metastatic melanoma. Melanoma-derived EVs were also found to upregulate CD36 in macrophages, which can induce immunosuppressive function. Cutaneous melanoma patients show a higher proportion of CD36 in lymphatic EVs compared to the control (p=0.03). Spatial imaging data demonstrate that cells in tumor-involved SLNs exhibit a higher likelihood of CD36 expression than cells from control. **CONCLUSIONS:** Overall, our results suggest that tumor derived lymphatic EVs draining into the SLN directly modulate resident lymphatic macrophages in a fashion that permits metastatic melanoma survival, thereby creating a pre-metastatic niche.

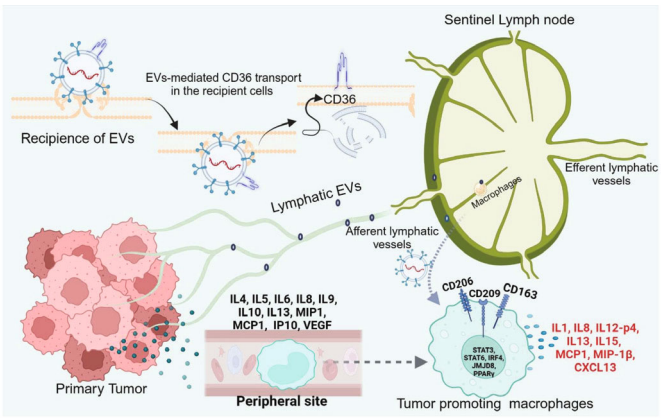


Figure. Primary-melanoma-secreted EVs and cytokines synergize to generate tumor-promoting macrophages and formation of premetastatic niche. Melanoma-secreted mediators contribute to creating a conducive environment for tumor proliferation by fostering the generation of tumor-promoting macrophages through exposure to melanoma-secreted EVs. These EVs upregulate CD36, thereby promoting immune evasion within the sentinel lymph node (SLN).

67. Peripheral Natural Killer cell transcriptomic features predict response to immune checkpoint blockade in patients with metastatic melanoma.

Piyush Kumar Sharma, MD PhD[1]; Chelsea Taylor, PhD[2]; Orion Tong, PhD[3]; Rosalin Cooper, MBBS PhD[4]; Robert A Watson, MBBS PhD[5]; Surya Koturan, PhD[6]; Alba Verge de los Aires[7]; Weiyu Ye, MBBS[8]; Isar Nassiri, PhD[9]; James Gilchrist[10]; Mark R Middleton, FRCP, PhD[11]; Benjamin P Fairfax, MRCP PhD[12]
[1]University of Miami Sylvester Cancer Center; University of Oxford, Miami, FL, US; [2]Department of Oncology, University of Oxford, Oxford, GB; [3]Department of Oncology, University of Oxford, Oxford, GB; [4]Department of Oncology, University of Oxford, Oxford, GB; [5]Department of Oncology, University of Oxford, Oxford, GB; [6]Department of Oncology, University of Oxford, Oxford, GB; [7]Department of Oncology, University of Oxford, Oxford, GB; [8]Department of Oncolgy, University of Oxford, Oxford, GB; [9]Department of Oncology, University of Oxford, Oxford, GB; [10]Weatherall Institute of Molecular Medicine, University of Oxford, Oxford, GB; [11]Churchill Hospital and University of Oxford, Oxford, GB; [12]Department of Oncology, University of Oxford, Oxford, GB

INTRODUCTION: Early changes in peripheral CD8+ T cell transcriptome and TCR repertoire have been shown to be predictive of response to immune check point blockade (ICB) in patients with metastatic melanoma (MM). Despite Natural Killer (NK) cells being indispensable for full therapeutic effect of ICB, its effect on peripheral NK cell transcriptome has hitherto remained uncharacterized. **METHODS:** We analysed 134 pre and post treatment peripheral NK cells transcriptomes from a prospectively maintained cohort of MM patients receiving anti-PD-1 alone (sICB) or in combination with anti-CTLA-4 (cICB) at Oxford University Hospitals. We also performed multi-parametric flow cytometry to assess changes in NK cell subsets and expression of cell surface and intracellular markers of NK cell cytotoxicity, maturation and activation. We quantified maximal variance in expression of genes associated with IFNγ, TNFα and Granzyme B as independent transcriptomic scores. **RESULTS:** By comparing baseline expression profiles (day 0) with those post-treatment (day 21) we identified 477 and 1100 transcripts (FDR<0.05) modulated by sICB and cICB respectively, which were far fewer than those modulated in CD8+ T cells. Gene sets preferentially modulated by cICB aligned with activation of mTORC1 complex and upregulation of mitotic and interferon pathways. We did not observe any change in frequency of circulating NK cell subsets with either sICB or cICB but noted a significantly higher proportion of $CD56^{dim}CD16^{bright}$ NK cells post treatment in responders post sICB treatment. For patients treated with cICB, pre-treatment granzyme B and post treatment IFNγ scores were linked with improved overall survival (OS) and progression free survival (PFS) probability (Fig 1 A, B) whereas for patients treated with sICB higher pre or post treatment TNFα scores were associated with improved OS probability (Fig 1 C, D). **CONCLUSIONS:** Analysis of peripheral NK cell transcriptomic signatures both before and during treatment holds prognostic potential in MM patients receiving ICB.

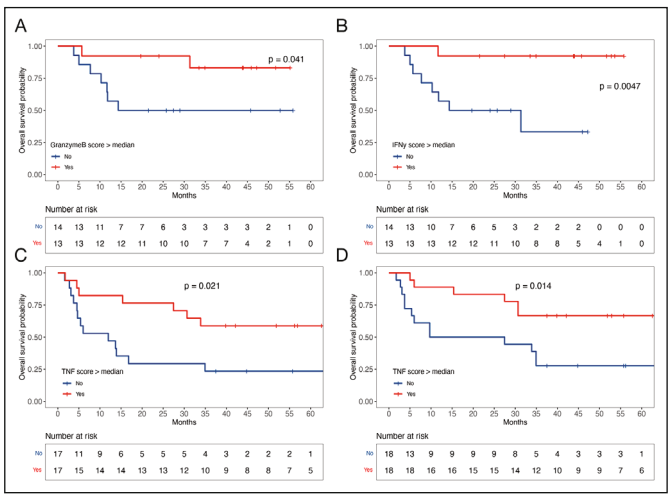


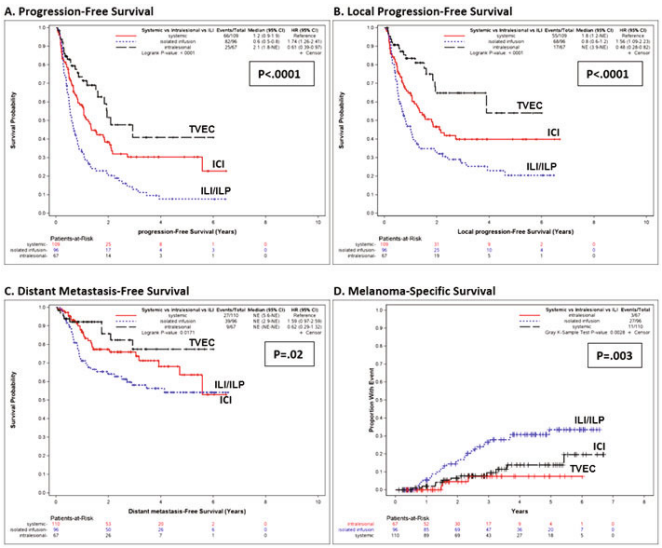
Figure 1. Kaplan-Meier curves showing improved OS probability in patients treated with cICB with higher than median (A) pre-treatment granzyme B score (B) post-treatment IFNγ score, and patients treated with sICB with higher than median TNFa scores (C) before and (D) after treatment (two-sided log-rank test).

68. A comparison of isolated limb infusion/perfusion, immune checkpoint inhibitors, and intralesional therapy as first-line treatment for patients with melanoma in-transit metastases

Michelle M. Dugan, MD[1]; Danielle K. DePalo, MD[2]; Syeda Mahrukh Hussnain Naqvi, MD, MPH[3]; David W. Ollila, MD[4]; Tina J. Hieken, MD[5]; Matthew S. Block, MD, PhD[6]; Winan J. van Houdt, MD, PhD[7]; Sophie J. M. Reijers, MD[8]; Nethanel Asher, MD[9]; Kristy K. Broman, MD, MPH[10]; Hayden Snow, MBBS[11]; Jeffrey M. Farma, MD, FACS[12]; John T. Vetto, MD[13]; Madison Kolbow, BS[14]; Robyn P.M. Saw, MBBS, MS[15]; Georgina V. Long, PhD, MBBS[16]; Lars Ny, MD, PhD[17]; Alexander C.J. Van Akkooi, MD, PhD[18]; Roger Olofsson Bagge, MD, PhD[19]; Jonathan S. Zager, MD[20]

[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4]University of North Carolina, Chapel Hill, NC, US; [5]Mayo Clinic, Rochester, MN, US; [6]Mayo Clinic, Rochester, MN, US; [7]Netherlands Cancer Institute, Amsterdam, NL; [8]Netherlands Cancer Institute, Amsterdam, NL; [9]Skin Cancer and Melanoma Center, Rabin Medical Center, Beilinson Hospital, Petah Tikva, IL; [10]University of Alabama at Birmingham, Birmingham, AL, US; [11]Peter MacCallum Cancer Centre, Melbourne, Victoria, AU; [12]Fox Chase Cancer Center, Philadelphia, PA, US; [13]Oregon Health and Science University, Portland, OR, US; [14]University of Minnesota, Minneapolis, MN, US; [15]Melanoma Institute Australia, Sydney, New South Wales, AU; [16]Melanoma Institute Australia, Sydney, New South Wales, AU; [17]Sahlgrenska University Hospital, Gothenburg, SE; [18]Melanoma Institute Australia, Sydney, New South Wales, AU; [19]Sahlgrenska University Hospital, Gothenburg, SE; [20]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Isolated limb infusion and perfusion (ILI/ILP) has been mainstay treatment for unresectable melanoma in-transit metastases (ITM), but use of immune checkpoint inhibitors (ICI) and intralesional therapies (talimogene laherparepvec (TVEC)) has increased management options. This study compares first-line ILI/ILP, ICI, and TVEC for unresectable ITM. **METHODS:** A retrospective review from 12 international institutions included patients treated from 2016–2022 with first-line ILI/ILP, ICI, or TVEC for unresectable melanoma ITM. **RESULTS:** 274 patients were treated, 120 female/154 male; 96 treated with ILI/ILP, 111 with ICI, and 67 with TVEC. Median follow-up was 3.3 years. Number of ITM and Breslow thickness were lowest for TVEC and highest for ILI/ILP (P<.001 and P=.03, respectively). TVEC was most used in stage IIIB disease, and ILI/ILP in stage IIIC/D (P=.003). There were no differences in complete response (CR) rates between treatment modalities. Stage IIIB disease had higher CR rates than stage IIIC (OR 3.8 (95% CI 1.2-12.7); P=.03). Median progression-free survival (PFS) was 0.6 years for ILI/ILP, 1.2 years for ICI, and 2.1 years for TVEC (P<.0001). Median local PFS (LPFS) was 0.8 years for ILI/ILP, 1.8 years for ICI, and not reached (NR) for TVEC (P<.0001). Median distant metastasis-free survival (DMFS) was NR for any treatment modality, but was longest for TVEC (P=.02). Melanoma-specific survival (MSS) at 1/3/5 years was 95%/73%/67% for ILI/ILP, 98%/90%/86% for ICI, and 100%/93%/93% for TVEC (P=.003). On multivariable analysis using ICI as the reference category, TVEC had the longest LPFS (HR 0.4 (95% CI 0.2-0.8); P=.01) and ILI/ILP had the shortest LPFS (HR 2.2 (95% CI 1.2-4.2); P=.01) and PFS (HR 1.8 (95% CI 1.2-2.6); P=.002). Stage IIIB disease was associated with longer PFS (HR 0.3 (95% CI 0.1-0.8); P=.011), DMFS (HR 0.2 (95% CI 0.06-0.5); P<.001), OS (HR 0.06 (95% CI 0.02-0.2);.001), and MSS (HR 0.1 (95% CI 0.05-0.4);.001), compared to stage IIID. **CONCLUSIONS:** In conclusion, TVEC had superior LPFS compared to ILI/ILP and ICI. TVEC should be considered as first-line therapy for unresectable stage IIIB melanoma ITM, particularly with a minimal tumor burden and thinner Breslow depth.



69. Local Recurrence Following Management of Primary Merkel Cell Carcinoma

Fergal G Kavanagh, MD, PhD[1]; Hannah Kalvin[2]; Edmund K. Bartlett, MD[3]; Christopher Barker[4]; Charlotte Ariyan[5]; Mary Brady[6]; Danielle Bello[7]; Klaus J. Busam, MD[8]; Kathy Panageas[9]; Daniel Coit[10]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Slaon Kettering Cancer Center, New York, NY, US; [7]Memorial Slaon Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Merkel cell carcinoma (MCC) is an uncommon neuroendocrine cutaneous malignancy believed to have a high risk for local recurrence (LR) after surgical excision alone. The current study describes a large cohort of patients undergoing excision of primary MCC to clarify the true risk of LR. **METHODS:** Patients with clinically localized MCC excised with pathologically negative surgical margins were identified from a prospectively maintained single institution database from 11/1980 to 12/2023. Data were collected on patient, tumor, and treatment variables. Patients were followed with attention to LR. The cumulative incidence of LR was determined. We attempted to develop a model of risk factors predicting LR. Fisher's exact test and Wilcoxon rank sum test were used to describe differences between groups. **RESULTS:** 447 patients with clinically localized disease who underwent excision with pathologically negative resections were identified. The median age was 72 years (IQR: 64-78); 57% were male. The median follow-up among survivors was 5.3 years. Tumor locations included extremities (52%), head and neck (31%), and trunk/buttock (17%). The median clinical tumor size was 12mm (IQR: 7-20mm) and lymphovascular invasion (LVI) was reported in 246 tumors (55%). 393 patients (88%) were treated with surgery alone, 54 patients (12%) were treated with surgery and adjuvant RT to the primary site. The median clinical margin width was 15mm. Patients treated with adjuvant RT were deemed to have higher risk features for LR than those who underwent resection only; tumors in surgery alone group: median size 12 (IQR 7,20) mm vs RT group: median size 20 (IQR 11,39) mm; p<0.001, more LVI (83% vs 55%);0.001. LR occurred in 8 patients (1 year LR rate 1.6%; 95% CI 0.72%-3.2%, Figure 1), 7 within 12 months of initial treatment, and all in the surgery alone group (see figure 1). Among patients who recurred median clinical margin was 12.5mm. At time of LR, patients were effectively treated with surgery alone (3 patients), surgery + RT (3 patients) and RT alone (2 patients). At a median follow up of 4.5 years following LR; 4 patients had no evidence of disease, 3 patients died of other causes and 1 patient subsequently developed distant metastatic disease and died of disease. LR was too infrequent to identify any risk factors contributing to that event. **CONCLUSIONS:** Negative margin surgery offers effective local control with a low LR rate of 1.6%. Patients who developed LR were effectively rescued with further local treatment. The low number of events precluded creation of a model to identify factors predicting risk

of LR. The routine use of adjuvant RT for all patients after complete excision of primary MCC is not supported by these findings.

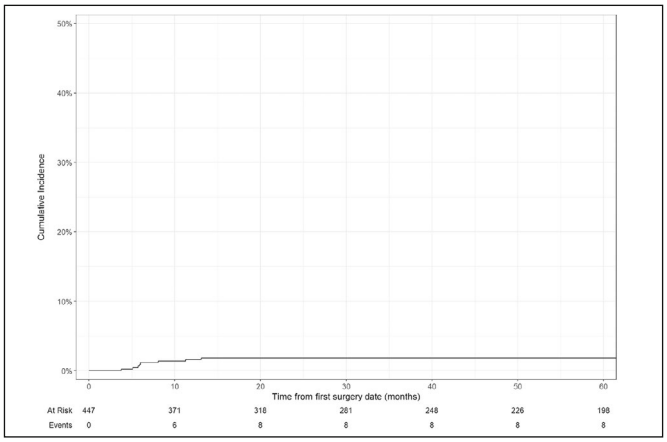


Figure 1. Cumulative incidence of local recurrence in patients that had surgery alone.

70. Outcomes of Patients Undergoing Sentinel Lymph Node Biopsy for Merkel Cell Carcinoma

Edmund K. Bartlett, MD[1]; Hannah Kalvin[2]; Christopher Barker[3]; Charlotte Ariyan[4]; Mary Brady[5]; Danielle Bello[6]; Joyce Chen[7]; Klaus J. Busam, MD[8]; Kathy Panageas[9]; Daniel Coit[10]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Slaon Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Merkel cell carcinoma (MCC) is a rare cutaneous malignancy with a propensity for nodal metastasis. Given the rarity of this malignancy and the variation in treatment patterns, characterization of the natural history of the disease remains limited. **METHODS:** All patients treated from 04/1996- 12/2022 with wide excision and sentinel lymph node (SLN) biopsy for clinically localized MCC were included from a prospectively maintained, single-institution database. Factors associated with a positive SLN were analyzed using logistic regression. Cumulative incidence functions were used to estimate recurrence and disease-specific death (DSD) with death from other causes as a competing risk. Competing risk regression was used to assess associations between outcomes of interest and pre-selected covariates. **RESULTS:** 342 patients with clinically localized MCC were identified. The median age was 70 (IQR: 63, 76) and the majority were male (60%). Tumors were located on the extremity (59%), head and neck (23%), and trunk (18%). Median tumor size was 1.4 cm (IQR: 0.8, 2.3) and lymphovascular invasion (LVI) was common (60%). The SLN was positive in 140 (41%). +SLN was associated with a larger tumor size (OR 2.2, p=0.006) and LVI (OR 3.2, p=0.001) after adjusting for time and primary tumor site. Even low risk patients (≤1cm tumors and without LVI) had a 17% incidence of +SLN. Of those patients with +SLN, 96% (134) underwent cross-sectional imaging (43 prior to surgery, 91 after finding +SLN), with metastasis detected in 2.2% (3/134). +SLN was the only factor identified to be independently associated with increased incidence of recurrence (39% vs. 12% at 5 years, OR 2.9, p<0.001). The 5-yr incidence of DSD was 3.5%, 10%, and 16% (p=0.002) for patients with Stage I, II, and IIIA respectively. Figure 1. Of the 202 with a negative SLN, only 6 recurred within 3 years in the same nodal basin, for a false-negative rate of 3.0%. 104 patients with a positive node were treated with adjuvant nodal basin radiation (RT), 11 underwent completion lymphadenectomy (CLND), 6 patients had both CLND and nodal RT, and 19 were observed. At 3 years, only 4 (2.9%) of these patients experienced a recurrence within the same nodal basin. **CONCLUSIONS:** SLN biopsy for patients with MCC is frequently positive and associated with an increased risk of recurrence and DSD. Even in the absence of identifiable risk factors for SLN metastasis, the SLN positivity rate is above 10%. SLNB appears to play an important prognostic role in MCC and guides exceptional regional control for both those with positive and negative SLNs.

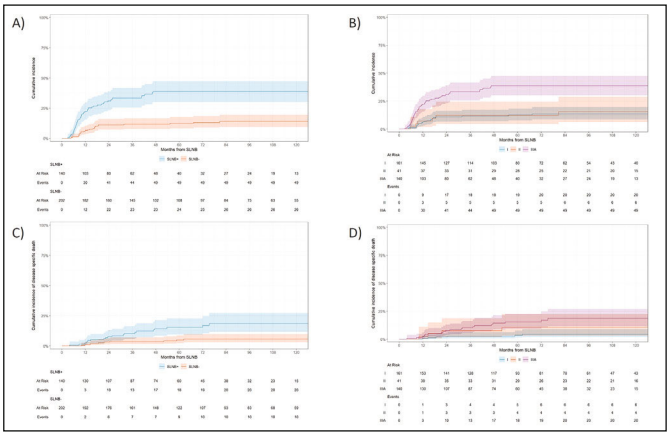


Figure 1. Outcomes in Merkel Cell Carcinoma following Wide Excision and Sentinel Lymph Node Biopsy. A) Cumulative incidence of recurrence by SLN status. B) Cumulative incidence of recurrence by pathological state. C) Cumulative incidence of disease specific death by SLN status. D) Cumulative incidence of disease specific death by pathological stage. Included patients were Stage IIIA due to positive SLN. Death from other cause was considered competing risk.

GI

71. International Multi-Institutional Validation Study of Novel Deep Machine Learning Artificial Intelligence Model to Predict Risk of Peritoneal Carcinomatosis in Gastric Cancer

Arsha Ostowari[1]; Kathryn T. Chen[2]; Oleksii Dobrzhanskyi[3]; Hyoung-Il Kim[4]; Jingjing Yu[5]; Bima J Hasjim[6]; Chanon Chantaduly[7]; Stefania Montero[8]; Brittany G Sullivan[9]; Yingjoy Li[10]; Shaun Daly[11]; Marcelo Hinojosa[12]; Brian Smith[13]; Ninh Nguyen[14]; Nataliya V Uboha[15]; Farshid Dayyani[16]; Peter D Chang[17]; Maheswari Senthil[18]

[1]University of California, Irvine Medical Center, Orange, CA, US; [2]Harbor-UCLA Medical Center, Torrance, CA, US; [3]Ukraine National Cancer Institute, Kiev, UA; [4]Yonsei University College of Medicine, Seoul, KR; [5]University of California, Irvine Medical Center, Orange, CA, US; [6]Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [7]University of California, Irvine School of Medicine, Irvine, CA, US; [8]Harbor-UCLA Medical Center, Torrance, CA, US; [9]Duke Department of Surgery, Durham, NC, US; [10]University of California, Irvine School of Medicine, Irvine, CA, US; [11]University of California, Irvine Medical Center, Orange, CA, US; [12]University of California, Irvine Medical Center, Orange, CA, US; [13]University of California, Irvine Medical Center, Orange, CA, US; [14]University of California, Irvine Medical Center, Orange, CA, US; [15]University of Wisconsin-Madison Department of Medicine, Madison, WI, US; [16]Universty of California, Irvine Medical Center, Orange, CA, US; [17]University of California, Irvine Medical Center, Orange, CA, US; [18]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US

INTRODUCTION: Image-occult peritoneal carcinomatosis (PC) occurs in about 30-40% of gastric cancer (GC) cases. Although staging laparoscopy is recommended, compliance is poor. In this study, we propose a deep learning artificial intelligence (AI) tool to assess the risk or presence of PC based on computed tomography (CT) scans. This study benefits from an international multi-ethnic cohort spanning three institutions to develop and evaluate model performance across diverse populations and hospital settings. **METHODS:** Patients with primary gastric/GEJ cancer treated at one of three institutions between 2010-2023 and who had pretreatment CTs available were included in the study. PC risk was defined as evidence of PC at the time of diagnosis or development of PC within the first year after diagnosis based on surgical and/or image findings. Clinical covariates including patient age, race, tumor stage, location, and grade were recorded. A convolutional neural network (CNN) based on the VGG-16 backbone with deep supervision was developed to predict PC risk. Clinical covariates were introduced to the CNN as a six-element feature vector concatenated to pooled feature maps generated by convolutional layers. In an initial experiment, only data from our institution was used to train a model. In a second experiment, data from all three institutions were pooled to develop a combined model. All experiments were evaluated using five-fold

cross-validation. **RESULTS:** The total cohort consisted of 255 patients with a median age of 60 years; in total; 137 (53.7%) were male, 108 (42.4%) were Hispanic, and 100 (39.2%) were White. Most tumors were poorly differentiated (n=183, 71.7%) and 94 (36.9%) had signet ring components. Utilizing only local institutional data, our CNN model combining pretreatment CTs and high-risk clinical features yielded a high accuracy for predicting PC risk with AUC 0.95, accuracy of 0.923, sensitivity of 0.986, positive predictive value (PPV) of 0.877 and negative predictive value (NPV) of 0.984. Utilizing the aggregate dataset, the combined model yielded similar high-performance characteristics with AUC of 0.948, accuracy of 0.933, sensitivity of 0.966, PPV of 0.943, and NPV of 0.903. **CONCLUSIONS:** We have developed and validated a deep learning AI model than can accurately predict the risk of PC in GC patients using pretreatment CTs and clinical risk factors. Improved accuracy of PC risk assessment can aid in developing risk-adjusted treatment approaches including consideration of intraperitoneal chemotherapy.

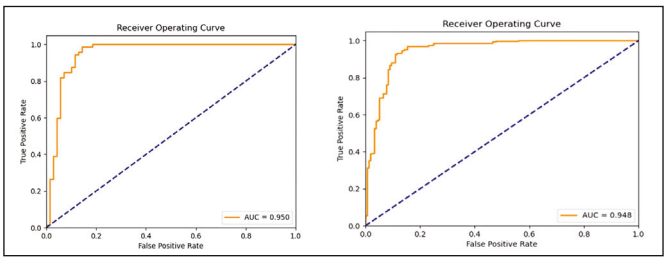


Figure 1. Deep learning model performance for characterization of PC risk using area under the receiver operating curve (AUC) demonstrating overall similar performance for (A) single local institutional cohort, and (B) aggregate multi-institutional international cohort.

72. Knockdown of the tumor suppressor FAM46C induces mesenchymal transformation in gastric adenocarcinoma

Ning Fu[1]; Karineh Kazazian[2]; Deanna Ng[3]; Shelly Luu[4]; Tao Wang, PhD[5]; Ream Abdullah[6]; Karina Pacholczyk[7]; Carol J Swallow[8]

[1]McMaster University, Hamilton, ON, CA; [2]University Health Network, Toronto, ON, CA; [3]University of Toronto, Toronto, ON, CA; [4]Mount Sinai Hospital, Toronto, ON, CA; [5]Toronto General Hospital, University Health Network, Toronto, ON, CA; [6]University of Toronto, Toronto, ON, CA; [7]Mount Sinai Hospital, Toronto, ON, CA; [8]Mount Sinai Hospital, Toronto, ON, CA

INTRODUCTION: In patients with node positive gastric adenocarcinoma (GCa), FAM46C loss in tumor tissue is associated with an adverse prognosis following curative intent resection (Luu et al., JGO 2024). The mechanism by which FAM46C exerts its tumor suppressive effect in GCa remains controversial. As a non-canonical RNA polymerase, FAM46C has the potential to alter gene expression through transcriptional regulation, yielding a more invasive cellular phenotype. **METHODS:** FAM46C and CDH1 gene expression in fresh frozen GCa specimens were examined by RNASeq. We used a xenograft NOD/SCID/Gamma mouse model to assess the effect of FAM46C depletion on AGS GCa tumor growth and invasion *in vivo*. One shGFP and two independent shFAM46C knockdown lines were created by lentiviral infection, and flank tumors induced by subcutaneous injection at 6 weeks of age (n=5 mice/group). Tumors were followed, excised at 9 weeks after injection, measured, examined with H&E staining, and gene expression measured by qPCR. Statistical comparison between groups was performed using one-way ANOVA and multiple comparisons test with Dunnett's correction. **RESULTS:** Loss of FAM46C was correlated with loss of the epithelial marker and cell adhesion protein CDH1 in human GCa (N=21, Welch two sample t-test). In the xenograft model, FAM46C knockdown caused faster GCa tumor growth (Fig 1. panels A-C, $p<0.03$), and more invasion into the surrounding soft tissue and underlying flank muscle (Fig 1. panels D, E, $p<0.0001$). This enhanced tumor progression was associated with alterations in expression of mesenchymal markers, with mean fold changes of 5.9, 2.1, 1.5 and 0.5 in SNAI2, TWIST, MMP-2 and VIM, respectively, between shFAM46C vs. shGFP AGS tumors grown *in vivo*. **CONCLUSIONS:** The subgroup of GCa with a mesenchymal phenotype are known to have a particularly poor prognosis. By upregulating expression of EMT genes, FAM46C loss can drive mesenchymal transformation, leading to more aggressive growth and invasion. Targeted pharmacologic restoration of FAM46C could rescue GCa cells back towards an epithelial phenotype.

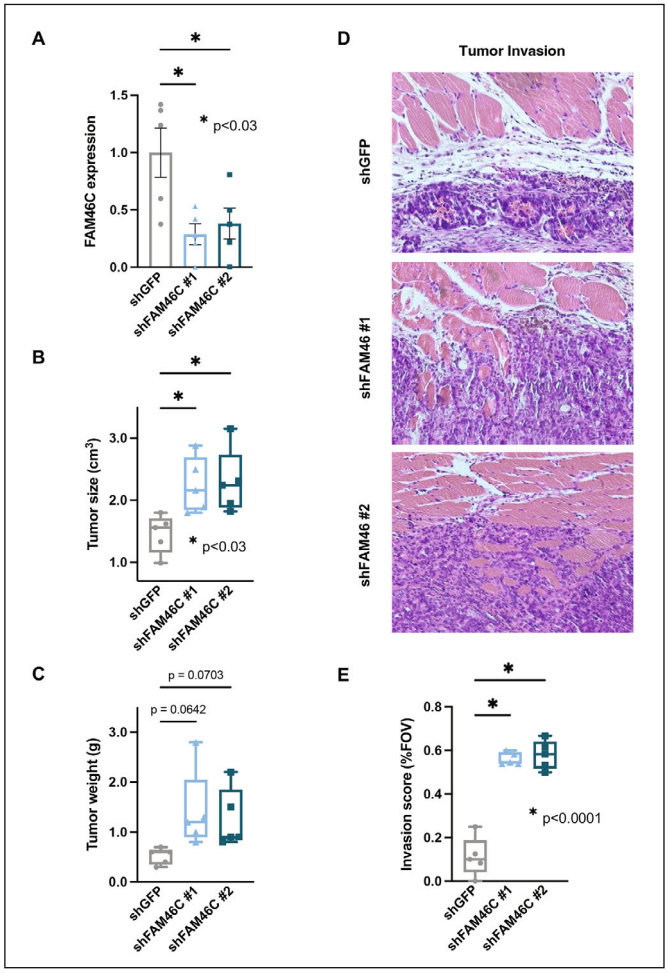


Figure 1. FAM46C knockdown in AGS xenografts increases tumor growth and invasion. A) mRNA expression (ΔΔCt) of FAM46C normalized to GAPDH in shFAM46C xenografts, relative to shGFP control. n=5 mice/group. Data are means ± SEM. B) Size and C) Weight of excised xenograft tumors. Boxes show median and IQR, whiskers represent full range. D) Representative sections of xenograft tumors showing microscopic appearance in relation to surrounding soft tissue, H&E stain. E) Invasion score, calculated as proportion of Fields od View (FOV) where invasion was present for each xenograft tumor.

73. Clinicogenomic comparison of early- and average-onset gastric cancer

Hannah McDonald, MD, PhD[1]; Anna Reagan, MD[2]; Abu Saleh Mosa Faisal, PhD[3]; Ryan Goettl, PhD[4]; Chi Wang[5]; Irada Ibrahim-Zada, MD[6]; Leah Winer, MD[7]; Prakash K. Pandalai, MD[8]; Michael Cavnar, MD[9]; Joseph Kim, MD[10]; Mautin Barry-Hundeyin, MD[11]

[1]University of Kentucky Department of Surgery, Lexington, KY, US; [2]University of Kentucky, Lexington, KY, US; [3]University of Kentucky, Lexington, KY, US; [4]University of Kentucky, Lexington, KY, US; [5]University of Kentucky, Lexington, KY, US; [6]University of Kentucky, Lexington, KY, US; [7]University of Kentucky, Lexington, KY, US; [8]University of Kentucky, Lexington, KY, US; [9]University of Kentucky, Lexington, KY, US; [10]University of Kentucky, Lexington, KY, US; [11]University of Kentucky, Lexington, KY, US

INTRODUCTION: In recent decades, there has been an unprecedented rise in gastric cancer among younger individuals, contrasting with a decline among older individuals. However, the biological underpinnings of gastric cancer in younger individuals remain poorly understood. We aimed to elucidate the clinicopathologic and genomic characteristics of early onset gastric cancer (EOGC) compared to average onset gastric cancer (AOGC). **METHODS:** Using the prospective Oncology Research Information Exchange Network (ORIEN) database, we compared demographic, clinicopathologic, genomic, and survival outcomes between EOGC (≤50 years) and AOGC (>50 years). Kaplan-Meier curves compared overall survival (OS). Whole exome

sequencing data were processed to identify significant somatic mutations. RNASeq data facilitated differential gene expression, pathway enrichment, and immune cell deconvolution analyses. **RESULTS:** We analyzed 166 patients including 40 with EOGC and 126 with AOGC. The median age at diagnosis was significantly lower in the EOGC group (45 vs 66 years; p<0.0001). There were no differences in body mass index, race, smoking, or alcohol consumption. EOGC patients exhibited significantly higher rates of pain at diagnosis (57% vs 29% p=0.004), but not anemia or reflux. EOGC patients were more likely to present with stage III/IV disease (70% vs 45% p<0.01) and diffuse/signet ring histology (57.5% vs 24% p=0.0002). Consequently, OS was decreased in the younger cohort (HR 0.54; p=0.041). Somatic mutational load was decreased in young patients (p=0.009). Significantly mutated genes in the entire cohort included *CDH1*, *ARID1A*, *P53*, *PIK3CA*, *TGFBR2* and *TYRO3,* but *CDH1* was more frequently mutated in EOGC (47% vs 19% p=0.001). Significant differences in RNA expression were observed, with upregulated epithelial cell signaling in H. pylori, *P53* signaling, and DNA damage repair. Immune deconvolution revealed a predominance of M2 macrophages, mast cells, and CD4^{+} T cell subsets, but no differences between cohorts. **CONCLUSIONS:** Young patients with gastric cancer have a unique clinicogenomic signature. They are more likely to present with aggressive disease characterized by pain, advanced stage, diffuse/signet histology, poorer OS, diminished mutational load and higher CDH1 mutational frequency. Pathway dysregulation in EOGC may contribute to tumorigenesis and therapy resistance. This study underscores the need for further research into novel therapies and biomarker discovery in younger individuals.

74. Mapping the precancer immune microenvironment of diffuse gastric cancers using single-cell resolution spatially resolved transcriptomics

Amber F Gallanis, MD[1]; Yunhe Liu[2]; Cassidy Bowden[3]; Sun A Kim[4]; Andrew M Blakely[5]; Jonathan M Hernandez[6]; Linghua Wang[7]; Jeremy L. Davis, MD[8]
[1]National Cancer Institute, National Institutes of Health, Bethesda, MD, US; [2]MD Anderson Cancer Center, Houston, TX, US; [3]National Cancer Institute, National Institutes of Health, Bethesda, MD, US; [4]National Institutes of Health, Bethesda, MD, US; [5]National Institutes of Health, Bethesda, MD, US; [6]National Institutes of Health, Bethesda, MD, US; [7]MD Anderson Cancer Center, Houston, TX, US; [8]National Cancer Institute, Bethesda, MD, US

INTRODUCTION: Occult, early-stage (pT1a) signet ring cell (SRC) lesions are an expected finding in individuals with germline *CDH1* loss-of-function variants, irrespective of age and family history of gastric cancer. SRC lesions exhibit clinically indolent behavior; however, the drivers of progression to advanced gastric cancer remains unknown. We investigated the tumor immune microenvironment (TIME) of early SRC to determine how the precancer niche may contribute to tumorigenesis. **METHODS:** We performed a spatial transcriptomic analysis using the 10X Genomics Xenium platform at subcellular resolution of early (pT1a) SRC lesions from twelve patients with germline *CDH1* mutations at risk of hereditary diffuse gastric cancer. A customized gastric cancer panel based on previous SRC whole transcriptomic analysis and a pre-designed 10X Genomics Multi-Tissue and Cancer panel were used for analysis. SRC TIME was investigated using a 50µm perimeter around the cancer region of interest and single-cell profiling strategy. Enrichment analyses using KEGG database and gene ontology were performed. **RESULTS:** Sub-cellular spatial transcriptomic analysis demonstrated 63 genes (9.1%, 63/694) were differentially expressed between early-stage SRC lesions and adjacent non-SRC gastric tissue ($p<0.05$, $\log_2FC\geq2$). Multiple differentially expressed genes were related to extracellular matrix (ECM) remodeling and epithelial-to-mesenchymal transition, including *COL3A1*, *COL1A2*, *VIM*, and *FXYD5*; and immune cell infiltration and trafficking, including *ALDH1A3*, *RGS1*, *DCN*, and *CPA3*. Mapping of the SRC TIME demonstrated significantly larger immune (p=0.002), proliferating (p=0.003), and stromal (p=0.047) compartments compared to non-SRC adjacent gastric tissue. Within the immune compartment, plasma cells (p=0.004) and macrophages (p=0.009) were more abundant within the SRC TIME. Enrichment analyses of differentially expressed genes in plasma cells (*FAM3D*, *SCGB2A1*, *C15orf48*) and macrophages (*CTSE*, *FCGR3A*, *PIGR*) in the SRC TIME demonstrated upregulation of inflammatory responses to antigenic stimulus and antigen processing, immune receptor activity, and antigen presentation. **CONCLUSIONS:** High-resolution spatial transcriptomic analysis of the SRC TIME demonstrates an expanded immune compartment with enrichment of immunogenic factors, which may contribute to the indolent behavior of precancerous signet ring cell lesions that are frequent among *CDH1* variant carriers.

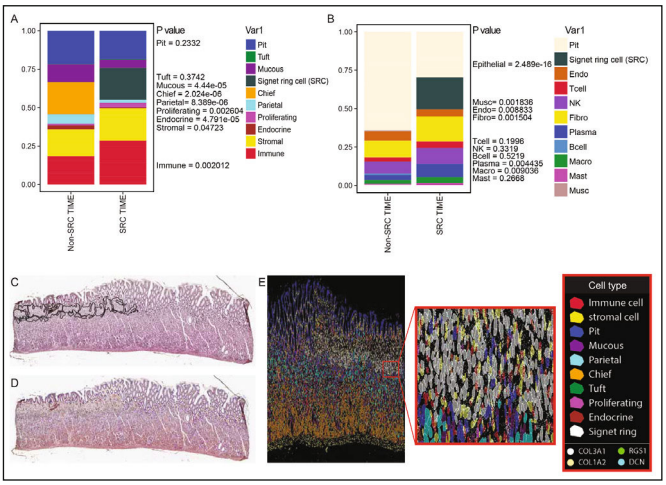
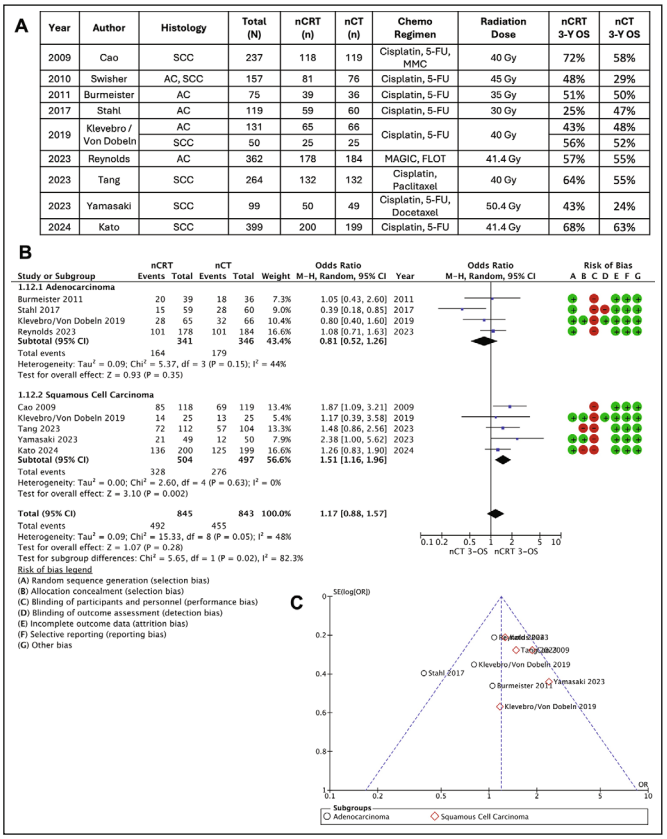


Figure 1. Composition of signet ring cell (SRC) lesion and non-SRC tumor immune microenvironments with annotation of (A) epithelial and (B) immune compartments. (C) Hematoxylin and eosin stained gastric tissue with SRC outlined and (D) multi-modal segmentation. (E) High-resolution spatial transcriptomic segmentation of SRC tumor immune microenvironment including gene transcripts of interest.

75. Neoadjuvant chemoradiation or chemotherapy for esophageal cancer – a histology-stratified update meta-analysis of randomized controlled trials

Andrew M Fleming, MD[1]; Brendan Sheridan, MD[2]; Angel Doño, MD[3]; Theresa Dinh, MD[4]; Jane Zhao, MD, MS[5]; Thomas Ng, MD[6]; Danny Yakoub, MD, PhD[7]
[1]The University of Tennessee Health Science Center / St. Jude Children's Research Hospital, Memphis, TN, US; [2]Department of Surgery, The University of Tennessee Health Science Center, Memphis, TN, US; [3]Department of Surgery, The University of Tennessee Health Science Center, Memphis, TN, US; [4]Department of Surgery, The University of Tennessee Health Science Center, Memphis, TN, US; [5]Department of Surgery, The University of Tennessee Health Science Center, Memphis, TN, US; [6]Department of Surgery, The University of Tennessee Health Science Center, Memphis, TN, US; [7]Department of Surgery, Augusta University Medical Center, Augusta, GA, US

INTRODUCTION: The benefit of neoadjuvant radiation for localized esophageal squamous cell carcinoma (SCC) and adenocarcinoma (AC) remains controversial. The current study comprises a histology-stratified pooled analysis of data from randomized controlled trials (RCTs) comparing neoadjuvant chemoradiation (nCRT) to neoadjuvant chemotherapy alone (nCT) for esophageal cancer (EC). **METHODS:** A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 -compliant systematic review was performed (PROSPERO ID: CRD42024509325) (IRB 24-09847-NHSR). RCTs comparing nCRT to nCT for EC were included. Random-effects meta-analysis was performed. Histology-stratified pooled odds ratios (OR) with 95% confidence intervals (CI) were calculated. Heterogeneity, publication bias, and study quality were assessed. **RESULTS:** Data from 9 RCTs published from 2009-2024 were included, comprising 1,893 patients (947 nCRT, 946 nCT) (Figure 1A). Most received cisplatin with 5-fluorouracil, and median radiation dose was 40.0 gray. Patients with SCC undergoing nCRT vs. nCT more often made it to resection (OR 1.94; CI 1.05—3.60, P=.03), and had a pathologic complete response (ypCR) (OR 11.4; CI 3.73—34.79, p<.0001), with similar odds of R0 resection (OR 2.18; CI 0.81—5.90; P=.12) and anastomotic leaks (OR 0.91; CI 0.55—1.49; P=.70). For AC, nCRT associated with similar resection rates (OR 0.92; CI 0.46—1.80; P=.80), but higher rates of ypCR (OR 3.88; CI 2.00—7.51; P<.0001), and more R0 resections (OR 4.21; CI 2.28—7.79;.00001) with similar leak rates (OR 0.96; CI 0.52— P=.91). nCRT was associated with a decreased number of local recurrences for SCC (OR 0.58; CI 0.40—0.86; P=.006), but not AC (OR 1.04; CI 0.70—1.53; P=.86) (subgroup test P=.04) and increased odds of 3-year overall survival for SCC (OR 1.51; CI 1.16—1.96; P=.002), but not AC (OR 0.81;1.26; P=.35) (subgroup test P=.02) (Figure 1B). There was no funnel plot asymmetry, and only 1 study fell outside the pseudo 95% CI (Figure 1C). **CONCLUSIONS:** The addition of neoadjuvant radiation appears to confer meaningful improvement in long -term outcomes for SCC, but not AC.



Year	Author	Histology	Total (N)	nCRT (n)	nCT (n)	Chemo Regimen	Radiation Dose	nCRT 3-Y OS	nCT 3-Y OS
2009	Cao	SCC	237	118	119	Cisplatin, 5-FU, MMC	40 Gy	72%	58%
2010	Swisher	AC, SCC	157	81	76	Cisplatin, 5-FU	45 Gy	48%	29%
2011	Burmeister	AC	75	39	36	Cisplatin, 5-FU	35 Gy	51%	50%
2017	Stahl	AC	119	59	60	Cisplatin, 5-FU	30 Gy	25%	47%
2019	Klevebro / Von Dobeln	AC	131	65	66	Cisplatin, 5-FU	40 Gy	43%	48%
		SCC	50	25	25			56%	52%
2023	Reynolds	AC	362	178	184	MAGIC, FLOT	41.4 Gy	57%	55%
2023	Tang	SCC	264	132	132	Cisplatin, Paclitaxel	40 Gy	64%	55%
2023	Yamasaki	SCC	99	50	49	Cisplatin, 5-FU, Docetaxel	50.4 Gy	43%	24%
2024	Kato	SCC	399	200	199	Cisplatin, 5-FU	41.4 Gy	68%	63%

76. DNA methylation-based liquid biopsy model for the identification of lymph node metastasis in patients with early gastric cancer

Keisuke Okuno[1]; Adwait Joshi[2]; Shuichi Watanabe[3]; Sakiko Asano[4]; Masanori Tokunaga[5]; Yusuke Kinugasa[6]

[1]Department of Gastrointestinal Surgery, Institute of Science Tokyo, Tokyo, JP; [2]Imperial College School of Medicine, London, GB; [3]Department of Hepatobiliary and Pancreatic Surgery, Institute of Science Tokyo, Tokyo, JP; [4]Department of Gastrointestinal Surgery, Institute of Science Tokyo, Tokyo, JP; [5]Department of Gastrointestinal Surgery, Institute of Science Tokyo, Tokyo, JP; [6]Department of Gastrointestinal Surgery, Institute of Science Tokyo, Tokyo, JP

INTRODUCTION: Early gastric cancer (EGC) is defined as a cancer that is limited to the mucosa or submucosa, and most patients with EGC have no lymph node metastasis (LNM), with rates of 3% for T1a and 20% for T1b EGC. However, due to the difficulty of accurate preoperative diagnosis of LNM, many EGC patients receive invasive radical gastrectomy with lymphadenectomy. To prevent overtreatments and occurrence of postgastrectomy syndromes, there is an imperative clinical need for the development of biomarkers that can accurately identify LNM prior to treatment. In this study, we established a cell-free DNA (cfDNA) methylation-based liquid biopsy assay for the pretreatment identification of LNM for patients with EGC. **METHODS:** A comprehensive biomarker discovery was performed through analyzing publicly accessible genome-wide DNA methylation profiling. DNA methylation-based biomarkers were validated in 191 formalin-fixed, paraffin-embedded (FFPE) clinical specimens using quantitative methylation-specific polymerase chain reaction (qMSP) assays. Finally, these biomarkers were translated into liquid biopsy assay by analyzing cfDNA extracted from plasma specimens of 100 patients with EGC using qMSP assays. **RESULTS:** We identified 6 novel differentially methylated regions, which were regions within 100bp including at least two differentially methylated CpG probes (|Delta-beta| >0.12 and P <0.05), through analyzing genome-wide DNA methylation profiling. Using qMSP assays in FFPE clinical specimens, pretreatment LNM-identification model was established through multivariate logistic regression analyses, with an area under the curve (AUC) value of 0.85. Finally, this model was translated into a liquid biopsy assay using qMSP assays in cfDNA specimens, and this liquid biopsy model can robustly identify LNM in EGC patients with an AUC value of 0.84. The diagnostic performance of this model was further improved by combining with common clinicopathological features. **CONCLUSIONS:** We successfully established a cfDNA methylation-based liquid biopsy diagnostic assay for the pretreatment identification of LNM in patients with EGC. This model has the potential to guide optimal and less invasive treatment options for patients with EGC.

77. Postoperative chemotherapy may not confer survival benefit for patients who experience pathologic complete response in treatment of stage I gastric cancer

Siqi Cao Brough[1]; Jasmine Huynh[2]; Madison Herin[3]; David Lee[4]

[1]Inova Fairfax Medical Campus, Falls Church, VA, US; [2]Inova Fairfax, Falls Church, VA, US; [3]Inova Farifax, Falls Church, VA, US; [4]Inova Fairfax, Falls Church, VA, US

INTRODUCTION: For patients with locally advanced gastric cancer, perioperative chemotherapy is recommended before and after surgery. However, as systemic treatment improves, benefit of adjuvant chemotherapy for patients with pathologic complete response (pCR) may not be significant for a subset of patients. The aim of this study is to identify patients with pCR who may not benefit from additional chemotherapy. **METHODS:** We analyzed data from National Cancer Database (NCDB) from 2004 to 2020. We included patients with stage I-III gastric cancer who underwent neoadjuvant chemotherapy and curative intent gastrectomy who had a pCR. We then compared overall survival (OS) of those who went on to receive adjuvant treatment to those who did not receive further treatment. Patients were stratified by AJCC cancer stage. **RESULTS:** We identified 592 patients who had primary tumor pathologic complete response on surgical specimen. We compared the outcomes of 183 patients who received both neoadjuvant and adjuvant chemotherapy to the 409 who received neoadjuvant only. Patients receiving further adjuvant chemotherapy were younger (63 years vs 65; p=0.03). There were no significant differences between the two groups in sex (71% male), race (57% white), Charlson-Deyo comorbidity score, tumor location, tumor grade or type of gastrectomy. Tumor histologies included 431 (73%) adenocarcinoma of unspecified type, 81 (14%) signet ring cell carcinoma, 66 (11%) intestinal type adenocarcinoma, 6 (<1%) diffuse type carcinoma, 4 mucinous adenocarcinoma, 3 tubular adenocarcinoma and 1 papillary adenocarcinoma; there were no differences in histology types between the two groups. Patients receiving further adjuvant chemotherapy were more likely to have greater than 15 lymph nodes harvested (77% vs 66%, p=0.01). On multivariable analysis, adjuvant chemotherapy was not associated with longer OS for patients with stage I disease (HR 0.76, 95% CI 0.36 – 1.58; p=0.49) – it was, however, associated with longer OS in patients with either stage II (HR 0.43, 95% CI 0.23 – 0.81, p=0.009) or stage III disease (HR 0.34, 95% CI 0.19 – 0.60, p=0.0002), adjusting for year of diagnosis, age, sex, race/ethnicity, tumor grade, lymphadenectomy >15, and signet ring cell histology. **CONCLUSIONS:** In this study of patients from NCDB with gastric cancer and pathologic complete response following neoadjuvant chemotherapy, adjuvant chemotherapy was associated with longer OS for patients with stage II and III disease but not for patients with stage I disease.

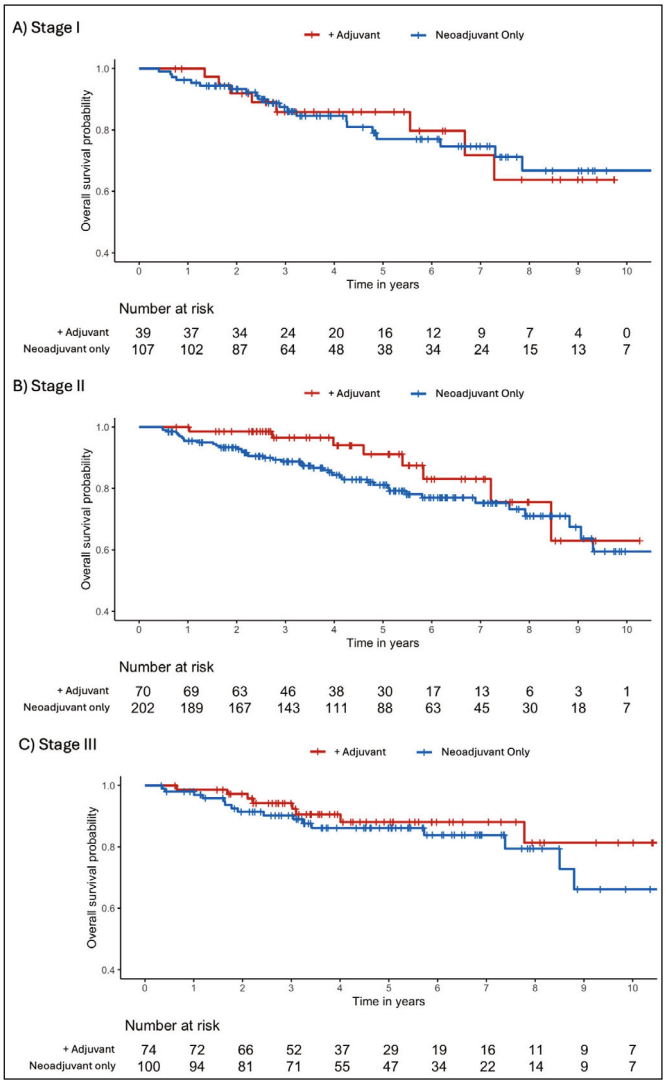


Figure 1. Impact of adjuvant chemotherapy on overall survival for patients with pathologic complete response following neoadjuvant chemotherapy.

78. Upfront Surgery Versus Neoadjuvant Chemotherapy for cT2N0M0 Gastric Cancer

Jessica A Steadman, MBBS[1]; EeeLN Buckarma, MD[2]; Mojun Zhu[3]; Mark Truty[4]; Cornelius Thiels[5]; Michael L Kendrick, MD[6]; Travis E. Grotz, MD, FSSO[7]
[1]Mayo Clinic, Rochester, MN, US; [2]Mayo Clinic, Rochester, MN, US; [3]Mayo Clinic, Rochester, MN, US; [4]Mayo, Rochester, MN, US; [5]Mayo Clinic, Rochester, MN, US; [6]Mayo Clinic, Rochester, MN, US; [7]Mayo Clinic, Rochester, MN, US

INTRODUCTION: While surgery alone may be adequate for early gastric adenocarcinoma (GC), locally advanced GC benefits from neoadjuvant chemotherapy (NAC). Stage Ib (cT2N0M0) lies in the transition from early versus locally advanced GC and there is limited data regarding the best management in Western populations. **METHODS:** Patients with clinical stage Ib (cT2N0M0) GC on endoscopic ultrasound (EUS) and subsequently underwent gastrectomy at a single institution between 2000-2023 were included in this retrospective review. Patients were stratified by upfront surgery (UFS) or NAC. Primary outcomes of interest were overall survival (OS) and recurrence-free survival (RFS) from the date of diagnosis. Secondary outcomes were accuracy of clinical staging, and rates of receiving peri-operative therapy. Cox proportional hazards regression models were used to evaluate RFS and OS before and after adjusting for age. **RESULTS:** Of 61 patients included in the study, 27 (44%) received NAC and 34 received UFS. The two groups were well balanced in terms of baseline demographic, clinical and pathological variables except for age. The UFS cohort were older (median age 71 IQR 66-81 years) than the NAC cohort (67 IQR 61-78 years) (p = 0.004). NAC patients received more cycles of therapy, median 8.0 (IQR 5.0-8.0) vs 5.0 (IQR 3.8-8.0), p=0.08. In UFS patients, EUS correctly staged GC in only 3 (9%) patients, understaged 23 (68%) and overstaged 8 (24%). Adjuvant therapy was recommended to the 23 understaged UFS patients. Of them, only 11 (48%) initiated adjuvant therapy and 7 completed therapy. Reasons for non-receipt of adjuvant therapy were poor performance status (n=5) and patient refusal (n=7). OS and RFS were significantly longer in the NAC group vs UFS (figure) (OS HR=0.37, 95% CI 0.15-0.91, p=0.03; RFS HR=0.36, 95% CI 0.15-0.89, p = 0.02) in univariate analysis. After adjusting for age, NAC was no longer associated with improved OS or RFS (p = 0.2). **CONCLUSIONS:** In patients who underwent UFS, more than two thirds were understaged by EUS and less than half received adjuvant therapy. NAC resulted in a trend towards completion of more cycles of chemotherapy and was associated with significantly improved OS and RFS in univariate analysis. These data suggest NAC may be beneficial in patients with stage 1b (cT2N0M0) GC.

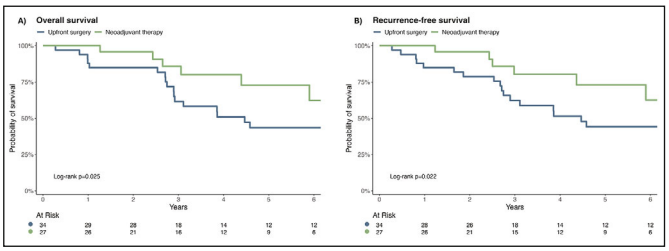


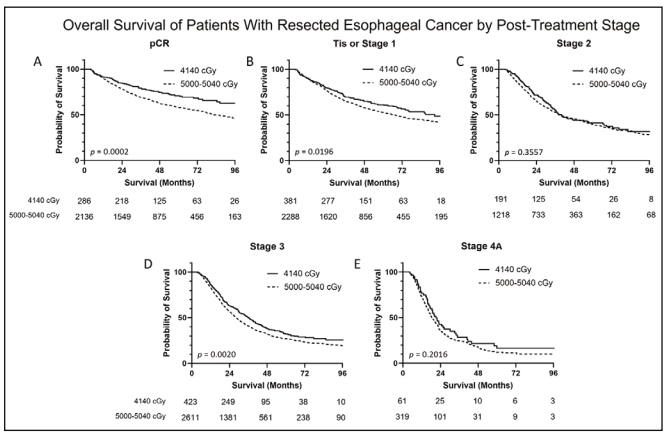
Figure. Kaplan Meier curve showing overall survival (A) and recurrence free survival (B) in cohort of 61 stage Ib gastric cancer patients treated with upfront surgery vs neoadjuvant chemotherapy.

79. Higher Neoadjuvant Radiation Dose is Associated with Lower Overall Survival in Resected Esophageal Cancer: A Propensity-Matched National Cancer Database Analysis

Thomas L Sutton, MD MCR[1]; Ranish Patel, MD[2]; Mohamed Elsheikh, MD[3]; Cymon Kersch[4]; Aaron G Grossberg[5]; Alia Qureshi[6]; John Hunter[7]; Nima Nabavizadeh, MD[8]; Stephanie Wood, MD[9]
[1]Cedars-Sinai Medical Center, Los Angeles, CA, US; [2]Oregon Health & Science University, Portland, OR, US; [3]Oregon Health & Science University, Portland, OR, US; [4]Oregon Health & Science University, Portland, OR, US; [5]Oregon Health & Science University, Portland, OR, US; [6]Oregon Health & Science University, Portland, OR, US; [7]Oregon Health & Science University, Portland, OR, US; [8]Oregon Health & Science University, Portland, OR, US; [9]Oregon Health & Science University, Portland, OR, US

INTRODUCTION: Following publication of the Chemoradiotherapy for Oesophageal Cancer Followed by Surgery Study (CROSS), neoadjuvant chemoradiation has become standard of care for most esophageal cancer (EC). Patients most commonly receive either 41.4 Gy (per CROSS) or 50-50.4 Gy, but few data comparing outcomes in the post-CROSS era have been reported. **METHODS:** A retrospective review of the National Cancer Database (NCDB) was performed for patients with EC receiving neoadjuvant chemoradiation followed by resection in the NCDB from 2012-2020 (n=10,810). Patients were grouped by neoadjuvant radiation dose (41.4 Gy or 50-50.4 Gy). Overall survival (OS), post-treatment stage, and receipt of 41.4 Gy dosing were evaluated in the cohort using Kaplan-Meier and Cox proportional hazards modeling, following propensity-score matching based on relevant clinicopathologic characteristics. **RESULTS:** 10,810 patients were identified with 1,450 (13.4%) receiving 41.4 Gy of radiation and 9,360 (86.6%) receiving 50-50.4 Gy. Pathologic complete response (pCR) was higher in patients receiving 50-50.4 Gy versus 41.4 Gy (22.8% versus 19.7%, P=0.009). Median duration of follow-up was 61.6 months from diagnosis (range 3-132.7 months). Median OS was 59.9 months (95% CI 51.6-68.1 months) in patients receiving 41.4 Gy and 45.5 months for patients receiving 50-50.4 Gy (95% CI 43.4-47.5 months, log-rank P<0.001). Following stratification for post-treatment stage, 41.4 Gy dosing remained associated with improved OS compared to 50-50.4 Gy acoss stages, but was most pronounced for patients with pCR (median OS 110.0 vs 82.4 months, P<0.001) and Tis or Stage I residual disease (median OS 92.8 vs. 67.2 months, P=0.02, Figure). Propensity matching yielded 1,458 clinicopathologically similar patients per group. On multivariable analysis, receipt of 41.4 Gy was independently associated with improved OS (HR 0.82, 95% CI 0.76-0.89, P<0.001). **CONCLUSIONS:** In the first large nationwide database study in the post-CROSS era, lower neoadjuvant radiation dosage is associated with

improved OS following resection of EC, with the greatest improvement in patients with pCR or near-pCR. Until prospective trials are completed, higher radiation doses should be reserved for definitive treatment in patients ineligible for surgery due to potential harms derived from higher radiation doses.



80. Endoscopic resection vs gastrectomy for early stage gastric cancer: the impact and predictors of nodal upstaging

Omid Salehi[1]; Abdul Saied Calvino[2]; Ponnandai Somasundar[3]; N Joseph Espat[4]; Mohammad Ali[5]; Sasha L Lightfoot, DO[6]; Sung Kwon, MD MPH[7]
[1]Roger Williams Medical Center, Providence, RI, US; [2]Roger Williams Medical Center, Providence, RI, US; [3]Roger Williams Medical Center, Providence, RI, US; [4]Roger Williams Medical Center, Providence, RI, US; [5]Roger Williams Medical Center, Providence, RI, US; [6]Roger Williams Medical Center, Providence, RI, US; [7]Roger Williams Medical Center, Providence, RI, US

INTRODUCTION: Endoscopic resection (ER) is increasingly favored as a first-line curative treatment over surgery for early gastric cancer (EGC) with minimal risk of lymph node metastasis. Our objective is to explore predictors of pathologic nodal upstaging that are important to consider when considering ER vs. gastrectomy. **METHODS:** A retrospective analysis of the National Cancer Database from 2010 to 2021 for patients with cT1aN0M0 gastric adenocarcinoma was performed stratified by ER vs. gastrectomy. Our main outcomes of interest were overall survival (OS) and pathologic nodal positivity rates. Multivariate logistic regression and Cox proportional hazards models were used. **RESULTS:** 1848 patients were identified; 766 (41.5%) had ER, 1082 (58.5%) had gastrectomy. On average, ER patients were more likely to be male (71.5% vs 60.5%, p<.01), older (69.7 ± 11 vs 65.4 ± 13.2 years, and white (86.0% vs 76.3%, p<.01). ER tumors were smaller (10mm [IQR 5-15] vs 15mm [IQR 8-30], lower grade (82.6% vs 56.5% well and moderately differentiated, more often found in the cardia (74.8% vs 35.1%, lower rate of LVI (8.4% vs 15.3%, and less signet morphology (2.6% vs 20.7%, p=.02). ER resulted in higher margin positivity (15.3% vs 4.4%, shorter length of stay (0 [IQR 0-0] vs 7 [IQR 5-11] days, and fewer readmissions (2.0% vs 7.2%, p<.01). Median OS was comparable between ER and gastrectomy (134.3 vs 137.8 months, p=.58), however 5-year OS was worse for ER (38.8% vs 48.7%, p<.01). Predictors of pathological nodal upstaging included tumor size (OR 1.03, 95% CI 1.01-1.04, poor differentiation (OR 2.55, 95% CI 1.04-6.24, p=.04), LVI (OR 14.44, 95% CI 8.4-24.84, p<.01) and margin positivity (OR 3.74, 95% CI 1.39-10.05, p=.01), while female sex was protective (OR 0.51, 95% CI 0.28-0.94, p=.03). The 5-year survival in pN0 patients was similar between ER and gastrectomy (45.2% vs 52.6%, p=.35). **CONCLUSIONS:** In the real-world practice of EGC treatment, ER is predominantly used in smaller, lower grade tumors with lower rate of LVI and signet morphology yet was associated with a lower 5-year survival compared to gastrectomy. Importantly, ~15% of gastrectomy patients had nodal upstaging on pathology and the 5-year survival was similar among those with pN0 status. We found tumor size, grade, margin positivity, and particularly LVI to be important clinical predictors of pathologic nodal upstaging that should be considered in EGC treatment decision-making.

Best Papers II

81. Primary efficacy, safety, survival, and initial biomarker data from the registration-intended cohort of patients with anti–PD-1–failed melanoma from the IGNYTE trial of RP1 plus nivolumab

Georgia Beasley, MD, MHSc[1]; Caroline Robert, MD, PhD[2]; Mohammed M Milhem, MBBS[3]; Joseph J Sacco, MBChB, MSc, MRCP, PhD[4]; Judith Michels, MD, PhD[5]; Gino K In, MD[6]; Eva Muñoz-Couselo, MD, PhD[7]; Dirk Schadendorf, MD[8]; Jiaxin Niu, MD, PhD[9]; Bartosz Chmielowski, MD, PhD[10]; Trisha M Wise-Draper, MD, PhD[11]; Tawnya L Bowles, MD[12]; Katy K Tsai, MD[13]; Céleste Lebbé, MD, PhD[14]; Caroline Gaudy-Marqueste, MD, PhD[15]; Mark R Middleton, FRCP, PhD[16]; Adel Samson, PhD[17]; Junhong Zhu, PhD[18]; Marcus Viana, MD[19]; Michael K Wong, MD, PhD[20]
[1]Duke University, Durham, NC, US; [2]Gustave Roussy and Paris-Saclay University, Villejuif, FR; [3]Holden Comprehensive Cancer Center, University of Iowa, Iowa City, IA, US; [4]The Clatterbridge Cancer Centre and University of Liverpool, Liverpool, GB; [5]Département de Médecine Oncologique, Gustave Roussy, Villejuif, FR; [6]University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA, US; [7]Vall d'Hebron Institute of Oncology (VHIO) and Vall d'Hebron Hospital Medical Oncology Department, Barcelona, ES; [8]West German Cancer Center, University Hospital Essen, Essen, DE; [9]Banner MD Anderson Cancer Center, Gilbert, AZ, US; [10]Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, CA, US; [11]University of Cincinnati Cancer Center, University of Cincinnati, Cincinnati, OH, US; [12]Intermountain Medical Center, Murray, UT, US; [13]Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA, US; [14]Université Paris Cité, AP-HP Dermato-Oncology and CIC, Cancer Institute APHP. Nord–Université Paris, Paris, FR; [15]Aix-Marseille Université, APHM, Centre de Recherche en Cancérologie de Marseille (CRCM), INSERM, U10, Marseille, FR; [16]Churchill Hospital and University of Oxford, Oxford, GB; [17]Leeds Institute of Medical Research at St. James's, University of Leeds, Leeds, GB; [18]Replimune, Inc., Woburn, MA, US; [19]Replimune, Inc., Woburn, MA, US; [20]University of Texas MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Treatment options for patients (pts) with advanced melanoma that has progressed on anti–PD-1 therapy are limited and associated with high toxicity. RP1 (vusolimogene oderparepvec) is an HSV-1–based oncolytic immunotherapy expressing GM-CSF and a fusogenic glycoprotein (GALV-GP-R−). The registration-intended cohort of the IGNYTE trial tested RP1 + nivolumab (nivo) in pts with advanced melanoma (NCT03767348). **METHODS:** Pts with unresectable advanced melanoma and confirmed progression on treatment with anti–PD-1 alone or combined with anti–CTLA-4 for ≥8 weeks as the last prior treatment, including as adjuvant therapy, were enrolled. RP1 was given intratumorally at 1×10^6 PFU/mL initially, then Q2W at 1×10^7 PFU/mL for up to 7 doses (≤10 mL/cycle) combined with nivo (240 mg IV); nivo was then given alone (240 mg Q2W or 480 mg Q4W IV) for up to 2 years, with further RP1 allowed if indicated. The primary endpoint was ORR by independent central review (ICR) using modified RECIST (mRECIST) v1.1. **RESULTS:** Of the 140 enrolled pts, 48.6% had stage IVb/c/d disease, 65.7% had primary anti–PD-1 resistance, 56.4% were PD-L1–negative, 37.9% had BRAF mutations, 46.4% had prior anti–PD-1 + anti–CTLA-4 therapy, and 25.7% had anti–PD-1 as adjuvant therapy only. The confirmed ORR by ICR was 33.6% (15.0% CR) by mRECIST v1.1. Responses were observed in injected and non-injected, including visceral lesions. Among responders, 98.7% of injected (n=79) and 98.4% of non-injected lesions (n=123) had reductions, with 93.7% and 79.7%, respectively, reduced by ≥30%. The median (range) DOR was 21.6 (1.2–43.5) months. Table 1 lists ORR by clinical subgroup. One-, 2-, and 3-year overall survival (OS) rates were 75.3%, 63.3%, and 54.8%, respectively; median OS was not reached. Most treatment-related adverse events (TRAEs) were grade 1–2 (grade 3–4: 12.8%). Initial biomarker assessment showed immune activation as measured by increased CD8+ T-cell infiltration (20/50) and PD-L1 levels (CPS; 26/49) vs baseline in available biopsies. **CONCLUSIONS:** RP1 + nivo was well tolerated and provided durable, clinically meaningful antitumor activity in pts with advanced melanoma and confirmed disease progression on prior anti–PD-1 therapy, including in poor prognostic subgroups. TRAEs were mostly grade 1–2. Biomarker analysis from tumor biopsies showed that RP1 + nivo increased CD8+ T-cell infiltration and PD-L1 expression, demonstrating that the combination can treat anti–PD-1–refractory disease.

Table 1. ORR by clinical subgroup

	ORR n/N (%)
All patients	**47/140 (33.6)**
Subgroups	
Stage IIIb-IVa	29/72 (40.3)
Stage IVb-IVd	18/68 (26.5)
Primary anti-PD-1 resistance	33/92 (35.9)
Secondary anti-PD-1 resistance	14/48[a] (29.2)
Single agent anti-PD-1	29/75 (38.7)
Prior anti-PD-1 + anti-CTLA-4	18/65 (27.7)
Prior anti-PD-1 as adjuvant	16/36 (44.4)
Prior anti-PD-1 not as adjuvant	31/104 (29.8)

[a]Includes 1 patient with unknown resistance status.

CTLA-4, cytotoxic T-lymphocyte antigen 4; ORR, objective response rate; PD-1, programmed cell death protein 1.

82. Genomic differences between primary tumor and lymph node metastasis in patients with clinically node-positive breast cancer: Prospective cohort study within TAXIS (OPBC-03, SAKK 23/16, IBCSG 57-18, ABCSG-53, GBG 101)

Michael Knauer[1]; Daniel Egle[2]; Stefanie Hayoz[3]; Ákos Sávolt[4]; Christoph Tausch[5]; Susanne Bucher[6]; Colin Simonson[7]; Rok Satler[8]; Jörg Heil[9]; Inga Bekes[10]; Vesna Bjelic-Radisic[11]; William Audeh[12]; Giang Thanh Lam[13]; Ryu Jai Min[14]; Simone Muenst[15]; Valerijus Ostapenko[16]; Christian Kurzeder[17]; Miranda Kleijn[18]; Walter Paul Weber[19]

[1]Tumor and Breast Center Eastern Switzerland, St. Gallen, CH; [2]ABCSG, Austrian Breast and Colorectal Cancer Study Group; Breast Cancer Center Tirol, Department of, Vienna; Innsbruck, AT; [3]Competence Center of SAKK, Bern, CH; [4]Department of Breast and Sarcoma Surgery, National Institute of Oncology, Budapest, HU; [5]Breast Centre Zurich, Zurich, CH; [6]Lucerne Cantonal Hospital, Lucerne, CH; [7]Department of Gynecology, Centre Hospitalier du Valais Romand (CHVR), Hôpital de Sion, Sion, CH; [8]Breast Center, Cantonal Hospital Winterthur, Winterthur, CH; [9]Breast Center Heidelberg, Heidelberg, DE; [10]Breast Center, St. Gallen Cantonal Hospital, St. Gallen, CH; [11]Breast Unit, Helios University Clinic, University Witten/Herdecke, Wuppertal, DE; [12]Agendia NV, Amsterdam, NL; [13]Breast Center, University Hospital of Geneva, Geneva, CH; [14]Samsung Medical Center, Gangnam-gu, Seoul, KR; [15]University of Basel; Institute of Medical Genetics and Pathology, University Hospital Basel, Basel, CH; [16]National Cancer Institute, Vilnius, LT; [17]University of Basel; Breast Clinic, University Hospital Basel, Basel, CH; [18]Agendia NV, Amsterdam, NL; [19]University of Basel; Breast Clinic, University Hospital Basel, Basel, CH

INTRODUCTION: The correlation between gene expression analyses from the primary tumor and lymph node metastases in patients with breast cancer is currently unclear, which limits the use of molecular tests in nodal tissue. In this study, we investigated differences in risk classification and subtyping between the primary tumor and the corresponding lymph node metastases by use of two established molecular assays. **METHODS:** The study was prespecified within the international phase III TAXIS trial, which investigates the safety of omission of axillary dissection in patients with clinically node-positive breast cancer in the upfront surgery setting and in case of residual disease after neoadjuvant therapy. A total of 38 European centers provided samples and clinical data. Core needle biopsies or surgical samples from primary tumors and corresponding metastatic lymph nodes were assessed by two different multigene expression analyses. Results of the multigene tests were compared to clinical risk assessment based on established clinical risk factors and subtypes as assessed by immunohistochemistry (IHC). The primary aim of this study was to compare molecular subtype and recurrence risk between the primary tumor and the metastatic lymph node. **RESULTS:** Eighty-nine patients with stage II/III breast cancer and a median age of 63 years were included in this study. Lymph node metastases were palpable in 58% of patients and detected by imaging in 42%. In 16%, there was discordance in risk categorization between the primary tumor and lymph node metastasis according to MammaPrint (K=0.64). BluePrint showed consistent results for subtype between primary tumor and nodal metastases (84% overall agreement and 100% for basal and Her2-subtypes). 92% of patients were categorized as high risk by clinical assessment, whereas only 65% were classified as high risk by MammaPrint; risk agreement was 69% (K=0.13). Breast Cancer Subtype comparison between IHC and genomic assessment showed agreement in 58% (K=0.29) – no disagreement was shown regarding basal-like and Her2-positive cancers. **CONCLUSIONS:** In this preplanned translational study, the genomic risk differed substantially between primary tumor and nodal disease. Therefore, the present results limit the applicability of molecular tests in nodal tissue, for example in occult breast cancer or external referrals where the primary tumor tissue is no longer available for analysis.

83. Surgical considerations around neoadjuvant therapy in melanoma: surgical outcomes from the randomized phase 3 Nadina trial

Anke Kuijpers[1]; Winan J. van Houdt, MD, PhD[2]; Piotr Rutkowski[3]; Dirk Grunhagen[4]; Serigne Lo[5]; Andrew Spillane[6]; Robyn P.M. Saw, MBBS, MS[7]; Martin Klop[8]; Thomas Pennington[9]; Charlotte Zuur[10]; Kerwin Shannon[11]; Sydney Ch'ng[12]; David E. Gyorki, MD, MBBS[13]; Mark Faries[14]; Michael Rtshiladze[15]; Richard Scolyer[16]; Bart van der Wiel[17]; Georgina Long[18]; Christian Blank[19]; Alexander C.J. Van Akkooi, MD, PhD[20]

[1]Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, NL; [2]Netherlands Cancer Institute, Amsterdam, NL; [3]Maria-Sklodowska-Curie National Research Institute of Oncology, Warsaw, PL; [4]Erasmus MC, Rotterdam, NL; [5]Melanoma Institute Australia, Sydney, AU; [6]Melanoma Institute Australia, Sydney, AU; [7]Melanoma Institute Australia, The University of Sydney, Sydney, New South Wales, Australia, Sydney, New South Wales, AU; [8]Netherlands Cancer Institute, Amsterdam, NL; [9]Melanoma Institute Australia, Sydney, AU; [10]Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, NL; [11]Melanoma Institute Australia, Sydney, AU; [12]Melanoma Institute Australia, Sydney, AU; [13]Division of Cancer Surgery, Peter MacCallum Cancer Centre, and Sir Peter MacCallum Department of O, Melbourne, Victoria, AU; [14]The Angeles Clinic and Research Institute, Los Angeles, CA, US; [15]Melanoma Institute Australia, Sydney, AU; [16]Melanoma Institute Australia, Syendy, AU; [17]Netherlands Cancer Institute, Amsterdam, NL; [18]Melanoma Institute Australia, Sydney, AU; [19]Netherlands Cancer Institute, Amsterdam, NL; [20]Melanoma Institute Australia, Sydney, AU

INTRODUCTION: The recently published NADINA trial (Blank et al. NEJM 2024) randomized patients with resectable macroscopic stage III melanoma to either two cycles of neoadjuvant ipilimumab 80 mg plus nivolumab 240 mg Q3W followed by surgery, or upfront surgery followed by 12 cycles of adjuvant nivolumab (480 mg Q4W). The aim of this study was to evaluate whether neoadjuvant checkpoint inhibition in the NADINA trial altered surgical outcomes compared to surgery upfront. **METHODS:** Patients who underwent a therapeutic lymph node dissection (TLND) within the trial were included. We analyzed surgical adverse events according to the Clavien-Dindo (CD) scores at 3 and 12 weeks. In addition, we defined textbook outcome as no complications ≥CD2 / no re-admissions / R0 / no re-operation. Differences between arms were assessed using t-test for continuous outcomes and Chi-squared test for categorical outcomes. **RESULTS:** Out of the 423 randomized patients, 15 were excluded due to being non-evaluable, resulting in a total of 408 patients included in this analysis. The pathological outcomes were comparable between the neoadjuvant and upfront surgery groups, with both groups exhibiting similar numbers of lymph nodes resected (mean 22 vs. 20, NS) and equivalent rates of R0 resections (85.6 vs. 87.1%, NS). In general, CD scores were similar between arms at 3 and 12 weeks, however surgery was delayed in 34 patients in the neoadjuvant arm compared to 5 patients in the adjuvant arm (16% vs. 2%, p<0.001). Drug-related toxicity accounted for 50% of the delay in the neoadjuvant arm. The most prevalent complication after surgery was seroma (37.3 vs. 39.1 %, NS), followed by surgical site infection (20.2 vs. 21.7%, NS). The only complication that differed between groups was thromboembolic events, which occurred in 5 patients in the neoadjuvant arm and did not occur in the upfront surgery arm (p=0.021). Re-operation rates (5.1 vs 3.9%, re-admission rates (9.6 vs. 8.3 %, NS) and re-intervention rates (30.8 vs 28.8%, NS) did not differ either. Textbook outcome was evaluable in 296 patients and was not significantly different between groups with 47.7% of patients in the neoadjuvant group and 57.1% of patients in the upfront surgery group meeting the textbook outcome criteria (NS). **CONCLUSIONS:** Patients receiving neoadjuvant immunotherapy demonstrate comparable surgical outcomes to those undergoing upfront surgery overall, except for the risk of delay of surgery and the risk of thromboembolic events.

84. Targeting neutrophil extracellular traps improves efficacy of immunotherapy in colorectal liver metastasis

Kaelyn C Cummins[1]; Yunwei Zhang[2]; Susan J Kim[3]; Samantha M Ruff[4]; Hongji Zhang[5]; Allan Tsung[6]
[1]University of Virginia Health, Charlottesville, VA, US; [2]University of Virginia Health, Charlottesville, VA, US; [3]University of Virginia Health, Charlottesville, VA, US; [4]University of Virginia Health, Charlottesville, VA, US; [5]University of Virginia Health, Charlottesville, VA, US; [6]University of Virginia Health, Charlottesville, VA, US

INTRODUCTION: Immune checkpoint inhibitors (ICI) restore the anti-tumor function of T cells. While they are effective in microsatellite instability-high (MSI-H) colorectal cancer (CRC) tumors, little progress has been made in their treatment of microsatellite stable (MSS) tumors, which make up 85% of CRCs. Thus, identifying new therapeutic strategies and ways to sensitize MSS tumors to ICI therapy is critical. Neutrophil extracellular traps (NETs) play a vital pro-tumorigenic role in the microenvironment of CRC liver metastases (CRCLM) and are associated with worse prognosis. Our recent findings show that disruption of NETs with DNase I significantly reduces the growth of CRCLM in MSI-H murine models. We set out to better understand the role of NETs in MSS CRCLM to identify novel therapeutic applications. **METHODS:** To model MSS CRCLM, CT26 CRC cells were injected into the portal vein of mice. Tumor growth was measured by *in vivo* bioluminescent imaging weekly and gross tumor nodules were counted upon sacrifice three weeks after surgery. Anti-PD-1 or IgG2a isotype antibody and DNase I were administered intraperitoneally on post-operative day 5. Bulk RNA sequencing for tumor cells was conducted. CD45+ immune cell populations and CD8+ T cell function in the tumor were quantified by flow cytometry. **RESULTS:** ICI treatment alone improved survival in murine models of MSI-H but not MSS CRCLM. Adding DNase I in an MSS model resulted in decreased tumor-associated neutrophils and NET formation *in vivo*, reduced resistance to anti-PD-1 blockade, and attenuated tumor growth. Expression of MMR proteins MSH2 and MSH6 was significantly reduced in the combination treatment group compared to ICI treatment alone; multiple tumor suppressor genes were also upregulated. Neutrophil infiltration into the TME and NET formation were both decreased in mice treated with combination therapy, while CD8+ infiltration was increased. Inhibiting NETs with DNase I reverses ICI resistance by reducing expression of MMR proteins in tumor cells and increases CD8+ T cell infiltration and cytotoxicity compared to anti-PD-1 treatment alone. **CONCLUSIONS:** Five-year survival for patients with CRCLM remains low (~30%). These findings represent a novel approach to targeting the tumor microenvironment using DNase I in combination with ICIs in MSS tumors. This impactful work has the potential to expand ICI use to the majority of CRC patients with MSS tumors.

85. Total Neoadjuvant therapy (TNT) for locally advanced gastric cancer results in improved completion rates of intended therapy

EeeLN Buckarma, MD[1]; Shelby Yee, MD[2]; Robert Veirkant[3]; Emily L Siegler[4]; Mojun Zhu, MD[5]; Cornelius Thiels[6]; Mark Truty[7]; Michale Kendrick[8]; Travis E. Grotz, MD, FSSO[9]
[1]Mayo Clinic, Rochester, MN, US; [2]Mayo Clinic, Rochester, MN, US; [3]Mayo Clinic, Rochester, MN, US; [4]Mayo Clinic, Rochester, MN, US; [5]Mayo Clinic, Rochester, MN, US; [6]Mayo Clinic, Rochester, MN, US; [7]Mayo, Rochester, MN, US; [8]Mayo, Rochester, MN, US; [9]Mayo Clinic, Rochester, MN, US

INTRODUCTION: Perioperative chemotherapy (PC) is currently the standard of care for locally advanced gastric cancer (LAGC). In practice, this strategy can be difficult to implement with many patients unable to complete adjuvant therapy. A total neoadjuvant therapy (TNT) approach may result in improved patient adherence and outcomes. **METHODS:** Single institution retrospective review of LAGC from 2008 to 2023. Associations of therapy strategy with clinical, pathological, and perioperative outcomes were examined using multivariable linear regression and multivariable logistic regression. Kaplan-Meier curves and cox proportional hazards regression models were used for DFS and OS. **RESULTS:** Of the 202 patients who met inclusion criteria, 71 (35%) were treated with TNT and 131 (65%) with a PC strategy. The two groups were well matched with no differences in baseline demographics, clinical stage, tumor grade or location. Patients treated with TNT received more cycles of perioperative treatment (median 8, IQR 6-9) compared to a PC strategy (median 6, IQR 4-8) ($p < 0.001$). Only 65% of the PC patients, initiated adjuvant chemotherapy and only 43% of those patients completed ≥ 3 cycles. There was no significant difference in postoperative EBL, hospital length of stay, readmissions or morbidity between TNT and PC. There was a similar (20% vs 22%) rate of pCR, and margin negative resections (99% vs 98%) between groups, respectively. TNT approach was associated with improved 18-month RFS and 5-year OS on univariate but not multivariable analysis. Significantly, more (93%) patients in the TNT group received ≥ 6 cycles of chemotherapy compared to PC (50%), $p = 0.002$. Patients who received ≥ 6 cycles of chemotherapy were found to have improved 18-month RFS and 5-year OS (figure) when compared to those who received < 5 (RFS HR=2.93, 95%CI 1.59-5.41, $p<0.001$, OS HR=2.32, 95%CI 1.39-3.92, $p = 0.002$). This remained significant on multivariable analysis. **CONCLUSIONS:** The TNT strategy for LAGC results in a higher rate of completing all intended therapy. The completion of ≥ 6 cycles of chemotherapy was independently associated with improved recurrence free and overall survival.

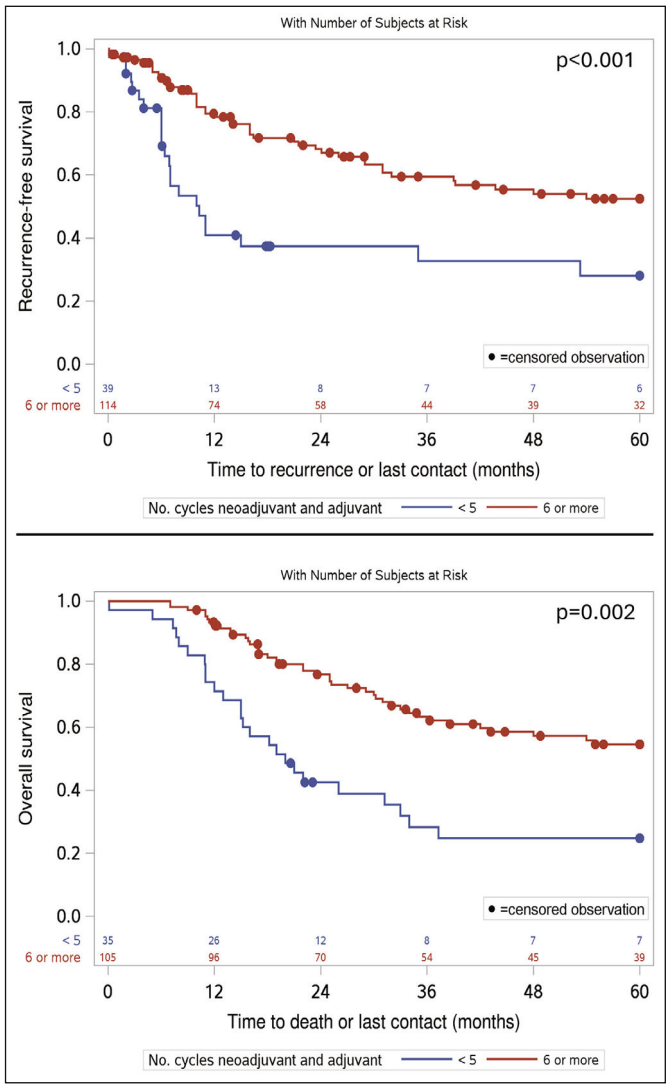


Figure. Kaplan Meier curves showing recurrence free and overall survival by number of chemotherapy cycles.

86. Phase II Study of Organ Preservation in Node-negative low Rectal Cancer : Updated Clinical and Patient Reported Outcomes

Hannah Buettner, MD[1]; Vanessa Wookey, MD[2]; Jeffrey M. Farma, MD, FACS[3]; Joshua Meyer, MD[4]; Eric Ross, PhD, ScM[5]; Erika Jerome, MA, MS[6]; Tanu Singh, MS, PhD[7]; Ryan Romasko[8]; Rosanna Veggeberg, MS[9]; Efrat Dotan, MD[10]; Michael J Hall, MD, MS, FASCO[11]; Matthew Philp, MD[12]; Juhi Mittal, MD[13]; Katrina Bynum[14]; Stephanie Greco, MD, FACS[15]; Sanjay S Reddy, MD, FACS[16]; Elin Sigurdson, MD, PhD, FACS, FRCS[17]; Namrata Vijayvergia, MD[18]
[1]Fox Chase Cancer Center, Philadelphia, PA, US; [2]Fox Chase Cancer Center, Philadelphia, PA, US; [3]Fox Chase Cancer Center, Philadelphia, PA, US; [4]Fox Chase Cancer Center, Philadelphia, PA, US; [5]Fox Chase Cancer Center, Philadelphia, PA, US; [6]Fox Chase Cancer Center, Philadelphia, PA, US; [7]Fox Chase Cancer Center, Philadelphia, PA, US; [8]Fox Chase Cancer

Center, Philadelphia, PA, US; [9]Fox Chase Cancer Center, Philadelphia, PA, US; [10]Fox Chase Cancer Center, Philadelphia, PA, US; [11]Fox Chase Cancer Center, Philadelphia, PA, US; [12]Lewis Katz School of Medicine at Temple University, Philadelphia, PA, US; [13]Fox Chase Cancer Center, Philadelphia, PA, US; [14]Fox Chase Cancer Center, Philadelphia, PA, US; [15]Fox Chase Cancer Center, Philadelphia, PA, US; [16]Fox Chase Cancer Center, Philadelphia, PA, US; [17]Fox Chase Cancer Center, Philadelphia, PA, US; [18]Fox Chase Cancer Center, Philadelphia, PA, US

INTRODUCTION: Total mesorectal excision (TME) is a highly effective treatment for rectal cancer (RC) but is associated with significant morbidity and mortality. Organ preservation (OP) approaches for locally advanced RC have been successful but not well studied for node-negative (NN) low RC. The objective of this investigator-initiated trial (IIT) is to determine the feasibility of performing successful local excision (LE) after neoadjuvant chemotherapy (CTX) in NN low RC. **METHODS:** With IRB approval, patients (pts) with clinical stage T1-3, N0 low rectal adenocarcinomas (<6 cm from anal verge) were included in this single arm phase II IIT. Pts received 6 cycles of FOLFOX (5-FU bolus 400 mg/m2 and infusion 2400 mg/m2, Leucovorin 400 mg/m2, Oxaliplatin 85 mg/m2). Those with evidence of a response underwent LE (transanal excision) 6-12 weeks later. To target occult nodal metastases and reduce in-bowel recurrences, LE was followed by chemoradiotherapy ([CXRT] capecitabine 825 mg/m2 and long course RT to 54 Gy). The primary endpoint was the proportion of pts with successful LE after neoadjuvant CTX (NCT03548961). **RESULTS:** Nineteen pts with low RC were enrolled; nine were female, and the mean age at diagnosis was 65 years. T stage was as follows: T1- 1(5%), T2 - 11(58%), T3 - 7(36%). Eighteen (95%) pts completed at least 5 cycles of neoadjuvant CTX and 16/19 (84%) underwent LE. Negative margins were achieved in 79% (15/19), meeting our primary endpoint ($p < 0.001$). Ten (53%) were downstaged, and complete pathological response was achieved in 5/16 (31%) of pts who underwent LE. Four (21%) pts (all T2 stage) did not meet the primary endpoint (3 with inadequate response to CTX and 1 with LE and positive margins). Of these, three were salvaged (2 with CXRT; 1 with TME), and one died of infection (unrelated complication). All 16 who underwent LE completed CXRT. Of the 15 pts with successful OP at a median follow-up of 25.5 months, no local recurrences have been reported and 1 pt with lung nodules below the threshold for metastases at study entry ultimately developed clear lung metastases. Median DFS was not reached. PRO assessment revealed a slight decline in physical health scores after neoadjuvant CTX but improved to baseline at follow-up. No decline was seen in mental health scores. **CONCLUSIONS:** Neoadjuvant CTX and LE allows for OP in NN low RC and results in a margin negative LE in over three fourths of pts with durable long term local control and preserved QOL. Ongoing trials are investigating OP approach in NN RC (NCT03259035). Our approach adds to the mounting evidence and will provide early data of the benefit of adjuvant chemoradiation to target occult nodes in this setting.

87. Estrogen receptor blockade suppresses gastrointestinal stromal tumor growth and Kit signaling in mouse model

Taylor E Hartlein, MD[1]; Susan Zeng, PhD[2]; Ferdinando Rossi, PhD[3]; Juan Esteban Perez, MD[4]; Iulia Barbur, MD[5]; Ronald DeMatteo, MD, FSSO[6]
[1]University of Pennsylvania, Philadelphia, PA, US; [2]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [3]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [4]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [5]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [6]The University of Pennsylvania HospitalUS

INTRODUCTION: Gastrointestinal stromal tumor (GIST) is the most common human sarcoma and is usually driven by an activating mutation in Kit. While tyrosine kinase inhibitors are initially effective, most patients with advanced GIST become resistant. We discovered that tumor cells in our genetically engineered $Kit^{V558\Delta/+}$ mouse model expressed estrogen receptor-alpha (ER) and therefore assessed it as a novel therapeutic target. **METHODS:** Experiments were performed on $Kit^{V558\Delta/+}$ mice that develop a cecal GIST with 100% penetrance. Tumors were harvested and tested for ER RNA by PCR, ER protein by immunohistochemistry, and tumor cell ER protein by flow cytometry. ER inhibition was modeled by treating mice with tamoxifen gavage or ovariectomy and resultant Kit signaling assessed by flow cytometry and western blot. Xenografts from the human cell lines GIST T1 (imatinib-sensitive) and HG130 (imatinib-resistant) (HG130) were treated with imatinib, tamoxifen, or both. **RESULTS:** Bulk $Kit^{V558\Delta/+}$ tumors expressed ER RNA by quantitative PCR and flow cytometry showed that Kit+ tumor cells from both male and female mice expressed ER protein. Bilateral ovariectomy in 5 week old female $Kit^{V558\Delta/+}$ mice resulted in smaller tumors ($p= 0.0022$) 4 weeks later vs. sham laparotomy (n=8/group). Tamoxifen treatment (n=7) of 14 week old $Kit^{V558\Delta/+}$ mice reduced tumor size ($p=0.001$) vs. control (n=5). Tamoxifen-treated tumors had much lower Kit expression by IHC and flow and western blot confirmed downregulation of kit and downstream phosphorylated proteins. In xenograft experiments, tamoxifen reduced the growth of and Kit expression of established imatinib-resistant HG130 (n=8, $p<0.0001$) and imatinib-sensitive T1 tumors (n=7, $p=0.0008$) compared to controls. **CONCLUSIONS:** Mouse and human GIST express ER and tamoxifen reduced tumor growth and Kit in a genetically engineered mouse model of GIST as well as imatinib-sensitive and -resistant human GIST xenografts. ER inhibition is an unexplored therapeutic target in GIST that may be effective in treating imatinib-resistant tumors.

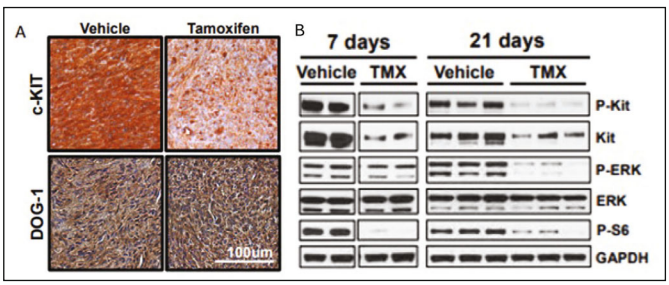


Figure 1. ER inhibition reduces tumor cell kit expression and downstream signaling (A)Matched Kit and DOG-1 immunohistochemistry of GIST paraffin sections from KitV558Δ/+ mice treated with 21 days of tamoxifen versus vehicle. (B) Western blot of Kit and downstream signaling proteins from vehicle versus tamoxifen-treated KitV558Δ/+ mice.

88. Patient-level evaluation of optimal margin width for lumpectomy with radiation in DCIS: an analysis of 8,070 patients in the NCDB Special Study

Amanda L Nash[1]; Yan Li[2]; Samantha M Thomas, MS[3]; Akiko Chiba[4]; Astrid Botty van den Bruele[5]; Jennifer K Plichta, MD[6]; Laura H Rosenberger, MD[7]; Amanda B Francescatti, MS[8]; Anne McCarthy[9]; Ronald J Weigel, MD, MBA, PhD[10]; Thomas Lynch, PhD[11]; Elizabeth Frank, EdM[12]; Ann Partridge[13]; Alastair M Thompson, MBChB MD[14]; Marc D Ryser, PhD[15]; E. Shelley Hwang, MD, MPH, FSSO[16]
[1]Department of Surgery, Duke University Medical Center, Durham, NC, US; [2]Duke Cancer Institute Biostatistics Shared Resource, Duke University, Durham, NC, US; [3]Duke University, Durham, NC, US; [4]Duke University Medical Center, Durham, NC, US; [5]Duke University Medical Center, Durham, NC, US; [6]Duke University Medical Center, Durham, NC, US; [7]Duke University Medical Center, Durham, NC, US; [8]American College of Surgeons, Chicago, IL, US; [9]American College of Surgeons, Chicago, IL, US; [10]American College of Surgeons, Chicago, IL, US; [11]Duke University Medical Center, Durham, NC, US; [12]Dana Farber Cancer Institute, Boston, MA, US; [13]Dana-Farber Cancer Institute, Boston, MA, US; [14]Baylor College of Medicine, Houston, TX, US; [15]Duke University, Durham, NC, US; [16]Duke University, Durham, NC, US

INTRODUCTION: The recommended margin width for pure DCIS treated with breast-conserving surgery (BCS) and adjuvant radiation (RT) has been established as 2mm. These recommendations were based on a study-level meta-analysis without individual patient data. We analyzed a large retrospective cohort of patients with DCIS who received BCS with RT to determine whether the 2mm margin recommendation is supported by patient-level data. **METHODS:** A stratified random sample of patients with DCIS who received BCS with RT was derived from 1,330 National Cancer Database (NCDB) Commission on Cancer-accredited sites. Data were abstracted from primary source documentation at each site for up to 10 years of follow-up. The primary predictor variable was margin width, and the primary outcome was ipsilateral recurrence. Final margin width was defined as positive (ink on tumor), 0.01-0.9mm, 1.0-1.9mm, and ≥2mm on the final surgical specimen. Group differences in patient and tumor characteristics were compared using the Chi-squared test for categorical variables, and the analysis of variance for continuous variables. The Kaplan Meier method was used to estimate cumulative recurrence rates according to margin width. Relative treatment effects were estimated using Cox models. Propensity-score based overlap weights were used for covariate balancing between treatment groups and were combined with survey weights to obtain population-averaged survival estimates. **RESULTS:** 8,070 patients met inclusion criteria. 5,181 DCIS lesions were ≤2 cm and 6,613 were estrogen

receptor (ER) positive. Median age at diagnosis was 59 years and 42.7% of DCIS were grade 3. Margin width was positive in 14.9% (n=1204), 0.01-0.9mm in 25.6% (n=2062), 1.0-1.9mm in 6.0% (n=484), and ≥ 2mm in 53.5% (n=4320). At a median follow-up of 68.1 months, there were 268 (3.3%) ipsilateral events, consisting of 108 invasive cancers and 160 DCIS recurrences. In the propensity-weighted analysis, only patients with positive margins had an increased risk of recurrence when compared to patients with ≥ 2mm margins (positive margin: HR 1.9 (95% CI 1.2-3.2); margin 0.01-0.9mm: HR 0.92 (95% CI 0.6-1.5); margin 1.0-1.9mm: HR 1.1 (95% CI 0.6-2.1)). Similarly, only patients with a positive margin had a significantly increased cumulative recurrence rate compared to standard 2mm margins (Figure 1). **CONCLUSIONS:** These data suggest that in patients with DCIS who undergo BCS and adjuvant RT, only patients with positive margins have a significantly increased risk of ipsilateral recurrence compared to patients with margin width ≥ 2mm. These data support that patients with clear but narrow margins after BCS for DCIS do not benefit from re-excision.

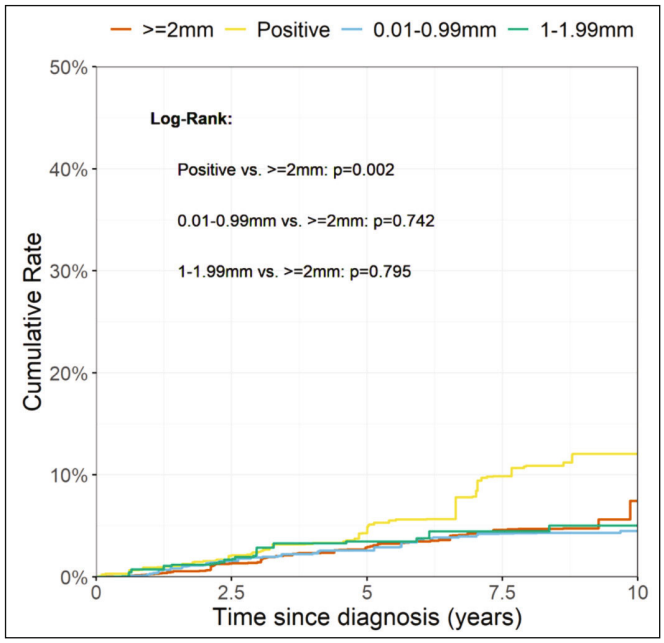


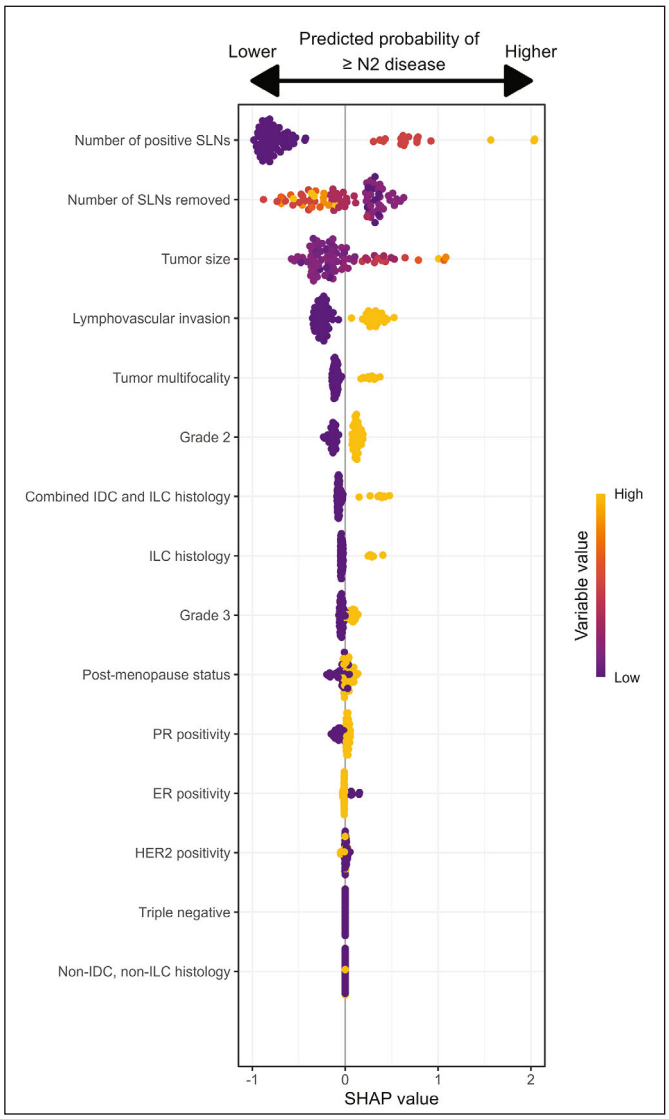
Figure 1. Weighted Kaplan Meier curve showing cumulative recurrence rate according to margin size in patients with DCIS who received adjuvant radiation. Log-rank tests were used to test between-group differences.

89. Predicting Pathologic N2 Breast Cancer in Pre- And Post-Menopausal Patients With Positive Sentinel Lymph Nodes

Kerollos N Wanis, MD[1]; Puneet Singh, MD[2]; Nina Tamirisa, MD[3]; Wenli Dong[4]; Sarah M DeSnyder, MD[5]; Kelly K. Hunt, MD, FSSO[6]; Isabelle Bedrosian, MD[7]; Abigail S Caudle, MD[8]; Henry Kuerer, MD[9]; Funda Meric-Bernstam, MD[10]; Taiwo Adesoye, MD[11]; Yu Shen[12]; Susie X Sun, MD[13]; Rosa F Hwang, MD[14]

[1]UT-MD Anderson Cancer Center, Houston, TX, US; [2]UT-MD Anderson Cancer Center, Houston, TX, US; [3]UT-MD Anderson Cancer Center, Houston, TX, US; [4]UT-MD Anderson Cancer Center, Houston, TX, US; [5]UT-MD Anderson Cancer Center, Houston, TX, US; [6]MD Anderson Cancer Center, Houston, TX, US; [7]UT-MD Anderson Cancer Center, Houston, TX, US; [8]UT-MD Anderson Cancer Center, Houston, TX, US; [9]UT-MD Anderson Cancer Center, Houston, TX, US; [10]UT-MD Anderson Cancer Center, Houston, TX, US; [11]UT-MD Anderson Cancer Center, Houston, TX, US; [12]MD Anderson Cancer Center, Houston, TX, US; [13]UT-MD Anderson Cancer Center, Houston, TX, US; [14]UT-MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: The distinction between pathologic category N1 and ≥N2 breast cancer impacts treatment decisions. For patients with 1-3 positive sentinel lymph nodes (SLNs), completion axillary dissection (ALND) allows for clarification of pathologic nodal status but causes morbidity. Our prior work showed that postmenopausal women with early stage cN0 breast cancer have a very low risk of ≥pN2 disease. This study aimed to develop predictive models for ≥pN2 disease in both pre- and post-menopausal women. **METHODS:** We utilized data from a single institution on women with cN0 invasive breast cancer undergoing upfront sentinel lymph node biopsy (SLNB) and completion ALND between 1993 and 2007. A machine learning model, using gradient boosted logistic regression trees, was trained to predict the probability of ≥pN2 disease based on clinicopathologic variables. Preoperative ultrasound of the regional lymph node basins started in 2000. Model performance was tested in a held-out sample (20%) and contrasted with standard logistic regression. Performance was validated using 2018-2020 data from the National Cancer Database (NCDB). Shapley additive explanations were used to quantify variable contributions. **RESULTS:** Of 3,574 patients with cN0 breast cancer, 415 (11.6%) had a positive SLN and underwent ALND. The mean age and tumor size were 54 years (range: 22-83) and 2.3 cm (range: 0.2-11.0). Most patients (86.5%) had ER positive tumors, and the median number of SLNs removed was 3 (range: 1-9) with a median of one positive (range: 1-3). The machine learning trained algorithm achieved an AUC of 0.87 (95% CI: 0.74, 0.97) and Brier score 0.073 (95% CI: 0.038, 0.12) in the test sample. In contrast, a parametric logistic regression model had AUC of 0.80 (95% CI: 0.61, 0.96) and Brier score 0.084 (95% CI: 0.043, 0.13). The AUC was 0.78 (95% CI: 0.76, 0.79) in the NCDB data. Number of positive SLNs and the total number of SLNs removed had the greatest influence on model predictions (Figure). Menopausal status, tumor grade, and lobular histology had less impact. In the overall cohort, the probability of ≥pN2 disease in cN0 patients was 15.4% (64 of 415). The probability was 6.2% for those with 1 positive SLN, 28.8% for those with 2 positive SLNs, and 48.4% for those with 3 positive SLNs ($p < 0.001$). The number of negative SLNs removed was inversely associated with ≥pN2 disease. **CONCLUSIONS:** We developed a machine learning model that effectively predicts the probability of ≥pN2 disease in cN0 patients with positive SLNs, providing guidance for the management of breast cancer patients.



90. Deep Learning for Pediatric Rhabdomyosarcoma Subtype Classification from Histology Images

Adam H Thiesen[1]; Sergii Domanskyi[2]; Ali Foroughi Pour[3]; Todd B Sheridan[4]; Steven B Neuhauser[5]; Alyssa Stetson[6]; Katelyn Dannheim[7]; Danielle B Cameron[8]; Shawn Ahn[9]; Hao Wu[10]; Emily R Christison-Lagay[11]; Carol J Bult[12]; Jeffrey H Chuang[13]; Jill C Rubinstein[14]

[1]The Jackson Laboratory, Farmington, CT, US; [2]The Jackson Laboratory, Farmington, CT, US; [3]St. Jude Children's Research Hospital, Memphis, TN, US; [4]Hartford Healthcare, Hartford, CT, US; [5]The Jackson Laboratory, Farmington, CT, US; [6]Massachusetts General Hospital, Boston, MA, US; [7]Massachusetts General Hospital, Boston, MA, US; [8]Massachusetts General Hospital, Boston, MA, US; [9]Yale School of Medicine, New Haven, CT, US; [10]Yale School of Medicine, New Haven, CT, US; [11]Yale School of Medicine, New Haven, CT, US; [12]The Jackson Laboratory, Bar Harbor, ME, US; [13]The Jackson Laboratory, Farmington, CT, US; [14]UConn School of Medicine, The Jackson Laboratory, Hartford Healthcare, Farmington, CT, US

INTRODUCTION: Pediatric sarcoma is both rare and histologically heterogeneous, making it difficult to amass sufficiently powered datasets to allow accurate subtype identification. The need for molecular testing to help guide diagnosis leads to unequal access to care. Deep learning is a form of artificial intelligence that can extract imaging features from digitized Hematoxylin & Eosin (H&E)-stained images and train models for classification tasks. These models are reproducible, implementable at a distance, and mitigate against inter-observer bias, but can be prone to overfitting in training. To address this overfitting we amassed a multi-institutional dataset and designed a computational pipeline, implementing the latest in deep learning backbones to perform automated classification of alveolar and embryonal rhabdomyosarcomas (RMS) using H&E-stained images alone. **METHODS:** We collected 561 H&E-stained images from numerous centers. After focus checking, resolution standardization, stain normalization, and image format conversion we define optimal parameters (tile size, magnification power, single- vs. multi-scale feature extraction). We compare InceptionV3 and CTranspath deep learning backbones, implementing our published SAMPLER method to create imaging feature sets from each backbone to use as input for alveolar vs embryonal RMS and RMS vs non-RMS classifiers. Finally, we benchmark the resulting SAMPLER classifiers with a transformer based deep learning architecture. **RESULTS:** Both SAMPLER and transformer methods achieved superior performance to published models (Area Under the Curve (AUC) for embryonal vs alveolar subtyping > 0.93 for both models, prior best 0.85). CTranspath outperformed InceptionV3 across all tests. Top performance was achieved using SAMPLER with multiscale resolution (20x + 40x), and nuclear morphology features (AUCs: alveolar vs embryonal 0.95, RMS vs non-RMS 0.94). In feasibility analysis SAMPLER runs successfully on standard computational architecture in minutes and is significantly faster than comprable models, with less computational resources needed. **CONCLUSIONS:** Our multi-institutional pediatric sarcoma dataset is the broadest harmonized resource of this type to our knowledge. Using a multiscale approach, cell morphological features, and optimized tiling parameters, we demonstrate accurate, computationally efficient RMS classification that is robust to center of origin, bringing promise that automated image review will accurately and remotely identify sarcoma histology, improving subtype-specific delivery of care.

Task	Model and Scale	AUC (std.)
Alveolar vs Embryonal	SAMPLER 20x	0.9445 (0.0201)
	Transformer 20x	0.9363 (0.0291)
	SAMPLER 20x + 10x	0.94922 (0.017)
	Transformer 20x + 10x	0.9369 (0.0293)
	SAMPLER 20x +40x	0.94943 (0.018)
	Transformer 20x+40x	0.9344 (0.0266)
	SAMPLER 20x+40x+Q[Eccentricity, Area]*	**0.9525 (0.02939)**
RMS vs NRSTS	SAMPLER 20x+40x+Q[Eccentricity, Area]*	**0.937 (0.0214)**

HPB II

91. Pre-Transplant Metabolic Tumor Volume Predicts Recurrence Following Liver Transplantation for Colorectal Metastasis: A Multicenter Validation Study

Chase J Wehrle, MD[1]; Mariana Chavez-Villa[2]; Matthew Byrne[3]; Abby Gross, MD[4]; Paresh Mahajan[5]; Jamak Modaresi Esfeh[6]; Maureen Whitsett Linganna[7]; Koji Tomiyama[8]; Andrea Schlegel, MD[9]; David CH Kwon[10]; Samer A Naffouje, MD[11]; Pal-Dag Line[12]; Charles Miller[13]; Koji Hashimoto[14]; Roberto Hernandez-Alejandro[15]; Federico Aucejo[16]

[1]Cleveland Clinic, Cleveland, OH, US; [2]University of Rochester, Rochester, NY, US; [3]University of Rochester, Rochester, NY, US; [4]Cleveland Clinic, Cleveland, OH, US; [5]Cleveland Clinic, Cleveland, OH, US; [6]Cleveland Clinic, Cleveland, OH, US; [7]Cleveland Clinic, Cleveland, OH, US; [8]University of Rochester, Rochester, NY, US; [9]Cleveland Clinic, Cleveland, OH, US; [10]Cleveland Clinic, Cleveland, OH, US; [11]Cleveland Clinic - Cleveland, OH, Cleveland, OH, US; [12]University of Oslo, Olso, NO; [13]Cleveland Clinic, Cleveland, OH, US; [14]Cleveland Clinic, Cleveland, OH, US; [15]University of Rochester, Rochester, NY, US; [16]Cleveland Clinic Foundation, Cleveland, OH, US

INTRODUCTION: Liver transplant (LT) for colorectal cancer liver metastases (CRLM) is increasingly popular, yet the ideal selection criteria remain unknown. Pre-transplant PET metabolic tumor volume (MTV) has been described as predicting recurrence, with a proposed cut-off of MTV ≥70 cm^3. This approach has not been validated. Patients undergoing LT for CRLM at two academic transplant centers (1/1/2017-12/1/2023) were included. PET-MTV was calculated by a blinded staff radiologist from the most recent PET-scan before LT using the published protocol. **RESULTS:** Twenty-six patients were included. Median follow-up was 609days (IQR 320-1069) and from PET to LT was 1.9 months (1.3-2.6). Nearly all (n=24, 92.3%) received living donor transplantation. Absolute recurrence rate was 30.8% (n=8). Actuarial unadjusted 1-, and 2-year RFS were 83% (n=15/18), and 62% (n=8/13); 1- and 2-year OS were 100% (n=18/18), and 85% (n=11/13). The incidence of recurrence-per-year follow-up was 0.35 when MTV≥70cm^3 vs 0.10 if MTV<70cm^3 (p<0.001). Median RFS using Kaplan-Meier product-estimate was 0.83 years (95%CI 0.43-1.23) in MTV≥70cm^3 vs 4.1 years (95%CI 2.90-5.22) when MTV<0.001); this was also associated with improved OS (p=0.003). MTV≥70cm^3 demonstrated HR=2.42 (95%CI 2.2-62.2, p=0.006) for association with RFS on univariate Cox-proportional hazards analysis, and an Area-Under-the-Curve (AUC)=0.771 (95%CI 0.560-0.981) for predicting recurrence (p=0.030),sans-serif'>Nineteen patients (69.2%) had histologically viable tumor, which was associated with recurrence (43% vs. 0%, p=0.039) and reduced RFS (log-rank p=0.019). PET-MTV was associated with presence of histologically-viable tumor (AUC=0.763, 95%CI 0.583-0.944). **CONCLUSIONS:** PET-MTV ≥70 cm^3 was associated with reduced RFS and OS after LT for CRLM, confirming findings from the Norway group. This is likely due to its' ability to identify residual viable tumors, which are independently associated with recurrence. PET-MTV should be a key selection criterion prior to LT for CRLM.

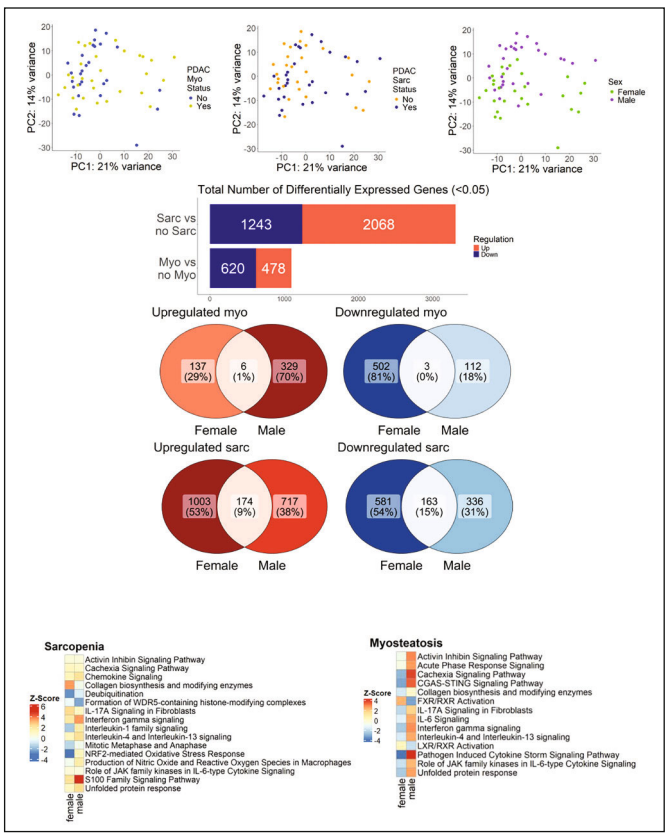
92. Sex-Based Differences in Cachexia, Skeletal Muscle Transcriptomics, and Survival in Pancreatic Adenocarcinoma

Thomas L Sutton, MD MCR[1]; Peter Pham[2]; Thai Nguyen[3]; Heike Mendez[4]; Peter Levasseur[5]; Ali Gunesch[6]; Aylmer Tan[7]; Brett Sheppard[8]; Aaron G Grossberg[9]

[1]Cedars-Sinai Medical Center, Los Angeles, CA, US; [2]Oregon Health and Science University, Portland, OR, US; [3]Oregon Health and Science University, Portland, OR, US; [4]Oregon Health and Science University, Portland, OR, US; [5]Oregon Health and Science University, Portland, OR, US; [6]Oregon Health and Science University, Portland, OR, US; [7]Oregon Health and Science University, Portland, OR, US; [8]Oregon Health and Science University, Portland, OR, US; [9]Oregon Health & Science University, Portland, OR, US

INTRODUCTION: Cachexia is a disease-associated metabolic syndrome characterized by anorexia, skeletal muscle and adipose tissue loss, myosteatosis, and functional impairment. CT-assessed changes in body composition such as sarcopenia and myosteatosis have been associated with chemotherapy intolerance as well as poor oncologic and perioperative outcomes across a variety of malignancies, including pancreatic ductal adenocarcinoma (PDAC). However, the impact of body composition measures and its regulatory mechanisms remains unclear, especially at the sex-specific level. **METHODS:** All patients with PDAC undergoing curative-intent resection from 2011 to 2022 at our institution with pre-operative CT imaging were identified. AutoMATiCA software was used to autosegment and measure cachexia-related endpoints including skeletal muscle cross-sectional area (CSA) and intermuscular adipose

tissue (IMAT). Patients were classified by the presence of sarcopenia and myosteatosis. Rectus muscle biopsies were collected at time of surgery, and RNA sequencing and analysis were performed to identify differentially expressed genes (DEGs) between study groups. **RESULTS:** A total of 203 patients were identified over the study period, with 116 meeting criteria for sarcopenia and 120 meeting criteria for myosteatosis. Median follow-up was 33.5 months. Median OS was 21.8 months (in patients with sarcopenia and 21.3 months in patients without sarcopenia regardless of sex (P=0.88). In contrast, male patients with myosteatosis had significantly shorter survival than patients without (median OS 16.3 vs 39.9 months, log-rank P=0.0006), but not in female patients (median OS 17.5 vs 24.9 months, log-rank P=0.37). The measured differences in OS were not attributable to differences in progression-free survival. Analysis of n=57 patients with paired CT body composition and muscle RNAseq data revealed that sex was the largest determinant of transcriptional profile. We observed stark differences in skeletal muscle transcriptomics between male and female patients both for myosteatosis and sarcopenia, with <1% overlap in DEGs for myosteasosis and <15% overlap for sarcopenia (Figure). **CONCLUSIONS:** Both the associations of myosteatosis and sarcopenia with survival and the molecular pathways underlying these changes are sex-dependent. Myosteatosis is a poor prognostic factor in males, and additional study of sex-specific cellular pathways involved in myosteatosis and sarcopenia is needed and may uncover targetable pathways to mitigate cachexia-related adverse outcomes during the treatment of PDAC.



93. Adjuvant hepatic arterial infusion pump chemotherapy after repeat hepatectomy for patients with liver confined recurrence of colorectal cancer – a multicenter phase II study

Loubna Outmani[1]; Wills Filipe[2]; Bas Groot Koerkamp[3]; Leni van Doorn[4]; Marjolein Homs[5]; Niels Kok[6]; Koert Kuhlmann[7]; Bianca Mostert[8]; Maarten Vermaas[9]; Cornelis Verhoef[10]; Dirk Grunhagen[11]

[1]Erasmus Medical Center, Rotterdam, NL; [2]Erasmus Medical Center, Rotterdam, NL; [3]Erasmus Medical Center, Rotterdam, NL; [4]Erasmus Medical Center, Rotterdam, NL; [5]Erasmus Medical Center, Rotterdam, NL; [6]Antoni van Leeuwenhoek, Amsterdam, NL; [7]Antoni van Leeuwenhoek, Amsterdam, NL; [8]Erasmus Medical Center, Rotterdam, NL; [9]IJsselland Hospital, Capelle aan den Ijssel, NL; [10]Erasmus Medical Center, Rotterdam, NL; [11]Erasmus MC, Rotterdam, NL

INTRODUCTION: Approximately 70% of patients develop recurrent colorectal liver metastasis (rCRLM), half of which is confined to the liver. Treatment with hepatic arterial infusion pump (HAIP) chemotherapy allows high dosage chemotherapy to be directed solely into the liver. A retrospective study including 374 patients treated in MSKCC and the Erasmus MC showed that patients who received adjuvant HAIP chemotherapy after repeat hepatectomy for CRLM had a median hepatic disease free survival (hDFS) of 46 months (95% CI 29-81 months) compared to 18 months (95% CI 15-26 months) in patients treated with resection and/or ablation alone (p=0.001). The aim of this study is to evaluate the efficacy of repeat hepatectomy and adjuvant HAIP chemotherapy in patients with recurrent resectable CRLM. **METHODS:** This is a multi-centre phase II study, and has been conducted in three medical centres in the Netherlands. Study population consists of adults with resectable recurrent CRLM without evidence extrahepatic disease (EHD). HAIP patients were included between March 2021 and November 2023. Control group consists of adults treated with repeat hepatectomy between January 2000 and December 2019. HAIP chemotherapy with floxuridine was administered in 6 cycles. The primary endpoint was hDFS. Secondary endpoints include overall survival (OS), postoperative complications and adverse events. HDFS and OS was compared using the Kaplan-Meier method and log-rank test. **RESULTS:** In total, 280 patients were included in this analysis: 45 patients underwent resection and received adjuvant HAIP chemotherapy and 235 were treated with resection alone. The HAIP group was characterized by a higher percentage of patients with more than 1 rCRLM (77% vs 36%, p <0.001) and more than one previous treatment for CRLM (38% vs 29%, p <0.025). All 45 patients started HAIP chemotherapy, 51% received the intended 6 cylces (n=23). The median hDFS was 18 months in HAIP patients compared to 24 months in resection only group (p=0.18). HAIP pump-related complication with a Clavien-Dindo grade 3 or higher occurred in 6 patients (13%) and HAIP chemotherapy related complications with a CTCEA grade 3 or higher occurred in 5 patients (11%). **CONCLUSIONS:** Hepatic disease free survival rates were similar among patients who were treated with adjuvant HAIP chemotherapy with floxuridine after repeat resection for CRLM and patients who underwent resection alone.

94. Multianalyte blood-based risk stratification of incidental pancreas lesions

Clayton T Marcinak[1]; Michelle D Stephens[2]; Bradon R McDonald, PhD[3]; Nabeel Merali, MBBS[4]; Elise C Dietmann[5]; Stephanie M McGregor, MD, PhD[6]; Sean M Ronnekleiv-Kelly, MD[7]; Sharon Weber, MD[8]; Everlyne N Nkadori, MPH[9]; Peter G Stadmeyer, MD[10]; Mark E Benson[11]; Deepak V Gopal, MD[12]; Syed Nabeel Zafar, MD, MPH[13]; Kaitlyn J Kelly, MD, MS[14]; Ali Pirasteh[15]; Adam E Frampton, MBBS, PhD[16]; Patrick R Pfau, MD[17]; Shivan Sivakumar, MBBS, PhD[18]; Rebecca Minter, MD FACS[19]; Muhammed Murtaza, MD, PhD[20]

[1]University of Wisconsin–Madison, Madison, WI, US; [2]University of Wisconsin-Madison, Madison, WI, US; [3]University of Wisconsin-Madison, Madison, WI, US; [4]University of Surrey, Surrey, GB; [5]University of Wisconsin-Madison, Madison, WI, US; [6]University of Wisconsin-Madison, Madison, WI, US; [7]University of Wisconsin-Madison, Madison, WI, US; [8]University of Wisconsin - Madison, Madison, WI, US; [9]University of Wisconsin-Madison, Madison, WI, US; [10]University of Wisconsin-Madison, Madison, WI, US; [11]University of Wisconsin-Madison, Madison, WI, US; [12]University of Wisconsin-Madison, Madison, WI, US; [13]University of Wisconsin-Madison, Madison, WI, US; [14]University of Wisconsin-Madison, Madison, WI, US; [15]University of Wisconsin-Madison, Madison, WI, US; [16]University of Surrey, Guildford, GB; [17]University of Wisconsin-Madison, Madison, WI, US; [18]University of Birmingham, Birmingham, GB; [19]University of Wisconsin-Madison, Madison, WI, US; [20]University of Wisconsin-Madison, Madison, WI, US

INTRODUCTION: Incidental detection of pancreas lesions is common and creates an opportunity to intercept pancreatic ductal adenocarcinoma (PDAC). However, identifying patients at risk for progression who can benefit from surgical resection remains challenging. The current role of blood tests for risk stratification in patients with incidental pancreas lesions (IPLs) is limited. **METHODS:** We evaluated the performance of circulating glycoproteins (CA 19-9, CEA and CA 125), plasma DNA fragmentation analysis, and their combination, in 99 asymptomatic patients with IPLs, to detect advanced pathology (high-grade dysplasia or invasive carcinoma). Genomewide plasma DNA fragmentation was analyzed using a machine learning model, adapted to detect PDAC in 242 patients with cancer and 300 healthy individuals. **RESULTS:** During 18.8 months of median follow-up by a multidisciplinary clinical team, 11 of 99 patients with IPLs were diagnosed with high-grade dysplasia or invasive carcinoma. We observed AUCs of 0.78, 0.63, 0.54 and 0.74 for detection of advanced pathology using CA 19-9, CEA, CA 125 and plasma

DNA fragmentation, respectively. Combined analysis of CA19-9, CA 125 and plasma DNA fragmentation showed an AUC of 0.93, with 91% sensitivity at 90% specificity. In a subset of 25 patients with histologically confirmed diagnoses, AUC improved to 0.96. In one patient with an equivocal initial endoscopy, multi-analyte blood analysis predicted cancer 3 months before diagnosis of stage IA cancer. **CONCLUSIONS:** Our results demonstrate the promise of a multianalyte blood test combining glycoprotein biomarkers with plasma DNA fragmentation to complement current clinical workflows for cancer detection in patients with IPLs.

95. Diagnostic Value of Diffusion-Weighted MRI for the Detection of Peritoneal and Liver Metastases in High-Risk Pancreatic Ductal Adenocarcinoma: A Pilot Study

Janyssa Charbonneau[1]; Patricia Noël[2]; Étienne Ouellet[3]; Jean-François Ouellet[4]; Jean-François B Ouellet[5]; Carl Daigle[6]; Isabelle Deshaies[7]; Alexandre Brind'Amour;[8]
[1]CHU de Québec - Université Laval, Québec, QC, CA; [2], , , US; [3], , , US; [4], , , US; [5], , , US; [6], , , US; [7], , , US; [8], , , US

INTRODUCTION: Metastatic presentation is frequent in pancreatic adenocarcinoma and is not always detected on staging imagery, considering the highly variable sensitivity of CT-scan for peritoneal metastases. This study aimed to evaluate the added value of preoperative diffusion-weighted MRI (DWI-MRI) in patients with high-risk pancreatic adenocarcinoma for the detection of peritoneal metastases. **METHODS:** This was a prospective single-center pilot study, conducted from 2022 to 2024, with an aimed sample size of 40 patients. Eligible patients had pancreatic adenocarcinoma, no evidence of distant metastases on preoperative CT-scan, resectable or borderline resectable tumor and at least one high risk feature for peritoneal metastases (tumor size >/= 3cm and/or CA19-9>400U/mL). All patients underwent preoperative DWI-MRI**. RESULTS:** Forty patients were recruited, and 38 patients were included for analysis. Upfront resectable tumors represented 47.4% of cases. Mean tumor size on CT-scan was 37.3mm. Median CA19-9 level was 495U/mL. DWI-MRI revealed missed peritoneal metastasis in 5.3% of cases (n=2), but unsuspected liver metastases in 34.2% of cases (n=13). DWI-MRI's sensitivity was 83.3% for liver metastases and 78.9% for overall abdominal metastases. Its NNT was 2.9 for the detection of liver metastases, and 2.5 for overall abdominal metastases. Unnecessary surgical exploration was avoided in 39.5% of the cohort. Ultimately, 18 patients were selected for curative-intent surgery, but metastases were found intraoperatively in four additional patients. At six months, three additional patients had developed metastatic disease and three had presented with local recurrence. **CONCLUSIONS:** DWI-MRI revealed few missed peritoneal metastases, but a significant number of liver metastases. Although this was a small pilot study, our findings seem to suggest that performing preoperative liver MRI in patients with pancreatic adenocarcinoma and high-risk features could be beneficial.

Table. DWI screening results and associated operative settings

DWI findings	N= 38 n (%)
Negative for abdominal metastases	23 (60.5)
Positive for abdominal metastases	15 (39.5)
Peritoneal carcinomatosis	2 (5.3)
Hepatic metastases	13 (34.2)
Other surgical contraindications	**N = 5 n (%)**
Disease progression or insufficient response under chemotherapy	4
Significant chemotherapy complication or associated decease	1
Operative outcomes	**N = 18 n (%)**
Oncologic resection completed	
Yes	15 (83.3)
No	3 (16.7)
Distant metastasis confirmed at surgery	4 (22.2)
Peritoneal carcinomatosis	1 (5.6)
Hepatic metastasis[a]	2 (11.1)
Distant nodal metastasis	1 (5.6)
Type of surgery	
Whipple	10 (55.6)
Distal subtotal pancreatectomy + splenectomy	5 (27.8)

[a]One patient presented suspect hepatic lesions at surgery. Lesions were biopsied and sent for frozen section examination, which came back negative. Final pathology report confirmed metastases afterwards.

96. Outcomes of Surveillance in Patients with IPMNs Tested Negative for High-Risk Mutations in Next-Generation Sequencing (NGS): A Large Multi-Center Study

Amudhan Kannan, MD[1]; Gilbert Z Murimwa, M.D[2]; John C Mansour, MD[3]; Alex Jones, MD[4]; Tarek Sawas, MD[5]; Oscar Ramirez, MD[6]; Dana Ley, MD[7]; Daniel Ellis, MD[8]; Hendrikus Vanderveldt, MD[9]; Veronica Coleman, PA-C[10]; Samantha Foley, PA-C[11]; Ali Abbas[12]; Naveen Rajamohan, MD[13]; Gaurav Khatri, MD[14]; Patrick R Pfau, MD[15]; Rebecca Minter, MD FACS[16]; Aatur D Singhi, MD[17]; Herbert J Zeh, MD[18]; Nisa M Kubiliun, MD[19]; Patricio M. Polanco, MD[20]
[1]University of Texas Southwestern Medical Center, Dallas, TX, US; [2]UTSouthwestern Medical Center, Dallas, TX, US; [3]UT Southwestern Medical Center, Dallas, TX, US; [4]University of Texas Southwestern Medical Center, Dallas, TX, US; [5]University of Texas Southwestern Medical Center, Dallas, TX, US; [6]University of Wisconsin-Madison, Madison, WI, US; [7]University of Wisconsin-Madison, Madison, WI, US; [8]University of Texas Southwestern Medical Center, Dallas, TX, US; [9]University of Texas Southwestern Medical Center, Dallas, TX, US; [10]University of Texas Southwestern Medical Center, Dallas, TX, US; [11]University of Texas Southwestern Medical Center, Dallas, TX, US; [12]University of Texas Southwestern Medical Center, Dallas, TX, US; [13]University of Texas Southwestern Medical Center, Dallas, TX, US; [14]University of Texas Southwestern Medical Center, Dallas, TX, US; [15]University of Wisconsin-Madison, Madison, WI, US; [16]University of Wisconsin-Madison, Madison, WI, US; [17]UPMC Medical Center, Pittsburgh, PA, US; [18]UT Southwestern Medical Center, Dallas, TX, US; [19]University of Texas Southwestern Medical Center, Dallas, TX, US; [20]University of Texas Southwestern Medical Center, Dallas, TX, US

INTRODUCTION: High-risk mutations in cyst fluid NGS (TP53, SMAD4, CTNNB1, mTOR) have demonstrated high sensitivity and specificity for predicting advanced neoplasia in patients with IPMNs. However, the outcomes of surveillance in patients who tested negative for these high-risk mutations have not been investigated in prior studies. This study aimed to evaluate the progression-free survival of patients with negative NGS results for high-risk mutations and study the predictors of progression in these patients. **METHODS:** We conducted a retrospective review of prospectively collected data from patients who underwent cyst fluid NGS testing using the same generation assay between 2021 and 2022 in two pancreatic cancer prevention programs. Patients with IPMNs (i.e., positive for KRAS/GNAS) and those with at least one follow-up imaging post-NGS were included. Patients with high-risk mutations were excluded from the study. Progression was defined as the development of new or additional worrisome features or high-risk stigmata (as per Kyoto guidelines), or advanced neoplasia (high-grade dysplasia/invasive cancer) following NGS testing. A Cox proportional hazards regression model was used to identify predictors of progression, while Kaplan-Meier survival analysis was employed to estimate progression-free survival, with survival curves compared between subgroups. **RESULTS:** A total of 573 patients underwent NGS testing across the two programs, of which 125 were tested using the same NGS assay and included for analysis. The median post-NGS follow-up duration was 20.5 months (IQR = 13–26.2). Of these, 30 patients developed progression after NGS testing. The most common type of progression was an increase in cyst size ≥ 2.5mm, a worrisome feature. A total of 7 patients underwent surgical resection, with 2 of them found to have high-grade dysplasia. None of the patients developed invasive cancer. Predictors of progression included a history of smoking (HR = 2.46; 95% CI = 1.08 – 5.6), larger cyst size (HR = 2.03; 95% CI = 1.22 – 3.37), and the presence of a dilated main pancreatic duct (MPD) (HR = 3.13; 95% CI = 1.34 – 7.32) prior to NGS testing. When grouping worrisome features together, the presence of any worrisome feature was significantly predictive of progression (HR = 3.34; 95% CI = 1.5–7.4). The median time to progression was 33 months for patients with worrisome features, 35.4 months for those with cysts ≥ 3cm, and 36 months for those with any smoking history. **CONCLUSIONS:** Patients who test negative for high-risk mutations in NGS are not exempt from the risk of progression. Any smoking history and presence of any worrisome features before NGS testing showed to be independent predictors of disease progression. For patients with smoking history or worrisome features or cysts ≥ 3 cm, frequent surveillance should be recommended following NGS testing. Further studies are needed to assess the role of repeat cyst fluid NGS testing in patients showing progression.

Table 1. Cox proportional hazards regression models for identifying the predictors of progression

Variables	Hazards ratio (HR)	95% CI	P-value
Age	0.98	0.94 – 1.01	0.22
Male sex	0.55	0.21 – 1.41	0.214
White race	1	0.4 – 2.53	0.99
Family h/o pancreatic cancer	0.76	0.2 – 2.92	0.7
Any h/o smoking	2.46	1.08 – 5.6	**0.032***
Diabetes	1.21	0.46 – 3.05	0.735
Pre-NGS cyst size (cm)	2.03	1.22 – 3.37	**0.006***
Pre-NGS dilated MPD (≥5 mm)	3.13	1.34 – 7.32	**0.008***
Pre-NGS mural nodules	0.66	0.08 – 5.34	0.7

97. Preoperative Exercise Therapy Mitigates Surgical Stress Induced Colorectal Cancer Liver Metastasis through Kupffer Cell-Mediated Anti-Tumor Immunity

Susan J Kim[1]; Yunwei Zhang[2]; Chengli Shen[3]; Kaelyn C Cummins[4]; Hongji Zhang[5]; Allan Tsung[6]

[1]University of Virginia Health, Charlottesville, VA, US; [2]University of Virginia Health, Charlottesville, VA, US; [3]University of Virginia, Charlottesville, VA, US; [4]University of Virginia Health, Charlottesville, VA, US; [5]University of Virginia, Charlottesville, VA, US; [6]University of Virginia Health, Charlottesville, VA, US

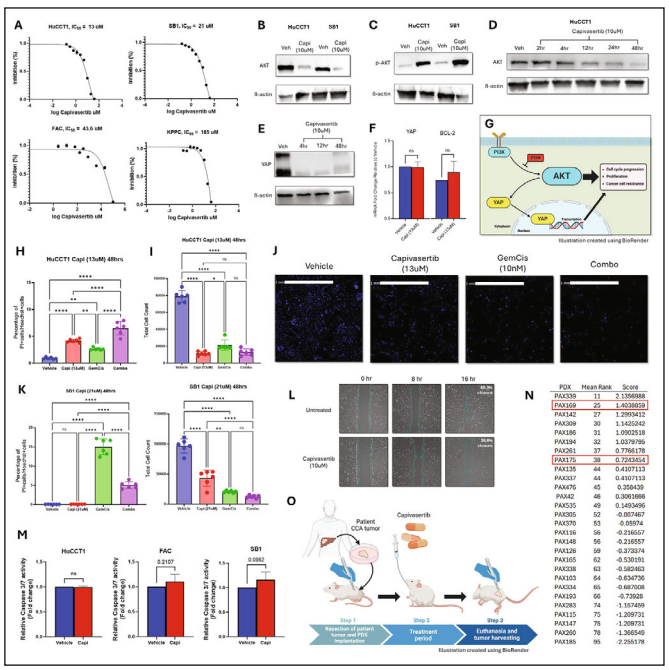
INTRODUCTION: Colorectal cancer mortality is primarily driven by hepatic metastasis, which affects 50-60% of patients. While metastasectomy is an integral component of treatment, surgery itself can induce a robust inflammatory response, which can lead to post-operative recurrence. Pre-operative exercise (PEx) has shown potential in mitigating the pro-inflammatory response following surgery which is largely mediated by Kupffer cells (KC). The purpose of our study is to determine the mechanism by which KCs orchestrate an anti-tumorigenic hepatic environment generated by surgical stress in the setting of colorectal cancer liver metastases (CRCLM). **METHODS:** 8 weeks-old male C57BL/6 mice were randomly stratified into PEx or Sedentary groups. PEx mice were exercised on a treadmill at 12.5m/min for 6 min/day, 5 days/week, for 4 weeks. Subsequently, CRCLM were induced by portal vein injection of 2 x 10^5 GFP-labeled MC38 colon cancer cells, followed by a 70% hepatic ischemia reperfusion (I/R) model to stimulate surgical stress. Tumor growth was measured *in vivo* with bioluminescent imaging, and mice were euthanized 3 weeks after index surgery. Tumoral immune cells from groups were submitted for single-cell RNA sequencing and flow cytometry, followed by gene ontology and KEGG enrichment analysis. **RESULTS:** 4 weeks of PEx significantly reduced surgical-stress induced CRCLM tumor growth compared to Sedentary controls. scRNA-seq of the PEx tumors demonstrated a significant shift toward an anti-tumor phenotype in KCs. On further gene ontology analysis of the PEx group, KCs were shown to upregulate CXCL9 production, a chemokine known to recruit CD8+ T-cells through its receptor, CXCR3. Additionally, tumors from the PEx group demonstrated increased CD8+ T-cell infiltration with enhanced cytotoxicity as indicated by increased IFN-gamma and TNF-alpha expression. Furthermore, administration of either CXCL9 antibody or CXCR3 antagonists led to loss of the protective effects of exercise, confirming the anti-tumor functionality of the KC-CD8+ T-cell interaction through the CXCL9/CXCR3 axis. **CONCLUSIONS:** Our research demonstrates how PEx mitigates surgical stress induced CRCLM by promoting a tumoricidal phenotype in KCs, offering a novel modality to reduce post-operative recurrence and improve outcomes in cancer patients undergoing liver surgery.

98. Investigating Capivasertib as a Therapeutic Strategy in Cholangiocarcinoma

Jack W. Sample, MD[1]; Danielle M. Carlson, MS[2]; Amro Abdelrahman, MBBS, MS[3]; Erik Jessen, PhD[4]; Nathan W. Werneberg[5]; Gregory J. Gores, MD[6]; Cornelius Thiels[7]; Rory L Smoot[8]

[1]Mayo Clinic, Rochester, MN, US; [2]Mayo Clinic, Rochester, MN, US; [3]Mayo Clinic, Rochester, MN, US; [4]Mayo Clinic, Rochester, MN, US; [5]Mayo Clinic, Rochester, MN, US; [6]Mayo Clinic, Rochester, MN, US; [7]Mayo Clinic, Rochester, MN, US; [8]Mayo Clinic Rochester, Rochester, MN, US

INTRODUCTION: Cholangiocarcinoma (CCA) is an aggressive malignancy of the biliary epithelium, characterized by limited therapeutic options and poor long-term survival rates. The PI3K/AKT pathway is the most dysregulated signaling pathway in cancer, with its increased activation associated with metastasis and poor prognosis in CCA. We investigated capivasertib, a selective AKT inhibitor, as a therapeutic option in CCA. **METHODS:** *In vitro* studies were conducted using multiple human and murine CCA cell lines. Multiomics data were generated from patient-derived xenografts (PDX) tumor samples developed from 28 patients with surgically treated CCA. Following Institutional Animal Care and Use Committee approval, *in vivo* studies were performed using C57BL/6 and NOD/SCID mice. **RESULTS:** Dose-response curves were established in multiple human and murine CCA cell lines (Fig1a). Target knockdown was confirmed via immunoblot in both human and murine CCA cell lines, HuCCT1 and SB1, respectively; as expected, phosphorylated AKT levels increased (Fig 1b-d), owing to capivasertib locking AKT in a catalytically inactive phosphorylated state. Notably, we observed decreased expression of yes-associated protein (YAP), a downstream effector of the hippo pathway associated with gemcitabine and cisplatin (Gem/Cis) sensitivity in CCA (Fig 1e). However, there was no significant decrease in the expression of YAP or its canonical downstream target genes, suggesting a post-translation interaction (Fig 1F-G). Cell proliferation and death were evaluated by propidium iodide and Hoechst33342 staining using both capivasertib monotherapy and combination with Gem/Cis, revealing that capivasertib exhibits more of an anti-proliferative effect than an apoptotic effect in CCA (Fig 1H-L). These findings were validated by analysis of caspase 3/7 activity (Fig 1M). To translate these findings into a preclinical model, we employed a bioinformatics approach to identify CCA PDX models with the highest and lowest expression of AKT (Fig 1N). Corresponding PDX models are currently undergoing treatment with oral capivasertib (100mg/kg) versus vehicle (Fig 1O). Additionally, C57/Bl6 mice bearing orthotopically implanted CCA cells are undergoing treatment with capivasertib monotherapy versus capivasertib and Gem/Cis combinatory therapy. **CONCLUSIONS:** Capivasertib, a selective inhibitor of all three isoforms of the serine/threonine kinase, AKT, is a promising therapeutic for CCA that demonstrates significant anti-proliferative properties and interesting interactions with other well-established cell signaling pathways.



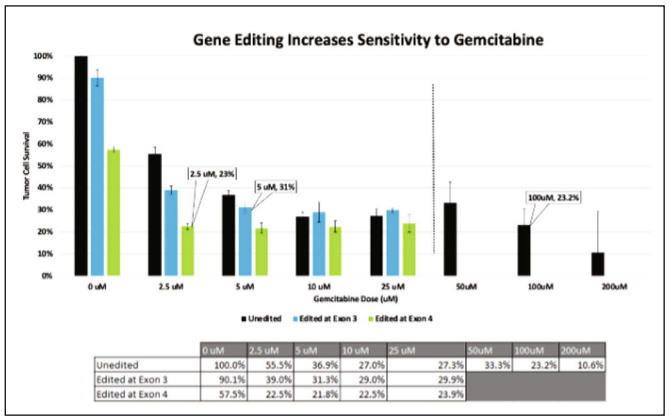
99. CRISPR-directed gene editing as an augmentative therapy for the treatment of pancreatic ductal adenocarcinoma

Michelle Abramova, Resident Physician[1]; London McGill[2]; Kelly Banas[3]; Anthony Scholer[4]; Eric Kmiec[5]; Gregory Tiesi, MD, FACS[6]

[1]Hackensack JSUMC, Neptune, NJ, US; [2]Gene Editing Institute Christiana Care, Newark, DE, US; [3]Gene Editing Institute Christiana Care, Newark, DE, US; [4]Hackensack JSUMC, Neptune, NJ, US; [5]Gene Editing Institute ChristianaCare, Newark, DE, US; [6]Jersey Shore University Medical Center Hackensack Meridian, Neptune, NJ, US

INTRODUCTION: Pancreatic ductal adenocarcinoma (PDAC) is particularly difficult to treat due to high rates of resistance to systemic therapy. We've previously demonstrated that utilizing CRISPR/Cas gene editing to disable

the NRF2 gene, in a squamous lung cancer model, resulted in decreased chemoresistance. We sought to evaluate if a similar effect could be found for PDAC. **METHODS:** Synthetic single guide RNAs (sgRNAs) were designed to target DNA and create double stranded breaks within the functional domains of the NRF2 gene to disrupt protein production and function. sgRNAs were complexed with Cas9 and delivered in vitro into Panc1 cells via nucleofection. Cells were harvested for SANGER sequencing and downstream chemotherapy exposure. CellTiter Glo viability assay was used to evaluate chemosensitivity before and after editing and also compared to unedited cells. Evaluation of editing efficiency was done by aligning the SANGER sequencing output in the bioinformatics program DECODR to see the random insertions and deletions that had been created during the cellular repair process post CRISPR/Cas9 targeting. **RESULTS:** The editing efficiencies of sgRNAs designed to target exon 2 through exon 5 of the NRF2 gene ranged from 23% to 92%, with the sgRNAs falling within the transactivation domains having the highest overall occurrence of random insertions and deletions (indels). The top three editing efficiencies were on exon 3 sgRNA 5 (55%), exon 4 sgRNA 83 (70%) and exon 4 sgRNA 76 (92%). Preliminary off target in silico analysis was performed for all sgRNAs. sgRNA5 and sgRNA83 had the lowest potential off target hits within the human genome. Combined with high indel activity these were moved forward into chemosensitivity assays. Compared to unedited Panc1 cells, exon 3 and 4 sgRNAs alone showed reduction in cell viability (90.1%, 57.5% vs. 100%; p = 0.0195, 0.0001; respectively). Gemcitabine exposure led to high rates of cell death for exons 3 and 4 compared to unedited cells (Figure 1). Exon 4 achieved maximal killing at the lowest dose of 2.5uM (22.5% vs. 55.5%, p = 0.0007) and retained sensitivity at higher doses. Exon 3 showed a similar response, but stabilized around 5uM (31.3% vs. 36.9%, p = 0.0002). Unedited cells required a 40-fold greater concentration (100uM) of Gemcitabine to achieve similar cell death levels (23.2%) as exon 4 sgRNA. **CONCLUSIONS:** CRISPR/Cas9 gene editing of PDAC cancer cells was able to substantially increase sensitivity to standard chemotherapy and provides a potential novel therapeutic approach to chemoresistance in PDAC patients.



	0 uM	2.5 uM	5 uM	10 uM	25 uM	50uM	100uM	200uM
Unedited	100.0%	55.5%	36.9%	27.0%	27.3%	33.3%	23.2%	10.6%
Edited at Exon 3	90.1%	39.0%	31.3%	29.0%	29.9%			
Edited at Exon 4	57.5%	22.5%	21.8%	22.5%	23.9%			

100. Improving early detection of pancreatic cancer through metabolomics profiling of human serum

Mehrdad Zarei[1]
[1]Case Western Reserve University/University Hospitals, Cleveland, OH, US

INTRODUCTION: Currently, there are no validated early detection tests for pancreatic cancer. Consequently, over 50% of patients diagnosed with pancreatic cancer present with metastatic disease, making it one of the most lethal cancers. Importantly, pancreatic cancer is often resistant to current systemic therapies; however, multiagent chemotherapy regimens are more effective when tumor burden is limited. This study explores metabolomics profiling of human serum to identify metabolic signatures as potential early biomarkers, aiming to improve early diagnosis and survival outcomes for pancreatic cancer patients. **METHODS:** Serum samples from 106 patients, including both pancreatic cancer patients and controls, were analyzed using liquid chromatography-mass spectrometry (LC-MS) to profile approximately 300 metabolites**.** Data were normalized and analyzed with univariate and multivariate methods, to identify significantly altered metabolites. Differential abundant metabolites were identified with adjusted p-values (FDR < 0.05), metabolic pathway enrichment was conducted using the KEGG database to highlight key pathways associated with pancreatic cancer. **RESULTS:** Mass spectrometric profiling revealed significant differences in the serum metabolomes of pancreatic cancer patients compared to healthy controls, as visualized through multivariate analysis. Fifteen metabolites were identified as significantly altered in pancreatic cancer patients, many were involved in amino acid pathways, including spermine, proline, alanine, creatinine, and isoleucine. Additionally, gender-specific differences in metabolite profiles were noted, underscoring the potential for personalized early detection strategies. Among the 300 metabolites analyzed, approximately one-third showed significant differences between men and women. Pathway analysis revealed gender-specific alterations in amino acid metabolism, oxidative phosphorylation, and purine and pyrimidine metabolism. Further analysis identified 45 distinct metabolites in female pancreatic cancer patients compared to healthy female controls, while 25 distinct metabolites were identified in male pancreatic cancer patients compared to healthy male controls. **CONCLUSIONS:** These findings suggest that gender-specific metabolic signatures in pancreatic cancer patients could facilitate early detection through a minimally invasive blood test (< 1 mL), offering a promising tool for improving patient outcomes.

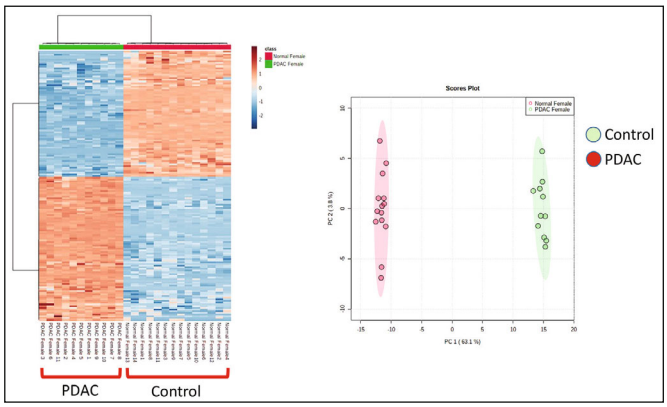


Figure 1. Metabolic profiling of human serum d ifferentiates PDAC from controls

PSM

101. Deep Machine Learning Model for Accurate Quantification of Treatment Response in Peritoneal Carcinomatosis

Shaina Sedighim[1]; Fatemeh Tajik[2]; Amy Y Li[3]; Belain Eyob[4]; Chanon Chantaduly[5]; Jingjing Yu[6]; Vinodh Kumar Radhakrishnan[7]; Aaqil M Khan[8]; Oliver S Eng[9]; Michael O'Leary[10]; Farshid Dayyani[11]; Peter D Chang[12]; Maheswari Senthil[13]
[1]UC Irvine Department of Surgery, Orange, CA, US; [2]University of California, Irvine, Orange, CA, US; [3]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [4]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [5]University of California, Irvine School of Medicine, Irvine, CA, US; [6]University of California, Irvine Medical Center, Orange, CA, US; [7]University of California, Irvine, Orange, CA, US; [8]University of California, Irvine, Orange, CA, US; [9]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [10]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [11]University of California, Irvine Medical Center, Orange, CA, US; [12]University of California, Irvine Medical Center, Orange, CA, US; [13]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US

INTRODUCTION: Peritoneal carcinomatosis (PC) poses unique management challenges as current imaging techniques are limited in ability to quantitatively characterize disease burden and treatment response. Moreover, PC is not considered a measurable disease based on Response Evaluation Criteria in Solid Tumors (RECIST) criteria, due to ill-defined borders. Hence, patients with PC are excluded from participation in many clinical trials. We sought to overcome this challenge by training a deep learning (DL) artificial intelligence (AI) model to accurately assess and quantify treatment response in PC. **METHODS:** An institutional database was used to identify patients with gastrointestinal PC between 2015-2020. Patients who received systemic therapy (ST) with corresponding pre- and post-ST computed tomography (CT) imaging were included in the study (n=105). A subset of the cohort was used for model development. PC regions were annotated with a 3D segmentation mask, verified

by an expert peritoneal malignancy surgeon. A 3D convolutional neural network with encoder-decoder architecture (16 layers and 714,212 trainable parameters) optimized with deep supervision was developed for per-voxel PC quantification. Automated AI measurements were compared to expert annotations using five-fold cross-validation with patient-level stratification, and to disease response as documented in the radiology report. **RESULTS:** A total of 44 CT exams from 23 patients were included. The median age was 56.5 years and 13/23 were female. AI generated volume estimates of PC burden showed high correlation with expert annotations (Pearson correlation of 0.802) with a per-voxel tumor sensitivity of 0.800, indicating reliable detection of tumor regions. All radiology reports documenting disease response exhibited a decrease in PC volume (average reduction of 589 cm3; Fig 1A-B), while those documenting disease progression exhibited an increase in PC volume (average increase of 1390 cm3; Fig 1C-D). For reports documenting stable disease, automated AI analysis identified a small decrease in tumor burden (average decrease of 140 cm3), a finding that often correlated to a subtle but verified reduction in PC disease (Fig E-F). **CONCLUSIONS:** The proposed AI model provides a novel method for accurate and objective quantification of PC disease burden with high correlation to expert-based assessment of treatment response. Ongoing work aims to validate this AI tool for quantifying treatment response in prospective patient care and future clinical trials.

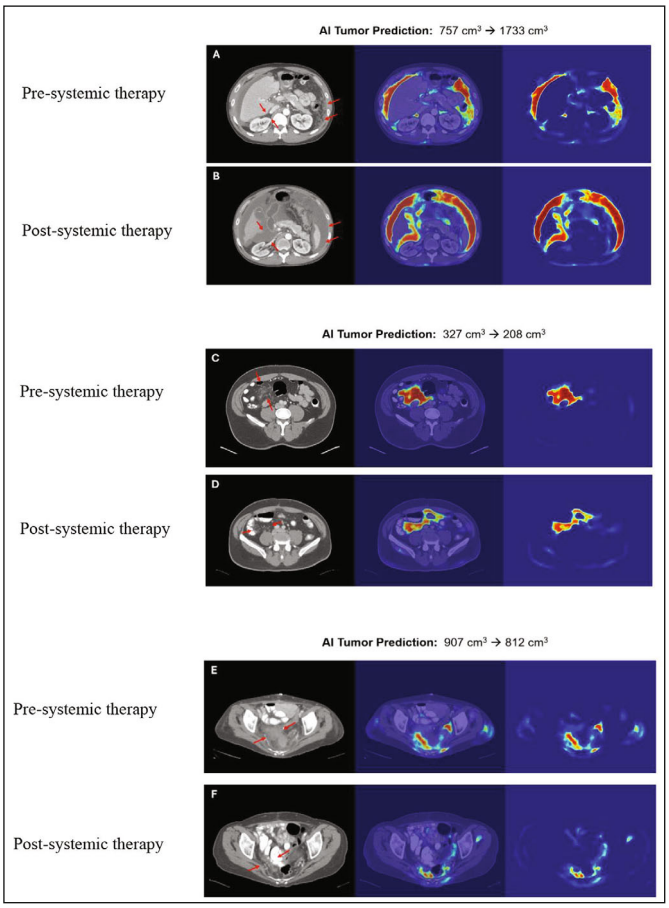
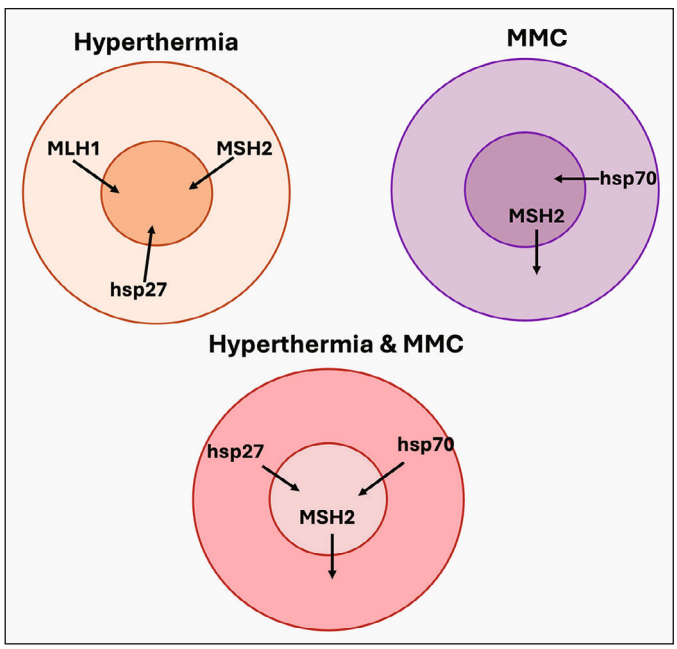


Figure 1. Representative images of AI-enabled volumetric quantification of carcinomatosis disease burden in patients pre- (top row, panels A/C/E) and post- (bottom row, panels B/D/F) systemic treatment. Panels 1A and 1B demonstrate a patient with tumor progression (757 cm3 to 1733 cm3). Panels 1C and 1D demonstrate a patient with tumor response (327 cm3 to 208 cm3). Panels 1E and 1F demonstrate a patient with an initial radiologic report documenting stable disease however with subtle reduction in PC burden most notable in the perirectal fat (907 cm3 to 812 cm3).

102. The impact of hyperthermia and mitomycin C on heat shock and mismatch repair proteins in colon cancer

Hannah G McDonald, MD, PhD[1]; Anna Reagan, MD[2]; Charles Bailey[3]; Breanna Knicely[4]; Eva Goellner, PhD[5]; Joseph Kim, MD[6]
[1]University of Kentucky Department of Surgery, Lexington, KY, US; [2]University of Kentucky, Lexington, KY, US; [3]University of Kentucky, Lexington, KY, US; [4]University of Kentucky, Lexington, KY, US; [5]University of Kentucky, Lexington, KY, US; [6]University of Kentucky, Lexington, KY, US

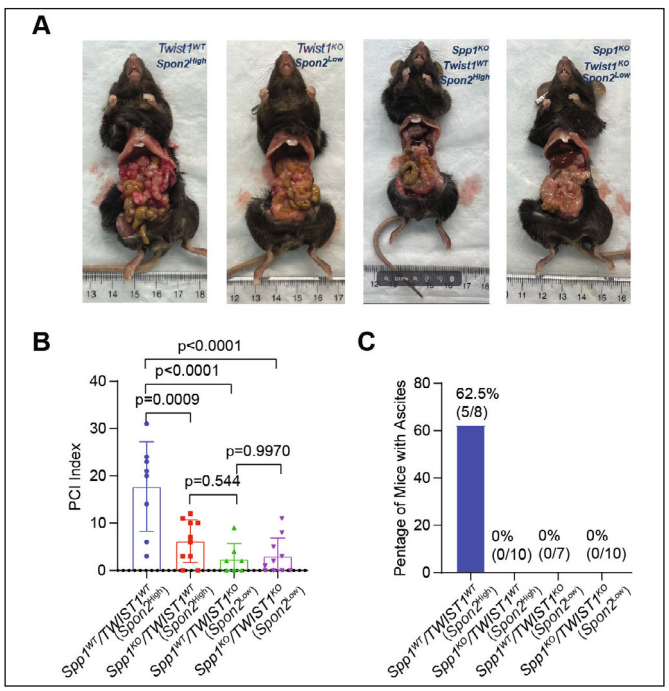
INTRODUCTION: The efficacy of heated intraperitoneal chemotherapy (HIPEC) is dependent on both hyperthermia and chemotherapy, which result in DNA damage. Mismatch repair (MMR) proteins and heat shock proteins (Hsps) are required for DNA repair. Given prior studies showing dysregulated MMR expression with exposure to hyperthermia and chemotherapy, we sought to characterize how HIPEC may impact Hsps and MMR proteins. **METHODS:** The HT29 MMR-proficient (pMMR) colon cancer cell line was utilized for all assays. The dose for 50% cytotoxicity (IC_{50}) from mitomycin C (MMC) 72h post-treatment was identified after 90 min treatment +/- hyperthermia (42°C vs 37°C). Cell viability was determined using CellTiter Glo®. The dose corresponding with average IC_{50} was utilized for all subsequent treatments with recovery periods of 4, 24, and 72h. Whole cell lysates, cytoplasmic, and nuclear fractions were isolated for western blot and ELISA quantification of MSH1, MSH2, hsp70, and hsp27. Immune fluorescence microscopy was utilized to further assess intracellular localization. Mass spectrophotometry (MS) was used to evaluate changes in the whole proteome following treatment conditions. **RESULTS:** After exposure of HT29 cells to MMC +/- hyperthermia, MMC IC_{50} was significantly higher at 42°C compared to 37°C (p=0.007). Additionally, expression levels of MMR proteins MLH1 and MSH2 decreased with both MMC and hyperthermia, whereas hsp70 expression increased. As expected, hsp27 expression increased with heat and decreased with MMC treatment. Exposure to heat resulted in nuclear localization of MLH1, MSH2, and hsp27 (Figure 1). MMC exposure resulted in cytoplasmic localization of MSH2 and nuclear localization of hsp70, as well as decreased cytoplasmic hsp27. Immune fluorescence microscopy corroborated these results, showing cytoplasmic translocation of MSH2 with heat and MMC and nuclear localization of hsp70 with MMC. MS results confirmed increased protein folding activity and decreased cell death cascade when hyperthermia and MMC were combined vs. MMC alone. **CONCLUSIONS:** Contrary to expectation, we discovered that hyperthermia increased MMC IC_{50} in pMMR colon cancer cells, suggesting that heat decreased the cytotoxic efficacy of MMC. Of great clinical interest, the combined exposure to hyperthermia and MMC resulted in cytoplasmic localization of MSH2, a condition that has been associated with MMR deficiency in colon cancer. Additional studies are examining whether this combined therapy may lead to microsatellite instability.



103. SPON2-SPP1 Molecular Circuit Drives Colorectal Cancer Peritoneal Metastasis Tumorigenesis and Chemoresistance

Zhuan Zhou[1]; Alessandro La Ferlita[2]; Manoj Palavalli[3]; Xiongfeng Chen[4]; Huocong Huang, MD PhD[5]; Alex C. Kim, MD/Ph.D.[6]
[1]UT Southwestern Medical Center, Dallas, TX, US; [2]The Ohio State University Medical Center, Columbus, OH, US; [3]The Ohio State University Medical Center, Columbus, OH, US; [4]UT Southwestern Medical Center, Dallas, TX, US; [5]UTSouthwestern Medical Center, Dallas, TX, US; [6]UT Southwestern Medical Center, Dallas, TX, US

INTRODUCTION: Colorectal cancer (CRC) carries a significant propensity for peritoneal metastasis (PM), a malignant spread of the cancer within the peritoneal cavity, affecting 10% of all patients and representing 25-35% of stage IV CRC. The patients with CRC PM have dismal prognosis with current median overall survival of PM patients at 16.3 months and with almost 0% survival at 5-years. Despite the current understanding of CRC metastasis, the molecular mechanism of CRC PM tumorigenesis and chemoresistance remains unknown. We identified direct TWIST1 downstream, novel SPON2-SPP1 cellular circuit that control of tumor microenvironment to drive for CRC PM tumorigenesis and chemoresistance. **METHODS:** CRISPR-cas9 knockout of SPON2 (*SPON2^{KO}*) was performed in mouse (MC38) and human (MDST8) cell lines. *In vitro* assay to assess tumorigenesis including invasion, migration, scratch-test, and sphere-formation assays were performed using *SPON2^{KO}* cells. MTT assay using *SPON2^{KO}* cells were performed to establish IC_{50} at various chemotherapy concentrations. Recombinant SPON2 (rSPON2) stimulation and co-culture system with MC38 and mouse mesothelial cells were utilized to assess fibroblast differentiation and SPP1 secretion. Lastly, *WT* and *Spp1^{KO}* transgenic mice were utilized to generate syngeneic CRC PM models with *Spon2* deficient cell lines. **RESULTS:** *SPON2^{KO}* cells demonstrated significant deficiency in migration, invasion, wound closure, and tumor sphere formation *in vitro*. Treatment of *SPON2^{KO}* cells with 5-FU, oxaliplatin, and SN38 resulted in significant increase in IC50 or chemosensitivity. Conversely, addition of rSPON2 rescued these *in vitro* phenotypes. Moreover, stimulation of undifferentiated mesothelial cells with rSPON2 or co-culture with WT cells resulted in mesothelial to antigen presenting cancer-associated fibroblast (CAF) differentiation demonstrated by upregulation of CAF markers including SPP1. Finally, establishment of syngeneic CRC PM model using WT and *Spp1^{KO}*transgenic mouse with *WT* and *Spon2* deficient MC38 cell lines resulted in significant decrease in tumor burden and ascites formation. **CONCLUSIONS:** We defined SPON2 as a novel downstream target of TWIST1 driving tumorigenesis and chemoresistance in CRC PM. SPON2-SPP1 axis actively regulates tumor microenvironment paracrine signaling between tumor epithelium and cancer-associated fibroblasts to drive the CRC PM virulence. Here, we establish a unique SPON2-SPP1 cellular circuit which may serve as new biomarkers and innovative therapeutic target.



104. Neutrophil-related and Other Innate Immune Pathways are Central to the Tissue Immune Microenvironment in Peritoneal Carcinomatosis

Christopher Sherry, DO[1]; Kunhong Xiao[2]; Neda Dadgar[3]; Hyun Park[4]; Rosie Blodgett[5]; Chelsea Knotts, MD[6]; Erin Grayhack[7]; Ashten Omstead[8]; Ali Zaidi[9]; Vera Donnenberg[10]; Albert Donnenberg[11]; David Bartlett, MD[12]; Patrick Wagner, MD[13]
[1]Allegheny Health Network, Pittsburgh, PA, US; [2]Allegheny Health Network, Pittsburgh, PA, US; [3]Cleveland Clinic Foundation, Cleveland, OH, US; [4]Allegheny Health Network, Pittsburgh, PA, US; [5]Allegheny Health Network, Pittsburgh, PA, US; [6]Allegheny Health Network, Pittsburgh, PA, US; [7]Allegheny Health Network, Pittsburgh, PA, US; [8]Allegheny Health Network, Pittsburgh, PA, US; [9]Allegheny Health Network, Pittsburgh, PA, US; [10]Allegheny Health Network, Pittsburgh, PA, US; [11]Allegheny Health Network, Pittsburgh, PA, US; [12]Allegheny Health Network, Pittsburgh, PA, US; [13]Allegheny Health Network, Pittsburgh, PA, US

INTRODUCTION: The immune contexture of peritoneal carcinomatosis remains incompletely defined, consisting both of peritoneal fluid as well as peritoneal tissue (mesothelium and immediately underlying mesenchymal tissue and immune infiltrate). To assess the peritoneal tissue microenvironment for key pathways relevant to tumor dissemination and disease progression, we performed a quantitative proteomics assessment on 'background' non-neoplastic peritoneal tissue samples obtained from patients with PC and compared them to patients without PC. **METHODS:** Paraffin-embedded peritoneal tissue samples from patients with (n=30) or without (n=44) PC were deparaffinized and homogenized, followed by protein extraction, trypsin digestion and liquid chromatography/tandem mass spectrometry analysis (Bruker timsTOF Pro2). Peptides were computationally filtered, matched to their cognate proteins, and assigned quantitative intensities that were in turn log2 transformed, with missing values imputed by replacement from normal distribution. Student's t test ($p<0.05$) was used to identify differentially expressed proteins (DEP) in PC-related samples. Go term enrichment and KEGG pathway analysis were performed on DEPs using Metascape, Enrichr-KG and DAVID (significance, Benjamini-Hochberg-corrected $p<0.05$). **RESULTS:** Among 881 verified proteins, 409 were quantified and 60 met criteria as DEPs, notable among them being members of the serine protease inhibitor (Serpin) family, heat shock proteins, and annexins. Pathway enrichment analysis (see Figure) revealed involvement of these DEPs in several key immune processes, including the neutrophil degranulation (n=16 distinct proteins, $p=1 \times 10^{-13}$), regulation of hydrolase activity (n=14, $p\sim1 \times 10^{-10}$), and innate immunity as a broad reactome category (n=22, $p=2.6 \times 10^{-9}$). **CONCLUSIONS:** The tissue milieu onto which peritoneal tumors adhere and grow is an important potential source for immunotherapy targets. In this study, analysis of 'background' peritoneal tissue revealed a proteomics signature in PC typified by neutrophil activation and innate immune-related responses. We hypothesize that the inflammatory milieu within peritoneal fluid and tissue in PC contributes to a tumor-promoting microenvironment in PC that impairs tumor-specific cytotoxic immunity and leads to consequences such as ascites, fibrosis and bowel obstruction. We identified a number of candidate proteins and pathways for further validation and mechanistic studies in hopes of illuminating potential targets for therapeutic intervention.

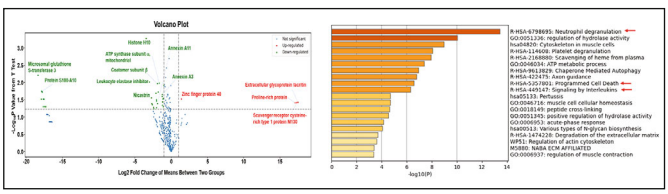


Figure. Proteomic comparison of carcinomatosis-related vs. benign peritoneal tissue illuminates neutrophil biology as a central element of the peritoneal immune microenvironment. Left panel, volcano plot identifying differentially expressed proteins with >50% change in carcinomatosis and $p<0.05$. Right panel, pathway enrichment analysis using DEPs to identify potential gene-gene and gene-pathway associations. Several overlapping neutrophil-related and other immunologic pathways (degranulation, regulation of hydrolase activity) were identified as over-expressed in carcinomatosis-related tissue.

105. Intra-Tumoral Mucolytic Therapy for Patients With Unresectable Pseudomyxoma Peritonei: Results of an Expanded Access Program

Shannon Altpeter, DMSc[1]; Michael M. Wach, MD[2]; Joshua Derby, MS[3]; H. Scott Beasley, MD[4]; James F. Pingpank, MD[5]; Melanie Ongchin, MD[6]; Sarah Valle, BMedSc BN[7]; David Morris, FRACS[8]; M. Haroon A. Choudry, MD[9]
[1]Department of Surgery, University of Pittsburg Medical Center, Pittsburgh, PA, US; [2]Department of Gastrointestinal Oncology, Moffitt Cancer Center, Tampa, FL, US; [3]Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, US; [4]Department of Radiology, University of Pittsburgh Medical Center, Pittsburgh, PA, US; [5]Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, US; [6]Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, US; [7]Research and Development, MucPharm Pty Ltd, Kogarah, AU; [8]Department of Surgery, Peritonectomy Unit, St George Hospital and University of New South Wales, Kogarah, AU; [9]Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, US

INTRODUCTION: Patients with advanced unresectable pseudomyxoma peritonei (PMP) have limited treatment options and a poor prognosis. An early phase single institution study from Australia demonstrated that repeated intra-tumoral administration of a mucolytic drug combination, comprising bromelain (Brom) and acetylcysteine (Ac), was feasible, safe, and effective at reducing the intraperitoneal mucinous tumor burden. We now aim to report the initial outcomes of an expanded access program for unresectable PMP patients treated with BromAc at a single institution in the US. **METHODS:** Eligible patients with unresectable PMP underwent image-guided placement of percutaneous catheters into one or more intraperitoneal mucinous tumors. This was followed by up to 6 sequential cycles of BromAc administration and aspiration of dissolved mucus, via the catheters. Mucolytic effect was assessed by the cumulative volume of aspirated mucus (ml), change in tumor volume by CT imaging, and change in patient reported symptoms using quality of life questionnaires. Treatment related complications were recorded. **RESULTS:** The median peritoneal carcinomatosis index of the 10 patients (mean age: 58.2 yr) was 31 (IQR=22-37). Twenty-three individual tumors (median volume: 538 cm^3 [IQR=257-1426]) were treated with BromAc in 44 separate treatment sessions (median BromAc treatments per patient 5 [IQR=3-6]). The median volume of mucus aspirated per tumor was 431 ml (IQR=155-985). There were 16 (36.4%) Clavien-Dindo Grade I and 10 (22.7%) Grade II adverse events. There was one (2.2%) Grade III adverse event of an enterocutaneous fistula formation. Two patients died within 30 days of protocol initiation from disease progression and clinical deterioration unrelated to therapy. Of the 8 patients that completed the 1-month post-treatment CT imaging, 14 of 17 tumors (82.4%) exhibited a reduction in mucinous tumor volume, with a median volume reduction of 48.9% [IQR=14.9-75.4] (Figure 1). An improvement in quality of life at 30 days was reported by 5 patients, especially related to abdominal pain and the ability to tolerate oral intake without nausea or vomiting. **CONCLUSIONS:** Intra-tumoral treatment with BromAc is a feasible, safe, and effective treatment option for patients with advanced unresectable PMP.

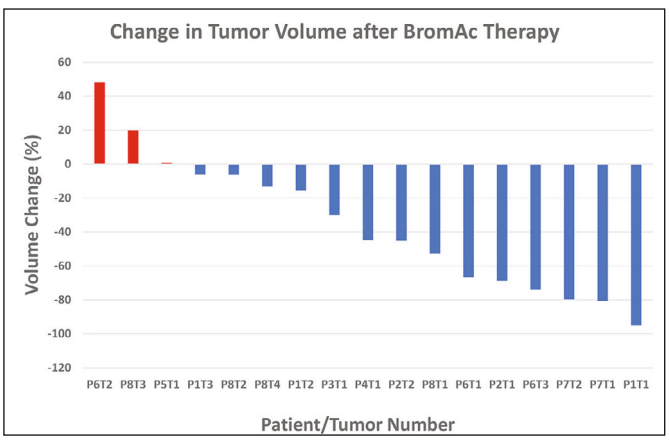


Figure 1. Change in tumor volume following BromAc therapy. Change in tumor volume was calculated for each individual tumor (T) in each individual patient (P). Tumor volume was calculated using the formula (4/3*Pi) * (x/2) * (y/2) * (z/2), where x, y, and z represent the largest measurement (cm) in the transverse, craniocaudal, and anteroposterior dimensions at the same location of representative pre-treatment and 1-month post-treatment CT image slices. The waterfall plot displays the percentage (%) change in tumor volume.

106. Patient-Reported Financial Toxicity of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy

Vladislav Kovalik, MD MSPH[1]; Vadim Gushchin, MD FACS[2]; Luis Felipe Falla-Zuniga, MD[3]; Mary Caitlin King, BS[4]; Abeerah Wasti, BA[5]; Sergei Iugai, MD[6]; Kseniia Uzhegova, MD[7]; Carol Nieroda, MD[8]; Teresa Diaz-Montes, MD MPH FACOG[9]; Armando Sardi, MD FACS[10]
[1]Mercy Medical Center, Baltimore, MD, US; [2]Mercy Medical Center, Baltimore, MD, US; [3]Mercy Medical Center, Baltimore, MD, US; [4]Mercy Medical Center, Baltimore, MD, US; [5]Mercy Medical Center, Baltimore, MD, US; [6]Mercy Medical Center, Baltimore, MD, US; [7]Mercy Medical Center, Baltimore, MD, US; [8]Mercy Medical Center, Baltimore, MD, US; [9]Mercy Medical Center, Baltimore, MD, US; [10]Mercy Medical Center, Baltimore, MD, US

INTRODUCTION: Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) may lead to substantial out-of-pocket expenses and income loss in cancer survivors. Based on survivor perspectives, we hypothesized that the financial toxicity (FT) of CRS/HIPEC is associated with poorer quality of life (QoL) and identified its risk factors. **METHODS:** A prospective single-center study enrolled CRS/HIPEC patients with peritoneal disease from various primary tumors (6/2024 – 10/2024). COST and FACT-G questionnaires were administered in-person during preoperative admission or routine follow-ups (<12 months, 1–2 years, and 2–5 years post-CRS/HIPEC). Lower COST and FACT-G scores indicated higher FT and poorer QoL, respectively. Spearman correlation between COST and FACT-G was assessed. Mean ± standard deviation (SD) COST scores were compared across clinical and socioeconomic variables using t-tests/ANOVA, and risk factors for lower COST scores were identified via multivariable linear regression (forward selection, p_e<0.05). **RESULTS:** In total, 106 patients were included: 17.0% (n=18) were surveyed before CRS/HIPEC, 29.2% (n=31) <12 months post-surgery, 19.8% (n=21) at 1-2 years, and 34.0% (n=36) at 2-5 years post-CRS/HIPEC. Mean±SD age was 57±12 years and 74.5% were females. Primary sites included appendix (42.5%), colon (16.0%), ovarian (34.9%), and other (6.6%) cancers. The peritoneal cancer index was ≥20 in 57.5%, 41.5% had neoadjuvant (NACT), and 31.1% had adjuvant chemotherapy (ACT). Overall, 43.4% had governmental insurance, 12.3% were unemployed, 32.0% were single, and 22.0% lived in areas with deprivation index >50. Mean±SD COST score was 28±11 and 35.8% of patients had moderate-to-severe FT (COST≤25). COST and FACT-G scores strongly correlated (rho=0.58, p<0.001) (Figure 1a). Mean±SD COST score was significantly lower in black, indigenous, or people of color (BIPOC) vs non-BIPOC patients (25±11 vs 31±10, p=0.012) and in patients who had NACT vs those who did not (25±12 vs 31±9, p=0.010). There were no associations between COST score and insurance, employment, marital status, area deprivation, tumor characteristics, or ACT. In the multivariable model, BIPOC (β=-4.7, p=0.023) and NACT exposure (β=-5.8, p=0.006) were associated with lower COST score, while being 2-5 year post-CRS/HIPEC led to a higher COST score (β=7.3, p=0.017) (Figure 1b). **CONCLUSIONS:** One in three CRS/HIPEC patients experience significant FT, which is strongly linked to QoL. BIPOC, patients starting cancer treatment with NACT, and those <2 years post-surgery are at higher risk for FT.

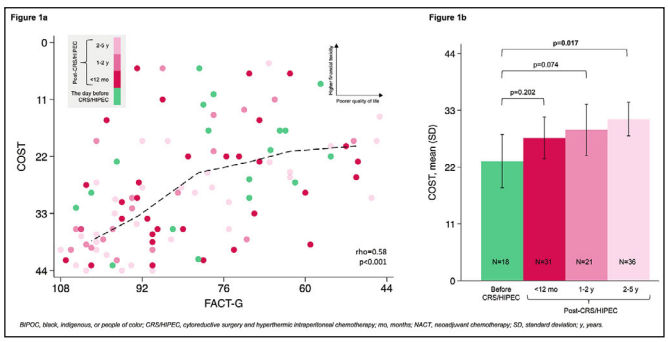


Figure 1a. The scatterplot illustrates individual data points for COST and FACT-G scores, representing financial toxicity and quality of life, respectively. The dashed line marks the median values. Spearman correlation analysis showed a significant moderate-to-strong correlation between COST and FACT-G (rho=0.58, p<0.001).
Figure 2b. Bar plots show differences in mean COST scores across time periods. The p-values are derived from a multivariable linear regression model, comparing each time period with pre-CRS/HIPEC assessment and adjusting for NACT exposure and BIPOC status.

107. Discovery of Drug Response-Associated Mutations in Mucinous Metastatic Appendiceal Cancer Using a Patient-Derived Tumor Organoid Platform

Daniel J. Gironda, BS[1]; Cecilia R. Schaaf, DVM, PhD[2]; Eleftherios A. Makris, MD, PhD[3]; Steven D. Forsythe, MS, PhD.[4]; Richard Andrew Erali, MD[5]; Ashok K. Pullikuth, M.Sc., PhD[6]; Perry Shen, MD[7]; Shay Soker, PhD[8]; Edward A. Levine, MD[9]; Konstantinos I. Votanopoulos, MD, PhD[10]; Lance D. Miller, [11]
[1]Wake Forest University School of Medicine, Winston-Salem, NC, US; [2]Wake Forest Institute for Regenerative Medicine, Winston-Salem, NC, US; [3]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [4]Center for Cancer Research, National Institutes of Health, Bethesda, MD, US; [5]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [6]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [7]Atrium Health Wake Forest Baptist Medical Center, Winston Salem, NC, US; [8]Wake Forest Institute for Regenerative Medicine, Winston Salem, NC, US; [9]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [10]Wake Forest Institute for Regenerative Medicine, Winston Salem, NC, US; [11]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US

INTRODUCTION: Metastatic appendiceal cancer (mAC) is an aggressive orphan disease that affects ~1/100,000 patients in the U.S. every year. Clinically, mAC presents as multiple tumor lesions colonizing spatially distinct sites throughout the peritoneal cavity, with no group yet to assess the molecular heterogeneity between distinct metastases in regard to drug responsiveness. **METHODS:** With IRB approval, we created patient-derived tumor organoids (PTOs) from 25 mAC patients treated at our institution to model the role of intra-patient tumor heterogeneity on drug responsiveness. We performed PTO drug screening with standard chemotherapies (FOLFOX, FOLFIRI) to enrich for chemo-sensitive or -resistant tumor cell subclones. **RESULTS:** PTOs derived from anatomically distinct locations within the same patient and treated with equimolar doses of FOLFOX or FOLFIRI showed, in some instances, differential drug responses as measured by ATP release. We then selected 30 tumors from 10 patients that demonstrated robust chemo-sensitivity or -resistance between treatments for downstream whole exome sequencing (WES). PTO DNA was extracted from 90 total treated PTO groups (vehicle, FOLFOX, FOLFIRI) and 10 corresponding saliva samples (healthy controls), analyzed for integrity and quantity, then analyzed by WES using the Illumina NextSeq 6000 platform. Resulting data were processed and analyzed for mutation calls using GATK and DRAGEN pipelines. The variant allele frequency (VAF) was quantified and compared between vehicle-treated and FOLFOX or FOLFIRI-treated PTOs- an increase in VAF post-treatment represented possible chemo-resistance, with decrease in VAF representative of possible chemo-sensitivity. Recurrent mutations solely associated with chemo-resistant PTOs and present in ≥40% (n=4/10) of our mAC patients were associated with impaired G-coupled protein receptor function, dysregulated Wnt signaling, inhibition of DNA damage repair, and inhibition of intrinsic apoptosis. Alterations exclusive to chemo-sensitive PTOs and present in ≥30% (n=3/10) of mAC patients include negative regulators of fatty acid metabolism, inducers of epithelial to mesenchymal transition (EMT), and repressors of t-cell invasion. **CONCLUSIONS:** These preliminary data suggest that the underlying biology of chemo-sensitivity or -resistance in mAC may be predicted through the PTO-modeled identification of recurrent mutations across inter- and intra-patient lesions. Follow up analyses on a larger cohort of mAC PTOs will be needed to validate these findings.

Table. Selected Cases to Represent Inter-Patient Tumor Organoid Modeling of Chemotherapy Sensitivity or Resistance. Patient 1 presents with four peritoneal surface tumors, two of which contain EZH1 mutations. After FOLFIRI treatment, the residual cells in the PTO had a statistically significant depletion in cells containing the EZH1 mutation, suggesting EZH1 mutation may associate with drug sensitivity. Patient 2 also presents with four peritoneal surface tumors, and two of which contain SLC22A5 mutations. In patient 2's liver stripping, treatment of FOLFIRI enriched for SLC22A5 mutant clones to increase in the PTO, which associated with an overall gain in PTO viability after treatment. Patient 2's tumor spleen, despite having an overall chemo-sensitivity associated response, selected for an increase in SLC22A5 mutant cells after FOLFOX treatment. SLC22A5 mutant clones only appear after FOLFOX/ FIRI treatment, which suggests that SLC22A5 mutation may confer a chemo-resistant phenotype after chemotherapy. Further analyses will integrate multiple gene mutations for molecular pathways identification and for the prediction peritoneal surface disease drug response.

Patient One (Tumor Site for PTO)	Chemotherapy Treatment	EZH1 Mutant or Wild Type	Average PTO Viability (%)	PTO Sensitive/ No Response
Primary Appendix	Control	Wild Type	100%	
	FOLFOX	Wild Type	104%	No Response
	FOLFIRI	Wild Type	122%	No Response
Omentum	Control	Wild Type	100%	
	FOLFOX	Wild Type	104%	No Response
	FOLFIRI	Wild Type	106%	No Response
Small Bowel	Control	**Mutant**	100%	
	FOLFOX	Wild Type	73%	No Response
	FOLFIRI	Wild Type	47%	**Sensitive**
Left Ovary	Control	**Mutant**	100%	
	FOLFOX	Wild Type	75%	No Response
	FOLFIRI	Wild Type	53%	**Sensitive**
Patient Two (Tumor Site for PTO)	**Chemotherapy Treatment**	**SLC22A5 Mutant or Wild Type**	**Average PTO Viability (%)**	**PTO Sensitive/ No Response**
Left Ovary	Control	Wild Type	100%	
	FOLFOX	Wild Type	72%	No Response
	FOLFIRI	Wild Type	69%	No Response
Liver Stripping	Control	Wild Type	100%	
	FOLFOX	Wild Type	116%	No Response
	FOLFIRI	**Mutant**	**114%**	**No Response**
Omentum	Control	Wild Type	100%	
	FOLFOX	Wild Type	122%	No Response
	FOLFIRI	Wild Type	147%	No Response
Tumor Spleen	Control	Wild Type	100%	
	FOLFOX	**Mutant**	57%	**Sensitive**
	FOLFIRI	Wild Type	79%	No Response

108. Safety, Feasibility and Immunomodulatory Activity of Intra-peritoneal, Intra-tumoral Lipopolysaccharide in Patients with Peritoneal Carcinomatosis: Results of the Regional Immuno-Oncology Trial (RIOT)-1

Christopher Sherry, DO[1]; Neda Dadgar[2]; Hyun Park[3]; Rosie Blodgett[4]; Chelsea Knotts[5]; Erin Grayhack[6]; Ashten Omstead[7]; Kunhong Xiao[8]; Ali Zaidi[9]; Vera Donnenberg[10]; Albert Donnenberg[11]; David Bartlett[12]; Patrick Wagner[13]
[1]Allegheny Health Network, Pittsburgh, PA, US; [2]Cleveland Clinic Foundation, Cleveland, OH, US; [3]Allegheny Health Network, Pittsburgh, PA, US; [4]Allegheny Health Network, Pittsburgh, PA, US; [5]Allegheny Health Network, Pittsburgh, PA, US; [6]Allegheny Health Network, Pittsburgh, PA, US; [7]Allegheny Health Network, Pittsburgh, PA, US; [8]Allegheny Health Network, Pittsburgh, PA, US; [9]Allegheny Health Network, Pittsburgh, PA, US; [10]Allegheny Health Network, Pittsburgh, PA, US; [11]Allegheny Health Network, Pittsburgh, PA, US; [12]Allegheny Health Network, Pittsburgh, PA, US; [13]Allegheny Health Network, Pittsburgh, PA, US

INTRODUCTION: Intra-tumoral immunotherapy is an attractive option for treating advanced cancers, but its utility in intra-abdominal tumors has been limited by the need for invasive procedures to access these tumors. We investigated the safety and feasibility of intra-peritoneal tumor injection with E. coli 0113-derived lipopolysaccharide (LPS), a toll-like receptor 4 (TLR4) agonist, and assessed biomarkers of immune response within the tumor microenvironment after injection. **METHODS:** The Regional Immuno-Oncology Trial-1 (RIOT-1; NCT05751837) was a Phase I trial in which patients with peritoneal carcinomatosis underwent a single 1 μg dose of LPS by intra-tumoral injection during a diagnostic laparoscopy in anticipation of a subsequent laparotomy. All patients were scheduled to undergo standard-of-care laparotomy on day 14 following injection, for definitive cytoreduction or palliative surgery,

at which time LPS-injected tumors and saline-injected intra-patient control tumors were harvested. In addition to primary safety outcomes, biomarkers of immunomodulatory activity were assessed on harvested tissues. **RESULTS:** LPS injection was performed in 12 patients and was asymptomatic without any study-related adverse events observed. All patients returned for planned laparotomy on day 14 post-injection. Evidence of immunomodulatory activity was seen in a a 54% reduction in CD8+ lymphocyte density and 62% decrease in CD8+:CD3+ lymphocyte ration, with concomitant increase in both M1-like (176% increase and M2-like (162% increase) macrophages. None of thes statistically significant alterations (p<0.0001), was observed in the intra-patient control (saline-injected) tumors. **CONCLUSIONS:** Intra-abdominal, intra-tumoral injection of the TLR4 agonist LPS was feasible and safe in this Phase I study, and was associated with specific, measurable alterations in the tumor immune microenvironment at 14 days post-injection. Additional delineation of immunologic response biomarkers is currently underway. Harvesting of injected tumors at subsequent laparotomy represents a window-of-opportunity concept to assess the performance of laparoscopically injected immunotherapeutic agents in peritoneal surface malignancies. Further investigation is warranted to explore the therapeutic implications of these findings.

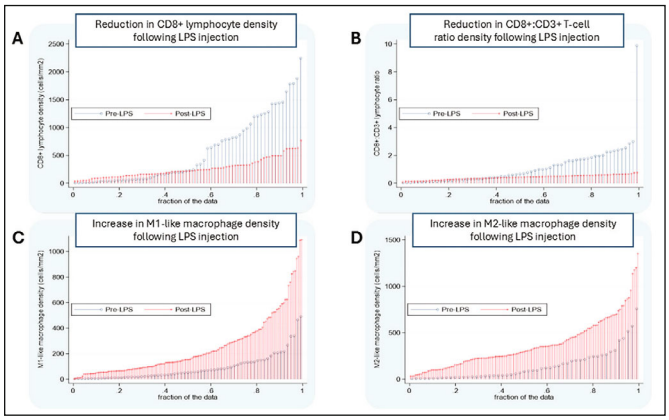


Figure 1. Immune cell modulation following LPS injection. Reductions were seen in CD8+ T-cell density (mean -54%, p<0.0001, panel A) and the CD8+CD3+ T-cell ratio (mean -62%, p<0.0001, panel B). Macrophage densities, on the other hand, substantially increased following LPS injection for both M1-like (mean +176%, p<0 .0001, panel C) and M2-like (mean +162%, p<0.0001, panel D) macrophages.

109. Hyperthermia-Mediated Immunogenic Changes Increase Susceptibility of Colorectal Cancer Metastases to Immunotherapy

Michael Tasker[1]; Eran Nizri[2]
[1]Sorasky medical center, Kaplan medical center, Tel Aviv, IL; [2]Tel-Aviv Sourasky Medical Center, Tel-Aviv, IL

INTRODUCTION: Peritoneal metastases (PM) of colorectal cancer (CRC) are currently treated by cytoreductive surgery (CRS) and heated intra-peritoneal chemotherapy (HIPEC). However, tumor recurrence is common even after complete macroscopic resection, and the efficacy of current HIPEC regimens is debated. In previous experiments, we demonstrated that HIPEC induced immunogenic changes that increased tumor cells' susceptibility to immunotherapy. This study aims to investigate whether hyperthermia alone can achieve similar effects. **METHODS:** PM-CRC was induced in C57BL mice via intraperitoneal injection of 1x10^6 MC38 cells. After 7 days and establishment of PM, mice were treated according to the following groups: sham, HIPEC (with mitomycin C at a human equivalent dose of 0.01 mg/ml), HIPEC + anti-PD-1 (a-PD-1), Hyperthermia (Hyp), and Hyp + a-PD-1. Mice were monitored for overall survival (OS) and weight. Tumor tissue was collected at various time points post-treatment to analyze immune cell infiltration using FACS. In vitro studies on MC38 cells assessed the effects of Hyp and HIPEC on immunogenicity markers, specifically danger-associated molecular patterns (DAMPs) such as calreticulin, HSP70, HSP90, HMGB-1, MHC-class-I and PDL-1. **RESULTS:** HIPEC treatment increased animal survival compared to sham (median OS: 25 vs. 18 days, 95% CI: 2.3-33.7 days). The combination of HIPEC and a-PD-1 further improved OS (29 days, 95% CI: 28.12-29.9), with Hyp + a-PD-1 showing the best outcomes (31 days, 95% CI: 27.1-34.9, p<0.001). HIPEC treatment resulted in increased CD8+ activity within metastases compared to sham (CD8+Ki-67+ positivity: 35% vs. 22%). Hyperthermia alone significantly increased the expression of calreticulin and HSP70 on MC38 cells (1.56 ± 0.02 vs. 1; 2.61 ± 0.65 vs. 1.2, respectively, $p < 0.05$), while HIPEC was more efficient in up-regulating HSP90 (2.37 ± 1.5 vs. 1.3 ± 0.2, $p < 0.05$). In vitro studies demonstrated a significant increase in PD-L1 and MHC class I expression on tumor cells treated with hyperthermia or HIPEC. **CONCLUSIONS:** Hyperthermia, administered without chemotherapy, induces immunogenic changes in tumor cells, enhancing the efficacy of immunotherapy for treating peritoneal metastases from colorectal cancer (PM-CRC) in experimental models. Both in vivo and in vitro findings suggest that hyperthermia is non-inferior to HIPEC in augmenting tumor immunogenicity signals. This study could pave the way for novel applications of combined hyperthermia and immunotherapy in the treatment of PM-CRC.

110. Whole genome sequencing reveals distinct mutational signatures in appendiceal cancer subtypes

Marc Attiyeh, MD[1]; Alexandra Gangi, MD, FSSO[2]; Allan Silberman, MD PhD[3]; Mustafa Raoof, MD[4]; Cristina R. Ferrone, MD, MS, FSSO[5]
[1]Cedars-Sinai Medical Center, Los Angeles, CA, US; [2]Cedars-Sinai Medical Center, Los Angeles, CA, US; [3]CedarsSinaiMC, Los Angeles, CA, US; [4]City of Hope Medical CenterUS; [5]Cedars-Sinai Medical Center, Los Angeles, CA, US

INTRODUCTION: Appendiceal cancers encompass histological subtypes with distinct clinical behaviors and biology. Whole genome sequencing (WGS) can characterize their mutational landscapes and identify subtype-specific signatures. Understanding these genomic differences can help uncover tumor biology and potential therapeutic strategies. **METHODS:** Sixteen WGS samples comprised of adenocarcinoma (AD), goblet cell adenocarcinoma (GCA), mucinous adenocarcinoma (MUC), and signet ring cell carcinoma (SRC) were obtained from the Hartwig Medical Foundation (Amsterdam, Netherlands). Variant types/counts and transition/transversion (Ts/Tv) ratios were extracted, and mutational signatures were identified using the SigProfiler software package (Wellcome Sanger Institute), focusing on contributions from single base substitutions (SBS), doublet base substitutions (DBS), and insertions/deletions (indels). **RESULTS:** ADs demonstrated a mean Ts/Tv ratio of 1.20, suggesting a balanced mutational profile, with contributions from SBS18 (oxidative damage) and SBS13 (cytidine deamination). GCAs had contributions from SBS17a and SBS17b, which are associated with oxidative stress, possible exposure to chemotherapy agents (e.g., 5-FU), and genomic instability. MUCs had the highest mutational burden (23,156 variants/sample) with a notable contribution from SBS88, which is associated with exposure to colibactin, a bacterial genotoxin produced by *E. coli* linked to colorectal cancer development. SRCs had a mean Ts/Tv ratio of 1.00, significantly lower than ADs ($p < 0.05$) and MUCs ($p < 0.01$), indicating increased genomic instability or defective DNA repair. SRCs displayed a heterogeneous genomic landscape with no single dominant SBS signature. One SRC sample, an outlier with a high variant count and disproportionate SBS44 contribution (associated with mismatch repair deficiency), was excluded from analysis. **CONCLUSIONS:** WGS reveals distinct mutational patterns across appendiceal cancer subtypes. MUCs show a high mutational burden and Ts/Tv ratio, potentially linked to microbiome-associated mutagenesis driven by colibactin exposure. GCAs show signatures tied to oxidative stress and chemotherapy exposure. ADs exhibit mixed mutational processes with contributions from oxidative damage and cytidine deamination. SRCs have a lower Ts/Tv ratio, indicating genomic instability or defective DNA repair. These findings highlight distinct mechanisms driving appendiceal cancer subtypes, suggesting implications for treatment and prognosis.

Type	N	TMB	Variants	SNPs	MNPs	Indels	Ts/Tv ratio	Dominant signatures
Adenocarcinoma	5	6.95 ± 4.40	20,852 ± 13,202	14,811 ± 9,423	96 ± 70	5,936 ± 5,103	1.20 ± 0.31	SBS18 (oxidative damage), SBS13 (cytidine deamination)
Goblet cell adenocarcinoma	3	3.23 ± 1.13	9,682 ± 3,398	7,893 ± 2,346	39 ± 11	1,750 ± 1,043	1.04 ± 0.34	SBS17a, SBS17b (oxidative stress-associated)
Mucinous adenocarcinoma	2	7.72 ± 5.60	23,156 ± 16,809	18,397 ± 14,101	79 ± 25	4,680 ± 2,683	1.39 ± 0.06	SBS88 (colibactin exposure)
Signet ring cell adenocarcinoma	5	6.09 ± 2.15	18,264 ± 6,454	14,223 ± 4,906	121 ± 78	3,920 ± 1,687	1.00 ± 0.23	Heterogenous without a dominant SBS

Mean ± standard deviation; TMB: tumor mutational burden (mutations/megabase); SNP: single nucleotide polymorphism; MNP: multiple nucleotide polymorphism; Indel: insertion or deletion; Ts/Tv ratio: transition/transversion ratio.

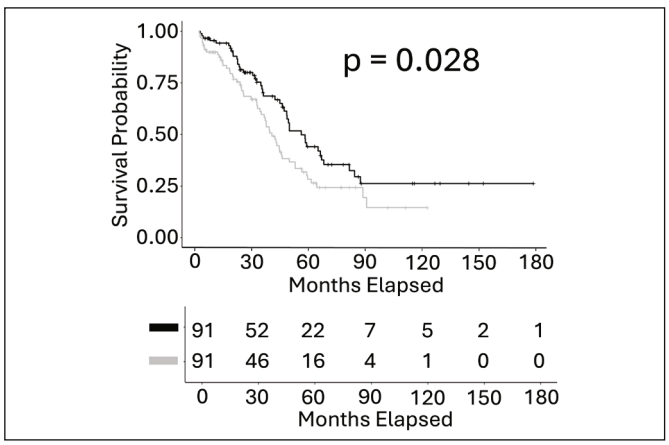
Quality/Disparities

111. Higher Chemical Complementarity Between Epstein-Barr Virus Epitopes and Immunoglobulin Heavy Chain CDR3 Regions Correlates with Better Outcomes for Ovarian Cancer Patients

Madeline C. Baker, Medical Student[1]; Nandini Goel, Medical Student[2]; Rahul Jain, Medical Student[3]; Taha I. Huda, MD[4]; Andrea Chobrutskiy, MD[5]; Boris I. Chobrutskiy, MD[6]; Joanna J. Song, Medical Student[7]; Veda Naga Priya Vangala, MS[8]; George Blanck, PhD[9]

[1]University of South Florida Morsani College of Medicine, Tampa, FL, US; [2]University of South Florida Morsani College of Medicine, Tampa, FL, US; [3]University of South Florida Morsani College of Medicine, Tampa, FL, US; [4]University of South Florida Morsani College of Medicine, Tampa, FL, US; [5]Department of Pediatrics, Oregon Health and Science University Hospital, Portland, OR, US; [6]Department of Internal Medicine, Oregon Health and Science University Hospital, Portland, OR, US; [7]University of South Florida Morsani College of Medicine, Tampa, FL, US; [8]University of South Florida Morsani College of Medicine, Tampa, FL, US; [9]University of South Florida Morsani College of Medicine, Tampa, FL, US

INTRODUCTION: Ovarian epithelial carcinoma is the deadliest gynecological cancer, and the link between Epstein-Barr Virus (EBV) and ovarian cancer is not well understood. This study aimed to assess whether higher chemical complementarity scores (CSs) between EBV epitopes and immunoglobulin heavy chain (IGH) CDR3 amino acid sequences affect survival outcomes in ovarian cancer patients. **METHODS:** This retrospective, quantitative study analyzed NIH dbGaP data, focusing on the TCGA-Ovarian dataset. IGH CDR3 recombination sequences were mined from RNASeq files, and CSs between IGH CDR3s and EBV epitopes were calculated via an Adaptive Match tool. EBV epitopes with significant survival distinctions were identified through univariate Cox regression and log-rank p-values, with Kaplan-Meier curves made to compare the upper and lower 50th percentile CS groups. This analysis was repeated for two additional datasets, NCICCR-Diffuse Large B-cell Lymphoma (DLBCL) and CGCI-Burkitt Lymphoma Genome Sequencing Project (BLGSP), due to the known association of EBV with lymphomas. **RESULTS:** For each dataset, higher complementarity to specific EBV epitopes correlated with better survival outcomes. TCGA-OV IGH cases in the upper 50th percentile for Hydro CSs with EBV epitope IEDB*30951 showed improved overall survival (OS), progression-free survival (PFS), and disease-specific survival (DSS) in KM analyses (p=0.028 for OS, p=0.034 for PFS, and p=0.049 for DSS). With both BLGSP and DLBCL, high Hydro CSs based on IGH CDR3s and high-survival EBV epitopes showed better OS. Given that certain lymphomas are associated with EBV infections, the findings suggest that lymphoma may occasionally be misdiagnosed as ovarian epithelial carcinoma. This misdiagnosis may explain the improved survival in patients with higher CSs, as lymphomas typically have a better prognosis than ovarian cancer. While the exact mechanism is not understood, higher EBV complementarity may reflect a stronger immune response to the cancer. **CONCLUSIONS:** This study highlights the importance of an accurate diagnosis, as treatment varies significantly between lymphoma and ovarian epithelial carcinoma. It also suggests the value of testing EBV antibody titers, which could help identify misdiagnoses and predict survival in ovarian cancer patients, as better complementarity to EBV is associated with improved survival outcomes.



112. Social Vulnerability and Clinical Trial Enrollment Among Breast Cancer Patients: How Do the Highest Mortality States Compare?

Rachel A Sachs, MD[1]; Shruthi R Perati, MD[2]; Sana M Mohayya[3]; Ernie Shippey[4]; Xiang Gao[5]; Larissa Pamen[6]; Shicha Kumar[7]; Coral Omene[8]; Henry A. Pitt, MD[9]; Mariam F. Eskander, MD[10]

[1]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, US; [2]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, US; [3]Rutgers Cancer Institute, New Brunswick, NJ, US; [4]Vizient Clinical Database Inc, Irving, TX, US; [5]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, US; [6]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, US; [7]Rutgers Cancer Institute, New Brunswick, NJ, US; [8]Rutgers Cancer Institute, New Brunswick, NJ, US; [9]Rutgers Cancer Institute, New Brunswick, NJ, US; [10]Rutgers Cancer Institute, New Brunswick, NJ, US

INTRODUCTION: Clinical trials are an important part of breast cancer treatment, but disadvantaged populations face barriers to enrollment. This study assesses the impact of social vulnerability on national breast cancer clinical trial enrollment, with state-specific analyses in the four states with the highest breast cancer mortality rates. **METHODS:** The national Vizient Clinical Database was queried for outpatients with breast cancer between January 2018 and June 2024. This dataset includes 98% of academic medical centers and more than 110 cancer hospitals. Social vulnerability was measured by the Vizient Vulnerability Index (VVI), a novel marker of social drivers of health at the census tract level made up of 9 domains. A multivariable analysis was performed evaluating the association of each social vulnerability domain with clinical trial participation. State-specific multivariable analyses were performed in Louisiana (LA), Mississippi (MS), Nevada (NV), and Oklahoma (OK). **RESULTS:** 2,121,567 patients were identified nationally; 1.8% enrolled in a clinical trial. Trial participants were more likely to be young, White, privately insured, have metastatic disease, and live in a less vulnerable census tract. On multivariable analysis, living in the most vulnerable VVI quartile both on a national (OR 0.48; 95% CI 0.45-0.50, p<0.0001) and state level (LA: OR 0.02; 95% CI 0.01-0.05, p<0.0001; MS: OR 0.02; 95% CI 0.01-0.02, p< OK: OR 0.01; 95% CI 0.002-0.01, p<0.0001) was associated with decreased odds of clinical trial enrollment. On a national level, the highest social vulnerability quartiles (ref: least vulnerable) in the VVI domains for economic (OR 0.92; 95% CI 0.75-1.00, p<0.0001), education (OR 0.98; 95% CI 0.91-0.99, p=0.002), housing (OR 0.32; 95% CI 0.30-0.33, social environment (OR 0.76; 95% CI 0.72-0.8, and transportation (OR 0.62; 95% CI 0.59-0.65, p<0.0001) were associated with decreased enrollment. Results by state are portrayed in Table 1. **CONCLUSIONS:** Patients with breast cancer living in socially vulnerable census tracts are 50% less likely to enroll in a clinical trial. This impact is greatly amplified in high-mortality states. Nationally, communities vulnerable in the economic, education, housing, social environment, and transportation domains have lower odds of clinical trial enrollment. However, states with varying demographics and geography face different barriers. Interventions targeting social vulnerability must be locally tailored to increase equity in clinical trials.

Table 1. Select state-specific domain multivariate analysis; ORs represent odds of clinical trial enrollment for most vs. least vulnerable quartile.

Location	VVI Domain	OR	95% CI	p-value
LA	*Education*	0.23	0.09-0.42	0.0003
	Healthcare Access	0.67	0.54-0.85	0.0322
	Neighborhood Resources	0.27	0.22-0.39	0.0012
	Social Environment	0.22	0.12-0.40	<0.0001
	Public Safety	0.06	0.04-0.09	<0.0001
MS	*Economic*	0.03	0.01-0.15	<0.0001
	Education	0.26	0.08-0.90	0.0338
	Healthcare Access	0.04	0.01-0.20	<0.0001
	Neighborhood Resources	0.20	0.05-0.74	0.016
	Social Environment	0.02	0.01-0.06	<0.0001
	Public Safety	0.55	0.53-0.67	0.0031
NV	*Education*	0.78	0.72-0.93	0.0271
	Healthcare Access	0.04	0.01-0.20	<0.0001
	Housing	0.18	0.04-0.75	0.0183
	Public Safety	0.14	0.04-0.54	0.004
OK	*Economic*	0.65	0.55-0.78	<0.0001
	Education	0.26	0.08-0.90	0.0338
	Healthcare Access	0.52	0.30-0.90	0.0184
	Public Safety	0.46	0.36-0.72	0.0349

113. Analyzing Financial Toxicity for Breast Cancer Care in India

Abhirup C Are[1]; Shilpa Murthy, MD, MPH[2]; Nisha Hariharan, MBBS, MS[3]; Makayla Schissel, MPH[4]; Subramanyeshwar R Thammineedi, MBBS, MS, MCh[5]; Srijan Shukla, MBBS, MS, DNB (General Surgery), DNB (Surgical Oncology)[6]

[1]Northwestern University, Evanston, IL, US; [2]Yale School of Medicine, New Haven, CT, US; [3]Basavatarakam Indo American Cancer Hospital & Research Institution, Hyderabad, Telangana, IN; [4]University of Nebraska Medical Center, Omaha, NE, US; [5]Basavatarakam Indo American Cancer Hospital & Research Institute, Hyderabad, Telangana, IN; [6]Basavatarakam Indo American Cancer Hospital & Research Institute, Hyderabad, Telangana, IN

INTRODUCTION: Breast cancer is one of the most common cancers affecting women in India. Breast cancer patients are known to experience varying levels of financial toxicity (FT) that can have a detrimental effect on their care. The aim of this study is to analyze the level of FT associated with breast cancer care in India by utilizing a survey tool to measure a) financial distress, b) out-of-pocket expenditure (OOPE), and c) distress financing (DF). **METHODS:** The study was conducted at a tertiary care cancer center in India (7/9/2024 to 8/20/2024) that treats a large volume of breast cancer patients across the entire economic spectrum, but with a high volume of patients from the lower socio-economic strata (LSES). Financial distress was assessed using a survey tool that included questions from previously validated survey instruments: FACIT-COST (range 0-44, with a higher score indicating better financial well-being) and PROFFIT (range 0-100, lower score indicating lower levels of financial toxicity). Out of pocket expenditure (OOPE) data was obtained and measured as a percentage of household income. Distress financing (DF) was measured as the type of personal assets and the number of times these assets were sold to sustain cancer care. All analyses were conducted using SAS version 9.4. **RESULTS:** A total of 151 patients with a median age of 51 years were included in the study. Most patients were of LSES, with 80% having a monthly household income of less than 25,000 INR (~298 USD). Nearly 50% of patients were within one year of initial diagnosis, with 52% having Stage III disease. Nearly all patients (99%) were enrolled in State-sponsored health insurance programs. Extreme levels of financial toxicity were noted in the majority of patients when measured by both FACIT-COST [low median score of 12 (IQR 8-17)] and PROFFIT tools [high median score of 85.7 (IQR 81-95.2)]. OOPE was documented in 100% of patients. For 130 patients (86%), OOPE accounted for 76-100% of their monthly household income. DF was reported by 123 patients (82%), with 106 (70%) of them having to dispose assets more than once that consisted of house, land and jewelry to fund their care. A total of 126 patients (84%) reported partial or complete loss of livelihood/employment. **CONCLUSIONS:** The results of our study demonstrate extreme levels of financial toxicity in patients undergoing breast cancer care in India. Despite being enrolled in State-sponsored health insurance programs, the majority of patients reported OOPE and DF. Further studies are required to drive policy changes that can help to ameliorate financial toxicity for breast cancer care in India.

114. Mutational landscape of gastric cancer in Black patients

Carolina M Larrain[1]; John G Aversa[2]; Darryl Nousome[3]; Jack Victory[4]; Tracey Pu, MD[5]; Alyssa Eade[6]; Lindsay R Friedman[7]; Imani Alexander[8]; Justin A. Drake[9]; Michael M Ittmann[10]; Daniel G Rosen[11]; Cecilia Monge[12]; Steven Hochwald[13]; Paxton V. Dickson, MD[14]; Kamran Idrees[15]; R. Taylor Ripley[16]; Jeremy L. Davis, MD[17]; Jonathan M Hernandez[18]

[1]National Institutes of Health, Bethesda, MD, US; [2]National Institutes of Health, Bethesda, MD, US; [3]National Institutes of Health, Bethesda, MD, US; [4]National Institutes of Health, Bethesda, MD, US; [5]National Cancer Institutes/ National Institutes of Health, Bethesda, MD, US; [6]National Institutes of Health, Bethesda, MD, US; [7]National Institutes of Health, Bethesda, MD, US; [8]National Institutes of Health, Bethesda, MD, US; [9]National Institutes of Health, Bethesda, MD, US; [10]Baylor College of Medicine, Houston, TX, US; [11]Baylor College of Medicine, Houston, TX, US; [12]National Institutes of Health, Bethesda, MD, US; [13]Roswell Park, Buffalo, NY, US; [14]University of Tennessee Health Science Center, Memphis, TN, US; [15]Vanderbilt University Medical Center, Nashville, TN, US; [16]Baylor College of Medicine, Houston, TX, US; [17]National Cancer Institute, Bethesda, MD, US; [18]National Institutes of Health, Bethesda, MD, US

INTRODUCTION: Gastric adenocarcinoma is a heterogenous disease that results from complex interactions between environmental and genetic factors, which may contribute to the disparate outcomes observed between different patient populations in the United States. Despite wide accessibility of next-generation sequencing, little is known about the molecular profile of gastric cancer in Black patients as this population has not been represented in large sequencing efforts. **METHODS:** Gastric cancer samples from Black patients were collected. DNA was extracted from formalin-fixed paraffin embedded tumor tissue and targeted sequencing was performed. Ancestry analysis was performed using Somalier with 1Kg samples as reference using the Tumor Data. Variant calling was performed using Mutect, Mutect2, Varscan, Vardict. Pathogenic variants or variants of undetermined significance were included. A comparative analysis with non-Hispanic White and Asian cohorts was performed using data obtained from the TCGA. **RESULTS:** Gastric cancer tumor DNA from 78 Black patients was analyzed. We analyzed ancestry from the tumor tissue, with results mostly consistent with African ancestry (Figure). TMB was low (4 patients with > 10mut/MB) for Black patients (Figure). The most frequently mutated gene was *TP53* (44.8%) (Figure), consistent with White (45.8%) and Asian (47.1%) patients. Black, White and Asian patients had similar locations of mutations and mutation type (e.g. missense) in the *TP53* gene protein domains (Figure). When comparing other frequently mutated genes in the Black cohort, we identified a significant increase in *ARSA* mutations compared to the White cohort [9% vs. <1%, x^2 (1, n=342) = 19.47, p = <0.01] and the Asian cohort [9% vs 1.2%, n=165) = 5.45, p = 0.02]. Likewise, HNF1A mutations were significantly elevated in the Black cohort compared to both the White cohort [8% vs. 2.6%, n=342) = 4.18, p=0.04] and the Asian cohort [8% vs 1.1%, n=165) = 4.33, p = 0.04]. When comparing the most frequently mutated genes in the White cohort with the Black cohort, we identified a significant decrease in MUC16 in the Black cohort (33% vs. 0%, n=342) = 35.01, p= <0.01). **CONCLUSIONS:** In examining gastric cancer tumor genetics in this large Black cohort, we identified some molecular differences from that of White and Asian patients. The impact of these differences is difficult to quantify, and it is highly likely that other factors such as socioeconomic status and access to care play a major role in disparate survival outcomes observed in this population. These results also highlight the importance of recruiting diverse patient populations to clinical studies.

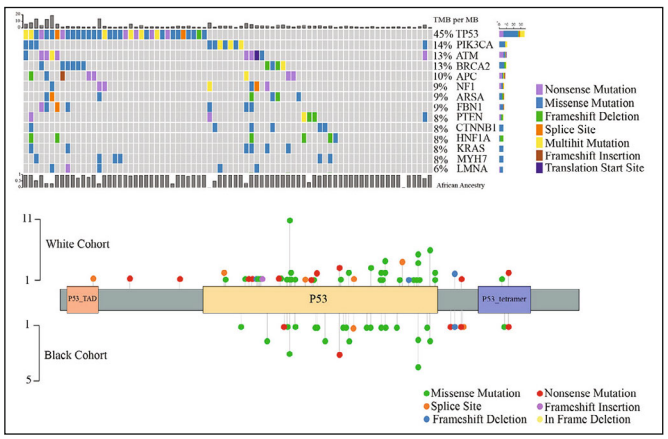


Figure. (Top) Oncoplot for Black patients with gastric cancer, including TMB status and African ancestry. (Bottom) Lollipop plot demonstrating location and type of TP53 mutations in the White and Black cohorts.

115. HOMECARE – need for homecare after cancer surgery for older adults: derivation and validation of a predictive tool.

Tiago Ribeiro, MD, MSc[1]; Amy Hsu[2]; Alyson Mahar[3]; Wing C Chan[4]; Daniel McIsaac[5]; Natalie G Coburn, MD, MPH[6]; Anna Gombay[7]; Anna Ding[8]; Jessica Armah[9]; Julie Hallet, MD[10]

[1]University of Toronto, Toronto, ON, CA; [2]Ottawa Hospital Research Institute, Ottawa, ON, CA; [3]Queens University, Kingston, ON, CA; [4]ICES, Toronto, ON, CA; [5]Ottawa Hospital Research Institute, Ottawa, ON, CA; [6]University of Toronto, Toronto, ON, CA; [7]Sunnybrook Research Institute, Toronto, ON, CA; [8]sunnybrook research institute, Toronto, ON, CA; [9]Sunnybrook Research Institute, Toronto, ON, CA; [10]NA, Toronto, ON, CA

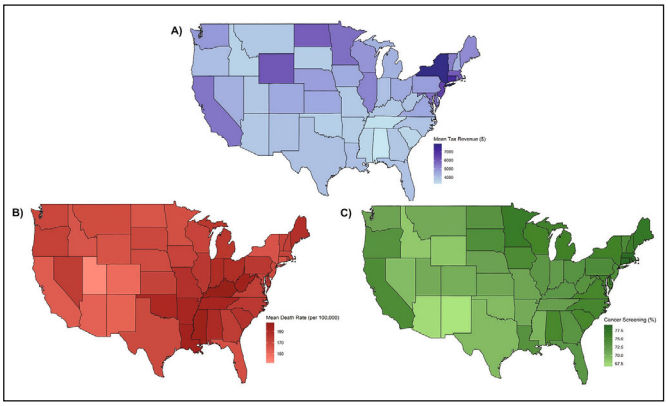
INTRODUCTION: Prognostication tools that report personalized risk estimates of patient-centred outcomes can improve discussions and preparation for older adults having cancer surgery. Need for home support after surgery is a patient-centred outcome and marker of functional recovery for older adults. Among older adults, over 15% become healthcare dependent in the year after cancer surgery. We developed and internally validated a risk prediction model, HOMECARE, to estimate the risk of requiring homecare for older adults after cancer surgery. **METHODS:** Using a population-based cohort

of adults ≥70 years old having surgery for solid malignancy (2007-2019), we developed a predictive model. The outcome was receipt of homecare, divided into 2 phases as per prior work: immediate (within 1 month; acute post-operative need focused on nursing care) and long-term (at 7-12 months; focused personal support services). Logistic regression models were used, with predictor variables selected among pre-operative information. We internally validated with bootstrapping using 500 samples with replacement. **RESULTS:** Of 93,883 patients included, 39,169 (41.72%) required immediate homecare; of the 88,252 alive after month 6 post-operatively, 22,031 (24.96%) required long-term homecare. The predictive model included age, sex, rural residence, previous cancer diagnosis, pre-operative frailty, pre-operative homecare use, cancer site, cancer stage, and type of surgery, and an interaction between cancer site and stage. For immediate homecare, the area under the curve was 0.77 and the deviation of predicted from observed probability was -0.02% (95%CI 0.04 to -0.08). For long-term homecare, the area under the curve was 0.76 and the deviation of predicted from observed probabilities was -0.004% (95%CI 0.002 to -0.009%). Deviation between predicted and observed probabilities ranged from -0.01% to 0.03 % across risk deciles for immediate homecare, and -0.04 to 0.04% for long-term homecare. **CONCLUSIONS:** The HOMECARE tool makes use of information available pre-operatively to predict the probability of requiring homecare immediately and long-term after cancer surgery for older adults. It presents good discrimination and is well calibrated. Individualized risk estimates from this tool can be obtained from an online calculator and used for counselling, setting of expectations and preparation of older adults selected for cancer surgery, as well as planning of support and healthcare resources. External validation and clinical usability testing are underway.

116. Impact of State-level Tax Policy on Cancer Screening and Mortality Rates in the United States

Odysseas P. Chatzipanagiotou[1]; Mujtaba Khalil[2]; Usama Waqar[3]; Selamawit Woldesenbet[4]; Giovanni Catalano[5]; Tim Pawlik[6]
[1]The Ohio State University, Columbus, OH, US; [2]The Ohio State University, Columbus, OH, US; [3]Emory University, Atlanta, GA, US; [4]The Ohio State University, Columbus, OH, US; [5]The Ohio State University, Columbus, OH, US; [6]The Ohio State University, Columbus, OH, US

INTRODUCTION: The Healthy People 2030 initiative has set national cancer screening targets for breast, colon, and cervical cancer, as well as goals to reduce cancer mortality. State-level tax policy is an underappreciated social determinant of health that may improve cancer screening and mortality via public financing of healthcare and the redistribution of wealth towards the mitigation of socioeconomic and health disparities. We sought to assess the impact that state-level tax revenue and tax progressivity may have on the rates of cancer screening and mortality. **METHODS:** A cross-sectional study design was utilized to examine state-level tax policy (1998-2019) relative to cancer screening and mortality in the US using the Centers for Disease Control and Prevention PLACES and WONDER databases. State-level tax policy was proxied by tax revenue per capita and the Suits index of tax progressivity, with progressive taxation equaling higher taxes for wealthier populations. Multivariable models adjusting for year, federal transfer revenue, other revenue, as well as socioeconomic and demographic variables were utilized. **RESULTS:** A total of 1,100 state-years (1999-2020 for 50 states) were evaluated. Median tax revenue per capita was $4,060 (IQR $3,903-$4,937, Figure). The median number of cancer-related deaths was 8,082 (IQR 3,024-13,481) across all state-years. Of note, each $1,000 increase in tax revenue per capita was associated with a 5.9% increase in odds of colon cancer screening [adjusted Odds Ratio (aOR) 1.059, 95% Confidence Interval (CI) 1.021-1.097], an 8.2% increase in the likelihood of breast cancer screening (aOR 1.082, 95%CI 1.040-1.126), and 4.0% higher odds of cervix cancer screening (aOR 1.040, 95%CI 1.016-1.064). Moreover, a +0.10 difference in a state's Suits index was associated with a 5.3% increase in odds of colon cancer screening. In terms of mortality,000 increase in tax revenue per capita was associated with a 4.7% decrease in cancer mortality (aIRR 0.953, 95% CI 0.927–0.980). Importantly, overall mortality rate decreased by 5.3% among White individuals (aIRR 0.947, 95% CI 0.919–0.977) versus only 1.6% among Black individuals (aIRR 0.984, 95% CI 0.971–0.998). **CONCLUSIONS:** Increase in tax revenue and higher progressivity in tax policy were associated with increased odds of higher state-level cancer screening rates, as well as decreased cancer mortality. However, progressive tax policies primarily benefited White populations. State-level policies based on tax revenue need to focus on improving health equity for all patients with cancer.



117. Impact of reaching the Medicare Part D Drug benefit threshold on surgical care and health outcomes among patients newly diagnosed with gastrointestinal cancer

Odysseas P. Chatzipanagiotou, MD[1]; Eshetu Worku[2]; Selamawit Woldesenbet[3]; Mujtaba Khalil[4]; Tim Pawlik[5]
[1]The Ohio State University, Columbus, OH, US; [2]Ohio State University, Wexner Medical Centre, Columbus, OH, US; [3]The Ohio State University, Columbus, OH, US; [4]The Ohio State University, Columbus, OH, US; [5]The Ohio State University, Columbus, OH, US

INTRODUCTION: Medicare Part D covers outpatient prescription drugs for elderly beneficiaries but requires full cost coverage once the coverage gap threshold is reached. We assessed the impact on out-of-pocket costs (OOP), timely treatment, and outcomes for gastrointestinal cancer patients. **METHODS:** Individuals newly diagnosed with gastrointestinal cancer between 2007 and 2019 were identified from the SEER-Medicare database. OOP costs were calculated for the year of diagnosis. Multivariable regression models compared timely surgical care and mortality risk among patients who reached the coverage gap threshold in the year of diagnosis versus individuals who did not. **RESULTS:** Among 35,745 Medicare beneficiaries diagnosed with colorectal (50.7%), pancreatic (19%), and liver (30.4%) cancer, median age was 76 years (IQR: 71-82), and 56.6% of the cohort were female. Notably, 48.9% (17,479) of patients reached the Medicare Part D threshold in the year of their cancer diagnosis. The mean OOP cost for individuals who reached the threshold was $1,060 (SD: $1,417) versus $268 (SD: $270, p-value < 0.0001) for patients who did not. On multivariable analysis, patients who reached the threshold were more likely to delay [OR: 1.13, 95% CI: 1.03-1.24, p-value = 0.010] or not receive surgery [OR: 1.40, 95% CI: 1.27-1.54, p-value < 0.0001], and had a higher risk of 5-year mortality [HR 5-year: 1.12, 95% CI: 1.09-1.15, p-value < 0.0001] regardless of comorbidity status, cancer site, and disease stage. **CONCLUSIONS:** Reaching the coverage gap threshold reduced receipt of surgical treatment and increased mortality risk among patients with gastrointestinal cancer. Policy initiatives aimed at increasing the coverage gap threshold may reduce financial strain thereby improving access to surgical care and enhancing health equity among cancer patients.

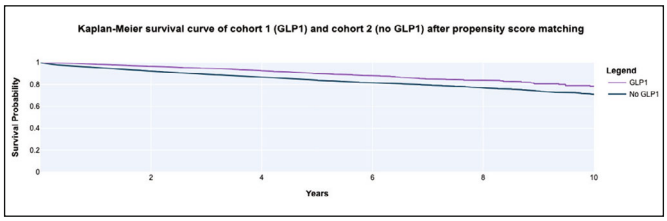
Breast II

118. The Effect of Glucagon-Like Peptide 1 Receptor Agonists on Postmenopausal Breast Cancer Outcomes

Jennifer Den[1]; Nicole Nelson[2]; Kamil Khanipov[3]; Raj Vaghjiani[4]; Douglas Tyler[5]; Vicki S Klimberg[6]
[1]The University of Texas Medical Branch at Galveston, Galveston, TX, US; [2]University of Texas Medical Branch - Galveston, TX, Galveston, TX, US; [3]University of Texas Medical Branch - Galveston, TX, Galveston, TX, US; [4]University of Texas Medical Branch - Galveston, TX, Galveston, TX, US; [5]University of Texas Medical Branch - Galveston, TX, Galveston, TX, US; [6]University of Texas Medical Branch - Galveston, TX, Galveston, TX, US

INTRODUCTION: Studies have shown that obesity increases the risk of postmenopausal breast cancer (BC) by 30-60% and is associated with poorer outcomes. This is believed to be related to continued exposure to estrogen and prolonged inflammation. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have been suggested to significantly lower the risk of several obesity-

associated cancers (OACs). We hypothesize that GLP-1RAs can improve outcomes in obese postmenopausal BC patients. **METHODS:** We conducted a retrospective cohort study using the TriNetX database to compare the outcomes of female BC patients ≥45 years old with a BMI of ≥35 kg/m². We created two cohorts: those who took GLP-1RAs with a Stage I-III BC diagnosis and those who never had exposure to GLP-1RAs. Patients' propensity score was matched based on age, BMI, diabetes, socioeconomic status, and genetic carrier status. Our outcomes of interest were 10-year overall survival (OS) and local recurrence (LR). **RESULTS:** We identified 10,498 patients who used GLP-1RAs and 93,174 patients who did not. After matching, 19,348 patients were identified, with 9,674 per cohort. 10-year OS with the Kaplan-Meier analysis was significantly greater in patients on GLP-1RAs (79%) compared to those not on GLP-1RAs (71%), log-rank test p-value <0.0001. The risk of LR was significantly lower (HR 0.481, 95% CI (0.425-0.546)). **CONCLUSIONS:** Postmenopausal breast cancer patients with a BMI ≥35 who took GLP-1RAs after diagnosis had a significantly greater 10-year OS and a lower risk of LR. GLP-1RAs should be investigated as a breast cancer adjunct in high-risk overweight or obese BC patients.



119. Retrospective, population-based cohort study on the associations between tumor size, receptor status, and regional nodal positivity rates for early-stage breast cancer: implications for the decision between upfront surgery vs neoadjuvant systemic therapy

Yerin R. Lee, BHSc[1]; Vasily Giannakeas, PhD, MPH[2]; David W. Lim, MD, CM, MEd, PhD[3]

[1]Women's College Hospital & University of Toronto, Toronto, ON, CA; [2]Women's College Hospital, Toronto, ON, CA; [3]Women's College Hospital & University of Toronto, Toronto, ON, CA

INTRODUCTION: For clinically node-negative T1-T2 breast cancers, the ASCO/Ontario Health guidelines discourage staging axillary ultrasound (AxUS). At the same time, neoadjuvant systemic therapy (NST) is recommended for HER2-positive (+) and triple negative (TN) breast cancers >2 cm, with controversy whether cT1cN0 HER2+ and TN tumors should receive NST or upfront surgery. We evaluated the regional lymph node positivity rates across T1a - T2 tumor sizes for hormone receptor (HR)-negative HER2+, HR+HER2+, HR+HER2-, and TN breast cancers. **METHODS:** We performed a population-based, retrospective cohort study using administrative health databases at ICES Ontario. Data from the Ontario Cancer Registry was extracted for all female patients with invasive breast cancer between 2000 – 2019 in Ontario, Canada. The following variables were analyzed: T stage, regional lymph node status, and estrogen, progesterone, and HER2 receptor statuses. The proportion of patients with positive lymph nodes (N1-3) was calculated for each receptor subtype. Chi-square tests (significance of P <0.05) with post-hoc Marascuilo correction were conducted. Analyses were conducted using SAS® and Python software. **RESULTS:** There were 36,168 T1a – T2 breast cancers, including 1,478 HR-HER2+ (4%), 3,649 HR+HER2+ (10%),688 TN (10%), and 27,353 HR+HER2- (76%). Increasing tumor size was associated with increasing regional nodal positivity rates across all receptor subtypes (P < .001 for all). For T1a lesions, all subtypes showed significant differences in pairwise comparisons, except between HR-HER2+ vs HR+HER2+, and HR-HER2+ vs TN. For T1b and T1c lesions, pairwise comparisons were significantly different between all subtypes. For T2 lesions, all pairwise comparisons were significant, except between HR+HER2- vs HR+HER2+. **CONCLUSIONS:** While current guidelines discourage AxUS for cT1-T2N0 breast cancers, at the population-level, pathologic regional nodal positivity rates are not insignificant for T1-T2 tumors, especially TN and HER2+ tumors. Upfront surgery for patients with pathologically positive nodes results in undertreatment. Furthermore, for cT1c tumors, regional nodal positivity rates reached 34%, 26%, and 20% for HR-HER2+, HR+HER2+, and TN, respectively. These data need to be shared with patients with cT1c tumors when deciding between NST or upfront surgery. Finally, we advocate considering staging AxUS for all HER2+ and TN T1-T2 tumors, irrespective of tumor size.

HR- HER2+					
	Count	Total	Percent	L 95 CI	U 95 CI
T1a	13	118	**11.02**	2.84	12.42
T1b	32	138	**23.19**	10.45	22.88
T1c	133	395	**33.67**	20.55	29.07
T2	320	827	**38.69**	23.36	29.36

HR- HER2- (TN)					
	Count	Total	Percent	L 95 CI	U 95 CI
T1a	10	120	**8.33**	2.79	12.21
T1b	34	292	**11.64**	5.92	12.57
T1c	236	1186	**19.90**	13.69	17.84
T2	660	2090	**31.58**	21.77	25.41

HR+ HER2+					
	Count	Total	Percent	L 95 CI	U 95 CI
T1a	17	151	**11.26**	3.63	12.26
T1b	50	354	**14.12**	8.99	15.87
T1c	312	1199	**26.02**	18.31	22.89
T2	849	1945	**43.65**	30.01	34.16

HR+ HER2-					
	Count	Total	Percent	L 95 CI	U 95 CI
T1a	67	1396	**4.80**	3.3	5.44
T1b	392	4594	**8.53**	7.06	8.61
T1c	2572	11229	**22.90**	19.51	20.99
T2	4437	10134	**43.78**	32.8	34.64

Figure 1. Number of patients with positive lymph nodes for TIa, TIb, TIc, and T2 lesions across HR-HER2+, HR+HER2+, TN, and HR+HER2- tumors.

120. Characterization of the germline pathogenic mutational landscape and oncologic outcomes among 877 patients with invasive lobular carcinoma

Victoria Huynh, MD[1]; Jason Mouabbi[2]; Henry Kuerer, MD[3]; Kerollos N Wanis, MD[4]; Hiam Abdel-Salam[5]; Angelica Gutierrez[6]; Helen Johnson[7]; Anthony Lucci, MD[8]; Kelly K. Hunt, MD, FSSO[9]; Banu Arun[10]

[1]University of Texas MD Anderson Cancer Center, Houston, TX, US; [2]University of Texas MD Anderson Cancer Center, Houston, TX, US; [3]UT-MD Anderson Cancer Center, Houston, TX, US; [4]UT-MD Anderson Cancer Center, Houston, TX, US; [5]University of Texas MD Anderson Cancer Center, Houston, TX, US; [6]University of Texas MD Anderson Cancer Center, Houston, TX, US; [7]University of Texas MD Anderson Cancer Center, Houston, TX, US; [8]UT-MD Anderson Cancer Center, Houston, TX, US; [9]MD Anderson Cancer Center, Houston, TX, US; [10]University of Texas MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Invasive lobular carcinomas (ILC) are histologically and biologically distinct from invasive ductal carcinomas. There is a paucity of published literature on the landscape of hereditary breast cancer in patients with ILC. This study was designed to characterize the pathogenic germline mutational landscape of patients with ILC and to compare clinicopathologic variables and treatment outcomes between those with and without germline pathogenic variants (PVs). **METHODS:** A prospectively maintained database was used to identify all patients diagnosed with stage I-III ILC who had genetic counseling and germline genetic testing. Clinicopathologic variables were compared. Survival and recurrence were compared using log-rank tests, and Cox proportional hazards models were used to describe associations between clinicopathologic factors and cancer events. **RESULTS:** Of 4,398 patients with stage I-III ILC seen between 1989 and 2024, 1,170 patients were evaluated by genetic counselors, and 877 underwent genetic testing. Eighty-three (9.5%) had pathogenic or likely pathogenic variants. 72.2% (N=83) had BRCA1/2, CHEK2, or CDH1 PVs. Ten patients (12%) had other breast cancer predisposition PVs and 13 patients (15.6%) had PVs detected that were not previously known to be breast cancer-associated. Comparisons of clinicopathologic and treatment characteristics (Table) showed that patients with PVs were significantly (p<0.01) more likely to be less than 40 years old, premenopausal, have high grade and triple negative breast cancer, and undergo mastectomy compared to those without a PV. Groups did not differ significantly by family history (55% overall) or other characteristics. During a median follow-up of 80 months, there was no significant difference in the rate of contralateral breast cancers, distant and local-regional recurrence-free, and overall survival among patients with and without PVs. **CONCLUSIONS:** In this largest single-institutional analysis, patients with ILC were shown to have a distinct landscape of germline PVs in breast cancer and non-breast cancer predisposition genes. A significant proportion of patients with ILC have PVs, and these findings have potentially actionable implications.

Table. Invasive lobular carcinoma patient, tumor, and treatment characteristics and outcomes among those with and without a pathogenic germline variant identified

Variable	Level	Overall	Negative	Positive	p
No.		877	794	83	
Race	Asian	27 (3.1)	27 (3.4)	0 (0.0)	0.182
	Black	62 (7.1)	57 (7.2)	5 (6.0)	
	Hispanic	110 (12.5)	102 (12.8)	8 (9.6)	
	Other	21 (2.4)	17 (2.1)	4 (4.8)	
	White	657 (74.9)	591 (74.4)	66 (79.5)	
Family History	No	399 (45.5)	365 (46.0)	34 (41.0)	0.418
	Yes	478 (54.5)	429 (54.0)	49 (59.0)	
Age	≥ 40	828 (94.4)	758 (95.5)	70 (84.3)	<0.001
	< 40	49 (5.6)	36 (4.5)	13 (15.7)	
Menopause Status	Post	509 (58.0)	471 (59.3)	38 (45.8)	0.019
	Pre	368 (42.0)	323 (40.7)	45 (54.2)	
Cancer Laterality at Diagnosis	Bilateral	51 (5.8)	47 (5.9)	4 (4.8)	1.000
	Unilateral	826 (94.2)	747 (94.1)	79 (95.2)	
T Category at Diagnosis[a]	T1	389 (44.4)	348 (43.8)	41 (49.4)	0.865
	T2	284 (32.4)	260 (32.7)	24 (28.9)	
	T3	178 (20.3)	162 (20.4)	16 (19.3)	
	T4	23 (2.6)	21 (2.6)	2 (2.4)	
	Unknown	3 (0.3)	3 (0.4)	0 (0.0)	
N Category at Diagnosis[b]	N+	280 (31.9)	255 (32.1)	25 (30.1)	0.823
	N0	596 (68.0)	538 (67.8)	58 (69.9)	
	Unknown	1 (0.1)	1 (0.1)	0 (0.0)	
Stage at Diagnosis[c]	I	351 (40.2)	318 (40.2)	33 (39.8)	0.870
	II	342 (39.1)	311 (39.3)	31 (37.3)	
	III	181 (20.7)	162 (20.5)	19 (22.9)	
Hormone Receptor Status[d]	HR Negative	37 (4.3)	26 (3.3)	11 (13.4)	<0.001
	HR Positive	832 (95.7)	761 (96.7)	71 (86.6)	
HER2/neu Status[e]	HER2 Negative	805 (94.5)	730 (94.7)	75 (92.6)	0.439
	HER2 Positive	47 (5.5)	41 (5.3)	6 (7.4)	
Grade[f]	I	236 (27.6)	221 (28.6)	15 (18.8)	0.018
	II	522 (61.1)	473 (61.1)	49 (61.3)	
	III	96 (11.2)	80 (10.3)	16 (20.0)	
Subtype[g]	HR-HER2+	10 (1.2)	8 (1.0)	2 (2.5)	0.001
	HR+HER2-	778 (91.3)	712 (92.3)	66 (81.5)	
	HR+HER2+	37 (4.3)	33 (4.3)	4 (4.9)	
	TNBC	27 (3.2)	18 (2.3)	9 (11.1)	
Initial Surgery[h]	BCS	304 (35.0)	284 (36.2)	20 (24.1)	0.029
	Mastectomy	564 (65.0)	501 (63.8)	63 (75.9)	
Chemotherapy	No	429 (48.9)	389 (49.0)	40 (48.2)	0.909
	Yes	448 (51.1)	405 (51.0)	43 (51.8)	
Radiation	No	389 (44.4)	351 (44.2)	38 (45.8)	0.817
	Yes	488 (55.6)	443 (55.8)	45 (54.2)	
Endocrine Therapy	No	197 (22.5)	164 (20.7)	33 (39.8)	<0.001
	Yes	680 (77.5)	630 (79.3)	50 (60.2)	
Follow Up (Months, Median [IQR])		79.5 [38-135]	64 [36-113]	80 [38-136]	
Overall Survival	5 years	95.0 (93.5-96.7)	95.2 (93.5-96.8)	94.1 (88.6-99.9)	0.57
	10 years	88.6 (85.9-91.4)	89.2 (86.5-92.1)	81.6 (70.9-94.0)	
Local-regional Recurrence	5 years	2.7 (1.5-3.9)	2.3 (1.1-3.4)	6.9 (0.8-12.5)	0.087
	10 years	5.6 (3.4-7.7)	5.4 (3.1-7.6)	6.9 (0.8-12.5)	
Distant Metastases	5 years	7.3 (5.4-9.2)	6.8 (4.9-8.7)	12.2 (3.8-20.0)	0.5
	10 years	14.4 (11.4-17.4)	13.9 (10.7-16.9)	20.7 (8.1-31.6)	
Contralateral Breast Cancer	5 years	3.1 (1.8-4.4)	3.2 (1.8-4.6)	1.9 (0.0-5.4)	0.93
	10 years	6.1 (3.8-8.4)	6.2 (3.8-8.6)	4.9 (0.0-11.5)	

Numbers are No. (%) or % (95% CI) unless otherwise indicated. Abbreviations: HR, hormone receptor. TNBC, triple negative breast cancer. BCS, breast conserving surgery. IQR, interquartile range.
[a] 3 with information not recorded.
[b] 1 with information not recorded.
[c] 3 with information not recorded.
[d] 8 with information not recorded.
[e] 25 with information not recorded.
[f] 23 with information not recorded.
[g] 25 with information not recorded.
[h] 9 with information not recorded.

121. Risk of locoregional recurrence according to residual breast disease among clinical N1 patients who achieve nodal downstaging following neoadjuvant chemotherapy

Kate R Pawloski, MD, MPH[1]; Giacomo Montagna, MD, MPH[2]; Andrea V Barrio, MD[3]; Varadan Sevilimedu, MBBS, DrPH[4]; Monica Morrow, MD[5]; Atif J Khan, MD[6]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Following neoadjuvant chemotherapy (NAC), the risk of locoregional recurrence (LRR) is influenced by tumor biology and treatment response in the breast and lymph nodes. Node-positive (cN1) patients who achieve a nodal pathologic complete response (pCR) have a lower risk of LRR and may be candidates for omission of regional nodal irradiation (RNI). However, the effect of residual tumor in the breast on LRR in cN1/ypN0 patients is uncertain. **METHODS:** From 4/2013-12/2022, we identified patients with cT1-3, cN1 breast cancer who received NAC +/- immunotherapy followed by breast conservation therapy (BCT) with whole breast radiotherapy or mastectomy and downstaged to ypN0. RNI was given per physician discretion. Clinicopathologic and treatment characteristics were compared between patients with and without residual invasive breast disease. The cumulative incidence of LRR and any recurrence (LRR and/or distant) were compared by ypT stage. Crude rates of LRR in patients treated without RNI were reported. Univariable analysis identified factors associated with LRR. **RESULTS:** Of 494 patients identified, median (interquartile [IQR]) age was 49 (40-58) years, 56% were pre-menopausal, 49% underwent lumpectomy and 99% SLNB (Table 1). The median (IQR) follow-up was 4.3 (2.2-6.2) years. Overall, 16% of BCT patients and 19% of mastectomy patients did not receive RNI. In total, 337 (68%) had a breast pCR (ypT0/Tis) and 157 (32%) had residual breast disease (ypT1-2) with a median (IQR) invasive residual tumor size of 0.5 cm (0.2-1.2 cm). Among ypT1-2 patients, non-ductal histology (6.4% vs. 2.1%, p=0.015), ER+/HER2- disease (30% vs. 9.8%, p<0.001) and multifocal/centric disease at presentation (35% vs. 21%, p<0.001) were more frequent than in ypT0/Tis patients. The overall 5-year LRR rate was 1.7% and was similar between ypT0/Tis and ypT1-2 groups (1.4% vs. 2.1; p=0.7). The overall 5-year rate of any recurrence was 7.0% and was also similar between ypT0/Tis and ypT1-2 groups (6.4% vs. 8.5%; p=0.3). Among BCT patients, there were no LRR events in those treated without RNI. The crude rate of LRR was 4.3% in mastectomy patients treated without PMRT/RNI and 0.5% in those who had PMRT/RNI. LRR was not statistically significantly associated with clinicopathologic factors. **CONCLUSIONS:** In this cohort of cN1/ypN0 patients predominantly treated with RNI prior to reporting of the NSABP B-51 trial, locoregional control was excellent irrespective of residual tumor burden in the breast. Further study on the impact of the extent of residual breast disease on the risk of LRR in the absence of RNI is warranted.

Table 1. Characteristics of cT1-3, cN1 patients rendered ypN0 following NST stratified ypT stage

Characteristic	Overall N = 494[1]	ypT0/Tis N = 337[1]	ypT1-2 N = 157[1]	p-value[2]
Age	49 (40, 58)	50 (41, 59)	48 (39, 58)	0.2
Race				0.2
Asian	70 (15%)	44 (14%)	26 (17%)	
Black	80 (17%)	61 (19%)	19 (13%)	
Other	32 (6.8%)	24 (7.5%)	8 (5.3%)	
White	288 (61%)	190 (60%)	98 (65%)	
Unknown	24	18	6	
Ethnicity				0.4
Hispanic	56 (12%)	41 (13%)	15 (9.9%)	
Non-Hispanic	414 (88%)	278 (87%)	136 (90%)	
Unknown	24	18	6	
Menopausal status				0.2
Postmenopausal	217 (44%)	155 (46%)	62 (39%)	
Premenopausal	277 (56%)	182 (54%)	95 (61%)	
Clinical T stage				0.5
1	100 (20%)	72 (21%)	28 (18%)	
2	300 (61%)	205 (61%)	95 (61%)	
3	94 (19%)	60 (18%)	34 (22%)	
Histology				0.015
IDC	477 (97%)	330 (98%)	147 (94%)	
Other	17 (3.4%)	7 (2.1%)	10 (6.4%)	
Subtype				<0.001
ER+/HER2-	80 (16%)	33 (9.8%)	47 (30%)	
ER+/HER2+	154 (31%)	99 (29%)	55 (35%)	
ER-/HER2+	126 (26%)	110 (33%)	16 (10%)	
ER-/HER2-	134 (27%)	95 (28%)	39 (25%)	
LVI	83 (18%)	48 (16%)	35 (22%)	0.077
Unknown	30	30	0	
Multifocal/centric disease at presentation	127 (26%)	72 (21%)	55 (35%)	0.001
Breast surgery				0.064
BCT	241 (49%)	174 (52%)	67 (43%)	
Mastectomy	253 (51%)	163 (48%)	90 (57%)	
Axillary surgery				0.10
SLNB	490 (99%)	336 (100%)	154 (98%)	
ALND	4 (0.8%)	1 (0.3%)	3 (1.9%)	
Multiple foci of residual invasive disease	55 (35%)	0 (NA)	55 (35%)	>0.9
Unknown	337	337	0	
Largest focus of residual invasive disease (cm)				<0.001
0	337 (68%)	337 (100%)	0 (0%)	
0.1-1.0	113 (23%)	0 (0%)	113 (72%)	
1.1-2.0	27 (5.5%)	0 (0%)	27 (17%)	
2.1-5.0	17 (3.4%)	0 (0%)	17 (11%)	

122. HER2 discordance between primary tumors and nodal metastases and correlation with the 21-gene recurrence score in early-stage, estrogen receptor-positive, node-positive breast cancer

Serena Zheng, MD[1]; Peggy S Sullivan, MD[2]; Kumkum Vadehra, MD[3]; Jiyoon Kim[4]; Rena D Callahan, MD[5]; Mediget Teshome, MD, MPH, FACS[6]; Chi-Hong Tseng[7]; Aditya Bardia, MD, MPH[8]; Nimmi S Kapoor, MD, FACS[9]

[1]UCLA Medical Center, Los Angeles, CA, US; [2]UCLA Medical Center, Los Angeles, CA, US; [3]UCLA Medical Center, Los Angeles, CA, US; [4]UCLA Medical Center, Los Angeles, CA, US; [5]UCLA Medical Center, Los Angeles, CA, US; [6]UCLA Medical Center, Los Angeles, CA, US; [7]UCLA Medical Center, Los Angeles, CA, US; [8]UCLA Medical Center, Los Angeles, CA, US; [9]UCLA Medical Center, Los Angeles, CA, US

INTRODUCTION: The RXPonder trial demonstrated the utility of the 21-gene recurrence score (RS) in predicting chemotherapy benefit in early-stage hormone receptor-positive, HER2-negative, node positive breast cancer. While biomarker status is clinically defined by the primary tumor, discordance between the primary breast tumor and nodal metastases occurs in 6-30% of cases. Moreover, emerging treatments for HER2-low tumors underscore the need for accurate HER2 characterization. This study aims to identify the rate of estrogen receptor (ER) and HER2 discordance between primary tumors and concurrent lymph node metastases and correlation to the RS. **METHODS:** Patients with ER-positive, HER2-negative, node-positive breast cancer who underwent surgery between 2016-2020 with RS data were identified retrospectively. Patient demographics, tumor histopathologic data, and RS were recorded. ER and HER2 immunohistochemical (IHC) staining was performed on single nodal metastases from archived tissue for comparison. ER discordance between primary and nodal staining was scored "0" if the difference was <25%, "1" for 25-50%, and "2" if >50%. HER2 discordance was scored " for no differences in IHC stains, "for 1-point difference and " for 2-point difference. Associations between clinical characteristics, receptor discordance, and RS were evaluated using Fisher's exact test, pairwise comparisons, and linear regression. **RESULTS:** A total of 81 patients met the study criteria, and 40 had nodal biomarkers evaluated. The median RS for the whole cohort was 15 (range 1-42) and 75% (30/40) had some degree of ER and/or HER2 nodal biomarker discordance. Lower progesterone receptor positivity (≤10%), 2 or more nodal metastases, or any amount of nodal discordance were significantly associated with RS≥16 (p=0.01, p=0.04, and p=0.02, respectively, Table I). No significant differences in age, ER positivity, tumor size, or ER nodal discordance and RS were observed. No nodal metastasis had ER-negative or HER2 IHC 3+ expression, but HER2 discordance between primary tumors and nodal metastases was seen in 70% of cases (28/40), and more discordance was associated with higher RS (p=0.01). **CONCLUSIONS:** HER2 expression discordance between breast primary and nodal metastasis is frequent and more discordance appeared to be associated with higher RS. Larger studies are needed to assess the clinical significance of HER2 nodal discordance in ER-positive HER2-negative primary breast cancer.

Table 1. Clinical and Pathologic Characteristics by Oncotype Score

	Oncotype Score		
	≤ 15 (n=44)	≥16 (n=37)	P-value
Age			
Age, median (range)	56 (33-78)	53 (37-80)	0.64
Age <50	12 (27%)	14 (38%)	0.60
Age 50-65	23 (52%)	15 (41%)	
Age >65	9 (20%)	8 (22%)	
Grade			
Low	11 (25%)	10 (27%)	0.59
Intermediate	30 (68%)	22 (59%)	
High	3 (7%)	5 (14%)	
ER Positivity			0.06
≤ 10%	0 (0%)	0 (0%)	
10%-90%	9 (20%)	15 (41%)	
>90%	35 (80%)	22 (59%)	
PR Positivity			**0.01**
≤ 10%	3 (7%)	12 (32%)	
10%-90%	32 (73%)	18 (49%)	
>90%	9 (20%)	7 (19%)	
HER2 IHC			0.53
0	6 (14%)	4 (11%)	
1+	23 (52%)	24 (65%)	
2+	15 (34%)	9 (24%)	
3+	0 (0%)	0 (0%)	
Tumor Size			
Median (range)	2 (0.6-9.8)	2.5 (0.7-41.3)	0.58
≤1cm	3 (7%)	3 (8%)	0.41
(1-2] cm	20 (45%)	12 (32%)	
(2-5] cm	16 (36%)	19 (51%)	
>5cm	6 (14%)	3 (8%)	
Number of Positive Nodes			
1	39 (89%)	27 (73%)	**0.04**
2	4 (9%)	10 (27%)	
3	0 (0%)	0 (0%)	
>3	1 (2%)	0 (0%)	
Nodal Staining (n=40)	n=18	n=22	
Any Nodal Discordance			**0.02**
Yes	10 (56%)	20 (91%)	
No	8 (44%)	2 (9%)	

123. Comparison of health-related quality of life outcomes in older breast cancer patients undergoing breast conserving surgery, mastectomy, and reconstruction: a prospective study

Claire Liu[1]; Rebecca Warburton, MD, FRCSC[2]; Amy Bazzarelli, MD, FRCSC[3]; Melina Deban[4]; Carol Dingee, BMSc, MD, CCFP, FRCSC[5]; Jin-Si Pao, MD, FRCSC[6]; Jieun Newman-Bremang, MD, MSc, FRCSC[7]; Kathryn Isaac, MD, FRCSC[8]; Jason Sutherland, MSc, PhD[9]; Elaine McKevitt, MEd, MD, FRCSC[10]

[1]University of British Columbia, Vancouver, BC, CA; [2]University of British Columbia, Vancouver, BC, CA; [3]University of British Columbia, Vancouver, BC, CA; [4]University of British Columbia, Vancouver, BC, CA; [5]University of British Columbia, Vancouver, BC, CA; [6]University of British Columbia, Vancouver, BC, CA; [7]University of British Columbia, Vancouver, BC, CA; [8]University of British Columbia, Vancouver, BC, CA; [9]University of British Columbia, Vancouver, BC, CA; [10]University of British Columbia, Vancouver, BC, CA

INTRODUCTION: Modern day treatments have improved breast cancer survival, making health related quality of life (HRQoL) after treatment increasingly important in breast cancer survivorship. There is a knowledge gap in the HRQoL outcomes of older patients undergoing breast cancer surgery. This study evaluated the preoperative and six-month postoperative change in patient-reported HRQoL in several aspects of mental and physical health,

comparing outcomes for breast conserving surgery (BCS), total mastectomy no reconstruction (TM), and total mastectomy with immediate reconstruction (TM+R) in older patients. **METHODS:** This prospective cohort study enrolled breast cancer patients between 2016 – 2023. Participants completed surveys that measured their mental and physical health. Surveys were completed preoperatively after surgical consultation and again six-months postoperatively. The BREAST-Q questionnaire was used to assess breast cancer specific outcomes including breast satisfaction, psychosocial, sexual, and chest physical well-being. General patient-reported outcomes were categorized in depression, anxiety, pain, and perceived health. **RESULTS:** This study had 259 breast cancer patients ≥70 years old meeting inclusion/exclusion criteria complete their pre- and six-month postoperative surveys. Of these, 191 underwent BCS, 55 TM, and 13 TM+R. On average, patients who underwent TM and TM+R experienced clinically significant reductions in breast satisfaction (-5.8, -5.6) and sexual well-being (-5.4, -9.1). TM patients also had decreased psychosocial (-4.2) and chest physical well-being (-5.0), while BCS patients showed no significant changes. In the multivariable linear regression model, BCS (β = 13.6, 95% CI: [4.0, 23.2], p = 0.006) and TM+R (β = 19.1, 95% CI: [3.1, 35.1], p = 0.02) were significantly associated with higher postoperative breast satisfaction scores compared to TM, controlling for tumor factors, neoadjuvant, and adjuvant therapies. BCS was also associated with higher postoperative chest physical well-being compared to TM (β = 8.8, 95% CI: [0.9, 16.6], p = 0.03). There was no significant difference in the change in depression, anxiety, or pain scores within and across the surgical modalities. **CONCLUSIONS:** BCS has improved HRQoL outcomes overall compared to mastectomy. Older breast cancer patients should be counselled to undergo BCS when feasible.

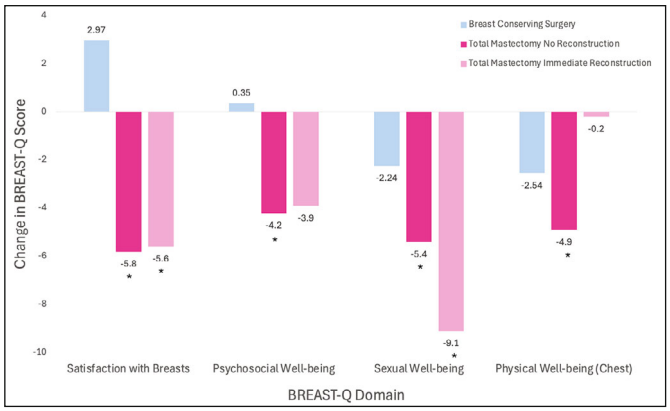


Figure 1. Preop- to 6-month Postop Change in Core BREAST-Q Scores

124. Breast Conserving Therapy for Multiple Ipsilateral Breast Cancer after Neoadjuvant Systemic Therapy

Monika K Masanam, MD[1]; Jennifer R Bellon, MD[2]; Elizabeth A Mittendorf, MD, PhD, MHCM[3]; Tari A. King, MD, FACS, FSSO[4]; Olga Kantor, MD, MS[5]
[1]Brigham and Women's Hospital/Dana-Farber Cancer Institute, Boston, MA, US; [2]Brigham and Women's Hospital/Dana-Farber Cancer Institute, Boston, MA, US; [3]Brigham and Women's Hospital/Dana-Farber Cancer Institute, Boston, MA, US; [4]Brigham and Women's Hospital/Dana-Farber Cancer Institute, Boston, MA, US; [5]Brigham and Women's Hospital/Dana-Farber Cancer Institute, Boston, MA, US

INTRODUCTION: The ACOSOG Z11102 trial demonstrated the safety of breast conserving surgery (BCS) with adjuvant radiation in women with multiple ipsilateral breast cancer (MIBC) with 5-year local-regional recurrence (LRR) of ~3%. However, patients treated with neoadjuvant systemic therapy (NST) were excluded from the trial; thus, the oncologic safety of BCS in women with MIBC receiving NST remains uncertain. **METHODS:** Adult patients diagnosed with non-metastatic MIBC who underwent BCS following NST from 2016 to 2022 were identified in a prospectively maintained institutional database. MIBC was defined as the presence of 2-3 foci of biopsy-proven breast cancer with at least 2 cm of intervening normal breast tissue between tumor foci. At least one tumor focus was invasive, with ductal carcinoma in situ (DCIS) permitted as additional foci. Descriptive statistics were applied to summarize the collected data. **RESULTS:** 73 patients met criteria for MIBC. The median age was 56 years (range 25-84). 60 (82.2%) patients received neoadjuvant chemotherapy (NAC), and 13 (17.8%) patients received neoadjuvant endocrine therapy (NET). Most patients had invasive ductal cancer (76.7%) and presented with grade 3 tumors (57.5%). The distribution of tumor subtypes was HR+/HER2- in 27 (37%) patients, HR-/HER2- in 20 (27.4%) patients and HER2+ in 26 (35.6%) patients. Most patients were clinical stage II (79.5%) at diagnosis with clinical T2 or higher tumors. Preoperative magnetic resonance imaging (MRI) was performed in 63% of patients. 20 (27.4%) patients had a pathologic complete response. For surgical approach, 48 (65.7%) patients had MIBC resected as a single site lumpectomy, 23 (31.5%) had 2 site lumpectomy, and 2 (2.7%) underwent 3 site lumpectomy. Baseline characteristics were similar among patients regardless of surgical approach (Table). The re-excision rate was 20.6% with one patient undergoing two re-excisions. For adjuvant therapy, 70 (95.9%) patients received radiation therapy, 42 (57.5%) patients received chemotherapy, and 35 (47.9%) patients received endocrine therapy. After a median follow-up of 34.7 months from the time of initial surgery, there was 1 (1.4%) local recurrence and 4 (5.5%) distant recurrences with a breast cancer-specific mortality rate of 4.1%. **CONCLUSIONS:** In this retrospective analysis of women with MIBC who underwent BCS after NST, the observed local recurrence rate was 1.4% at 3-year median follow-up. These findings suggest BCS may be a safe surgical option for patients with MIBC receiving NST.

Table. Baseline patient and tumor characteristics and re-excision rates, stratified by surgical approach

Characteristic	Overall N=73 (%)	Single site lumpectomy N=48 (%)	Two or three site lumpectomy N=25 (%)
Age			
<40	12 (16.4)	7 (14.6)	5 (20.0)
40-49	8 (11.0)	6 (12.5)	2 (8.0)
50-59	27 (37.0)	20 (41.7)	7 (28.0)
60-69	16 (21.9)	7 (14.6)	9 (36.0)
≥70	10 (13.7)	8 (16.7)	2 (8.0)
Tumor histology			
IDC	56 (76.7)	35 (72.9)	21 (84.0)
ILC	3 (4.1)	2 (4.2)	1 (4.0)
Mixed IDC/ILC	13 (17.8)	10 (20.8)	3 (12.0)
Other	1 (1.4)	1 (2.1)	0 (0.0)
Clinical stage			
1	10 (13.7)	4 (8.3)	6 (24.0)
2	58 (79.5)	42 (87.5)	16 (64.0)
3	5 (6.8)	2 (4.2)	3 (12.0)
Pathological stage			
0	20 (27.4)	17 (35.4)	3 (12.0)
1	19 (26.0)	11 (22.9)	8 (32.0)
2	23 (31.5)	13 (27.1)	10 (40.0)
3	11 (15.1)	7 (14.6)	4 (16.0)
Grade			
1	6 (8.2)	4 (8.3)	2 (8.0)
2	25 (34.2)	15 (31.3)	10 (40.0)
3	42 (57.5)	29 (60.4)	13 (52.0)
Molecular subtype			
HR+/HER2-	27 (37.0)	17 (35.4)	10 (40.0)
HR-/HER2-	20 (27.4)	14 (29.2)	6 (24.0)
HR+/HER2+	19 (26.0)	13 (27.1)	6 (24.0)
HR-/HER2+	7 (9.6)	4 (8.3)	3 (12.0)
Pre-operative MRI			
Yes	46 (63.0)	29 (60.4)	17 (68.0)
No	27 (37.0)	19 (39.6)	8 (32.0)
Re-excisions			
0	58 (79.5)	41 (85.4)	17 (68.0)
1	14 (19.2)	7 (14.6)	7 (28.0)
2	1 (1.4)	0 (0.0)	1 (4.0)

IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; HR, hormone receptor; HER2, human epidermal growth factor receptor 2; MRI, magnetic resonance imaging

125. Identification of Novel Risk Factors Associated with Lymphedema Development After Sentinel Lymph Node Biopsy

Natalia Polidorio, MD, PhD[1]; Varadan Sevilimedu, MBBS, DrPH[2]; Rachel Supplice[3]; Monica Morrow, MD[4]; Babak J Mehrara[5]; Andrea V Barrio, MD[6]
[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Lymphedema rates in breast cancer patients treated with upfront sentinel lymph node biopsy (SLNB) are low, but less is known about risk after neoadjuvant chemotherapy (NAC) +/- nodal radiation (RT), particularly among those who downstage. In addition, the impact of race/ethnicity on lymphedema development after SLNB has not been well studied. We prospectively evaluated rates and risk factors for lymphedema in SLNB patients, and assessed long-term quality of life (QOL). **METHODS:** Between 11/2016-03/2020, patients undergoing unilateral SLNB +/- ALND were enrolled

in a lymphedema screening study. Race/ethnicity were self-reported. Volumetric arm measurements (perometer) and QOL (Upper Limb Lymphedema-27) were obtained at preoperative baseline and follow-up. Lymphedema rates were reported as crude incidence rates. Factors associated with lymphedema were assessed on univariate analysis (UVA) using multiple comparison correction. Factors associated with QOL were assessed. **RESULTS:** Of 827 patients enrolled, 411 had SLNB alone, and 176 returned for follow-up, comprising our cohort. Median age was 49 years, 29% were clinically node positive, 59% received NAC, and 30% nodal RT (Table). Receipt of NAC or nodal RT did not differ across racial/ethnic groups (p=0.3). At a median follow-up of 4.54 years (IQR 3.75, 5.09), 11 patients (6.3%) developed lymphedema. Lymphedema rates varied by race/ethnicity, with the highest incidence observed in Black women (21%) vs Asian (0%), Hispanic (0%) and White (5%) women (p=0.02). Lymphedema rates were also higher with NAC (9.6%) vs upfront surgery (1.4%) (p=0.03), with a 14% lymphedema rate among clinically node-positive patients who downstaged. After multiple comparison correction, Black race (adjusted p=0.04), NAC receipt (adjusted p=0.04) and nodal RT (adjusted p<0.001) were associated with higher lymphedema rates. Median follow-up QOL scores were lower among racial/ethnic minorities (Asian 92 [IQR 83, 100]; Black 91 [IQR 69, 97]; Hispanic 85 [IQR 68, 93] vs White 100 [IQR 95, 100], p<0.001), and among those receiving NAC (NAC 96 [IQR 83, 100] vs upfront surgery 100 [IQR 92, p=0.02). **CONCLUSIONS:** In this prospective cohort of SLNB patients, lymphedema rates were higher with NAC +/- nodal RT compared with upfront surgery but were lower than reported after ALND (~20-30%), confirming the benefit of NAC for downstaging. The disproportionately higher lymphedema rates in Black women suggest a biologic difference in response to lymphatic injury requiring further study.

Table. Clinicopathologic characteristics of SLNB cohort

Characteristic	Overall N = 176
Age, median (IQR)	49 (41, 57)
Baseline BMI, median (IQR)	25.0 (22.1, 29.2)
Surgery on dominant arm	88 (50%)
Race/Ethnicity	
Asian	28 (16%)
Black	28 (16%)
Hispanic	17 (10%)
Other	4 (2%)
White	99 (56%)
Insurance type	
Private	148 (84%)
Medicaid/Medicare	28 (16%)
Clinical T stage	
Tis	3 (2%)
T1	44 (25%)
T2	109 (62%)
T3	20 (11%)
Clinical N stage	
cN0	125 (71%)
cN1	49 (28%)
cN2	1 (0.6%)
cN3	1 (0.6%)
Histology	
Ductal	146 (83%)
Lobular	20 (11%)
Mixed	7 (4.0%)
Other	3 (2%)
LVI	38 (22%)
Unknown	4
Tumor subtype,	
HR+/HER2-	78 (45%)
HER2+	55 (32%)
HR-/HER2-	41 (24%)
Unknown	2
Breast surgery	
BCS	57 (32%)
Mastectomy	119 (68%)
Number of nodes removed, median (IQR)	4.00 (3.00, 5.00)
Neoadjuvant chemotherapy	104 (59%)
Adjuvant radiotherapy	82 (47%)
Nodal radiotherapy	52 (30%)

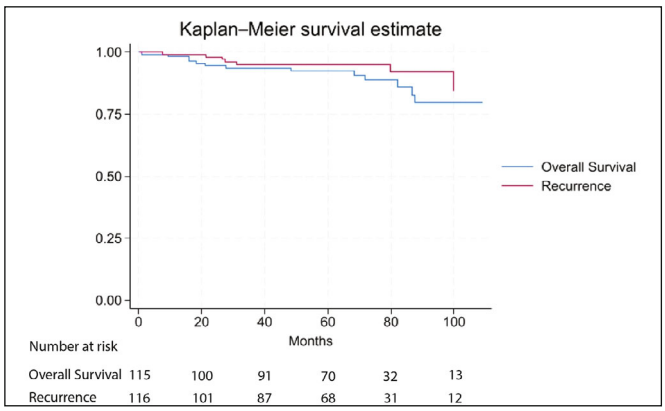
Abbreviations: BMI, body mass index; LVI, lymphovascular invasion; HR, hormone receptor, TNBC, triple-negative breast cancer, BCS, breast-conserving surgery.

126. Simultaneous Omission of Sentinel Lymph Node Biopsy and Radiation in Older Women with Early ER+ Breast Cancer

Chase E Cox[1]; Jessica R Schumacher, PhD[2]; Margaret R Lillie, MS[3]; Joshua R Carino, BA[4]; Dana C Casey, MD[5]; Julia M. Selfridge, MD[6]; David C Ollila, MD[7]; Caprice Greenberg, MD, MPH[8]; Kristalyn K Gallagher, DO[9]; Phillip Spanheimer, MD[10]

[1]University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US; [2]University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US; [3]University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US; [4]University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US; [5]University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US; [6]The University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US; [7]University of North Carolina, Chapel Hill, NC, US; [8]University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US; [9]University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US; [10]University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US

INTRODUCTION: The SSO and ASTRO suggest that women 70 years and over with early stage (cT1/2N0), estrogen receptor positive (ER+), HER2 negative breast cancer should not routinely receive sentinel lymph node biopsy (SLNB) or radiation. Several trials have shown that radiation provides a small local recurrence benefit with no effect on survival in this population leading to decreased utilization. However, oncologic outcome data on women with neither SLNB nor radiation is limited. We evaluated recurrence and survival in older women with early stage, ER+, HER2 negative breast cancer who underwent lumpectomy without SLNB or radiation. **METHODS:** Women treated for breast cancer at our institution from 2014 to 2022 were identified in a local tumor registry. Inclusion criteria were: women 65 years and older, Tumor size <= 5cm, ER+ > 10%, HER 2- invasive breast cancers treated with lumpectomy and adjuvant endocrine therapy without SLNB or radiation. Women with a history of an ipsilateral breast cancer were excluded. Data were abstracted from patient charts. Follow up was defined as the last appointment with any medical provider. The Kaplan-Meier method was used to estimate curves for mortality and recurrence. **RESULTS:** A total of 116 women meeting inclusion criteria were identified. Median age at time of surgery was 76 (IQR: 72, 80). The majority of patients were white (85%). 71% of patients had a family history of breast cancer. 11% had a personal history of contralateral breast cancer. Most patients had a T1 tumor (85%) and ductal histology (78%). 107 patients (92%) initiated adjuvant endocrine therapy with median therapy duration of 4.2 years. Median follow up time was 65 months. Of the 116 patients, 7 developed recurrence (6.0%). Of the 7 recurrences, 6 were locoregional: 5 in breast and 1 axillary. One patient first developed a local recurrence and years later developed distant recurrence. Three women with recurrence underwent mastectomy. 5-year locoregional recurrence free survival was 95%, 5-year disease specific survival was 100%, and 5-year overall survival was 92.5% (Figure 1). **CONCLUSIONS:** Locoregional recurrence was rare at a median follow up of over five years with simultaneous omission of SLNB and radiation in older women with low-risk ER+ breast tumors. Death from non-cancer causes was more common highlighting the competing risks in this population. These findings support the oncologic safety of omitting both SLNB and radiation in well selected patients.



127. Sentinel Lymph Node Involvement in Triple Negative Breast Cancer: Predictive Factors and Implications for Axillary Surgery Decision-Making

Ashley L Cairns[1]; Roland Bassett[2]; Kerollos N Wanis, MD[3]; Puneet Singh, MD[4]; Isabelle Bedrosian, MD[5]; Kelly K. Hunt, MD, FSSO[6]; Sarah M DeSnyder, MD[7]; Henry Kuerer, MD[8]; Min Yi, [9]; Abigail S Caudle, MD[10]; Funda Meric-Bernstam, MD[11]; Taiwo Adesoye, MD[12]; Susie X Sun, MD[13]; Nina Tamirisa, MD[14]; Rosa Hwang, MD[15]

[1]MD Anderson Cancer Center, Houston, TX, US; [2]UT-MD Anderson, Houston, TX, US; [3]UT-MD Anderson Cancer Center, Houston, TX, US; [4]UT-MD Anderson Cancer Center, Houston, TX, US; [5]UT-MD Anderson Cancer Center, Houston, TX, US; [6]MD Anderson Cancer Center, Houston, TX, US; [7]UT-MD Anderson Cancer Center, Houston, TX, US; [8]UT-MD Anderson Cancer Center, Houston, TX, US; [9]UT-MD Anderson Cancer Center, Houston, TX, US; [10]UT-MD Anderson Cancer Center, Houston, TX, US; [11]UT-MD Anderson Cancer Center, Houston, TX, US; [12]UT-MD Anderson Cancer Center, Houston, TX, US; [13]UT-MD Anderson Cancer Center, Houston, TX, US; [14]UT-MD Anderson Cancer Center, Houston, TX, US; [15]UT-MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Sentinel lymph node biopsy (SLNB) is the standard for axillary staging in early-stage breast cancer. The SOUND trial showed omission of axillary surgery was noninferior to SLNB, though most patients had hormone receptor-positive tumors, with a minority having triple-negative breast cancer (TNBC). TNBC status has been suggested as a negative predictor for sentinel lymph node (SLN) involvement. This study evaluates SLN positivity rates in clinically node-negative (cN0) TNBC patients and identifies associated predictive factors. **METHODS:** A prospective institutional database was used to analyze female patients with cN0 invasive breast cancer who underwent upfront surgery and SLNB from 1993-2007. Postmenopausal status was defined as age ≥ 50 years. All patients underwent axillary ultrasound staging. Wilcoxon rank-sum tests and Fisher's exact tests were used to compare continuous and categorical variables, respectively, between TNBC and non-TNBC groups. In TNBC patients, logistic regression was used to evaluate predictors of positive SLN. A multivariate regression model identified independent predictors of SLN positivity. Firth's penalized likelihood method was used in small sample categories. **RESULTS:** A total of 3,431 patients met inclusion criteria, of whom 379 (11%) had TNBC. Patients with TNBC were significantly younger (p=0.0005) and more likely to be pre-menopausal (p=0.0025) compared to non-TNBC patients. TNBC patients had a higher pathologic T category with more T2 tumors (29.4% vs. 18.6%; p=0.001) that were more likely to be high grade (80% vs. 25.2%; p=0.005). However, they were less likely to have any positive SLNs (13.5% vs. 23.6%, p<0.0001), with fewer positive SLNs that was not statistically significant (1 vs. 3, p=0.2) and less extranodal extension (9.8% vs. 21%, p=0.07). Multivariate analysis showed tumor size (OR 1.55; p<0.001) and lymphovascular invasion (LVI, OR 3.9;0.001) were significant predictors of SLN positivity. When limited to tumors ≤ 2 cm, 8.7% had a positive SLN (23 of 264) and LVI remained an independent predictor (OR 4.8; p=0.009). **CONCLUSIONS:** TNBC patients are less likely to have a positive SLN than those with other breast cancer subtypes, despite larger tumor size and higher grade. These results suggest a potential for SLNB omission particularly for T1 tumors in alignment with the SOUND trial. A multidisciplinary approach considering predictive factors such as tumor size and LVI, along with the use of nomograms, is recommended for predicting SLNB positivity.

Top-Rated Videos

128. Pleural Flap Closure to Mediastinalize the Gastric Conduit in Robotic Ivor Lewis Esophagectomy: A Novel Technique

Faisal S Jehan, MD, FICS[1]; Maureen Brady, PA-C[2]; Todd Demmy, MD[3]; Zachary Stiles, DO[4]; Moshim Kukar, MD[5]

[1]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [2]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [3]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [4]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [5]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US

INTRODUCTION: With the increasing adoption of Ivor Lewis (IL) esophagectomies, gastric conduit dysfunction is becoming a more common issue. Factors contributing to this complication include redundancy and the final lie and positioning of the gastric conduit. This positioning of the gastric conduit in the chest, as opposed to within the mediastinum, can cause angulation and narrowing at the level of the hiatus. These anatomical challenges can result in symptoms such as delayed gastric emptying, reflux, and patient discomfort, highlighting the need for improved techniques to optimize conduit placement and function. **METHODS:** In this video, we demonstrate a novel technique aimed at mediastinalizing the gastric conduit during a robotic Ivor Lewis esophagectomy. The method involves creating and securing a pleural flap over the gastric conduit in the chest, using robotic assistance. And closure of this pleural flap using a running 3.0 V-lock suture. **RESULTS:** The application of this novel technique for pleural flap closure successfully mediastinalized the gastric conduit as shown in the video. Postoperative assessments with Chest X-rays and CT esophagogram showed a significant reduction in conduit angulation and free flow of the contrast through the hiatus as shown in Figure 1. Patients demonstrated no immediate complications related to the pleural flap closure. **CONCLUSIONS:** In conclusion, the novel technique of pleural flap closure to mediastinalize the gastric conduit during robotic Ivor Lewis esophagectomy appears to be a safe and effective method to reduce conduit angulation and improve gastric emptying. With continued modification of our technique over the last decade, we believe that this modification has the most potential to improve quality-of-life while adding minimal time in the operating room and no additional morbidity.

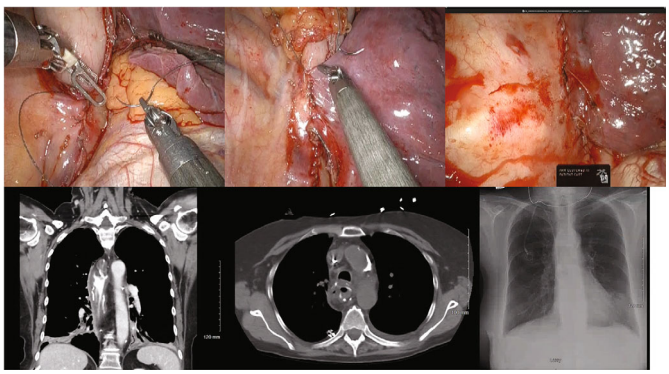


Figure 1. Top row showing pleural flap closure using 3.0 running V lock. Bottom row showing post operative CT esophagogram and Chest X-ray.

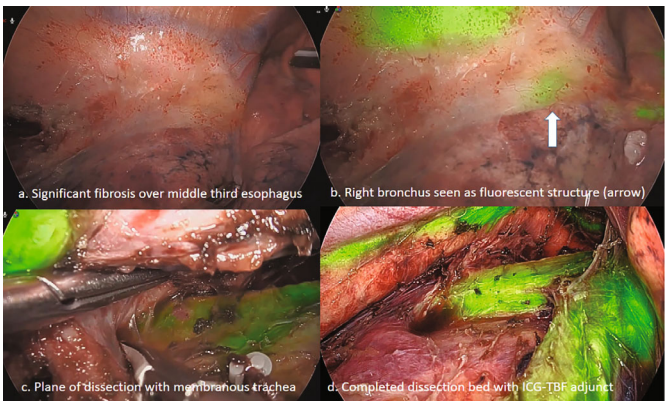
129. Tracheobronchial fluorescence (ICG-TBF) as an adjunct during minimally invasive salvage esophagectomy- a video presentation.

Srijan Shukla, MS, DNB (Surgical Oncology), FEBS (Fellow European Board of Surgery)[1]; Subramanyeshwar R Thammineedi, MCh, FRCS, FACS[2]

[1]Basavatarakam Indo American Cancer Hospital & Research Institute, Hyderabad, Telangana, IN; [2]Basavatarakam Indo American Cancer Hospital & Research Institute, Hyderabad, Telangana, IN

INTRODUCTION: Squamous cell carcinoma (SCC) is the predominant esophageal carcinoma in low to middle income countries (LMIC's). Salvage esophagectomy is a complex procedure with high conversion rates. The combined effect of radiation fibrosis and disease recurrence makes the planes between the esophagus and surrounding structures indistinct. The tracheobronchial complex is at risk of injury due to the thin membranous anatomy in contact with the esophagus. Tracheobronchial fluorescence (ICG-TBF) is a novel technique of aerosolization of indocyanine green (ICG) that utilizes the principles of fluorescence-guided surgery (FGS) to aid in a safe and reproducible minimally invasive esophagectomy. **METHODS:** The case reported in the video is of a 62-year-old male who had developed a recurrence of SCC of the middle third esophagus starting at 23 cm from incisors and extending above the carina on imaging. The patient had received definitive chemoradiation 16 months back. The preoperative whole-body PET CT scan and bronchoscopy revealed indentation but no invasion in the tracheobronchial tree. After induction of general anesthesia, ICG-TBF was administered with a 7.5 mg dose via a nebulizer. Right thoracoscopic mobilization of the esophagus was done in the overlay mode of a near-infrared (NIR) enabled camera. **RESULTS:** Dense adhesions were found between the involved esophagus, subcarinal nodes, and the tracheobronchial tree. Utilizing the ICG-TBF, a plane of dissection was created between the esophagus and membranous trachea above the growth. As the membranous trachea was highlighted with fluorescence, it was amenable to continue the dissection on the adherent segment while maintaining the accurate plane of dissection. The vagus nerve over the carina was thickened and indistinguishable from the trachea, however a lack of fluorescence over the nerve made the distinction pronounced enabling the surgeon to proceed. The thoracoscopic mobilization was completed in a minimally invasive technique with no inadvertent injuries. The patient had no allergic reaction to

the aerosolized ICG during or after the surgery. **CONCLUSIONS:** ICG-TBF is an affordable, safe, and reproducible technique that can help the esophageal surgeon successfully navigate the challenging scenario of salvage surgery in a recurrent SCC of the middle or upper third esophagus. Further studies are required to establish the benefit in terms of conversion rates, operative times, and tracheobronchial injury rates.



130. Robotic-Assisted Right Hepatectomy: An Efficient Technique for Intraparenchymal Pedicle Dissection

Laleh Foroutani[1]; Jane Wang[2]; Amir Ashraf Ganjouei[3]; Adnan Alseidi[4]; Mohamed A. Adam, MD[5]
[1]University of California San Francisco (UCSF), San Francisco, CA, US; [2]University of California San Francisco, San Francisco, CA, US; [3]University of California San Francisco, San Francisco, CA, US; [4]University of California San Francisco, San Francisco, CA, US; [5]University of California, San Francisco, San Francisco, CA, US

INTRODUCTION: This abstract presents a video demonstration of robotic-assisted right hepatectomy as an efficient technique for intraparenchymal approach for pedicle dissection and transection employing an ultrasonic surgical aspirator in a patient with a large hepatic adenoma. **METHODS:** A 45-year-old overweight female with a history of cutaneous melanoma and oral contraceptive use presented with symptomatic 10 cm hepatic masses in the right lobe of the liver and elevated alkaline phosphatase. A biopsy showed hepatocellular adenoma. Given the size and symptoms of the mass, robotic-assisted right hepatectomy was deemed the most appropriate surgical intervention. The patient was placed in the supine position (20° reverse Trendelenburg, 8° right side up), and a total of four robotic ports and a 12-mm port for the ultrasonic aspirator were placed. A laparoscopic ultrasonic surgical aspirator was utilized for intraparenchymal dissection and transection of the right pedicle, allowing for meticulous dissection and preservation of contralateral structures. Large crossing veins were clipped and transected. The specimen was extracted via a 4-cm Pfannenstiel incision. **RESULTS:** There was no bile leak or bleeding from the transection line. The procedure was completed successfully without any intraoperative complications. Robot console time was 148 minutes. The parenchymal transection was completed in 34 minutes with two intracorporeal Pringle maneuvers. The estimated blood loss was 50 mL. The patient had an uneventful postoperative recovery and was discharged on postoperative day three without requiring opioids at discharge. Pathology confirmed an inflammatory variant of hepatocellular adenoma with negative margins. The patient continues to do well in 5-month follow-up. **CONCLUSIONS:** This case highlights the efficacy and safety of robotic-assisted right hepatectomy using a CUSA-based intraparenchymal approach for right pedicle control. This robotic approach ensures the benefit of intraparenchymal pedicle dissection due to the enhanced visualization and precise control of vascular structures and ducts, reducing the risk of contralateral vessels and duct injury. The combined use of CUSA and the robotic approach maximizes the efficiency of parenchymal transection while minimizing blood loss and complications.

131. Nipple Sparing Mastectomy with Immediate Lift Using a Vertical Incision Pattern: Video Technique

Ilana G. Margulies, MD, MS[1]; Julian K. Marable, BA[2]; Monika K. Masanam, MD[3]; Kenneth Fan, MD[4]; David H. Song[5]; Lucy De La Cruz, MD[6]
[1]MedStar Georgetown University Hospital, Washington, DC, US; [2]MedStar Georgetown University Hospital, Washington, DC, US; [3]MedStar Georgetown University Hospital, Washington, DC, US; [4]MedStar Georgetown University Hospital, Washington, DC, US; [5]MedStar Georgetown University Hospital, Washington, DC, US; [6]MedStar Georgetown University Hospital, Washington, DC, US

INTRODUCTION: Nipple-sparing mastectomy (NSM) is a valuable surgical approach that allows for preservation of the nipple areolar complex (NAC) in mastectomy; however, patients who have large breasts with moderate to severe ptosis are typically not eligible for NSM secondary to increased risk of complications. We describe a novel technique through video illustration of NSM using a vertical lift incision pattern that can be used to reduce the breast envelope in ptotic breasts immediately prior to implant- or flap-based reconstruction. **METHODS:** The technical points of this novel technique are described in the presented video and include the design of a vertical incision pattern for a NSM for large and ptotic breasts, followed by a step-by-step guide discussing how to perform a mastectomy using this approach immediately prior to direct-to-implant reconstruction. **RESULTS:** The presented video demonstrates the markings used for this approach, the operative technique of the NSM through this incision pattern, and the use of subsequent direct-to-implant reconstruction. The vertical incision pattern is designed using principles of the vertical mastopexy technique. After incising a 38 mm diameter around the nipple, the remainder of the skin within the vertical incision pattern is de-epithelialized. The mastectomy then begins on lateral border of vertical incision pattern and proceeds in the superomedial direction down to chest wall. The use of a curved cautery device is discussed to assist with following the round contour of the mastectomy plane through this approach. The dissection is then extended superiorly, laterally, and inferiorly using a two-finger technique to allow for tissue retraction while ensuring appropriate mastectomy flap thickness. Our technique for direct to implant reconstruction is then illustrated as we wrap the implant using an acellular dermal matrix, place the implant into the mastectomy pocket, and close the vertical incision pattern in a layered fashion. **CONCLUSIONS:** NSM with immediate lift using a vertical incision pattern is described with video illustration. The use of mastopexy principles involving skin reduction with de-epithelialization and tissue in-folding maintains perfusion to promote NAC and skin flap survival. Careful selection criteria including BMI, breast size, and degree of breast ptosis should be used when offering this approach to patients to mitigate complication risk.

132. A Simplified Robotic-Assisted Inframesentric Duodenojejunostomy Technique for Distal Duodenal Resections

Jane Wang[1]; Amir Ashraf Ganjouei[2]; Laleh Foroutani[3]; Kenzo Hirose, MD[4]; Eric K. Nakakura, MD, PhD[5]; Carlos U. Corvera, MD[6]; Adnan Alseidi[7]; Mohamed A. Adam, MD[8]
[1]University of California San Francisco, San Francisco, CA, US; [2]University of California San Francisco, San Francisco, CA, US; [3]University of California San Francisco, San Francisco, CA, US; [4]University of California, San Francisco, San Francisco, CA, US; [5]University of California, San Francisco, San Francisco, CA, US; [6]University of California, San Francisco, San Francisco, CA, US; [7]University of California San Francisco, San Francisco, CA, US; [8]University of California, San Francisco, San Francisco, CA, US

INTRODUCTION: The traditional surgical approach for resecting distal duodenal gastrointestinal stromal tumors (GISTs) involves a Roux-en-Y D2 duodenojejunostomy. However, the Roux-en-Y reconstruction may increase the risk of delayed gastric emptying and injury to the major papilla. In this video abstract, we describe a robotic-assisted inframesentric duodenal reconstruction technique following resection of a D4 GIST, which obviates the need for Roux-en-Y reconstruction. **METHODS:** A 48-year-old male was diagnosed with a 4 cm GIST in the D4 segment of the duodenum. The procedure was performed using the da Vinci Xi robotic system. A segmental resection of the D3/D4 duodenum was carried out to achieve negative margins. To ensure the correct positioning of the jejunum inferior to the duodenum without torsion and to obviate the need for Roux-en-Y reconstruction, a 20 cm segment of the proximal jejunum was resected. Subsequently, a hand-sewn side-to-side inframesentric anastomosis was created between the proximal D3 segment of the duodenum and the jejunum. **RESULTS:** The procedure involved minimal blood loss (10 ml) and there were no intraoperative complications. The patient was discharged

on postoperative day four on a pureed diet and required no narcotics during his admission. Pathology confirmed GIST with clear tumor margins. At the six-month follow-up, no complications, readmissions, or mortality were reported and he was tolerating a regular diet. **CONCLUSIONS:** This approach simplifies the complexity of duodenal reconstruction by eliminating the need for Roux-en-Y duodenojejunostomy with its additional anastomosis. By anastomosing the jejunum to D3, this technique reduces the risk of injury to the major duodenal papilla in D2 and potentially improves drainage of the duodenum due to the caudal orientation of the duodenojejunostomy.

133. Robotic Partial Duodenectomy for Gastrointestinal Stromal Tumor

Parit T Mavani, MBBS[1]; Callie Goel, MD, MSc[2]; Sarah E Aptov[3]; David A. Kooby, MD[4]; Mihir M. Shah, MD[5]
[1]Emory University, Sandy Springs, GA, US; [2]Emory University, Atlanta, GA, US; [3]Emory Saint Joseph Hospital, Atlanta, GA, US; [4]Emory University School of Medicine, Atlanta, GA, US; [5]Emory University, Atlanta, GA, US

INTRODUCTION: Resection of duodenal Gastrointestinal Stromal Tumor (GIST) in the pancreaticoduodenal groove is challenging due to its proximity to the ampulla of Vater. Segmental resection using partial duodenectomy is possible with careful evaluation of the ampulla during duodenal closure. Understanding the technical steps associated with partial duodenectomy is important to avoid complex resection (i.e. pancreaticoduodenectomy) while maintaining oncologic safety. We aimed to demonstrate the technical steps of robotic partial duodenectomy for segmental resection of duodenal GIST located in close proximity to ampulla. **METHODS:** A 76-year-old woman was presented with syncope. On diagnostic workup, a CT scan of the abdomen noted a duodenal tumor closely abutting the pancreas, located anterior to the pancreaticoduodenal groove (Figure 1). Esophagogastroduodenoscopy with endoscopic ultrasound (EUS) revealed a duodenal tumor originating from the muscularis propria layer of the second portion of the duodenum. The Fine-Needle Aspiration (FNA) was consistent with a GIST. Further staging workup was negative for metastasis. We consented the patient for robotic partial duodenectomy, possible pancreatoduodenectomy. **RESULTS:** Our video case includes the following technical steps: division of the gastrocolic omentum, Kocherization of the duodenum, mobilization of the tumor, division of feeding vessels, resection of the tumor, duodenal closure in a continuous fashion, cholecystectomy, specimen retrieval and drain placement. Intraoperative endoscopy was performed prior to tumor resection, during duodenal closure and at the end of the closure. Intraoperatively, on endoscopy no mucosal component of the duodenal tumor was noted. The duodenal tumor was resected without rupture and with grossly negative margins. The endoscopy during duodenal closure noted no impingement of the ampulla by visualizing the ureteral stent passed through the cystic duct into the ampulla. After the duodenal closure, we passed the gastroscope through the closure revealing excellent patency and hemostasis, and confirmation of safe distance from the ampulla. Saline immersion leak test was negative. The patient recovered well from the surgery and was discharged on postoperative day 4. Surgical pathology revealed low-grade GIST with a low mitotic rate. **CONCLUSIONS:** Our video case demonstrates successful completion of robotic partial duodenectomy for a duodenal gastrointestinal stromal tumor with preservation of the ampulla and avoidance of pancreatoduodenectomy.

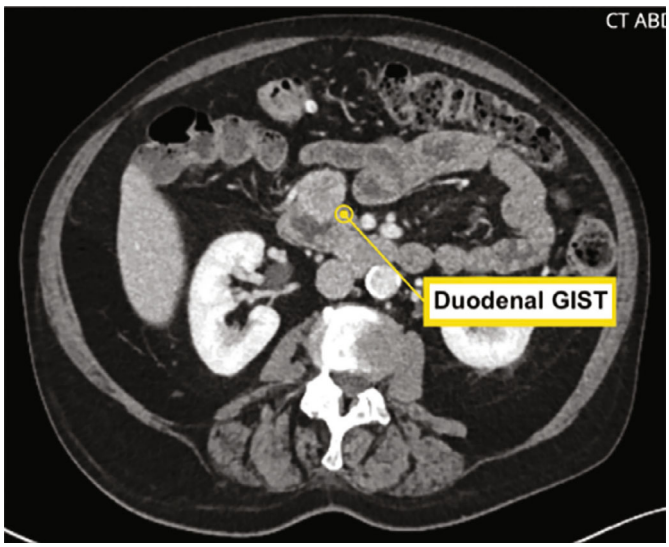


Figure 1. Duodenal mass anterior to the pancreaticoduodenal groove near the ampulla

134. Robotic Modified Puestow Procedure with Pancreaticogastrostomy

Mohammad S Ali, MD[1]; Ali Ahmad[2]
[1]Boston University-Roger Williams Medical Center, Providence, Rhode Island, RI, US; [2]University of Kansas School of Medicine-Wichita, Wichita, KS, US

INTRODUCTION: The Puestow procedure also known as the lateral pancreaticojejunostomy was invented by Charles B. Puestow and William J. Gillesby in 1958 for the management of chronic pancreatitis with a dilated pancreatic duct. Minimally invasive surgery has allowed for the Puestow procedure to be modified yet continues to be a option for patients with chronic pancreatitis. **METHODS:** Single institution video presentation of steps of a minimally invasive modified Puestow procedure robotic pancreaticogastrostomy as an efficient and effective option for management of chronic pancreatitis. **RESULTS:** Robotic Modified Puestow Procedure with Pancreaticogastrostomy demonstrated good outcomes with effective management of symptoms of chronic pancreatitis. **CONCLUSIONS:** Robotic modified Puestow procedure with pancreaticogastrostomy is a safe and effective technique as an alternative to the pancreaticojejunostomy.

135. Chest Wall Resection & Reconstruction - REAL WORLD solution

Rigved Nittala[1]
[1]Homi Bhabha Cancer Hospital & Research Centre, Visakhapatnam, Andhra Pradesh, IN

INTRODUCTION: Our video presents complex resection of Chest wall with forequarter amputation. Instead of Costly reconsruction methods, we have used Bone cement and steel wires for the rigid reconstruction. **METHODS:** This video presentation demonstrates the utility of bone cement & steel wires for rigid reconstruction. **RESULTS:** This presentation discusses a complex surgical case involving a chest wall resection and forequarter amputation performed on a patient diagnosed with a spindle cell sarcoma of the chest wall. The surgical procedure necessitated the removal of the anterolateral portions of the first four ribs on the left side, resulting in a significant structural defect.In addressing the reconstruction of this defect, various options were considered, including 3D reconstruction titanium rib implants, which could incur costs of approximately $300 per rib, totaling nearly $900. However, we opted for a more cost-effective solution using bone cement and steel wires, achieving a total reconstruction cost of around $50.This approach not only provides a rigid and stable reconstruction of the chest wall but also demonstrates a simple and reproducible technique that is particularly advantageous in resource-constrained environments. Our findings advocate for this method as a viable alternative for managing complex chest wall defects, emphasizing its affordability and practicality in real-world clinical settings. **CONCLUSIONS:** Bone Cement with steel wires is an affordable and safe rigid reconstruciton option for complex chest wall defects in resource constraints hospitals.

136. Robotic assisted central pancreatectomy for low-grade neuroendocrine tumor

Olivia E El Achtar, MD FACS[1]; Ricardo Jureidini, MD[2]; Thiago Costa Ribeiro, MD[3]; Guilherme Naccache Namur, MD[4]; Jose Jukemura, MD[5]; Ulysses Ribeiro, [6]; Paulo Herman, MD PhD[7]; Italo B Simoes, MD[8]

[1]Hospital das Clinicas FMUSP/Instituto do Cancer do Estado de Sao Paulo, Panama, Panama, PA; [2]Hospital das Clinicas FMUSP/Instituto do Cancer do Estado de Sao Paulo, Sao Paulo, Sao Paulo, BR; [3]Hospital Das Clinicas FMUSP/Instituto do Cancer do Estado de Sao Paulo, Sao Paulo, Sao Paulo, BR; [4]Hospital das Clinicas FMUSP/Instituto do Cancer do Estado de Sao Paulo, Sao Paulo, Sao Paulo, BR; [5]Hospital das Clinicas FMUSP/Instituto do Cancer do Estado de Sao Paulo, Sao Paulo, Sao Paulo, BR; [6]Hospital das Clinicas FMUSP/Instituto do Cancer do Estado de Sao Paulo, Sao Paulo, Sao Paulo, BR; [7]Hospital das Clinicas FMUSP/Instituto do Cancer do Estado de Sao Paulo, Sao Paulo, Sao Paulo, BR; [8]Hospital das Clinicas FMUSP/Instituto do Cancer do Estado de Sao Paulo, Sao Paulo, Sao Paulo, BR

INTRODUCTION: Pancreatic neuroendocrine tumors represent a rare sub type of pancreatic cancer. Surgical planning requires multidisciplinary evaluation including preoperative staging and careful consideration of morbidity depending on the location of the tumor and the type of surgery. The minimally invasive approaches have gained terrain in the treatment of this pathologies, aiding in the preservation of pancreatic tissue and critical structures around the pancreas. Currently the evidence of robotic vs laparoscopic approach is limited. Robotic central pancreatectomy is proposed as a safe alternative to major resections in benign and low-grade malignant tumors with better exocrine and endocrine pancreatic function, but worse rate of pancreatic fistula compared with distal pancreatectomy. **METHODS:** The patient is male, 68 years old, diabetic, with previous open surgery for hiatal hernia, presents with history of nausea, vomiting and abdominal pain. Abdominal ultrasound shows hiatal hernia and a suspicion for a pancreatic cystic lesion. Magnetic resonance cholangiopancreatography and endoscopic ultrasound imaging shows a cystic lesion of about 1.8 cm in the body of the pancreas without communication with the main pancreatic duct. Biopsy suggests a well differentiated neuroendocrine tumor. Follow up after one-year shows growing of the lesion by 5 mm. Surgical treatment is decided. **RESULTS:** The patient had a robotic assisted central pancreatectomy, lymphadenectomy and Roux-en-Y pancreaticojejunostomy. We describe all the steps of the surgery and the main anatomic relationships are shown. Total surgical time 7 hours, blood loss 150 mL. Postoperative course without complications. The patient went home at the 8th postoperative day, without evidence of pancreatic fistula. After one-year of follow up the patient has not had worsening of the diabetes or signs of exocrine insufficiency. Pathology report: Well-differentiated neuroendocrine tumor, grade 1, Mitotic index 0 mitoses/mm2, Ki-67: 1%, positive for chromogranin A, synaptophysin A and CK 8/18. Size 1.9 x 1.0 cm with clear surgical margins and 5 lymph nodes negative for metastases. **CONCLUSIONS:** Robotic assisted central pancreatectomy is safe and feasible for low grade neuroendocrine tumors minimizing exocrine and endocrine disfunction. The use of the robotic platform can aid the surgeon to perform this procedure in a safer way.

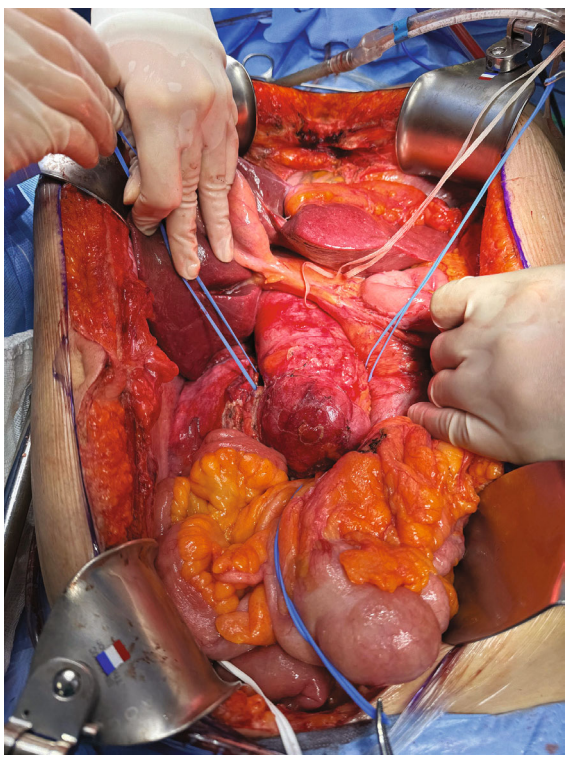


137. Leiomyosarcoma of the inferior vena cava with right atrium tumor thrombus. Early surgical resection to prevent secondary Budd-Chiari Syndrome is crucial.

Marcus Rodrigo Monteiro[1]

[1]Hospital Sirio Libanes, Sao Paulo, Sao Paulo, BR

INTRODUCTION: Leiomyosarcomas (LMS) of the inferior vena cava (IVC) are a rare form of retroperitoneal tumors, and their venous extension to the right atrium is also unusual. Represent a non-habitual surgical challenge and often require a multidisciplinary approach, within tumor board discussion and different surgical specialties. Type III IVC LMS were taught to be inoperable, with limited responsiveness to the chemotherapy regimens; but, nowadays, with better surgical approaches and preoperative management, surgery is now a safe option. **METHODS:** Female, previously healthy, 60 years old, with lower right back pain. CT scan revealed a extensive retroperitoneal mass, measuring 21,4 x 7,5 x 7,4cm, involving IVC, right kidney/renal veins and duodenum, with tumoral thrombus extension to the right atrium (transesophageal echocardiography showed a 2cm tumoral extension above the cavoatrial junction). CT-guided core biopsy was performed: low grade (G1) LMS. The tumor is located between the right atrium and IVC below the renal veins, comprising the retrohepatic cava and hepatic veins (secondary budd-chiari syndrome). Due to limited reponsiveness to neoadjuvant chemotherapy/radiotherapy, plus clinical features of budd-chiari like syndrome, the patient's case underwent multidisciplinary tumor board discussion and the decision was favorable to upfront surgery. **RESULTS:** Tumor was located at the mid-right side of the retroperitoneum, envolving the suprahepatic/retrohepatic/subhepatic IVC as previously mentioned; also duodenum and right kindney dislocated from the habitual position, without infiltration or hydronephrosis. Full Cattel-Braasch manouver to completely expose IVC and aorta; distal control of the vein, 5cm above the iliac bifurcation; both renal veins insertion were compromised by the tumor (not the arteries) Using piggyback approach, the IVC was deattached from the liver and also major hepatic veins and porta hepatis were dissecated At this time, the CV team conducted a sternotomy and cardiopulmonary bypass (CPB). The TEE showed a 2cm tumoral thrombus extension above the cavoatrial junction. After stapling the IVC and the renal veins, and also ligating lumbar veins, the tumor was completely isolated.The infrarenal IVC was removed en bloc along with the TT. The remaining IVC below the hepatic veins was sutured. A vascular graft was anastomosed with the proximal and distal cuffs of the IVC. Both renal veins were also reimplanted to the. **CONCLUSIONS:** Final pathology revealed a G2 LMS; all margins negative. She was discharged on 13 postop day.



ABSTRACTS

E-POSTERS

SSO 2025 ANNUAL MEETING

Society of Surgical Oncology

March 27-29, 2025

P1. Activated Hippo pathway is associated with worse response to Trastuzumab and survival in HER2-positive breast cancer

Masanori Oshi[1]; Akimitsu Yamada[2]; Itaru Endo[3]; Kazuaki Takabe, MD, PhD[4]
[1]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [2]Yokohama City University, Yokohama, JP; [3]Yokohama City University, Yokohama, JP; [4]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US

INTRODUCTION: Hippo signaling pathway, a highly conserved pathway that controls cell proliferation, apoptosis, cancer stemness, and consequently regulates homeostasis, is an emerging pathway regulating pro-cancerous processes. Hippo signaling was also reported to promote trastuzumab resistance in breast cancer. However, the clinical relevance of Hippo signaling in breast cancer patients remain unclear. **METHODS:** Clinical and transcriptome data were obtained from two independent large cohorts, METABRIC and TCGA cohorts. We used the "KEGG hippo pathway" gene set in KEGG collections, which contains 44 genes, and Gene set variation analysis algorithm to generate the score to quantify Hippo pathway activity. We defined the top tertile as Hippo pathway high group within each cohort. **RESULTS:** Patients with high Hippo pathway scores have significantly worse disease-specific survival (DSS) in HER2-poitive breast cancer, but not in the other subtypes. Hippo pathway score showed the largest hazard ratio (HR) of DSS in HER2-positive breast cancer compared with YAP1 and TAZ expressions consistently in both METABRIC and TCGA cohorts (HR = 1.11 [p = 0.48], 0.97 [p = 0.89], and 2.47 [p = 0.04], in the METABRIC, HR = 2.49 [p = 0.15], 0.64 [p = 0.37], and 41.8 [p = 0.03], in the TCGA, respectively). High Hippo pathway cancer enriched metastasis-related gene sets; epithelial mesenchymal transition, Notch signaling, Hedgehog signaling, transforming growth factor (TGF)-β signaling, as well as cell proliferation-related gene set; mitotic spindle, consistently in both cohorts. Hippo pathway high HER2-positive breast cancer was significantly infiltrated with low fraction of anti-cancer immune cell; T helper type 1 (Th1) cells, plasmacytoid dendritic cells (pDC), and M1 macrophages in both cohorts. Interestingly, pathological complete response (pCR) after trastuzumab-based neoadjuvant chemotherapy compared to residual disease, was significantly associated with lower Hippo pathway score, as opposed to there was no difference in YAP1 nor TAZ expression levels in GSE37946 cohort (p = 0.035, 0.247, and 0.755, respectively). **CONCLUSIONS:** Enhanced Hippo pathway was associated with high level of several metastasis-related gene sets, and less infiltration of anti-cancer immune cells, and that a resistance for neoadjuvant treatment may be associated with a worse prognosis for patients with HER2-positive breast cancer.

P2. Application of Choosing Wisely Recommendations to Axillary Management in Early-Stage HR+/HER2- Local Breast Recurrences

Eliza H Lorentzen, MD[1]; Tari A. King, MD[2]; Elizabeth A Mittendorf, MD, PhD, MHCM[3]; Olga A Kantor, MD, MS[4]; Christina A Minami, MD, MS[5]
[1]Brigham and Women's Hospital/Dana-Farber Brigham Cancer Center, Boston, MA, US; [2]Brigham and Women's Hospital/Dana Farber Cancer Institute, Boston, MA, US; [3]Brigham and Women's Hospital/Dana-Farber Cancer Institute, Boston, MA, US; [4]Brigham and Women's Hospital, Boston, MA, US; [5]Brigham and Women's Hospital/Dana Farber Brigham Cancer Center, Boston, MA, US

INTRODUCTION: Trial data support omission of axillary surgery in women ≥70 with early-stage HR+/HER2- breast cancers. Choosing Wisely recommendations discourage routine use of sentinel lymph node biopsy (SLNB) in this population but do not specify between primary and recurrent disease. While SLNB rates remain as high as 80% in women undergoing surgery for their first cancer, practice patterns in the management of early-stage, HR+ ipsilateral breast tumor recurrence (IBTR) are less well-defined. We aimed to examine how Choosing Wisely recommendations are being applied in the setting of IBTR. **METHODS:** Women with a history of breast conserving surgery (BCS) for non-metastatic breast cancer with subsequent ipsilateral T1-2N0 HR+/HER2- breast cancer were queried in SEER, 2018-2020, and stratified by age (<70 years vs. ≥70). Patients who underwent axillary lymph node dissection (ALND, defined as removal of ≥10 nodes) at the treatment of the index breast cancer or who did not undergo surgery for their IBTR were excluded. The outcome of interest was the performance of axillary surgery (SLNB, defined as removal of 1-9 nodes, or ALND). Multivariable logistic regression was used to identify patient- and disease-specific covariates associated with omission of axillary surgery. **RESULTS:** Of 1299 eligible patients, 676 (52.0%) were ≥70 years. The majority of all patients, 992 (76.4%), were Non-Hispanic White. Disease-free interval (DFI) was >10 years in 696 (53.6%) patients and there was no significant difference in DFI by age (p=0.599). A greater proportion of older women vs. younger women had omission of axillary surgery (≥70 years: 42.2% vs. <70: 21.0%, p<0.001) and repeat breast conservation (≥70 years: 49.0% vs. <70: 17.7%, p<0.001). On adjusted analysis, age ≥75 years compared to <70 (75-79 years: OR 1.78, 95% CI (1.08-2.95); 80-84 years: OR 4.90, 95% CI [2.81-8.55]; ≥85 years: OR 4.26, 95% CI [2.13-8.53]), rural residence compared to urban residence (OR 2.31, 95% CI [1.32-4.05]), and breast conserving therapy compared to mastectomy (OR 2.58, 95% CI [1.36-4.89]) were associated with a greater odds of omission of axillary surgery (Table). **CONCLUSIONS:** Axillary surgery rates in women ≥70 years with early-stage HR+/HER2- IBTRs are lower than in younger women and lower than reported national rates for SLNB in the setting of primary cancers. Further work exploring why providers feel more comfortable de-escalating locoregional therapy in select cases of IBTR is needed.

Table. Multivariable Analysis Predicting Omission of Axillary Surgery for Treatment of IBTR

	Odds Ratio (95% CI)	P-value
Age (years)		
<70	*Ref*	
70-74	1.30 (0.82-2.08)	0.269
75-79	**1.78 (1.08-2.95)**	0.024
80-84	**4.90 (2.81-8.55)**	<0.001
≥85	**4.26 (2.13-8.53)**	<0.001
Race and Ethnicity		
Non-Hispanic/Latinx White	*Ref*	
Hispanic/Latinx White	1.27 (0.68-2.36)	0.460
African-American/Black	0.74 (0.37-1.50)	0.410
Other/Unknown	0.95 (0.46-1.96)	0.882
Urban/Rural Status		
Urban	*Ref*	
Rural	**2.31 (1.32-4.05)**	0.003
DFI (years)		
<5	*Ref*	
5-10	4.45 (0.45-43.8)	0.201
>10	7.47 (0.81-68.9)	0.076
Surgery and RT		
BCS	0.63 (0.35-1.15)	0.131
BCT	**2.58 (1.36-4.89)**	0.004
Mastectomy	*Ref*	
Mastectomy + RT	1.28 (0.06-8.09)	0.765
Prior RT		
Yes	0.85 (0.56-1.28)	0.246
No	*Ref*	
Chemotherapy		
Yes	*Ref*	
No/unknown	1.28 (0.85-1.92)	0.246

IBTR: ipsilateral breast tumor recurrence; **CI:** confidence interval; **BCS:** breast conserving surgery; **BCT:** breast conserving therapy, defined BCS + RT; **RT:** radiation therapy

P3. Association between 21-gene Recurrence Score and Racial Differences in Chemotherapy in Premenopausal Breast Cancer

Sara Myers, MD, PhD[1]; Philip Poorvu[2]; Rachel Freedman[3]; Ann Partridge[4]; Elizabeth A Mittendorf, MD, PhD, MHCM[5]; Tari A. King, MD, FSSO[6]; Olga Kantor, MD[7]
[1]The Ohio State University Wexner Medical Center/ The James, Columbus, OH, US; [2]Dana-Farber Cancer Institute, Boston, MA, US; [3]Dana-Farber Cancer Institute, Boston, MA, US; [4]Dana-Farber Cancer Institute, Boston, MA, US; [5]Brigham and Women's Hospital/Dana-Farber Cancer Institute, Boston, MA, US; [6]Brigham and Women's Hospital/Dana Farber Cancer Institute, Boston, MA, US; [7]Brigham and Women's Hospital, Boston, MA, US

INTRODUCTION: Racial disparities in outcomes for premenopausal breast cancer (BC) have been well documented. Precision medicine is a possible solution to promote health equity. The OncotypeDX® 21-gene recurrence score (RS) predicts chemotherapy benefit in ER+HER2- BC. The TAILORx trial, which evaluated RS in node negative (pN0) disease, showed possible chemotherapy benefit in women <50 yo with RS 16-25. We characterized RS use

in women <50 yo as a first step in understanding how it impacts differences in chemotherapy receipt among premenopausal patients. **METHODS:** Women <50 yo with ER+HER2- pN0 invasive BC treated with upfront surgery from 2018-2021 were identified from the National Cancer Database. Cohort characteristics were compared by RS and chemotherapy receipt. RS was categorized as: <16, 16-20, 21-25, and >25. Low clinical risk disease was classified as low grade ≤3 cm, intermediate grade ≤2 cm, and high grade ≤1 cm, with all other disease considered high risk. Multivariable regression examined associations between sociodemographic/clinical factors and chemotherapy receipt by RS. **RESULTS:** Of 36,765 women with ER+HER2- pN0 BC <50yo, 85% were White, 10% were Black, 4% were Asian, and 7% were Hispanic. 67% had RS assessment. RS was least likely to be performed in Black (64% vs 67% Whites vs 70% Asians; p<0.001) and Hispanic (59% vs 62% non-Hispanic, p<0.001) women. RS assessment was more likely in high clinical risk disease (66% vs 60% low risk;0.001), lumpectomy (61% vs 63% mastectomy;0.001), and those who required radiation (62% vs 61% no radiation; p=0.035). Chemotherapy was received by 12% of patients with no RS, 1.1% of RS <15, 11% of RS 16-20, 52% of RS 21-25, and 89% of RS>25 (p<0.001). Black race (p=0.005), mastectomy (p<0.001), radiation (p<0.001), endocrine therapy (p<0.001), lower ER and PR percentages (p<0.001), and high-risk disease (p<0.001) were associated with receiving chemotherapy in patients who did not have RS performed (Table). Among patients with RS, race-based differences in chemotherapy dissipated for all with RS ≤25. High clinical risk remained associated with chemotherapy receipt for all with RS≤25. **CONCLUSIONS:** In this study, Black women <50 yo with ER+ pN0 BC were less likely to have RS assessment but more likely to receive chemotherapy. Among those with RS assay, there were no race-based differences in chemotherapy receipt for RS≤25. This data suggests RS may mitigate racial differences in the treatment of premenopausal pN0 BC and highlights the need to explore how precision oncology might enable health equity.

Table 1. Multivariable analysis of factors found to be significantly associated with chemotherapy use

	No RS	RS <15	RS 16-20	RS 21-25	RS>25
Variable [1]	OR, 95% CI	OR, 95% CI	OR, 95% CI	OR, 95% CI	OR, 95% CI
Race					
White	Ref	Ref	Ref	Ref	Ref
Black	1.34 (1.09, 1.64)*	0.73 (0.35, 1.56)	0.99 (0.68, 1.46)	0.81 (0.59, 1.11)	0.53 (0.36, 0.78)*
Asian/Pacific Islander	0.98 (0.71, 1.35)	0.89 (0.35, 2.26)	1.03 (0.67, 1.60)	0.73 (0.49, 1.08)	1.02 (0.47, 2.21)
Other	0.64 (0.40, 1.01)	0.57 (0.13, 2.55)	1.02 (0.50, 2.06)	1.09 (0.55, 2.15)	0.73 (0.29, 1.85)
Hispanic ethnicity	1.01 (0.79, 1.28)	1.26 (0.67, 2.36)	1.05 (0.72, 1.52)	0.91 (0.65, 1.29)	1.00 (0.61, 1.66)
ER%	0.99 (0.98, 0.99)*	0.99 (0.98, 1.00)	1.01 (1.00, 1.02)	1.00 (0.99, 1.01)	1.00 (0.99, 1.00)
PR%	0.99 (0.98, 0.99)*	0.99 (0.97, 0.99)*	0.99 (0.99, 0.99)*	0.99 (0.99, 1.00)*	0.99 (0.99, 0.99)*
Mastectomy	3.10 (2.34, 4.12)*	3.44 (1.75, 6.77)*	2.53 (1.59, 4.03)*	2.09 (1.29, 3.39)*	2.18 (1.19, 3.98)*
Radiation					
None	Ref	Ref	Ref	Ref	Ref
Breast/CW only	2.48 (1.85, 3.23)*	1.95 (0.95, 3.97)	1.60 (0.99, 2.58)	1.43 (0.88, 2.33)	1.60 (0.86, 2.98)
Breast/CW + RNI	4.22 (3.02, 5.90)*	5.51 (2.93, 10.36)*	2.30 (1.33, 3.98)*	1.61 (0.91, 2.85)	1.36 (0.63, 2.93)
Endocrine therapy	1.83 (1.45, 2.31)*	0.50 (0.26, 0.95)*	1.55 (0.88, 2.75)	1.67 (1.05, 2.65)*	7.65 (5.02, 11.66)*
High Clinical risk	5.19 (4.51, 5.98)*	3.44 (2.28, 5.18)*	2.57 (2.07, 3.21)*	1.66 (1.36, 2.04)*	1.32 (0.96, 1.81)

*Indicates p<0.05

[1]In addition to the covariates listed, multivariable models also included insurance status, income, and axillary staging procedure. Because these characteristics were not significantly associated with receipt of recurrence score assay or recurrence score category, they have not been included in the table.

Abbreviations: RS= Recurrence Score; ER= Estrogen Receptor; PR=Progesterone Receptor; SLNB= Sentinel Lymph Node Biopsy; ALND= Axillary Lymph Node Dissection; CW= Chest Wall; RNI= Regional Nodal Irradiation.

P4. Associations Between Language and Barriers to Care on Self-Reported Stress in Hispanic Breast Cancer Patients

Maria A Sierra, MD, MPH[1]; Peter A Borowsky, MD[2]; Alexandra E Hernandez, MD, MPH[3]; Michael H Antoni, PhD[4]; Maria M Llabre, PhD[5]; Neha Goel, MD, MPH[6]

[1]University of Miami Miller School of Medicine, Miami, FL, US; [2]University of Miami, Miami, FL, US; [3]University of Miami, Miami, FL, US; [4]University of Miami, Miami, FL, US; [5]University of Miami, Miami, FL, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Breast cancer outcome disparities persist, which may be in part attributed to stress and barriers to care, such as language. Research shows that stress and language impact health care beliefs and understanding, decisions and treatment. This study aims to better understand the association between preferred language and barriers to care on self-reported stress in a bilingual Hispanic breast cancer population. **METHODS:** From 2019-2024 patients were prospectively enrolled at an NCI-designated cancer center and sister safety-net hospital. Patients that identified as Hispanic and bilingual were included in this study. Patients were administered surveys which used Likert scales to evaluate current stress levels and barriers to care. Linear regression analyses assessed the association between barriers to care and stress, controlling for sociodemographic variables, including age, preferred language, and education level. **RESULTS:** 264 Hispanic women with mean (SD) age of 58.2 (12) were included. 238 (90.8%) identified as White, 13 (5%) as Black, and 13 (5%) as Other. 16 (6.1%) received no education or some elementary education, 79 (29.9%) had high school level education, 164 (62.1%) attended college or trade school and 5 (1.9%) preferred not to answer. 43 (16.3%) patients preferred to speak in English compared to 221 (83.7%) in Spanish. The Short Acculturation Scale for Hispanics (SASH) was used to confirm language preference with those who marked English as their preferred language scoring higher on the scale, indicating higher use of English language (3.53 vs. 1.40 for those who preferred English compared to Spanish). When accounting for age and education level, we found those who preferred Spanish language had lower levels of self-reported stress (B= -0.63, SE= 0.23, β= -0.18, t = -2.80, p= 0.006). Individuals with more barriers to care had higher levels of self-reported stress (B= 0.90, SE= 0.25, β= 0.22, t = 3.67, p< 0.001). Specifically, lack of transportation (B= 0.24, SE= 0.10, β= 0.14, t = 2.31, p= 0.022), unsure how to get there (B= 0.58, β= 0.16, t = 2.58, p= 0.01), and no family or friend to accompany to visits (B= 0.34, SE= 0.12, β= 0.18, t = 2.96, p= 0.003) were significant predictors of self-reported stress. **CONCLUSIONS:** Barriers to care are important factors associated with stress, and ultimately breast cancer outcomes. Importantly, Spanish language was protective of stress. This study highlights the importance of screening for barriers to care, including language, and stress given potential avenues to develop targeted cancer control interventions.

P5. Axillary Management in the Setting of Multicentric/Multifocal Breast Cancer: ACOSOG Z0011 Implications

Elizabeth M Fish, DO[1]; Walker Lyons, MD[2]; Austin D Williams, MD, MSEd[3]; Cecilia Chang, MS[4]; Allison A. Aggon, DO[5]; Andrea S. Porpiglia, MD[6]; Alycia L. So, MD[7]; Richard J. Bleicher, MD[8]

[1]Fox Chase Cancer Center, Philadelphia, PA, US; [2]Fox Chase Cancer Center, Philadelphia, PA, US; [3]Fox Chase Cancer Center, Philadelphia, PA, US; [4]NorthShore University HealthSystem, Evanston, IL, US; [5]Fox Chase Cancer Center, Philadelphia, PA, US; [6]Fox Chase Cancer Center, Philadelphia, PA, US; [7]Fox Chase Cancer Center, Philadelphia, PA, US; [8]Fox Chase Cancer Center, Philadelphia, PA, US

INTRODUCTION: ACOSOG Z0011 excluded "multicentric disease that is not amenable to a single lumpectomy." Meanwhile, Z11102 found that multicentric/multifocal (MC/MF) breast cancer is amenable to breast conservation therapy (BCT), but nodal management was not explored. Although MC/MF breast cancer definitions are subjective, particularly since 'quadrant' boundaries can be rotated, it remains unclear whether surgeons are treating the axilla differently in MC/MF vs unicentric (UC) disease and whether this affects survival. **METHODS:** Patients ≥18 having MC/MF and UC breast cancers (MC/MF vs UC examined/available for 2018-2021) and upfront surgery in the National Cancer Database were compared. Axillary management trends and overall survival (OS) for a Z0011-eligible subset was also assessed. **RESULTS:** Of 319,347 patients included, 295,283 (92.5%) were UC and 24,064 (7.5%) MC/MF. 79.8% of UC breast cancers were node-negative vs 65.7% of MC/MF tumors (p<0.001). A mean of 0.25 ± 0.77 nodes were positive in the UC group vs 0.44 ± 1.02 in the MC/MF group. MC/MF primaries were more common in those with lobular histology (OR=1.76, p<0.001), node positivity (OR=1.46, moderate (OR=1.35, p<0.001) or poor (OR=1.22, p<0.001) differentiation, and lymphovascular invasion (LVI; OR=1.25, p<0.001). MC/MF tumors were more common in Blacks (OR=1.13, p<0.001) and less common in Asians (OR=0.92, p=0.019) as compared with Whites. Being MC/MF was one of several multivariable predictors for nodal positivity (odds 49.6% higher, p<0.001). Nodal positivity was also associated with LVI (OR=1.21, cT3 (OR=4.44, p<0.001) and cT2 tumors (OR=3.61, moderate (OR=1.33, p<0.001) and poor (OR 1.21, OR <0.001) differentiation, and lobular histology (OR=1.15, among others. In a Z0011 subgroup (cT1/2 with 1-2+ nodes having BCT), 24,297 were UC and 1,695 MC/MF. Adjusting for patient/tumor factors, MC/MF tumors had a Z0011 paradigm as often as UC (p=0.881). Predictors of worse OS in the Z0011 subgroup were mixed histology (HR=3.18, p=0.009), poor differentiation (HR=1.82, and larger size (HR=1.02, p<0.001). Adjusted OS was similar for UC and MC/MF disease overall (p=0.3058) and in the Z0011 subgroup (p=0.164). Unadjusted OS is shown in the Figure. **CONCLUSIONS:** Despite the MC exclusion in Z0011, surgeons are applying the Z0011 paradigm to MC/MF breast cancer. Although there is an increase in nodal positivity in MC/MF disease, there is no OS impairment when treated via Z0011. Thus, excluding MC/MF disease and changing practice is not warranted.

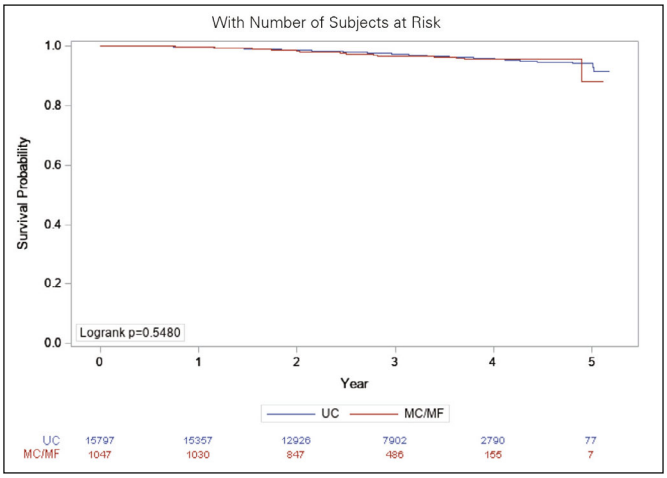


Figure. 5-Year OS in UC vs MC/MF Breast Cancers Treated with Z00II Paradigm

P6. Clinical Relevance of Sphingosine 1-Phosphate Receptor 4 (S1PR4) in Breast Cancer Using Bulk and Single-Cell Transcriptome Analysis

Sarah M McIntyre, MD[1]; Rongrong Wu[2]; Takashi Ishikawa[3]; Kazuaki Takabe, MD, PhD[4]

[1]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [2]Tokyo Medical University, Tokyo, JP; [3]Tokyo Medical University, Tokyo, JP; [4]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US

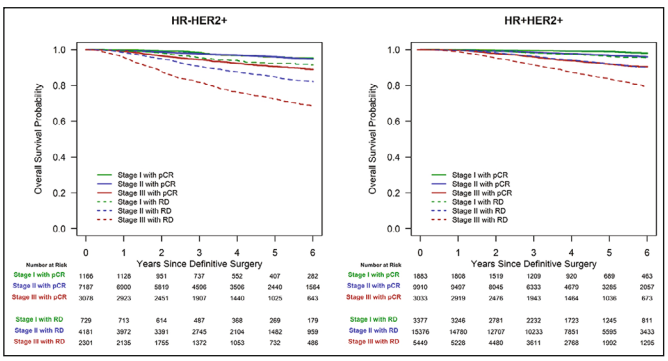
INTRODUCTION: Sphingosine 1-phosphate (S1P) generated in breast cancer (BC) cells is known to be exported and signal through its cell-specific interactions with five G protein coupled receptors in a paracrine manner. The Sphingosine 1-Phosphate Receptor 4 (S1PR4) has been implicated in the tumor immune response, and in vitro and murine models suggest that S1PR4 signaling may decrease T cell expansion and response to chemotherapy. In vitro work has also linked S1PR4 to HER2 signaling, but the clinical relevance of these findings has not been elucidated. This study aims to explore this through in Silico transcriptomic analyses of publicly available single-cell and bulk sequencing datasets. **METHODS:** In total, 5,364 patients with breast cancer from the TCGA, METABRIC, SCAN-B, and 4 single-cell cohorts were analyzed. The high expression group was defined as the top 10% of expression within each cohort. Gene set enrichment analysis (GSEA) and Kaplan Meier survival analyses were performed. **RESULTS:** S1PR4 expression was seen predominantly in T and B cell populations across the 4 single-cell cohorts. S1PR4 expression was higher in triple negative (TN) BC. Although not significant, S1PR4 high BC showed excellent overall survival in the HER2+ subtype in the TCGA and SCAN-B cohorts. High S1PR4 BC was associated with leukocyte fraction, stromal fraction, tumor infiltrating lymphocytes, and both BCR and TCR Shannon and Richness. High S1PR4 expression was associated with high levels of CD8+ and CD4+ T cells, B cells, M1 macrophage, dendritic cells, vascular and lymphatic endothelial cell infiltrations regardless of subtype in all cohorts ($p<0.05$). Interestingly, high levels of S1PR4 expression also correlated with high cytolytic activity score regardless of subtype across the cohorts ($p<0.05$). In the METABRIC and SCAN-B cohorts, high S1PR4 expression enriched immune-related gene sets; interferon-alpha response, interferon-gamma response, allograft rejection and inflammatory response, and enriched less cell proliferation-related gene sets; G2M checkpoint, E2F targets, mitotic spindle and MYC targets. S1PR4 expression correlated with pathologic complete response (pCR) after anthracycline and taxane neoadjuvant therapy in ER+/HER2- and TNBC (GSE163882 cohort). S1PR4 expression was higher in tumor that achieved pCR after immunotherapy for ER+/HER2- but not TN tumors in the I-SPY2 cohort. **CONCLUSIONS:** S1PR4 was predominantly expressed in T and B cells and its expression reflected their infiltration and cell killing activity. Further investigation is warranted to elucidate its utility as a biomarker for immunotherapy for ER+/HER2- BC.

P7. Clinical Stage at Diagnosis Impacts Overall Survival in Patients with Operable HER2+ Breast Cancer Regardless of Response to Neoadjuvant Chemotherapy

Nara Tashjian, MD, MBA[1]; Tanya Hoskin, MS[2]; Roberto Leon-Ferre, MD[3]; Judy C. Boughey, MD[4]

[1]Mayo Clinic, Rochester, MN, US; [2]Mayo Clinic, Rochester, MN, US; [3]Mayo Clinic, Rochester, MN, US; [4]Mayo Clinic, Rochester, MN, US

INTRODUCTION: Pathologic complete response (pCR) to neoadjuvant chemotherapy (NAC) in HER2+ breast cancer is associated with improved disease free, event free and overall survival (OS). This study evaluated the effect of disease extent at presentation in combination with therapeutic response to NAC on OS in HER2+ breast cancer. **METHODS:** Patients (pts) with stage I-III HER2+ breast cancer diagnosed 2013-2020 who underwent NAC and HER2-targeted therapy were identified from the National Cancer Database. pCR was defined as ypT0/Tis, ypN0/N0(i+). Clinical stage at presentation was categorized by AJCC 7th edition. OS was assessed by clinical stage at presentation and chemotherapy response, stratified by hormone receptor (HR) status, using the Kaplan-Meier method and multivariable Cox proportional hazards regression. **RESULTS:** A total of 57,671 pts were included. pCR rate was significantly higher in pts with HR- disease than in those with HR+ disease (61% vs 38%, $p<0.001$). Pts with pCR had significantly better OS than pts with residual disease (RD) (95% vs 89% at 5 years, $p<0.001$), and this was true for both HR- and HR+ disease. Clinical stage at presentation was associated with OS within each response group for both subtypes (see Figure). Among pts with pCR, OS at 5 years was 98% for stage I, 97% for stage II, and 91% for stage III ($p<0.001$). Among pts with RD, OS at 5 years was 95% for stage I, 91% for stage II, and 80% for stage III ($p<0.001$). On multivariable analysis, pts in the HR- subgroup who presented with stage III disease and had a pCR did not have significantly different OS compared to pts who presented with stage I and had RD (HR 1.29, 95% CI 0.94-1.76, $p=0.12$). In the HR+ group, pts who presented with stage II disease with pCR did not have significantly different OS than pts who presented with stage I disease with RD (HR 0.97, 95% CI 0.77-1.22, $p=0.79$). Additionally, pts with stage III disease with pCR had significantly worse OS than those stage I pts with RD after NAC (HR 2.17, 95% CI 1.71-2.75, $p<0.001$) and similar OS to stage II pts with RD (HR 1.00, 95% CI: 0.86-1.17, $p=1.0$). **CONCLUSIONS:** In pts with HER2+ breast cancer treated with NAC, the clinical stage at presentation impacted OS both in pts with pCR and RD. Pts with HER2+ disease (either HR+ or HR-) presenting with locally advanced disease who experienced pCR had similar or worse OS compared to those with early stage who had residual disease. These pts could benefit from further studies that evaluate potential escalation of adjuvant therapies in certain groups of pts with HER2+ disease with pCR.



P8. Closing the Gap: A longitudinal review of the trends of gender representation in the Society of Surgical Oncology committee membership and annual meeting presenters from 2010 to 2023

Natalie Gaughan, MD[1]; Sarah A McLaughlin, MD, FACS, FSSO[2]; Jacqueline S. Jeruss, MD, PhD, FACS[3]; Kelly K. Hunt, MD, FACS, FSSO[4]; Mediget Teshome, MD, MPH, FACS, FSSO[5]; Amanda Kong, MD, MS, FACS, FSSO[6]

[1]Medical College of Wisconsin, Milwaukee, WI, US; [2]Mayo Clinic, Jacksonville, FL, US; [3]University of Michigan, Ann Arbor, MI, US; [4]MD Anderson Cancer Center, Houston, TX, US; [5]UCLA Medical Center, Santa Monica, CA, US; [6]Medical College of Wisconsin, Milwaukee, WI, US

INTRODUCTION: Gender equity in surgery remains an ongoing focus of investigation and while there are more women entering the surgical workforce, disparities persist. Professional surgical organizations, such as the Society of

Surgical Oncology (SSO) are powerful engines for scientific advancement and career growth. Leadership roles in societies, positions on academic committees and presentations at annual meetings serve as surrogates for professional career achievement. The objective of our study was to evaluate gender representation related to participation and leadership within the SSO. **METHODS:** Data was obtained from the SSO database and included committee membership, leadership roles, and annual meeting information from 2010-2023. Gender of individuals was determined by self-report or from institutional websites. Committee leadership was defined as chair or vice chair. Information regarding first author presenters included invited talks, peer reviewed oral presentations and peer reviewed poster discussions. Data was analyzed using descriptive statistics. **RESULTS:** From 2010 to 2023, our analysis revealed a significant increase in female committee membership, with women comprising 49.3% of members in 2023, up from 25.5% in 2010, indicating a positive trend towards gender equity in committees ($p < 0.001$). Similarly, an increasing female representation was noted in gender distribution related to committee leadership. In 2010, women comprised 20.3% of leadership roles, with an increase to 62.5% in 2023 ($p < 0.005$). Over the past decade, membership on the executive council saw an increase in women representation from 30.5% to 44.4% ($p = 0.085$). The executive committee representation of women increased from 13.3% to 33.3% ($p = 0.067$). From 2013 to 2023, an increase in women SSO meeting presenters was found. In 2013, 38.8% of presenters were women and in 2023 this figure rose to 44.2% ($p = 0.06$). The highest year of women presenters was at 63.7% in 2021. Analyzed video presentations revealed 25% of video presenters were women in 2013 compared to 33% of presenters in 2023 (p=NS). **CONCLUSIONS:** Representation of women within the SSO committee leadership and presenters at the annual meeting has increased from 2010-2023. This finding reflects both broader societal advances towards inclusivity as well as SSO's ongoing efforts in working towards promoting career development for all members. Continued research and targeted interventions will be essential in advancing gender equity within SSO and the broader surgical community.

P9. Differential responses to neoadjuvant chemotherapy in non-BRCA1 genetic breast cancers

Avia D Wilkerson[1]; Rahul Rangan, MD[2]; Wei Wei, MS[3]; G. Thomas Budd[4]; Zahraa Al-Hilli, MD, MBA[5]

[1]Cleveland Clinic - Cleveland, OH, Cleveland, OH, US; [2]Cleveland Clinic - Cleveland, OH, Cleveland, OH, US; [3]Cleveland Clinic - Cleveland, OH, Cleveland, OH, US; [4]Cleveland Clinic - Cleveland, OH, Cleveland, OH, US; [5]Cleveland Clinic - Cleveland, OH, Cleveland, OH, US

INTRODUCTION: Previous study of neoadjuvant chemotherapy (NAC) response in women with BRCA1 mutations demonstrated that tumorigenic, mutation-specific biologic aberrancies may increase sensitivity of BRCA1-positive breast cancers to chemotherapies and improve rates of pathological complete response (pCR) when compared to sporadic breast cancers. This study aims to investigate how rates of primary breast tumor and axillary nodal disease response to NAC across other notable genetic breast cancers compare to BRCA1-associated cancers. **METHODS:** This was an IRB-approved, retrospective cohort study. Our institution's tumor registry and electronic health record were used to identify patients who underwent NAC between 2016 and 2023, from which those with pathogenic variants in BRCA1, BRCA2, CHEK2, PALB2, or ATM genes were identified. Demographics, tumor characteristics, and pathologic response within the breast and axilla were assessed. Fisher's exact test was used to compare factors between pathogenic variant groups. **RESULTS:** Of 1642 patients who underwent NAC during the study period, 132 (8%) patients with pathogenic variants in the genes of interest were identified (BRCA1 53, BRCA2 36, CHEK2 15, PALB2 12, ATM 16). The overall pCR rate was 41.7% (55/132). Greater intra-breast pCR was observed in BRCA1-associated breast cancers (58.5%) followed by ATM (43.8%), with the worst pCR seen in CHEK2 patients (20%), p=0.02. PALB2 patients had the greatest axillary nodal pCR rate (71.4%), followed by ATM (69.2%). CHEK2 patients also demonstrated the poorest pCR within the axilla (10%), p=0.02. There were also significant differences between pathogenic variant groups in estrogen receptor status (p=<0.0001) and age at presentation (p=0.0005). **CONCLUSIONS:** There appear to be differential responses to NAC across genetic breast cancers which may be of future interest to oncologists and surgeons in consideration of neoadjuvant treatment utility and potential for surgical de-escalation. While BRCA1 mutations are associated with improved NAC response within the breast, PALB2 and ATM may be associated with improved axillary response. Further investigation in a multi-institutional setting is needed to expand upon these findings.

	All	BRCA1	BRCA2	CHEK2	PALB2	ATM	P value
Median age at presentation	45	40	45	57	59.5	45	0.0005
ER status							<0.0001
Negative	56.1	83.0	47.2	6.7	58.3	31.3	
Positive	43.9	17.0	52.8	93.3	41.7	68.8	
PR status							<0.0001
Negative	64.4	96.2	50.0	6.7	58.3	50.0	
Positive	35.6	3.8	50.0	93.3	41.7	50.0	
HER2 status							0.02
Amplified	16.7	15.1	5.6	40.0	8.3	31.3	
Equivocal	0.8	0	2.8	0	0	0	
Non-amplified	82.6	84.9	91.7	60.0	91.7	68.8	
TNBC[1]	47.0	67.9	41.7	6.7	58.3	18.8	<0.0001
Breast NAC Response							0.02
None	13.6	7.6	25.0	20.0	0	12.5	
Partial	44.7	34.0	47.2	60.0	66.7	43.8	
pCR	41.7	58.5	27.8	20.0	33.3	43.8	
Axillary NAC Response[2]							0.02
None/Partial	47.5	36.0	56.0	90.0	28.6	30.8	
pCR	52.5	64.0	44.0	10.0	71.4	69.2	

All values represent percentage (%) values of respective cohort
1. Triple negative breast cancer
2. Includes only patients presenting with clinically node-positive (cN1) disease

P10. Evaluation of axillary management strategies for occult malignancy in contralateral prophylactic mastectomy

Christopher D Vetter, MD, MSc[1]; Judy C. Boughey, MD[2]; Jeffrey E Johnson, MD[3]

[1]Mayo Clinic, Rochester, MN, US; [2]Mayo Clinic, Rochester, MN, US; [3]Mayo Clinic, Rochester, MN, US

INTRODUCTION: The optimal strategy for evaluating the axilla in the setting of invasive occult malignancy (OM) found in contralateral prophylactic mastectomy (CPM) is unknown. Approaches include preoperative breast magnetic resonance imaging (MRI) with selective SLN mapping and delayed SLN for BIRADS 3-5, risk assessment (RA) and selective SLN surgery, RA and SLN mapping for delayed SLN surgery, omission of SLN surgery, and routine SLN mapping for delayed SLN surgery. Herein we evaluate the cost effectiveness of these strategies. **METHODS:** A decision tree representing the choices and outcomes was constructed (Figure 1) with event probabilities from literature review. For RA, high risk was defined as 7% risk of OM based on prior data. Cost data was obtained from the Nationwide Ambulatory Surgery Sample, via the Healthcare Cost and Utilization Project, a product of the Agency for Healthcare Research and Quality. A cost-effectiveness analysis was conducted to determine expected costs, number of SLN surgeries avoided in the absence of OM, number of diagnostic axillary lymph node dissections (ALND) avoided, and incremental cost effectiveness ratios for each of the approaches relative to the historical standard, mastectomy followed by diagnostic ALND if OM is identified. **RESULTS:** The pooled rate of OM in CPM for women with unilateral breast cancer was 1.55%. 19,574 CPM/year in the US were estimated. The evaluated strategies resulted in 0-303 ALND/year and 0-1,643 excess SLN surgeries/year. All variants of RA and selective SLN mapping resulted in cost savings and no excess SLN surgery. Routine SLN mapping for delayed SLN surgery resulted in no excess SLN surgeries and no ALND but came at the expense of $7.9 million/year. This is considerably less than the cost of preoperative MRI at $23.7 million / year which had similar minimization of diagnostic ALND and excess SLN surgery. RA and selective SLN surgery was more costly than all other strategies ($26-28 million/year) and resulted in a significant number of excess SLN surgeries (1,595-1,643). **CONCLUSIONS:** Different strategies for axillary management for CPM maximize different outcomes; no strategy was superior across all domains. The lowest cost strategy was RA and selective SLN mapping for delayed SLN surgery, but this resulted in some ALND. MRI with delayed SLN for BIRADS 3-5 was able to prevent ALND and excess SLN surgery, but at significant increased cost. Routine SLN mapping with delayed SLN surgery performed similarly to MRI, avoiding all diagnostic ALND and unnecessary SLN surgery at a lower overall cost.

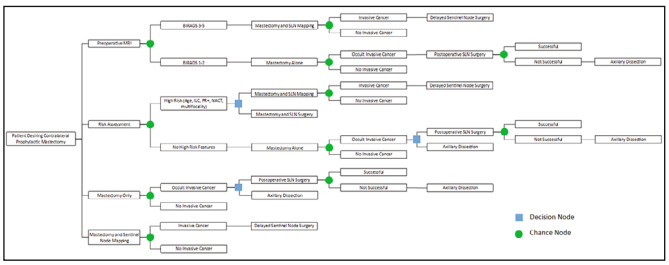


Figure 1. Decision tree for axillary management at the time of contralateral prophylactic mastectomy

P11. Genetic testing and impact on surgical management of breast cancer in the setting of new society guidelines

Christina Rutherford, BA[1]; Sarah Thacker, BS[2]; Anna Reagan, MD[3]; Brittany Levy[4]; Kelsey Karnik, PhD[5]; Tony Mangino, PhD[6]; Veronica Jones[7]; Erin E Burke, MD, MS[8]

[1]University of Kentucky College of Medicine, Lexington, KY, US; [2]University of Kentucky College of Medicine, Lexington, KY, US; [3]University of Kentucky, Lexington, KY, US; [4]University of Kentucky Department of Surgery, Lexington, KY, US; [5]University of Kentucky Department of Biostatistics, Lexington, KY, US; [6]University of Kentucky Department of Biostatistics, Lexington, KY, US; [7]University of Kentucky Department of Surgery, Lexington, KY, US; [8]Ohio State University, Columbus, OH, US

INTRODUCTION: In 2019, the American Society of Breast Surgeons (ASBrS) published a consensus statement recommending that genetic testing be made available to all patients with breast cancer. Approximately 10% of breast cancers are associated with a pathogenic germline variant, yet many patients remain undiagnosed even though genetic testing impacts treatment recommendations. We sought to investigate the impact of the ASBrS recommendations on rates of genetic testing, factors associated with genetic testing and possible impact of genetic testing on surgical treatment. **METHODS:** A retrospective chart review of all patients ≥18 years of age with a diagnosis of unilateral stage 0 to III breast cancer between 2011 to 2020 was performed at our institution. The patients were divided into two groups: before and after the 2019 ASBrS guideline. Demographic, clinicopathologic, genetic testing and treatment data were collected. Univariate and multivariate analysis was performed to assess factors associated with genetic testing. **RESULTS:** A total of 2,634 patients were identified. Of the entire cohort, 27.3% underwent genetic testing (21.7% before and 47.6% after guideline release). Of those who underwent genetic testing, 24.6% had pathogenic germline variants. After adjusting for demographic variables, individuals were 4.29 times more likely to receive genetic testing if diagnosed after the guideline release (CI (3.46, 5.33); p-value <0.001). Older patients, patients with Medicare and patients with race classified as other were less likely to receive genetic testing and this was statistically significant (all p <0.05). Patients were 2.22 times more likely to undergo unilateral or bilateral mastectomy as opposed to lumpectomy if they received genetic testing (p <0.001). Furthermore, patients were 2.56 times more likely to have bilateral mastectomy compared to unilateral mastectomy if they underwent genetic testing (p < 0.001). **CONCLUSIONS:** Genetic testing rates significantly increased in our cohort after the July 2019 ASBrS consensus statement release. There was an association with genetic testing and receipt of unilateral and bilateral mastectomy in this cohort. Further investigation is needed to understand this possible association to help personalize the testing and treatment provided to each individual patient with breast cancer.

Table 1. Patient demographics, tumor characteristics, surgical treatment and genetic testing data for the entire cohort and broken down by diagnosis before or after the release of the American Society of Breast Surgeons guidelines on genetic testing.

Variable	Entire Cohort N = 2,634 (%)	Before Guideline N = 2,071 (%)	After Guideline N = 563 (%)	p-value
Age (years)				**0.020**
18-39	169 (6.42)	145 (7.0)	24 (4.3)	
40-64	1,587 (60.2)	1,260 (60.8)	327 (58.1)	
65-79	776 (29.5)	590 (28.5)	186 (33.0)	
80+	102 (3.9)	76 (3.7)	26 (4.6)	
Race				**0.150**
White	2,448 (92.9)	1,930 (93.2)	518 (92.0)	
Black	148 (5.6)	116 (5.6)	32 (5.7)	
Other	38 (1.4)	25 (1.2)	13 (2.3)	
Insurance				**<0.001**
Private/Military	1,302 (49.4)	1,050 (50.7)	252 (44.8)	
Medicare	881 (33.4)	673 (32.5)	208 (36.9)	
Medicaid	373 (14.2)	283 (13.7)	90 (16.0)	
Uninsured	61 (2.3)	56 (2.7)	5 (0.9)	
Unknown	17 (0.6)	9 (0.4)	8 (1.4)	
Charlson Comorbidity Index				**< 0.001**
0-2	735 (27.9)	453 (21.9)	282 (50.1)	
3-4	654 (24.8)	550 (26.6)	104 (18.5)	
>5	1,245 (47.3)	1,068 (51.6)	177 (31.4)	
Body Mass Index (kg/m2)				**0.183**
<18.5	16 (1.1)	13 (1.3)	3 (0.6)	
18.5-24.9	334 (23.2)	228 (23.4)	106 (22.7)	
25-29.9	408 (28.3)	284 (29.2)	124 (26.6)	
30-40	512 (35.6)	346 (35.6)	166 (35.6)	
>40	169 (11.7)	102 (10.5)	67 (14.4)	
T Stage				**0.122**
Tis	467 (17.7)	362 (17.5)	105 (18.6)	
T1	1,311 (49.8)	1,049 (50.6)	262 (46.5)	
T2	651 (24.7)	490 (23.7)	161 (28.6)	
T3	156 (5.9)	127 (6.1)	29 (5.2)	
T4	28 (1.1)	25 (1.2)	3 (0.5)	
Unknown	21 (0.8)	18 (0.9)	3 (0.5)	
N Stage				**0.009**
N0	1,995 (76.1)	1,568 (76.1)	427 (76.0)	
N1	459 (17.5)	345 (16.7)	114 (20.3)	
N2	114 (4.3)	98 (4.7)	16 (2.8)	
N3	54 (2.1)	49 (2.4)	5 (0.9)	
ER Status				**<0.001**
Negative	560 (21.3)	473 (22.8)	87 (15.4)	
Positive	2,066 (78.4)	1,591 (76.8)	475 (84.4)	
Unknown	8 (0.3)	7 (0.3)	1 (0.2)	
PR Status				**0.012**
Negative	869 (33.0)	711 (34.3)	158 (28.1)	
Positive	1,757 (66.7)	1,353 (65.3)	404 (71.7)	
Unknown	8 (0.3)	7 (0.3)	1 (0.2)	
HER2 Status				**0.244**
Negative	2,314 (87.8)	1,808 (87.3)	506 (89.9)	
Positive	314 (11.9)	258 (12.4)	56 (9.9)	
Unknown	6 (0.2)	5 (0.2)	1 (0.2)	
Breast Surgery Performed				**0.056**
Lumpectomy	1,390 (52.8)	1,097 (53.0)	293 (52.0)	
Unilateral Mastectomy	654 924.8)	529 (25.6)	125 (22.2)	
Bilateral Mastectomy	589 (22.4)	444 (21.4)	145 (25.7)	
Lymph Node Surgery Performed				**0.003**
Sentinel Node Biopsy	1,788 (67.9)	1,376 (66.5)	412 (73.2)	
Axillary Node Dissection	437 (16.6)	368 (17.8)	69 (12.3)	
None	407 (15.5)	325 (15.7)	82 (14.6)	
Genetic Testing Performed				**< 0.001**
Yes	716 (27.3)	448 (21.7)	268 (47.6)	
No	1,909 (72.7)	1,614 (78.3)	295 (52.4)	
Provider Ordering Genetic Testing				**0.001**
Genetic Counselor	29 (6.3)	23 (9.7)	6 (2.7)	
Gynecologist	13 (2.8)	5 (2.1)	8 (3.6)	
Medical Oncologist	101 (21.9)	57 (24.0)	44 (19.6)	
Surgeon	303 (65.7)	140 (59.1)	163 (72.8)	
Primary Care Physician	4 (0.9)	3 (1.3)	1 (0.4)	
Other	11 (2.4)	9 (3.8)	2 (0.9)	
Genetic Testing Result				**0.159**
Negative	410 (75.1)	256 (73.1)	154 (78.6)	
Positive	136 (24.9)	94 (26.8)	42 (21.4)	

P12. Hospitalizations and emergency visits in breast cancer patients undergoing neoadjuvant chemotherapy with pembrolizumab: A population-based analysis

Gary Ko, MD, MSc[1]; Matthew Castelo, MD[2]; Qing Li, MMath[3]; Ning Liu, PhD[4]; Eitan Amir, MD[5]; Andrea Covelli, MD, PhD[6]; Antoine Eskander, MD, ScM[7]; Vivianne Freitas, MD[8]; C. Anne Koch, MD[9]; Jenine Ramruthan, MSc[10]; Emma Reel, MSW[11]; Amanda Roberts, MD[12]; Toni Zhong, MD, MHS[13]; Tulin D Cil, MD, MEd[14]

[1]University of Toronto, Toronto, ON, CA; [2]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, CA; [3]IC/ES, Toronto, ON, CA; [4]IC/ES, Toronto, ON, CA; [5]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, CA; [6]Sinai Health System - Mount Sinai Hospital, Toronto, ON, CA; [7]Sunnybrook Health Sciences Centre, Toronto, ON, CA; [8]University of Toronto, Toronto, ON, CA; [9]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, CA; [10]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, CA; [11]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, CA; [12]Sunnybrook Health Sciences Centre, Toronto, ON, CA; [13]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, CA; [14]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, CA

INTRODUCTION: Neoadjuvant chemotherapy regimens containing pembrolizumab are increasingly used for triple negative breast cancer (BC) treatment. However, these regimens can be associated with immune-related adverse events and may lead to emergency department (ED) visits and hospitalizations.The objective of this study was to assess the odds of ED visits and hospitalizations for BC patients undergoing neoadjuvant chemotherapy (NAC) with and without pembrolizumab. **METHODS:** BC patients who underwent NAC and surgery between April 1, 2022 - August 31, 2023 were included. Patients were classified into 3 groups based on NAC regimens received: pembrolizumab, anti-HER2 drug, or chemotherapy only group. The proportion of patients who had ED visits or hospitalizations during the neoadjuvant period (first date of chemotherapy to the day of surgery) and the post-operative period (day of surgery to 30 days after surgery) were calculated. Logistic regression was used to estimate the odds of an ED visit or hospitalization for patients receiving pembrolizumab compared to the other two groups, adjusting for age and comorbidities. **RESULTS:** The study cohort consisted of 1301 BC patients who had NAC. The median age was 52 and 94.7% of patients had no comorbidities. A total of 229 patients (17.6%) had pembrolizumab, 532 (41%) had an anti-Her 2 agent, and 540 (41.4%) had chemotherapy only. A higher proportion of patients on pembrolizumab had ≥1 ED visits (54.6%) during the neoadjuvant period compared to patients on anti-HER2 (54.6% vs. 42.3%, aOR 1.79, 95% CI 1.31-2.45) or chemotherapy only (54.6% vs. 40.0%, aOR 1.61, 95% CI 1.18-2.21). However, there was no significant difference in odds of ED visits in the post-operative period (chemotherapy alone: aOR 1.32, 95% CI 0.87-1.99 & anti-HER2: aOR 1.30, 95% CI 0.85-1.97 vs. anti-HER2). Patients receiving pembrolizumab had higher odds of hospitalization during the neoadjuvant period (chemotherapy alone: aOR 3.94, 95% CI 2.66 -5.83, anti-HER2 aOR 2.78 95% CI 1.92- 4.04). The odds of hospitalization during the post op period for patients receiving pembrolizumab was similar to patients undergoing anti-HER2 therapy (aOR 1.63, 95% CI 0.77, 3.43), but slightly higher than chemotherapy only (aOR 2.54, 95% CI 1.13, 5.72). **CONCLUSIONS:** BC patients undergoing NAC with pembrolizumab had significantly higher odds of ED visits and hospitalizations before surgery, but this not in the post-operative period. This study provides confirmatory population-level data regarding the integration of immunotherapy into NAC.

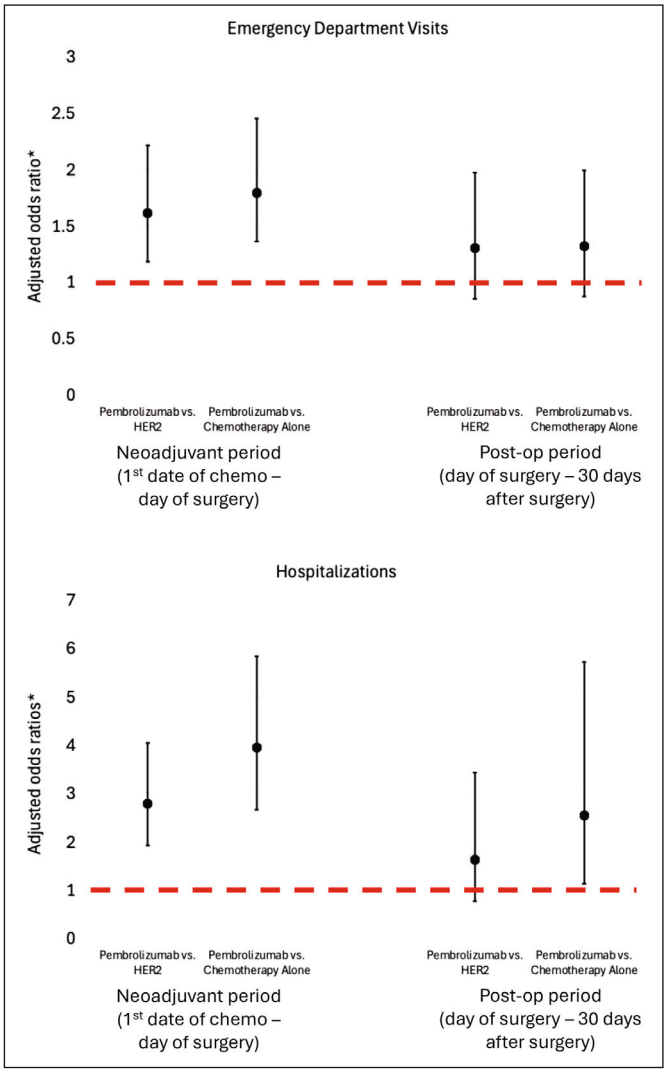


Figure 1. Odds ratio and 95% Confidence Interval adjusted for age and comorbidity of emergency department visits and hospitalization between patients receiving pembrolizumab containing NAC and non-pembrolizumab containing regimens

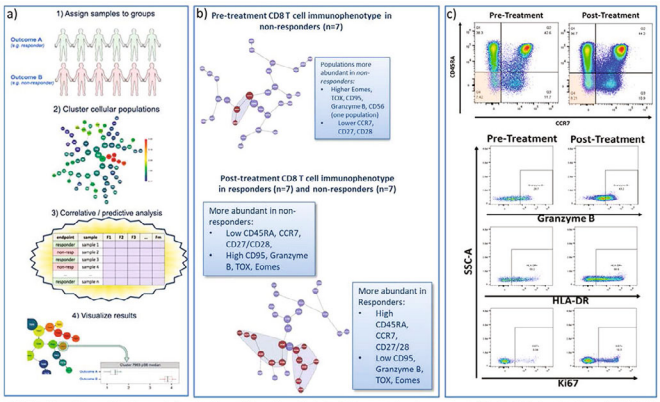
P13. Immunemodulatory effects of single preoperative pembrolizumab dose and a subablative radiotherapy fraction (7 Gy) in circulating immune cells – a multiparameter flow cytometric analysis of NCT04454528 particiants with early stage breast cancer

Julia Tchou[1]

[1]University of Pennsylvania, Philadelphia, PA, US

INTRODUCTION: We have recently demonstrated that a preoperative combination of a single low-dose radiotherapy (RT) fraction (7 Gy) and a single dose of pembrolizumab, an immune checkpoint inhibitor (ICI), for patients with early-stage breast cancer is safe, feasible, and resulted in clinically significant tumor shrinkage >30% (TΔ30) and pathological complete response (pCR) in 13 of 27 (48%) and 3 of 27 (11%) respectively. We hypothesize that RT+ICI may have pro-inflammatory immunemodulatory effects in circulating immune cells. **METHODS:** Deep immunophenotyping of pre- and post-treatment peripheral blood mononuclear cells (PBMCs) from NCT04454528 participants (n=20) was performed using twenty-eight color, high-dimensional flow cytometry encompassing various markers of T cell activation, differentiation and exhaustion and pre-gating to viable, single lymphocytes. An unbiased computational analysis of flow cytometric data was performed stratifying by treatment arms, response, and tumor subtypes as illustrated in Fig. 1a. Activation markers of a subpopulation of CD8+ CD45RA- CCR7- T cells, i.e. T effector memory cells (TEM), were further evaluated. **RESULTS:** Flow cytometric analyses of baseline PBMCs revealed

a CD8 T cell profile characterized by increased levels of Eomes and CD95, along with decreased CCR7, CD27, and CD28, indicating a more terminally differentiated state in non-responders. Post-treatment, CD8 T cell profile was characterized by high CCR7, CD28, and low CD95, Granzyme B, TOX, and Eomes in responders and low CCR7, and high CD95, Eomes in non-responders suggesting that RT + ICI have further amplified pre-existing immunophenotypes (Fig. 1b). Immunophenotype changes in TEM that has immune memory and surveillance roles demonstrated a higher level of Ki67 (6.9% to 16.3%), HLA-DR (59.% to 66.6%), and Granzyme B (28.7% to 43.2%) post-treatment (Fig. 1c). **CONCLUSIONS:** A single preoperative RT+ICI is sufficient in reshaping circulating immune cells towards a pro-inflammatory immune signature that includes TEM activation post-treatment. Deep TCR sequencing to evaluate shifts in TCR repertoire and antigen-specific TCR discovery in PBMC are underway. Expansion of this phase 2 study to increase sample size and to test whether preoperative ICI + RT can be implemented in diverse clinical setting is being considered.



a) Methodology of an unbiased computational analyses of flow cytometric data of 28 immunophenotype markers of T cells; b) Cluster abundance of CD8 T cell markers pre- and post-treatment – top panel: pre-treatment immunophenotype of TNBC non-responders (n=7), bottom panel: post-treatment immunophenotype of CD8 T cells in responders (n=7) (lower right clusters in red) vs. non-responders (n=7) (upper left clusters in red); c) Immunophenotype change pre- and post-treatment of CD8 CD45RA- CCR7- effector memory T cells (TEM): top panel: CD45RA- CCR7- gated CD8 T cells pre- and post treatment (lower left shaded area), bottom panel: increased levels of granzyme B (28.7% to 43.2%), HLA-DR (59.2% to 66.6%), and Ki67 (6.9% to 16.3%) in CD45RA- CCR7- CD8 T cells post-treatment.

Figure 1. Deep immunophenotyping of circulating CD8 T cells pre- and post-treatment collected from patients participating in NCT04454528

P14. Impact of mastectomy versus lumpectomy on mortality in patients with T4b breast cancer

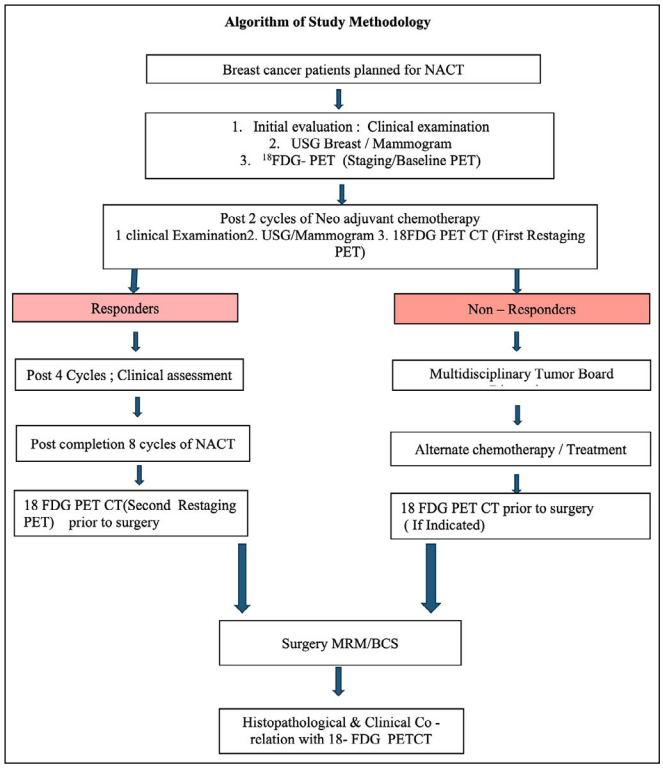
Maha Marshad[1]; Vasily Giannakeas, PhD, MPH[2]; David W Lim, MD, CM, MEd, PhD[3]
[1]University of Toronto, Toronto, ON, CA; [2]Women's College Hospital, Toronto, ON, CA; [3]University of Toronto & Women's College Hospital, Toronto, ON, CA

INTRODUCTION: Treatment for T4b breast cancer, defined as breast cancer involving the skin, involves a multimodal approach in management. While mastectomy is recommended for T4d lesions (inflammatory breast cancer), this is less clear for T4b lesions. We aim to characterize the surgical management of T4b breast cancer and compare differences in mortality between patients undergoing lumpectomy versus mastectomy. **METHODS:** We identified women diagnosed with invasive T4b breast cancer from 2000-2020 using data from the Surveillance, Epidemiology, and End Results 17 registry. We retrieved information on demographics, clinicopathological characteristics, and cancer treatment. Women were categorized based on operation performed: lumpectomy vs mastectomy, and were followed for up to 20 years for breast cancer-specific death. We compared clinical features between the surgical groups and used a Fine and Gray competing risks model to estimate the hazard ratio for breast cancer mortality, accounting for competing causes of death. All statistical analyses were performed using SAS®. P values <0.05 were considered significant. **RESULTS:** A total of 9265 women with T4b breast cancer were identified, with 8037 (86.7%) having mastectomy and 1228 having lumpectomy (13.3%). The mean age at diagnosis among women having lumpectomy and mastectomy were 64 and 61.4 (P< .01). There was no difference in race or marital status between groups. Women with higher income (>$80,000) had lumpectomy, while more women with income under $80,000 had mastectomy (P< .01). Women living in metropolitan areas were more likely to receive lumpectomy compared with rural areas (P = 0.02). Chemotherapy was received in 5851(72.8%) of women who had a mastectomy versus 770(62.7%) in those who underwent a lumpectomy. Radiation was given to 55.5% of patients undergoing a mastectomy versus 59.7% in the lumpectomy group. The 20 year breast cancer mortality was 42.7% for lumpectomy compared with 55.6% in mastectomy. After adjusting for patient, tumour and treatmetn factors, there was no difference in 20-year breast cancer mortality between the surgical groups (HR 1.07, 95% CI 0.95-1.21, P = 0.2). **CONCLUSIONS:** We observed no difference in 20-year breast cancer death in women with T4b breast cancer having lumpectomy versus mastectomy. Contrary to T4d breast cancer, this suggests that lumpectomy may be oncologically safe for T4b lesions. Surgical procedure was associated with sociodemographic factors, such as income and rurality, suggesting that social determinants may influence surgical procedure choice and receipt, which require further exploration.

P15. Importance of FDG PET/CT in early prediction of response to neoadjuvant chemotherapy in breast cancer patients: A tertiary care cancer center experience from India

Jeewan Ram Vishnoi, Surgical Oncology[1]; Arvind R Koslia, Surgical Oncology[2]; Nivedita R Sharma, Surgical Oncology[3]; Dharma Ram Poonia, Surgical Oncology[4]; Parmod Kumar, Medical Oncology[5]; Sameer Taywade, Nuclear Medicine[6]; Taruna Yadav, Radiodiagnosis[7]; Poonam Elhence, Pathology[8]; Rajesh Kumar, Nuclear Medicine[9]; Puneet Pareek, Radiation Oncology[10]; Sanjeev R Misra, Surgical Oncology[11]
[1]All India Institute of Medical Sciences, Jodhpur, Rajasthan, IN; [2]All India Institute of Medical Sciences, Jodhpur, Jodhpur, Rajasthan, IN; [3]All India Institute of Medical Sciences, Jodhpur, Jodhpur, Rajasthan, IN; [4]All India Institute of Medical Sciences, Jodhpur, Jodhpur, Rajasthan, IN; [5]All India Institute of Medical Sciences, Jodhpur, Jodhpur, Rajasthan, IN; [6]All India Institute of Medical Sciences, Jodhpur, Jodhpur, Rajasthan, IN; [7]All India Institute of Medical Sciences, Jodhpur, Jodhpur, Rajasthan, IN; [8]All India Institute of Medical Sciences, Jodhpur, Jodhpur, Rajasthan, IN; [9]All India Institute of Medical Sciences, Jodhpur, Jodhpur, Rajasthan, IN; [10]All India Institute of Medical Sciences, Jodhpur, Jodhpur, Rajasthan, IN; [11]All India Institute of Medical Sciences, Jodhpur, Jodhpur, Rajasthan, IN

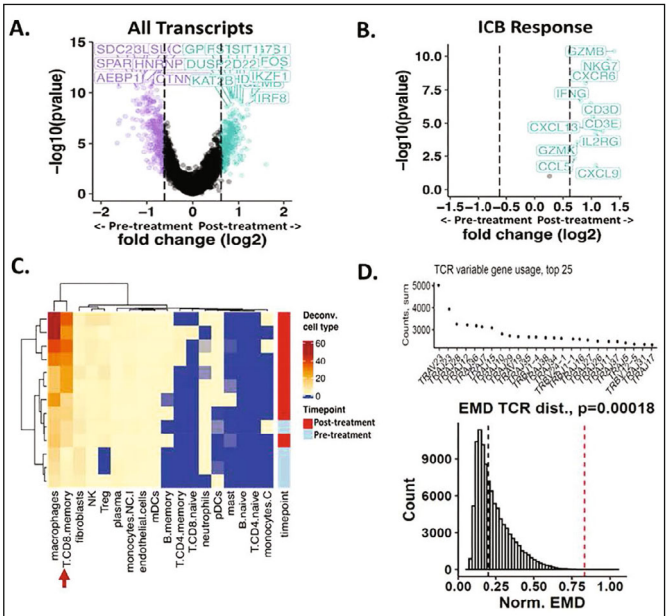
INTRODUCTION: Breast cancer is considered a heterogeneous disease, and its treatment has evolved towards personalized and precision medicine. Individualizing treatment and simplifying the switch to non-cross-resistant chemotherapeutic drugs can be facilitated by techniques that allow early prediction of therapeutic effectiveness, thus avoiding potentially ineffective therapies. The potential of FDG PET/CT to reveal metabolic alterations within the tumor enables early identification of response and prediction of treatment efficacy. The objective of the study was to evaluate whether PET/CT is an effective imaging modality in the early prediction of response to neoadjuvant chemotherapy in breast cancer. **METHODS:** A prospective study was conducted on a subset of breast cancer patients planned for neoadjuvant chemotherapy (NACT) followed by curative intent surgery at a tertiary care cancer center. Whole-body PET/CT scans were performed at baseline, after the 2nd or 3rd cycle of NACT, and after completion of NACT, prior to surgery, for all these patients. **RESULTS:** In our study, 51 patients with a mean age of 48.8 years (range: 26-74 years) were included. The majority of patients presented with a clinical T stage of cT2 (54.9%), followed by cT4 (23.5%) and cT3 (17.9%), and a clinical N stage of cN1 (72.5%), followed by cN2 (15.7%) and cN3 (7.8%). The receptor status was ER+/PR+ (50.9%), Her2neu+ (45%), and triple-negative breast cancer (TNBC) (25.4%). Most cases received adriamycin, cyclophosphamide, and taxane-based (CT+T) chemotherapy regimens. On follow-up (1st restaging PET/CT), the mean SUVmax for the responders (pathological group) was 4.39 (SD-2.229). PET/CT was significantly superior to clinical assessment in sensitivity (78.1% vs 30%), specificity (82.4% vs 25.6%), and accuracy (79.5% vs 26.5%). ROC analysis showed that a reduction in SUVmax value by 50.45% differentiated between pathological responders and non-responders, with sensitivity and specificity of 78.1% and 82.4%, respectively. The 2nd restaging PET/CT corroborated the findings of the 1st restaging PET/CT, suggesting that PET/CT after 8 cycles of NACT may be avoided in patients who are PET responders, which could be beneficial in resource-constrained settings. Receptor status (ER, PR, Her2neu), LVI, and PNI were not statistically significant with either SUVmax (after 2 cycles of chemotherapy) values or percent change in SUVmax. **CONCLUSIONS:** We conclude that 18-FDG PET/CT is a useful modality for predicting early response to chemotherapy and distinguishing pathological non-responders from responders with good sensitivity and NPV. This modality can help individualize treatment, avoid unnecessary chemotherapy, and reduce the financial burden on patients.



P16. In situ vaccine effects after a single preoperative pembrolizumab dose and subablative radiotherapy fraction (7 Gy) – evidence from spatial transcriptomic analyses of pre- and post-treatment tissues of NCT04454528 particiants

Julia Tchou[1]
[1]*University of Pennsylvania, Philadelphia, PA, US*

INTRODUCTION: We have recently demonstrated that a preoperative combination of a single low-dose radiotherapy (RT) fraction (7 Gy) and a single dose of pembrolizumab, an immune checkpoint inhibitor (ICI), for patients with early-stage breast cancer is safe, feasible, and resulted in clinically significant tumor shrinkage >30% (TΔ30) and pathological complete response (pCR) in 13 of 27 (48%) and 3 of 27 (11%) respectively. We hypothesize that RT + ICI may reshape the tumor immune microenvironment (TIME) resulting in an *in situ* vaccine effect. **METHODS:** An interim spatial transcriptomic analysis of matched pre- and post-treatment FFPE tumor blocks from responders (n=7) was performed using NanoString GeoMx® Platform. Immunostaining of tumor sections using pan-CK (tumor cells), CD3 (T cells) and CD11c (myeloid cells) was used to select regions of interest (ROI). Immune cell type spatial deconvolution, gene set variation, and TCR V-beta gene segment permutation analyses were performed to identify enrichment of transcriptomic changes, and shifts in immune cell type and TCR diversity in the TIME related to RT + ICI treatment. **RESULTS:** Spatially-resolved transcriptomic analyses of serial tumor sections with ROI (n = 126) from responders exhibited enrichment of gene signatures associated with cytolytic activity (e.g Granzyme B), antigen processing (e.g. CD70/CD27 axis) and ICI response (e.g. Granzyme B and INFγ) (Fig. 1A & B). Immune cell type deconvolution in the TIME post-treatment demonstrated a significant enrichment in memory CD8+ T cell in responders (Fig. 1C). A significant shift in TCR V-beta gene segment usage permutation pattern in the TIME, specifically segment TRAV23, was noted post-treatment in responders. Permutation of this shift was non-random as determined by Earth Mover's Distance calculation (P = 0.00018) supporting the emergence of new T cell responses (Fig. 1D). **CONCLUSIONS:** Preoperative RT + ICI resulted in pro-inflammatory changes in the TIME that is marked by signficant enrichment of memory CD8 T cells. These changes coupled with the emergence of new T cell response underscore the *in situ* vaccine effects of RT + ICI. Plans for a multi-site phase 2 study to validate these results with a larger sample size and to demonstrate study feasibility in diverse clinical sites are being considered.



(A) Volcano plot showing transcription changes of all transcripts pre- and post-treatment (up regulated genes are shown in turquoise while down regulated genes are shown in purple); (B) Volcano plot showing ICI response genes that were upregulated (turquoise) post-treatment in responders; (C) Heatmap of immune cell type deconvolution (each column represents the specific immune cell type of interest and each row represents a region of interest in the TIME pre- (light blue) or post-(red) treatment) illustrating markedly increased memory CD8+ T cells (red arrow) post-treatment in Patient 14; (D) Changes in TCR diversity in tumors following RT+ ICI. Upper panel: Histogram demonstrating the frequency of the top 25 TCR V-beta gene segments used in the TI ME post-treatment. Bottom panel: Earth mover's distance (EMD) analysis to assess whether TCR V-beta gene segment usage permutation post-treatment revealed a non-random permutation (black dotted line) p=0.00018. Note that a random permutation distance is marked by red dotted line.

Figure 1. Spatially-resolved transcriptomic analysis to evaluate effects of RT + ICI on tumor immune microenvironment (TIME) of NCT04454528 participants (n=7)

P17. Is Tumor PD-L1 Expression Predictive of Response after Neoadjuvant Chemoimmunotherapy in Triple Negative Inflammatory Breast Cancer?

Jennifer Chen[1]*; Salyna Meas*[2]*; Vanessa N. Sarli*[3]*; Megumi Kai*[4]*; Joshua Upshaw*[5]*; Azadeh Nasrazadani*[6]*; Vicente Valero, MD*[7]*; Wendy Woodward*[8]*; Anthony Lucci, MD*[9]
[1]*The University of Texas MD Anderson Cancer Center, Houston, TX, US;* [2]*The University of Texas MD Anderson Cancer Center, Houston, TX, US;* [3]*The University of Texas MD Anderson Cancer Center, Houston, TX, US;* [4]*The University of Texas MD Anderson Cancer Center, Houston, TX, US;* [5]*The University of Texas MD Anderson Cancer Center, Houston, TX, US;* [6]*The University of Texas MD Anderson Cancer Center, Houston, TX, US;* [7]*MD Anderson Cancer Center, Houston, TX, US;* [8]*The University of Texas MD Anderson Cancer Center, Houston, TX, US;* [9]*UT-MD Anderson Cancer Center, Houston, TX, US*

INTRODUCTION: Although studies report higher pathologic complete response (pCR) after neoadjuvant chemoimmunotherapy (NACI) in triple negative breast cancer, we previously observed lower than expected pCR rates in patients with inflammatory breast cancer (IBC). We sought to examine whether primary tumor PD-L1 expression would be predictive of pCR after NACI in triple negative IBC (TN-IBC). **METHODS:** Patients were enrolled in a prospective registry from 2019-2024 and underwent neoadjuvant chemoimmunotherapy prior to surgery. Positive PD-L1 status was defined as a combined positive score of ≥ 10 via IHC 22C3 assay. Chi-square, Fisher's exact, and student's t-tests were used to compare group differences. Univariate and multivariate logistic regression were performed to evaluate predictive value of tumor PD-L1 status on treatment response. **RESULTS:** In total, 30 TN-IBC patients with available

tumor PD-L1 status were included. Patients were predominantly White (23, 76.7%), followed by 10% (3) Black and 6.7% (2) Asian. Median age was 45.5 years (IQR 38.8-56.8) and 43.3% (13) had BMI ≥ 30 kg/m2. Most patients had ductal (24, 80%), high-grade (23, stage IIIB or IIIC disease (24, 80%). All patients underwent neoadjuvant chemoimmunotherapy – 86.7% (26) received KEYNOTE-522 regimen, pembrolizumab with TC (paclitaxel-carboplatin) followed by AC (doxorubicin-cyclophosphamide) while 13.3% (4) received atezolizumab with carboplatin. Tumor PD-L1 status was positive in 56.7% (17) and negative in 43.3% (13). All patients underwent surgical resection with the majority receiving modified radical mastectomy (28, 93.3%). Overall pCR rate was 33.3%. Among PD-L1 positive tumors, pCR rate was 47.1% (8/17) compared to 15.4% (2/13) in PD-L1 negative tumors (p = 0.07). There were no differences in age, race, ethnicity, BMI, stage, grade, and presence of LVI by tumor PD-L1 status. On univariate analysis, tumor PD-L1 status was not associated with pCR (OR 4.9, 95% CI: 0.8-29.1, p = 0.08, Table 1). On multivariate analysis including age, and grade as covariates, tumor PD-L1 status was not an independent predictor of pCR (OR 14.9, 95% CI: 0.9-254.3, p = 0.06). **CONCLUSIONS:** While pCR rate was higher for PD-L1 positive tumors, our results suggest there is clinical benefit of neoadjuvant chemoimmunotherapy use in TN-IBC irrespective of tumor PD-L1 status. However, given that the observed gap in pCR rates in TN-IBC is greater than that seen in TN non-IBC disease, further evaluation of neoadjuvant chemoimmunotherapy response in PD-L1 negative TN-IBC is warranted.

Table 1. Univariate and Multivariate Logistic Regression of Factors Associated with pCR after Neoadjuvant Chemoimmunotherapy

Variable	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Age	1.03	0.97-1.10	0.292	1.04	0.93-1.16	0.515
BMI	1.12	0.97-1.28	0.125	1.09	0.88-1.34	0.427
Race/ethnicity						
Non-Hispanic White	*Ref*			*Ref*		
Other	0.26	0.04-1.90	0.184	0.31	0.02-5.20	0.414
AJCC 8th ed. clinical stage						
IIIB	*Ref*			*Ref*		
IIIC	1.75	0.26-11.7	0.564	1.26	0.10-16.2	0.861
IV	0.50	0.03-7.45	0.615	0.08	0.00-4.79	0.227
Tumor grade						
Moderately differentiated	*Ref*			*Ref*		
Poorly differentiated	0.18	0.03-1.22	0.079	0.10	0.00-3.80	0.218
Tumor PD-L1 status						
Negative	*Ref*			*Ref*		
Positive	4.89	0.82-29.1	0.081	14.9	0.87-254.3	0.063

P18. Local control after preoperative radiotherapy + immune checkpoint blockade and surgical resection is mediated by CD8 T cells – a murine breast tumor model to reverse translate the local treatment effects of NCT04454528

Julia Tchou[1]
[1]*University of Pennsylvania, Philadelphia, PA, US*

INTRODUCTION: We recently demonstrated that a single radiotherapy (RT) fraction (7 Gy) combined with a single dose of pembrolizumab (αPD1), an immune checkpoint inhibitor, given preoperatively in patients with early stage breast cancer (NCT04454528) was feasible and resulted in significant tumor response in 13 of 27 (48%) participants. Whether preoperative RT+ αPD1 improves local control is unclear. We aimed to reverse translate NCT04454528 in a murine breast tumor model to investigate the local effects of RT+αPD1 in the tumor immune microenvironment (TIME) to gain insight on long-term outcomes of NCT04454528 participants. **METHODS:** Murine E0771 breast tumor cells (1x106) were implanted into the 4th nipple duct of wild type C57BL/6 female 5–6 week old mice on Day 0. There were 4 treatment groups (n=15 per group): 1) isotype only, 2) RT (5.5 Gy) + isotype, 3) αPD1 (3 intraperitoneal doses) only, and 4) RT + αPD1. αCD4 or αCD8 were given to cohorts 1 & 4 (n=5 per group) on Days 6, 10, 15, and 20. Tumor resection (n=10, groups 1 – 4 including those with CD4 or 8 depletion) was performed on Day 10. Local control on Day 24 was compared using Fisher-Irwin tests. On Day 15, mice without resection (n=5 per group) were sacrificed. Tumors were collected and analyzed by immunohistochemistry to quantify CD4 & CD8 T cells in TIME. **RESULTS:** ombination RT+ αPD1 treatment given prior to surgery was significantly more effective in local control than isotype or RT alone (p<0.05) (Fig. 1B). CD8 (but not CD4) T cells played a critical role in local control as CD8 depletion resulted in a lower local control rate regardless of preop RT+ αPD1 at Day 84 (p<0.05) (Fig. 1C). The magnitude of CD4 or CD8 T cell infiltration in the TIME was further evaluated. Combination RT+ αPD1 resulted in a significantly higher CD8 (but not CD4, data not shown) T cell density than RT or αPD1 only treatment on Day 15 (p < 0.05) (Figure 1D). **CONCLUSIONS:** pact of preoperative RT + αPD1 on the long term outcomes in NCT04454528 participants is limited by small sample size and short follow up. A murine model that can reverse translate NCT04454528 treatment effects may provide insight on disease outcomes. Our model showed that RT + αPD1 improved local control by invoking a local immune response mediated by CD8 T cells in TIME. Future work to elucidate mechanism of RT + αPD1 resistance and to test novel combination immunotherapy approaches is underway.

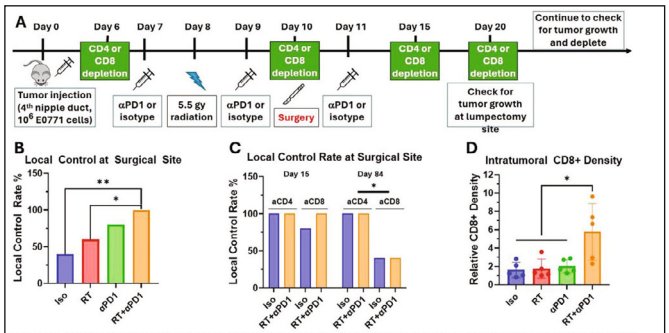


Figure 1. A) Schematic design for local control determination in CD4/CD8 depleted mice treated pre-operatively with either isotype or RT+ αPD-1. B) Local control rate at Day 24 (14 days post tumor resection) of isotype, RT, αPD-1, and RT+αPD-1 treated mice (Local control = # of mice without tumor re-growth / Total # of mice in cohort). C) Local control rates of CD4/CD8 depleted Isotype and RT+αPD-1 treated mice at Days 15 and 84 (5 and 74 days post tumor resection respectively). D) Relative density of CD8+ in tumors harvested on Day 15 from isotype, RT, αPD-1, and RT+αPD-1 treated mice. Relative density was determined via positive pixel analysis in Aperio Image Scope (Rel. Density = #positive pixels / #positive & negative pixels).

P19. Long-term safety of prophylactic and therapeutic nipple sparing mastectomies in BRCA1 and BRCA2 mutation carriers

Denise I Garcia, MD, MEd[1]*; Kyle J Kanderman*[2]*; Abigail E Daly*[3]*; Michele A Gadd*[4]*; Michelle C Specht*[5]*; Francys C Verdial, MD, MPH*[6]*; Tolga Ozmen, MD*[7]*; Rebecca M Kwait, MD*[8]*; Barbara Smith, MD, PhD*[9]
[1]*Massachusetts General Brigham, Boston, MA, US;* [2]*mass general hospital, Boston, MA, US;* [3]*Mass General, Boston, MA, US;* [4]*Massachusetts General Hospital, Boston, MA, US;* [5]*Massachusetts General Hospital, Boston, MA, US;* [6]*Massachusetts General Brigham, Boston, MA, US;* [7]*Massachusetts General Brigham, Boston, MA, US;* [8]*Massachusetts General Brigham, Boston, MA, US;* [9]*Massachusetts General Hospital, Boston, MA, US*

INTRODUCTION: BRCA1/2 mutation carriers have a 60-70% lifetime risk of breast cancer and an up to 2-3% annual risk of developing breast cancer. Although current data show that prophylactic nipple-sparing mastectomy (NSM) reduces this risk, the extent and durability of risk reduction is unknown. We assessed long-term risk reduction and oncologic safety of prophylactic and therapeutic NSM in BRCA1/2 mutation carriers. **METHODS:** Consecutive NSM in patients with and without pathogenic BRCA1/2 mutations from 10/2007 - 6/2019 at our institution were identified. Patient and tumor characteristics, treatments, and oncologic outcomes were collected. Rates of new cancers, locoregional and distant recurrence, and overall survival were determined. **RESULTS:** A total of 174 BRCA1/2 mutation carriers, 86 with BRCA1 mutations and 88 with BRCA2 mutations, underwent bilateral prophylactic NSMs with no tumor found on final pathology. At 98 months median follow-up (1393 woman-years), no patient had developed cancer in retained breast or nipple skin. One BRCA2 mutation carrier presented with ER+/PR+/HER2- axillary and bone metastases at 75 months follow-up, but without breast skin or nipple recurrence. The annual risk of any breast cancer event in this cohort was 0.072%. 124 BRCA1/2 mutation carriers, 70 with BRCA1 mutations and 54 with BRCA2 mutations, underwent 130 therapeutic NSMs and 118 contralateral prophylactic NSMs. Axillary nodes were positive in 22% of patients. Tumors were triple negative in 55% of BRCA1 and 20% of BRCA2 patients. At 104 months median follow-up, overall survival (OS) was 91%. There were 8 recurrences: 4 (3.2%) locoregional only (LRR) and 4 (3.2%) distant only (DR); no patient had both an LRR and DR. There were no nipple recurrences. At 1007 woman-years follow-up were no new primary ipsilateral breast cancers in any of the contralateral prophylactic NSMs. For comparison, at 89 months median follow-up of 1416 contemporaneous therapeutic NSM in women without documented BRCA mutations, OS was 93% (p = 0.680 vs. BRCA1/2 carriers), LRR was 3.7% (p = 1.00), the DR rate was 4.2% (p = 0.76), and the rate of both LRR and DR was 2.4% (p = 0.106). **CONCLUSIONS:** Prophylactic NSM provides excellent long-term reduction in annual risk of

new breast cancers in BRCA1 and BRCA2 mutation carriers. Long-term risks of nipple recurrence, and local and distant recurrence are low after therapeutic NSM in BRCA1 and BRCA2 mutation carriers. NSM is effective for breast cancer treatment and prevention in BRCA1/2 mutation carriers.

	BRCA1	BRCA2	*p*-values
Total Breasts/Procedures	**N = 70**	**N = 54**	
Median Follow-Up (months)	94	106	
Median Age (years)	45	47	P = 0.060
Tumor histology, n (%)			P = 0.870
IDC ± DCIS	52 (74.3%)	31 (57.4%)	
ILC ± DCIS	1 (1.4%)	2 (3.7%)	
DCIS with microinvasion	3 (4.3%)	-	
Pure DCIS	12 (17.1%)	18 (33.3%)	
Invasive Other	2 (2.9%)	3 (5.6%)	
Invasive Tumor Characteristics	N = 55	N = 36	
Median invasive tumor size, (range), cm	1.2 (0.2 - 5.3)	1.55 (0.12 - 4.8)	P = 0.749
Positive axillary nodes	12 (21.8%)	8 (22.2%)	P = 0.964
Invasive receptor status			**P = 0.003**
ER + / HER2 +	1 (1.8%)	4 (11.1%)	
ER + / HER2 -	23 (41.8%)	25 (69.4%)	
ER - / HER2 -	30 (54.5%)	7 (19.5%)	
ER - / HER2 +	1 (1.8%)	-	
DCIS receptor status	N = 15	N = 18	
ER+	10 (66.7%)	17 (94.4%)	P = 0.112
ER-	4 (26.7%)	1 (5.6%)	
Not Done	1 (6.6%)	-	
Tumor grade			**P = 0.004**
Low/Intermediate Grade (1-2)	14 (20.0%)	26 (48.1%)	
High Grade (3)	54 (77.1%)	27 (50.0%)	
Unreported	2 (2.9%)	1 (1.9%)	
Treatment Type (N, %)			
Any systemic therapy	60 (85.7%)	39 (72.2%)	P = 0.063
Radiation therapy	16 (22.9%)	12 (22.2%)	P = 0.933
Recurrence (N, %)			
Any Recurrence	4 (5.7%)	4 (7.4%)	P = 0.490
Locoregional only (not nipple)	2 (2.9%)	2 (3.7%)	P = 1.000
Nipple	0	0	
Distant only	2 (2.9%)	2 (3.7%)	P = 1.000
Locoregional and distant	0	0	

P20. Omission of radiation after breast conserving surgery for invasive lobular carcinoma: impact on early recurrence events in patients meeting PRIME II criteria

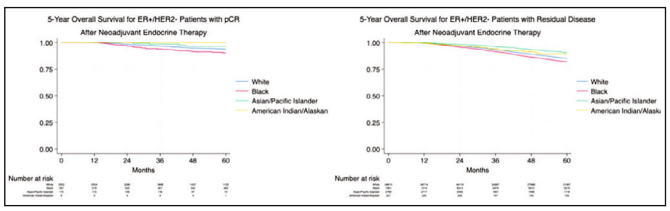
Mandeep Kaur[1]; Astrid Quirarte[2]; Anna Vertido[3]; Taron Torosian[4]; Thomas M. Li[5]; A. Jo Chien[6]; Nicolas Prionas[7]; Rita Mukhtar[8]
[1]University of California, San Francisco, San Francisco, CA, US; [2]University of California, San Francisco, San Francisco, CA, US; [3]University of California, San Francisco, San Francisco, CA, US; [4]University of California, San Francisco, San Francisco, CA, US; [5]University of California, San Francisco, San Francisco, CA, US; [6]University of California, San Francisco, San Francisco, CA, US; [7]University of California, San Francisco, San Francisco, CA, US; [8]University of California, San Francisco, San Francisco, CA, US

INTRODUCTION: In the PRIME II trial, omission of radiotherapy following breast conserving surgery (BCS) in appropriately selected patients resulted in low incidence of early recurrence events (4.8% local recurrence and 0.8% distant recurrence at 5 years). No studies evaluate the impact of omission of radiation specifically in patients with invasive lobular carcinoma (ILC), a histologic subtype of breast cancer known for its diffuse growth. We therefore evaluated radiotherapy omission patterns in patients with ILC and the incidence of early recurrence in the subset meeting PRIME II eligibility criteria. **METHODS:** We utilized a prospectively maintained single institution ILC database containing treatment and outcomes data for 823 cases of ILC. Among those who underwent BCS, we evaluated factors associated with omission of radiation using t-tests and chi square tests. We used the Kaplan Meier method to determine estimated cumulative freedom from local recurrence at 5 years with and without radiotherapy among patients meeting PRIME II study criteria (age ≥65 years, tumor size ≤3 cm, estrogen-receptor positive, margin-negative, node-negative status). **RESULTS:** Among the 401 patients who underwent BCS overall, 34.9% omitted adjuvant radiotherapy. Omission of radiotherapy was significantly associated with older age at diagnosis (mean 66.8 years vs. 60.5 years, p<0.0001), smaller tumor size (mean 1.7 cm vs. 2.3 cm, p=0.0017), a higher proportion of node-negative status (85.5% vs. 73.8%, p=0.022), and a higher proportion of progesterone receptor low status (45.3% vs. 32.3%, p=0.013). Among the 117 patients meeting PRIME II trial criteria, omission of radiotherapy was significantly more common compared to those who did not meet PRIME II criteria (50.4% omitting radiation vs. 28.5%, p<0.001). Estimated freedom from local recurrence at 5 years in patients who met PRIME II criteria and had radiotherapy was 97.8% (95% confidence interval [CI] 85.3-99.7%) and in those who omitted radiotherapy was 90.6% (95% CI 76.5-96.4%). **CONCLUSIONS:** Omission of radiotherapy after BCS was significantly more common among patients with ILC meeting PRIME II criteria, as would be expected. Interestingly, the estimated incidence of local recurrence events at 5 years for those meeting PRIME II criteria exceeded the reported local recurrence incidence in the trial. Whether omission of radiotherapy in patients with ILC may lead to higher risk of early local recurrence events should be explored in a larger dataset given the unique histologic growth pattern of this tumor type.

P21. Pathologic Complete Response and Survival after Neoadjuvant Endocrine Therapy Among Racial Groups in Hormone Receptor-Positive Breast Cancer

Selena J An, MD, MSPH, MA[1]; Julia M. Selfridge, MD[2]; Katherine Reeder-Hayes, MD[3]; Chris B Agala, PhD[4]; Phillip Spanheimer, MD[5]
[1]University of North Carolina, Chapel Hill, NC, US; [2]The University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US; [3]University of North Carolina, Chapel Hill, NC, US; [4]University of North Carolina, Chapel Hill, NC, US; [5]University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US

INTRODUCTION: Racial disparities in breast cancer (BC) outcomes are well-known. In patients receiving neoadjuvant endocrine therapy (NET), differences in pathologic complete response (pCR) among racial groups are not well-understood. This study aimed to identify factors associated with pCR after NET among different racial groups. **METHODS:** Adult women with stage 1-3 ER+/HER2- BC from 2006-2021 in the National Cancer Database who received NET were included. Patients receiving neoadjuvant chemotherapy were excluded. Rates of pCR, defined as no residual disease in the breast and axilla post-treatment, were compared among white, Black, Asian/Pacific Islander, and American Indian/Alaskan groups. Predictors of pCR were identified with multivariable logistic regression. Overall survival in patients with pCR was modelled with Kaplan-Meier analyses. **RESULTS:** 70,904 patients were included, with 58,401 (82.4%) white, 8,825 (12.5%) Black, 2,405 (4.8%) Asian/Pacific Islander, and 273 (0.4%) American Indian/Alaskan patients. A larger proportion of Black patients compared to other racial groups presented with more advanced disease (48.2% stage 2 and 26.8% stage 3) and had higher grade tumors (38.5% grade 3). A larger proportion of Asian/Pacific Islander patients compared to other racial groups had no comorbidities (87.6%). Overall, 5.2% achieved pCR (4.9% in white, 7.3% in Black, 6.0% in Asian/Pacific Islander, and 4.8% in American Indian/Alaskan groups, p<0.001). Adjusting for age, histology, grade, clinical stage, comorbidity, income, and treatment facility, Black compared to white race was associated with higher odds of achieving pCR (odds ratio [OR] 1.34, 95% confidence interval [CI] 1.16-1.55) in patients younger than 60. This association between pCR and race was not statistically significant in patients older than 60. Stratifying by pCR, 5-year overall survival differed by racial groups (figure). **CONCLUSIONS:** After neoadjuvant endocrine therapy, Black compared to white patients had higher pCR rate, while American Indian/Alaskan patients had the lowest rate. Younger Black compared to white patients had higher odds of achieving pCR relative to other racial groups. While overall survival was worst among Black patients with and without pCR, the effect size was similar. Further studies are needed to investigate potential biologic and socioeconomic etiology of the observed differences in survival among different racial groups.



P22. Post-Operative Impact of Negative Pressure Wound Therapy Following Oncoplastic Breast Surgery

Nicole Harris, MD[1]; Paige Aiello, MD[2]; David J Detz, MS, MD[3]; Diego Hanssen, MD[4]; Carly Farrell, PA-C[5]; Junmin Whiting[6]; Susan Hoover, MD[7]; Nazanin Khakpour, MD[8]; John Kiluk, MD[9]; Laura Kruper, MD, MSCE[10]; Christine Laronga[11]; Melissa Mallory, MD[12]; Marie C Lee, MD[13]; Brian Czerniecki, MD, PhD[14]
[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4]UT Health Houston, Houston, TX, US; [5]Moffitt Cancer Center, Tampa, FL, US; [6]Moffitt Cancer Center, Tampa, FL, US; [7]Moffitt Cancer Center, Tampa, FL, US; [8]Moffitt Cancer Center, Tampa, FL, US; [9]Moffitt Cancer Center, Tampa, FL, US; [10]Moffitt Cancer Center, Tampa, FL, US; [11]Moffitt Cancer Center, Tampa, FL, US; [12]Moffitt Cancer Center, Tampa, FL, US; [13]Moffitt Cancer Center, Tampa, FL, US; [14]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: The application of negative pressure wound therapy (NPWT) systems over closed surgical incisions purportedly lowers post-operative wound complications, however, there is little evidence to support its routine use in breast surgery. The Prevena™ system is an NPWT dressing placed in the operating room (OR) at the conclusion of skin closure, providing continuous negative pressure. The primary objective of this study was to compare major and minor wound complication rates in breast cancer (BC) patients undergoing oncoplastic procedures, with and without the use of the NPWT. **METHODS:** A prospectively maintained database of BC patients undergoing breast conserving oncoplastic procedures (lumpectomy with mastopexy/mammoplasty) with placement of NPWT system placed at a single institution was queried. This cohort was compared to a retrospective contemporaneous control group receiving primary two-layered suture and skin adhesive closure only. All patients were seen 2-4 weeks post-op to assess for complications. Major complications included abscess/hematoma/seroma needing drainage, and wound breakdown or asymmetry requiring return to the OR. Minor complications included breast lymphedema/erythema, minor nipple necrosis, and wound breakdown or mild asymmetry not requiring return to OR. Analyses were performed using Chi-square test or Fisher's exact test, where applicable, and univariate logistic regression models, with statistical significance set at $p < 0.05$. **RESULTS:** Of 157 patients, 64 had NPWT and 93 were controls. The median age of patients in both groups was 62, ranging from 34 to 83 years of age, and groups were well balanced with regard to smoking status, ethnicity, and comorbidities such as diabetes and obesity. There were significantly fewer major complications in the NPWT group (3% NPWT vs 14% control, p=0.027). The control group had a 5 times higher likelihood of major complications (odds ratio of 5.04, p=0.038). There were no significant difference in the rates of minor complications (12.5% NPWT vs 18.3% control, p = 0.331), and no difference in complication rates based on comorbidities or tumor characteristics. **CONCLUSIONS:** NPWT significantly decreases major post-operative wound complications in BC patients undergoing oncoplastic procedures. Surgeons should consider NPWT to minimize the need for post-op antibiotics, procedures, and returns to the OR in this subset of patients. Minimization of major post-op complications can help ensure the timely initiation of adjuvant therapy following breast conserving oncoplastic procedures.

Table 1. Univariate Association with Negative Pressure Wound Therapy

Covariate	Complication (Yes/No)	NPTW Used		P-Value
		No (N = 93)	Yes (N=64)	
Any Type of Complication	No	73 (78.5)	55 (85.9)	0.238
	Yes	20 (21.5)	9 (14.1)	
Major Post-Operative Complications	No	80 (86)	62 (96.9)	0.027
	Yes	13 (14)	2 (3.1)	
Minor Post-Operative Complications	No	76 (81.7)	56 (87.5)	0.331
	Yes	17 (18.3)	8 (12.5)	

P23. Residential Proximity to National Priorities List Superfund Sites and Exposure to Poor Air Quality Are Associated with Increased Likelihood of Triple Negative Breast Cancer in a South Florida Population

Peter A Borowsky[1]; Maria Alicia Sierra, MD, MPH[2]; Lauren Nahodyl, MS[3]; Erin Kobetz, PhD, MPH[4]; Neha Goel, MD, MPH[5]
[1]University of Miami, Miami, FL, US; [2]University of Miami Miller School of Medicine, Miami, FL, US; [3]University of Miami, Miami, FL, US; [4]University of Miami, Miami, FL, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Triple negative breast cancer (TNBC) is an aggressive form of breast cancer that has previously been spatiotemporally associated with disadvantaged neighborhoods and at-risk groups. Less is known about how environmental factors, including geospatial proximity of place of residence to National Priorities List (NPL) superfund (SF) sites and neighborhood air quality, influence likelihood of TNBC. This study sought to assess the association between place of residence proximity to NPL SF sites and air quality with likelihood of TNBC in a South Florida population. **METHODS:** A retrospective review was performed for breast cancer patients treated at one of two institutions (academic medical center and sister safety-net hospital) between 2005-2017. Patient addresses were collected and converted to census tract census-defined place (CDP) identification numbers. Those without valid tract numbers were excluded. U.S Environmental Protection Agency (EPA) data was used to geocode NPL-designated sites for CDP-linkage to patient addresses. EPA data was also used to measure particulate matter (pm) air quality levels within CDP regions, with levels grouped into categories of satisfactory (pm< 12), moderate (pm 12-35), and unhealthy (pm> 35). Multilevel analyses were performed to assess for association of distance between patient address and NPL site, along with air quality levels, and TNBC compared to ER+/HER2- and HER2+ disease, controlling for age, race, and ethnicity. **RESULTS:** 6,145 patients with a mean age of 55.9 ± 12.1 were included. 52.6% (n= 3,234) of patients were Hispanic, 26.3% (n= 1,615) non-Hispanic White, and 17.2% (n= 1,060) non-Hispanic Black. On multilevel analysis, patients living proximal to NPL SF sites (OR 1.30, 95% CI 1.03-1.64, p= 0.027) and those living in areas with poorer air quality (OR 2.28, 95% CI 1.45-3.55, p< 0.001) had a higher likelihood of TNBC compared to ER+/HER2- and HER2+ disease. **CONCLUSIONS:** Living near NPL SF sites and being exposed to unhealthy air quality were independently associated with a higher likelihood of TNBC. These findings remain to be validated in a larger population, but merit further inquiry on the role of environmental contaminants on breast cancer subtype development.

P24. Surgeon Practice Patterns in De Novo Oligometastatic Breast Cancer

Malia A. Brennan, MD[1]; Jennifer K Plichta, MD, MS[2]; Mariya Rozenbilt, MD[3]; Meghan R Flanagan, MD, MPH[4]
[1]University of Washington, Seattle, WA, US; [2]Duke University Medical Center, Durham, NC, US; [3]Yale University, New Haven, CT, US; [4]University of Washington, Seattle, WA, US

INTRODUCTION: Approximately 6% of breast cancer patients present with distant metastases. Randomized controlled trials have failed to consistently demonstrate a survival benefit with primary site local therapy, yet there remains ongoing debate about the role of surgery. The primary objective of this study is to understand the scope of current practice patterns among surgical oncologists treating patients with de novo oligometastatic breast cancer (dnOMBC). **METHODS:** Members of the Society of Surgical Oncology (SSO) who self-designated as performing breast surgery were surveyed (September-October 2024). Questions focused on practice patterns and considerations for offering primary site surgery in the setting of dnOMBC. Responses were summarized. **RESULTS:** 104/1068 (9.7%) individuals completed the survey. The majority practiced at an academic medical center (56%) followed by integrated health system (21%) and community practice (18%). Most had been in practice ≥10 years (61%). When considering number of metastatic sites, few (4%) would offer surgery for >3 metastatic lesions, though 20% indicated that multiple factors are considered. 85% of respondents consider the site of metastasis, and 68% consider receptor subtype. Patients with metastatic nodal disease (contralateral axillary, supraclavicular, cervical, mediastinal) and/or bone-only metastasis were most likely to be considered for surgery. Of the 69 respondents for whom receptor subtype influenced the decision, only 17% would offer surgery in the setting of triple negative disease. Ablative radiation to metastatic sites increased the likelihood to offer surgery among 75%, as did inflammatory

breast cancer (68%). Responses to clinical scenarios are reflected in Table 1. While 55% of respondents would not offer surgery in complete breast/axillary response but residual metastatic disease, the vast majority (94%) would offer surgery in residual or progressive local disease with complete response at metastatic sites. Regarding immediate breast reconstruction, 43% would only offer in the setting of sustained no evidence of distant disease, and 35% would consider irrespective of metastatic sites. **CONCLUSIONS:** There is variation in surgeon management of dnOMBC. Receptor subtype, location and number of lesions, response to systemic therapy, and ablative radiation of metastatic sites all influence decision making. Multi-disciplinary discussions are crucial to optimize treatment, and future clinical trials should seek to identify patients for whom surgery will improve outcomes.

Table 1. Responses to "I would offer surgical resection of the primary tumor and axillary lymph node sampling +/- adjuvant radiation in the following clinical scenarios"

	Irrespective of plan for ablative radiation to metastases	Only if ablative radiation to metastases originally planned	Only if sustained systemic therapy response, irrespective of radiation plan	Only if sustained systemic therapy response and plan for radiation	Would not offer surgery	If progression in breast/axilla and no progression in metastatic sites	Only for palliation of locoregional symptoms
If patient has complete response at **all sites of disease** (breast/axilla/ metastases)	16%	3%	35%	19%	19%		
If patient has complete response in breast/axilla but **residual metastatic disease**	4%	7%	13%	21%	55%		
If patient has complete response in metastatic lesions but **no/partial response in breast/axilla**	20%	3%	17%	13%	6%	30%	7%

P25. Survival in Older Women Receiving Adjuvant Radiation Monotherapy vs. Endocrine Monotherapy Following Lumpectomy for Invasive Breast Cancer

Tori Chanenchuk[1]; Kerri Anne Crowell[2]; Ton Wang[3]; Laura H Rosenberger, MD[4]; Gayle DiLalla[5]; Susan McDuff[6]; Gretchen Kimmick[7]; E. Shelley Hwang, MD, MPH, FSSO[8]; Jennifer K Plichta, MD[9]

[1]Duke University Medical Center, Durham, NC, US; [2]Duke University Medical Center, Durham, NC, US; [3]Duke University Medical Center, Durham, NC, US; [4]Duke University Medical Center, Durham, NC, US; [5]Duke University Medical Center, Durham, NC, US; [6]Duke University Medical Center, Durham, NC, US; [7]Duke University Medical Center, Durham, NC, US; [8]Duke University, Durham, NC, US; [9]Duke University Medical Center, Durham, NC, US

INTRODUCTION: Breast cancer is increasingly prevalent in older women. Most are diagnosed with hormone receptor positive (HR+) disease. For older women with HR+ breast cancer who are treated with 5-years of adjuvant endocrine therapy (ET), randomized trials have shown no detriment to survival outcomes with omission of radiation therapy (RT). However, many women have difficulty tolerating ET and may prefer not to take it. The aim of this study was to determine whether treatment with adjuvant RT monotherapy results in comparable overall survival (OS) to treatment with adjuvant ET monotherapy in women age ≥65yo diagnosed with early-stage breast cancer undergoing lumpectomy. **METHODS:** Women ≥65yo, diagnosed with ER+/HER2-, stage I breast cancer (cT1-2, N0), who underwent lumpectomy, were selected from the National Cancer Database (2010-2020). Those who received chemotherapy and/or any neoadjuvant therapy were excluded. Patient characteristics were summarized by N (%) for categorical and median (IQR) for continuous variables. OS was estimated via Kaplan-Meier (KM), with log-rank tests for group comparisons. A Cox Proportional Hazards model assessed the association between treatment group and OS, adjusting for covariates. **RESULTS:** The cohort included 30,177 patients, with 35.8% receiving RT and 64.2% receiving ET. The median follow-up for the entire cohort was 67.6 mos. Patients in the RT and ET groups were of similar age [median (IQR): RT 73yo (69-79) vs ET 75yo (71-80); p<0.001]. Patients in the ET group had minimally larger tumors [median tumor size (IQR): ET 1cm (0.7-1.5) vs RT 0.9cm (0.6-1.3);0.001], were less likely to have grade 3 tumors (ET 7.0% vs RT 8.4%;0.001), and were slightly more likely to have PR+ disease (ET 91.4% vs RT 89.6%;0.001). In the unadjusted KM analysis, patients receiving ET had a slightly lower 5-year OS compared to the RT group [ET 85.8% vs RT 88.9%;0.001]. A similar trend was observed when stratified based on age group, although less pronounced (all p<0.05). In the adjusted multivariable analysis, RT remained associated with a slightly better OS than ET [ET ref, RT hazards ratio 0.91 (95% CI 0.85-0.97); Table]. **CONCLUSIONS:** For older patients with early-stage, ER+/HER2- breast cancer, survival outcomes were largely similar for those who received adjuvant RT monotherapy vs adjuvant ET monotherapy. De-escalation of ET has not been as extensively explored. Prospective trials of RT vs ET may be warranted in this unique population.

Table. Cox proportional hazards modeling (OS), including demographic and disease variables, comparing only endocrine therapy vs only radiation therapy (N = 30177). In addition to the below variable, model also adjusted for education level, income level, insurance status, facility type, facility location, and community type.

Predictor (s)	HR (95% CI)	P Value	Overall P-Value
Therapy Group			0.002
Endocrine Therapy Only	REF		
Radiation Therapy Only	0.91 (0.85-0.97)	0.002	
Age Group			<0.001
65-69	REF		
70-74	1.28 (1.15-1.41)	<0.001	
75-79	1.93 (1.75-2.13)	<0.001	
80+	3.61 (3.29-3.96)	<0.001	
Sex			0.503
Female	REF		
Male	1.15 (0.77-1.71)	0.503	
Race/Ethnicity			0.009
Non-Hispanic White	REF		
Non-Hispanic Black	0.99 (0.88-1.11)	0.820	
Non-Hispanic Asian	0.77 (0.58-1.01)	0.060	
Hispanic	0.75 (0.62-0.91)	0.003	
Other	0.81 (0.54-1.2)	0.293	
Charlson/Deyo Comorbidity Score			<0.001
0	REF		
1	1.59 (1.5-1.7)	<0.001	
≥2	2.3 (2.11-2.51)	<0.001	
Clinical T-Stage			<0.001
cT1	REF		
cT2	1.24 (1.1-1.39)	<0.001	
Pathological T-Stage			<0.001
pT1	REF		
pT2	1.32 (1.18-1.47)	<0.001	
Grade			<0.001
1	REF		
2	1.08 (1.02-1.14)	0.009	
3	1.34 (1.22-1.47)	<0.001	

Abbreviations: HR = Hazards Ratio, CI=confidence interval

P26. The Impact of Neoadjuvant Immunotherapy on Lymphedema Rates in Triple Negative Breast Cancer Following Axillary Surgery

Sarah A. Kelly[1]; Natalia Polidorio[2]; Varadan Sevilimedu[3]; Giacomo Montagna[4]; Nour Abuhadra[5]; Monica Morrow[6]; Andrea V. Barrio[7]; Stephanie Downs-Canner[8]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New-York, NY, US

INTRODUCTION: Lymphedema is a major source of morbidity among breast cancer patients. While the pathophysiology is not fully understood, the addition of immunotherapy to neoadjuvant chemotherapy (NAC) has the potential to alter lymphedema rates through autoimmune pathways. We aimed to compare rates of lymphedema in patients with triple negative breast cancer (TNBC) who have undergone axillary surgery, stratified by receipt of neoadjuvant chemo-immunotherapy with pembrolizumab (NAC+P), or NAC. **METHODS:** This retrospective study compared 420 women with stage I-III TNBC treated with NAC+P (6/2021-9/2024) to 505 consecutive patients who received NAC (3/2010-9/2019) prior to neoadjuvant pembrolizumab approval. Patients without lymphedema assessment or loss of follow-up were excluded. Lymphedema was defined as provider documentation in the

electronic medical record. Lymphedema rates were compared across cohorts and stratified by axillary surgery type using non-parametric tests. A 1-year cut-off period for lymphedema development was employed to address follow-up time differences between groups. Multivariable analysis was utilized to determine the independent association of immunotherapy with lymphedema. **RESULTS:** Patients treated with NAC were more likely to undergo axillary lymph node dissection (ALND) than NAC+P patients. Compared to NAC patients, NAC+P patients were more likely to be stage 2 (vs stage 1), and to receive nodal irradiation and adjuvant capecitabine (reflective of time period). Median follow-up times differed significantly between NAC+P and NAC cohorts (1 year vs 3 years, $p < 0.001$). When restricted to 1-year follow up, lymphedema rates did not differ between NAC+P and NAC patients (20% vs 15%, $p = 0.087$). Among those who underwent ALND, lymphedema at 1 year occurred in 30% of NAC+P and 32% of NAC patients. For those who underwent sentinel node biopsy, lymphedema occurred in 11% of NAC+P and NAC patients at 1 year (Table). On multivariable analysis, receipt of immunotherapy was not associated with lymphedema after adjustment for axillary surgery, race, radiation type and the use of adjuvant capecitabine (OR 1.41 for NAC with KN522 as referent, 95% CI 0.97-2.05, $p = 0.08$). **CONCLUSIONS:** At 1-year follow-up, the addition of immunotherapy to chemotherapy was not associated with increased lymphedema rates compared to NAC, although longer follow-up is needed to provide further insight into its role. Rates of lymphedema post-neoadjuvant therapy may continue to decline with improved systemic therapy, and avoidance of both ALND and nodal irradiation.

Table. Clinicopathologic characteristics of the patients stratified by type of neoadjuvant treatment.

Characteristic		NAC+P (n = 420)		NAC only (n = 505)		p-value
		n	%	n	%	
Age, years (median, IQR)		52	41-62 (IQR)	50	41-59 (IQR)	0.2
BMI, kg/m^2 (median, IQR)		26	23-31 (IQR)	27	23-33 (IQR)	0.075
	Asian	69	16%	50	10%	0.021*
	Black, non-Hispanic	77	18%	109	22%	
	Hispanic	38	9%	60	12%	
	White, non-Hispanic	232	55%	273	55%	
	Other	3	0.7%	7	1%	
cT Stage	Tis/T1	51	12%	117	23%	< 0.001*
	cT2	294	71%	246	49%	
	cT3/T4	72	18%	139	28%	
cN Stage	cN0	224	53%	191	38%	< 0.001*
	cN1	175	42%	265	52%	
	cN2/N3	21	5%	49	10%	
Adjuvant Capecitabine		126	30%	115	23%	0.027
Breast Surgery	None	5	1%	0	0%	0.004*
	Lumpectomy	227	54%	243	48%	
	Mastectomy	188	45%	262	52%	
Axillary Surgery	SLNB	328	78%	284	56%	< 0.001*
	ALND	92	22%	221	44%	
Overall pCR		230	55%	184	36%	< 0.001*
Nodal pCR		128	65%	169	54%	0.016*
Adjuvant Breast RT	No RT	96	24%	93	19%	< 0.001
	PBI/WBRT	209	53%	219	44%	
	PMRT	87	22%	182	37%	
Nodal RT		170	41%	245	53%	< 0.001*
Lymphedema		77	18%	151	30%	< 0.001*
Lymphedema at 1 Year		65	15%	100	20%	0.087
Lymphedema at 1 Year, ALND Only		28	30%	70	32%	0.8
Lymphedema at 1 Year, SLNB Only		37	11%	30	11%	0.8

*Chi-square statistic is significant at the .05 level.

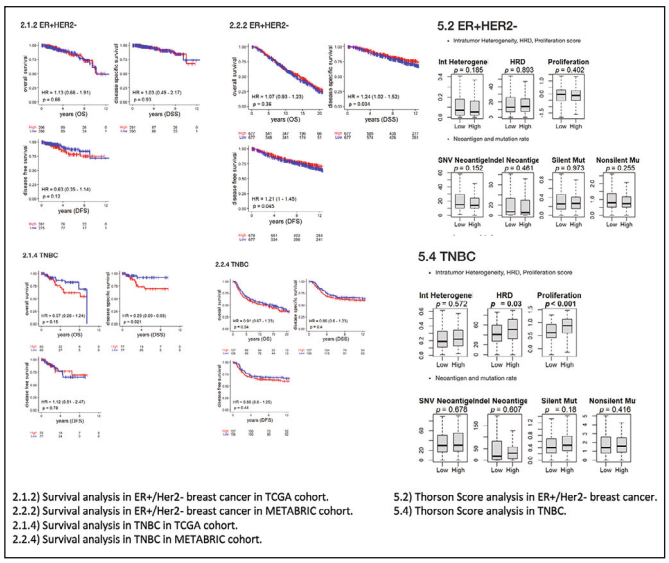
Abbreviations: NAC+P, neoadjuvant chemo-immunotherapy with pembrolizumab; NAC, neoadjuvant chemotherapy; BMI, body mass index; IQR, interquartile range; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; pCR, pathologic complete response; RT, radiation therapy; PBI, partial breast irradiation; WBRT, whole-breast radiation therapy

P27. The Role of Neutrophil in Breast Tumor Microenvironment and Association with Response to Neoadjuvant Therapy.

Faisal S Jehan, MD, FICS[1]; Rongrong Wu[2]; Takashi Ishikawa[3]; Kazuaki Takabe, MD, PhD[4]

[1]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [2]Tokyo Medical University, Tokyo, JP; [3]Tokyo Medical University, Tokyo, JP; [4]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US

INTRODUCTION: The tumor immune microenvironment (TIME) plays a crucial role in the progression and metastasis of breast cancer (BC). Once considered merely part of the body's innate immune defense, neutrophils are now recognized for their complex interactions within the TIME, influencing tumor growth, angiogenesis, and immune evasion. Recent studies suggest that tumor-associated neutrophils (TAN) can adopt both pro-tumorigenic and anti-tumorigenic phenotypes depending on the context. The aim of our study was to evaluate the association of TAN with biology and outcomes in BC. **METHODS:** Number of neutrophils was estimated by xCell algorithm on transcriptomics. Over 6300 breast cancer patients from three independent large cohorts: METABRIC, TCGA and SCAN-B, were analyzed. High and low neutrophil groups were divided by the median. We also performed Gene Set Enrichment Analysis (GSEA), and Thorson score analysis. **RESULTS:** High TAN was associated with better disease specific survival (DSS) and overall survival (OS) in ER+/HER2- of METABRIC, and was associated with worse DSS in the triple negative breast cancer (TNBC) of TCGA, but they were not validated by the other cohorts. High TAN had no correlation with the histological grade, tumor size, nodal metastasis or Ki67 expression regardless of subtypes in the three cohorts. Low TAN was associated with increased tumor immune activity by increased interferon alpha and gamma response, and allograft rejection in both the METABRIC and the SCAN-B cohorts in ER+/HER2-. No consistent enrichment of any pathways across the METABRIC and the SCAN-B cohorts based on TAN levels was seen in TNBC. High TAN was significantly associated with lower lymphocyte infiltration in the ER+/HER2-. In TNBC, high TAN was significantly associated with high Homologous Recombination Deficiency and high cell proliferation. Interestingly, cytolytic activity of high TAN was significantly lower in ER+/HER2- and HER2+, but not in TNBC, suggesting that TAN is associated with less immune cell killing in these subtypes. In agreement, CD8 and CD4 infiltrations were significantly lower in those subtypes. **CONCLUSIONS:** Our large clinical cohort study did not demonstrate any difference in survival or staging of ER+/HER2- and TNBC based on TAN. Understanding the specific mechanisms by which neutrophils contribute to the breast cancer microenvironment is critical for developing targeted therapies that could modulate their function for improved patient outcomes.



P28. Trends in Breast and Axillary Operations in Young Patients with Operable Breast Cancer from the National Cancer Database (NCDB): De-escalation of Axillary Surgery in Favor of Radiation

Marissa K. Boyle, MD[1]; Marc A. Attiyeh[2]; Farin Amersi, MD[3]; Alice Chung[4]; Jin Sun Lee[5]; Armando E. Giuliano[6]

[1]Cedars-Sinai Medical Center, Los Angeles, CA, US; [2]Cedars-Sinai Medical Center, Los Angeles, CA, US; [3]Cedars-Sinai Medical Center, Los Angeles, CA, US; [4]Cedars-Sinai Medical Center, Los Angeles, CA, US; [5]Cedars-Sinai Medical Center, Los Angeles, CA, US; [6]Cedars-Sinai Medical Center, Los Angeles, CA, US

INTRODUCTION: Young women ≤ 40 years old represent the minority of breast cancer patients and are often underrepresented in clinical trials. As a result, overtreatment with extensive surgery has been historically performed. This study compares trends in breast and axillary operations in young patients

with breast cancer over time and assesses for de-escalation of axillary surgery in favor of radiation. **METHODS:** Women ≤ 40 years old with stage 1–3 breast cancer who underwent surgery from January 2005 to December 2019 were identified from the National Cancer Database (NCDB). Patients were divided into two groups: those who were treated from 2005–2009 (Old) and 2015–2019 (New), to capture trends in demographic, clinical, and treatment data over time. **RESULTS:** 96,722 evaluable patients with a median age of 36.5 years (range 18–40) were identified. The comparison between Old (n=44,497) and New (n=52,225) groups demonstrated an increased proportion of patients of Hispanic (3,658 [8.9%] vs 5,194 [10.2%]) and Asian race (2,034 [4.9%] vs. 3,369 [6.6%]) (p<0.001). While most patients had invasive ductal carcinoma, more early stage cancers with better prognostic features were detected over time (cT1: 11,687 [26.3%] vs 18,764 [35.9%]; well differentiated: 3,933 [9.6%] vs 4,760 [9.9%]) (p<0.001). There was an increase in hormone receptor positive breast cancer (28,432 [68.4%] vs 37,792 [74.3%], p<0.001). For breast operations, partial mastectomies decreased significantly over time from 40.8% to 30.2% (p<0.001). Among patients who underwent mastectomies, the rate of nipple-sparing mastectomies increased from 0.3% to 9.5%, along with an increased use of reconstruction (p<0.001). Axillary lymph node dissections (ALND) decreased over time from 37.5% to 19.4% with a corresponding increase in the use of radiation (56.3% vs 57.4%, p<0.001). This trend was particularly pronounced in the node-positive cohort of 29,062 patients who underwent a mastectomy (ALND: 9,392 [72.4%] vs 5,967 [37.1%]; radiation: 7,255 [59.0%] vs 11,757 [75.5%]) (p<0.001) [Figure]. **CONCLUSIONS:** In young patients with stage 1–3 operable breast cancer, de-escalation of axillary surgery in favor of radiation is evident and results in non-inferior survival. These findings suggest that the addition of adjuvant radiation and improved systemic treatments may be responsible for the de-escalation of axillary surgery.

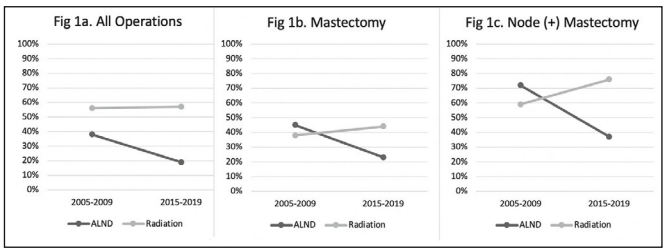


Figure. Rates of Axillary Lymph Node Dissections and Radiation Over Time in Young Women with Operable Breast Cancer

P29. Tumor antigen targeting type 1 conventional dendritic cells drive immune responses to eliminate metastasis initiating cancer cells

Caitlyn Balsay-Patel, MD[1]; Ganesan Ramamoorthi, PhD[2]; Grace Spiegelhoff, BS[3]; Carly Farrell, PA-C[4]; Marie C Lee, MD[5]; Ricardo Costa, MD[6]; Hyo Han, MD[7]; Marilin Rosa[8]; Brian Czerniecki, MD, PhD[9]

[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4]Moffitt Cancer Center, Tampa, FL, US; [5]Moffitt Cancer Center, Tampa, FL, US; [6]Moffitt Cancer Center, Tampa, FL, US; [7]Moffitt Cancer Center, Tampa, FL, US; [8]Moffitt Cancer Center, Tampa, FL, US; [9]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Dissemination and seeding of metastasis initiating cancer cells (MICs) in distant organs have been identified as the main source for overt metastasis outgrowth in breast cancer (BC) patients. There remains no specific therapy targeting these disseminated MICs. We have demonstrated that type 1 conventional dendritic cells (cDC1) mediated activation of anti-tumor immune effector cells can limit dissemination of MICs and its tumorigenesis in preclinical models. We therefore assessed the effect of cDC1 therapies on MICs in a pilot clinical study. **METHODS:** An IRB approved, single-center study collected bone marrow (BM) samples of BC patients undergoing surgery. The groups included (1) those with no prior treatment; (2) patients treated with standard neoadjuvant chemotherapy (NACT), or (3) tumor antigen targeting cDC1 intratumoral administration prior to NACT. The BM aspirates were processed for red blood cells lysis and MICs were isolated by immunomagnetic negative selection and EpCAM-based immunomagnetic enrichment. The isolated MICs were quantified and confirmed for cancer cell phenotype by histopathology. The statistical analysis was performed with GraphPad Prism. *P* values were calculated using two-tailed Mann–Whitney test. **RESULTS:** The BM of 17 BC patients at a single high-volume cancer center were collected. 6 of these received no NACT (group 1) while 7 received standard systemic NACT (group 2) and 4 received intratumoral injection of cDC1 prior to systemic NACT (group 3). The mean MIC count for group 1 was 5215 MICs per cc BM, while group 2 was 2640 MICs and group 3 was only 389 MICs. There were significantly less MICs in BM of patients from group 3 compared to groups 1 (p=0.0095) and 2 (p=0.0061). Group 3 also had more pathologic complete responses (pCR) with 4 (n=4) while group 2 had 2 pCR, 3 patients with residual cancer burden (RCB) II and 2 patients with RCB III (n=7). Implantation of MICs from untreated BC patients into immunodeficient (NSG) mice effectively developed tumors. Interestingly, these MICs after being treated with IFN-γ, lost their potential to grow into overt metastasis in NSG mice. **CONCLUSIONS:** Intratumoral cDC1 delivered prior to any standard NACT significantly decreases disseminated MICs in BM of BC patients. This may be the result of activation of IFN-γ secreting anti-tumor immune effector cells. Further investigation is warranted to determine if delivering cDC1 can subsequently prevent the outgrowth of overt metastasis and reduce mortality in BC.

Study group	Patient ID	BC subtype	Pathologic response	MIC counts per cc BM	*P* values
Group 1 – Untreated	Patient ID: 1	HER2+ER-PR-		3200 MICs	
	Patient ID: 2	HER2+ER-PR-		5960 MICs	
	Patient ID: 3	HER2+ER+PR+		3222 MICs	
	Patient ID: 4	HER2-ER-PR-		14875 MICs	
	Patient ID: 5	HER2-ER+PR+		1535 MICs	
	Patient ID: 6	HER2-ER+PR+		2500 MICs	
Group 2 – Neoadjuvant therapy	Patient ID: 7	HER2+ER-PR-	pCR	3194 MICs	*P* = 0.1807 vs group 1
	Patient ID: 8	HER2+ER+PR-	RCB II	1402 MICs	
	Patient ID: 9	HER2+ER-PR-	RCB II	1980 MICs	
	Patient ID: 10	HER2+ER+PR+	RCB II	2616 MICs	
	Patient ID: 11	HER2-ER+PR+	RCB III	5295 MICs	
	Patient ID: 12	HER2-ER+PR-	RCB III	2304 MICs	
	Patient ID: 13	HER2+ER+PR-	pCR	1690 MICs	
Group 3 – Intratumoral tumor antigen targeting DC1+ Neoadjuvant therapy	Patient ID: 14	HER2+ER+PR-	pCR	560 MICs	*P* = 0.0095 vs group 1 *P* = 0.0061 vs group 2
	Patient ID: 15	HER2+ER-PR-	pCR	173 MICs	
	Patient ID: 16	HER2-ER-PR-	pCR	479 MICs	
	Patient ID: 17	HER2-ER-PR-	pCR	345 MICs	

P30. Tumor hypoxia is associated with markers of increased tumor aggression and response to immunotherapy in ER+/HER2- breast cancer patients

Olivia A Martin, MD, MS[1]; Masanori Oshi[2]; Akimitsu Yamada[3]; Itaru Endo[4]; Kazuaki Takabe, MD, PhD[5]

[1]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [2]Yokohama City University Graduate School of Medicine, Yokohama, Kanagawa, JP; [3]yokohama city university, Yokohama, Please select -, JP; [4]Yokohama City University, Yokohama, JP; [5]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US

INTRODUCTION: Hypoxia in solid tumors is known to aggravate cancer and promote metastasis. Numerous studies have demonstrated that tumor hypoxia aggravates breast cancer (BC) in in vitro and in vivo systems, however, its relationship with tumor aggressiveness has not previously been assessed using multiple gene expression profiles on transcriptomics of large patient cohorts. **METHODS:** A total of 5226 BC patients from 3 independent cohorts, METABRIC (n = 1903), SCAN-B (GSE96058, n = 3273), and I-SPY2 (n=50) were analyzed. Hypoxia was quantified using gene set variant analysis (GSVA) of hypoxia gene set in the Molecular Signatures Database (MSigDB) collection on transcriptome. High and low hypoxia groups were divided by the median. False Discovery Rate (FDR) adjustment of p-values was performed to assess statistical significance. **RESULTS:** High hypoxia BC was significantly enriched in apoptosis, glycolysis, and coagulation gene sets regardless of subtype in both METABRIC and SCAN-B cohorts. High hypoxia was associated with lower Ki67 expression and lower proliferation score regardless of subtype. Lower homologous recombination deficiency, fraction alteration, and silent mutation rate were associated with tumor hypoxia only in ER+/HER2- BC. High hypoxia BC enriched for epithelial to mesenchymal transition pathway, TGF-beta signaling, and Hedgehog signaling regardless of subtype. Hypoxia was also significantly higher in triple negative (TNBC) compared to ER+/HER2- BC in both cohorts. Surprisingly, tumor size, lymph node status, distant metastasis, and overall survival were not significantly different by hypoxia, except for disease-free survival of TNBC in METABRIC. The angiogenesis gene set was enriched and fibroblasts, as well as pericytes, were highly infiltrated in high hypoxia BC

regardless of subtype, but vascular endothelial and lymphatic endothelial cells were significantly infiltrated only in ER+/HER2- BC. Inflammatory response, complement, TNF-α signaling, and IL-2 signaling were all enriched to high hypoxia regardless of subtype, whereas interferon-ϒ and IL-6 signaling were enriched only in ER+/HER2- BC. High hypoxia BC was associated with less CD8 and Th1 cell infiltrations in TNBC, whereas dendritic cell, M1 and M2 macrophage, as well as cytolytic activity score were all significantly higher in ER+/HER2- BC. In the ISPY-2 trial set, high hypoxia tumors were associated with significantly higher pCR rate in ER+/HER2- BC, but not in TNBC, after immunotherapy. **CONCLUSIONS:** We quantified hypoxia in BC patients using transcriptomics and found that it was associated with aggressive biology but not with survival. High hypoxia tumors were associated with myeloid cell infiltration, increased immune response, and better response to immunotherapy in I-SPY2 trial only in the ER+/HER2- BC subtype.

P31. Use of Neoadjuvant Chemotherapy for Local and Regionally Recurrent Triple Negative and HER2+ Breast Cancer

Mary M. Mrdutt[1]; Courtney N. Day, MS[2]; Amy Degnim, MD[3]; Judy C. Boughey, MD[4]; Roberto Leon-Ferre[5]
[1]Mayo Clinic, Rochester, MN, US; [2]Mayo Clinic, Rochester, MN, US; [3]Mayo Clinic, Rochester, MN, US; [4]Mayo Clinic, Rochester, MN, US; [5]Mayo Clinic, Rochester, MN, US

INTRODUCTION: Data on neoadjuvant chemotherapy (NACT) for local and regionally recurrent (LRR) breast cancer (BC) is sparse. We evaluated use of NACT for triple negative (TN) and HER2+ LRR BC and significance of pathologic complete response (pCR). **METHODS:** We identified patients (pts) with invasive TN or HER2+ LRR BC treated surgically (9/2008-5/2024). Pts with distant metastasis or second LRR were excluded. We evaluated demographics, index and LRR characteristics and treatment. NACT use over time was evaluated with Cochran Armitage Trend tests. Associations with biologic subtype and clinical nodal status were assessed with chi-square or Fisher's exact tests where appropriate. Cumulative incidence of distant recurrence (DR) was evaluated with death as a competing risk. **RESULTS:** 103 pts with LRRs were identified: 73 (70.9%) clinically node negative (cN0) local recurrences, 11 (10.7%) regional nodal recurrences, and 19 (18.4%) with local and nodal recurrence. LRR tumor subtype was 62.1% TN and 37.9% HER2+ in (28/39 hormone receptor (HR)+, 11/39 HR-). Proportion of cN0 recurrence was similar across subtype (TN 70.3% , HER2+ 71.8%). Median time from primary cancer surgery to LRR was 4.4 yr (IQR: 1.4,10.7, [TN 3.7 yr (IQR: 1.2, 11.3) vs HER2+ 5.4 yr (IQR:2.8, 10.5, p=NS)]. Chemotherapy data for LRR was available in 96 pts. 75 (78.1%) received chemotherapy, with no significant change over time (2008-2011: 73.3%, 2012-2015 76.9%, 2016-2019 70.0%, 2020-2024: 83.3%, p=NS). Chemotherapy was given neoadjuvantly in 50/75 (66.7%) with use increasing (2008-2011 36.4%, 2012-2015 40.0%, 2016-2019 78.6%, 2020-2024 77.5%; p=0.003). cN+ LRR were more likely to receive NACT (21/25, 84.0% vs cN0 29/50, 58.0%; p=0.04). Among 50 pts receiving NACT, 20 (40%) had a pCR (13/29 [45%] TN; 7/21 [33%] HER2+). 11/29 (37.9%) cN0 LR had a pCR as did 9/21 (42.9%) cN+ LRR (cN0: 37.5% TN, 38.5% HER2; cN+: 53.9% TN, 25.0% HER2+). Overall median follow-up was 2.0 (IQR: 0.5, 5.5) yr. Additional events included DR (20), isolated nodal recurrence (1), and radiation associated angiosarcoma (1). Median time to DR was 0.9 yr (IQR: 0.5, 3.0). 5-year cumulative incidence of DR was 26.9% overall (95% CI: 17.5, 41.4) and higher among those with NACT not achieving pCR (no pCR 43.5% (95% CI: 24.4, 77.6) vs pCR 0%, p=0.001). **CONCLUSIONS:** NACT for TN and HER2+ BC LRR has increased over time. 40% pts achieved pCR rate, associated with excellent clinical outcomes. Conversely, nearly half of patients not achieving pCR experienced DR by 5 years. NACT for resectable LRR warrants furture investigation in clinical trials.

P32. Variation in Locoregional Surgical Management of Stage IV Breast Cancer; Local/Institutional and Regional Geographic Considerations

Shruti Zaveri[1]; Zachary Whitham[2]; Anvy Nguyen[3]; Arushii Nadar, BS[4]; Ann Marilyn Leitch[5]; Glenda Delgado[6]; Deborah Farr[7]; Rachel Wooldridge[8]; Anthony Froix[9]; Stephanie Serres[10]
[1]The University of Texas Southwestern Medical Center, Dallas, TX, US; [2]The University of Texas Southwestern Medical Center, Dallas, TX, US; [3]The University of Texas Southwestern Medical Center, Dallas, TX, US; [4]The University of Texas Southwestern Medical Center, Dallas, TX, US; [5]The University of Texas Southwestern Medical Center, Dallas, TX, US; [6]The University of Texas Southwestern Medical Center, Dallas, TX, US; [7]The University of Texas Southwestern Medical Center, Dallas, TX, US; [8]The University of Texas Southwestern Medical Center, Dallas, TX, US; [9]The University of Texas Southwestern Medical Center, Dallas, TX, US; [10]The University of Texas Southwestern Medical Center, Dallas, TX, US

INTRODUCTION: Prior studies have demonstrated variation in surgical management of breast cancer. As randomized controlled trials have increasingly shown limited survival advantage with surgical management of stage IV breast cancer, the present study aimed to assess variation in surgical management of de novo stage IV breast cancer. **METHODS:** We conducted a retrospective cohort analysis of 68,670 patients diagnosed with de novo stage IV breast cancer from 2012 to 2021 using the National Cancer Database. The proportion of patients treated with locoregional surgical intervention was compared between year of diagnosis, facility type, geographic region, and facility volume, while controlling for demographic and clinical variables. **RESULTS:** Overall, 13,608 patients (19.82%) of stage IV breast cancer patients underwent breast and/or axillary surgical intervention. There was a statistically significant decrease from 27.4% to 15.0% in the proportion of patients undergoing surgery over the included timeframe (p <0.001). Significant variation in the proportion of patients receiving surgical intervention was noted among geographic regions ranging from 14.2% to 21.8% (Northeast and West, respectively; Midwest 17.6%, South 20.7%; p <0.001). Facilities with the lowest volume of stage IV patients were significantly more likely to offer surgical intervention, with 22.1% undergoing surgery at facilities in the lowest quartile of patient volume and 17.4% undergoing surgery at facilities in the highest quartile of patient volume (p <0.001). Patients treated at comprehensive community cancer centers were most likely to have surgical intervention, and those treated at academic centers (including NCI-designated comprehensive cancer centers) were least likely (21.1% vs. 15.6%, respectively, p <0.001). When considered at an individual facility level, proportions of patients treated with surgery ranged from 0% to 100% (median 18.8%, IQR 13.1-24.4%, Figure). In multivariate analyses, year of diagnosis, facility type, geographic region, and facility volume remained significant predictors of primary site surgery. **CONCLUSIONS:** Significant variation exists in locoregional surgical management of de novo stage IV breast cancer. Surgical intervention has decreased over time, likely due to evidence demonstrating limited survival advantage and improving systemic therapy. However, this study reveals that institutional and geographic factors may significantly impact surgical decision-making and management for these patients.

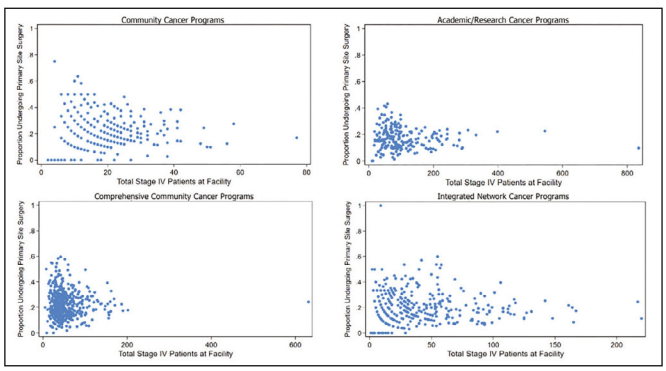


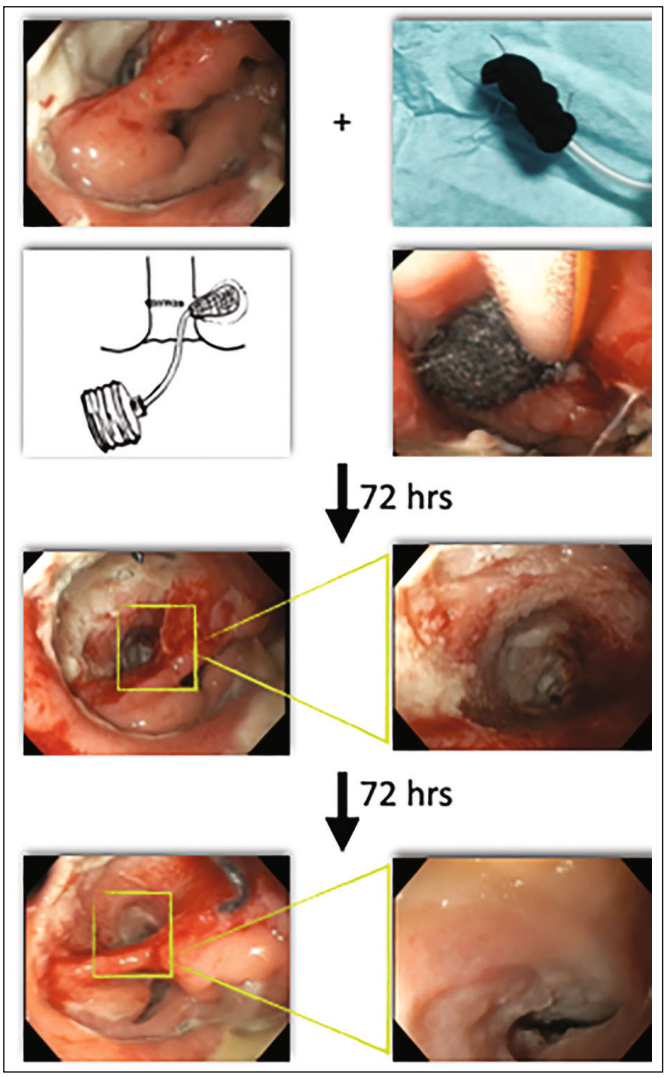
Figure. Proportion of Patients Undergoing Locoregional Surgical Intervention for De Novo Stage IV Breast Cancer By Facility Type

P33. A Low Cost Endoluminal Vacuum Therapy for Rectal Anastomotic Leaks in a Resource Constraint Setting: Outcomes and Insights of a Single Centre Experience

John J. Alapatt, MS (General surgery), DrNB (Surgical Oncology), FEBS, MRCS (Edinburgh)[1]
[1]MVR Cancer Centre and Research Institute, Kozhikode, Kerala, IN

INTRODUCTION: Anastomotic leaks in rectal cancer patients are a significant complication which may result in a disconnection of the anastomosis and end – colostomy .The commercially available endoluminal vacuum technology is expensive and not readily available in our resource limited setting.We aimed to evaluate the efficacy of a novel low cost endoluminal vacuum therapy as an alternative to the commercially available technology. **METHODS:** We retrospectively analyzed the prospective database of the group of patients who had a rectal anastomotic leak after a low anterior resection from January 2021 to July 2024. All patients who were diagnosed to have a extraperitoneal contained leak with no features of peritonitis and underwent a diversion colostomy were

included in the study.The initial set of patients , who were treated with IV antibiotics , pigtail insertion and drainage of pelvic collection was labelled as group A. All patients who were treated by endoluminal vacuum therapy was labelled as group B.The primary objective of the study was to ascertain the rates of stoma closure , time to stoma closure and the mean duration of hospital stay in the two groups. The technique (as illustrated) consisted of utilising a sterile sponge through with a channel is created by passing a redon curved needle of closed suction drain. The perforated end of the drain catheter remains within the body of the sponge. To further anchor the sponge to drain tube, a 0 – silk suture can be used to transfix the catheter at the top and the bottom. The sponge with drain catheter was railroaded over an endoscopic guide wire and placed in the anastomotic leak cavity in the pararectal space.Vacuum dressing was applied and connected to a portable reusable vacuum unit , set to 100 mm Hg pressure. The sponge was changed after every 48-72. **RESULTS:** We had a total of 28 patients in group A and 31 patients in group B. The rates of stoma closure in group A was 19 patients (67.8%).Two patients of group A , who had a persistent anastomotic leakage subsequently underwent endoluminal vacuum therapy and underwent successful closure of their stoma.28 patients of group B (90.3%) ,treated with endoluminal vacuum therapy underwent diversion colostomy closure.The time to stoma closure was 120 days and 76 days in group A and group B respectively.The mean duration of endoluminal vacuum therapy was 23 days .The average number of dressing changes was 6 for the endoluminal vacuum therapy.The total cost of one vacuum therapy dressing change in our technique came to 12.74 dollars.The total cost of one session of commercially available endoluminal technology is priced at 327.46 dollars. **CONCLUSIONS:** Our novel endoluminal vacuum setup is a low cost alternative to commercially available apparatus. This can be safely and effectively used to salvage failed rectal anastomoses in hospitals and patients with resource constraints



P34. A Novel Role of Secreted Methionine Adesnosyltransferase a2 in the Development of Colorectal Liver Metastases

Monica R Justo, MD[1]; Andrea Floris, PhD[2]; Youngyi Lim[3]; Swati Chandla, PhD[4]; Manisha Dagar, PhD[5]; Heping Yang, MD, PhD[6]; Alexandra Gangi, MD, FSSO[7]; Maria Lauda Tomasi, PhD[8]; Shelly C Lu, MD[9]

[1]Cedars Sinai Medical Center, Los Angeles, CA, US; [2]Cedars Sinai Medical Center, Los Angeles, CA, US; [3]Cedars Sinai Medical Center, Los Angeles, CA, US; [4]Cedars Sinai Medical Center, Los Angeles, CA, US; [5]Cedars Sinai Medical Center, Los Angeles, CA, US; [6]Cedars Sinai Medical Center, Los Angeles, CA, US; [7]Cedars-Sinai Medical Center, Los Angeles, CA, US; [8]Cedars Sinai Medical Center, Los Angeles, CA, US; [9]Cedars Sinai Medical Center, Los Angeles, CA, US

INTRODUCTION: Liver is the most common site of metastatic disease for patients with colorectal cancer (colorectal liver metastasis, CRLM). Methionine adenosyltransferase (MAT) is an essential enzyme that catalyzes the formation of S-adenosylmethionine (SAMe), the principal methyl donor, in mammalian cells. MAT1A (encodes for MATα1) is the isoform expressed mainly in normal adult liver, whereas MAT2A (encodes for MATα2) is expressed in all extrahepatic tissues. We reported MAT1A is a major defense against CRLM as loss of Mat1a sensitizes the liver to CRLM. In contrast, MAT2A is overexpressed in colon cancer and promotes cell proliferation and survival. Specifically, we reported MATα2 functions as a transcription factor that binds and activates the BCL-2 promoter. The aim of the current study was to elucidate the interplay between MAT2A and MAT1A and how they might influence CRLM. **METHODS:** Our study included in vitro experiments using human hepatocytes, RKO (human colorectal cancer, CRC) cells, extracellular vesicle (EV) isolation, chromatin immunoprecipitation (ChIP), ChIP-seq, western blotting, immunohistochemistry and immunofluorescence. We confirmed some of the findings using resected human CRLM and normal human liver specimens. **RESULTS:** MATα2 is secreted in free but truncated form and intact within EVs by CRC cells. MATα2 within EVs can be internalized by human hepatocytes and found within the nucleus, which then binds to the MAT2A promoter on ChIP analysis. MATα2 is predicted to bind the MAT1A promoter, and this was confirmed using ChIP-seq. Treatment of human hepatocytes with EVs from RKO cells overexpressing MAT2A lowered hepatocytes' MAT1A promoter activity and expression but increased MAT2A promoter activity. In human CRLM samples, hepatocytes in nontumor region express lower MATα1 but higher MATα2 as compared to normal liver. Treating RKO cells with EVs released from RKO cells overexpressing MAT2A promoted cell proliferation and invasion. **CONCLUSIONS:** Our results suggest CRC cells secretion of MATα2 in EVs can promote growth in an autocrine fashion as well as act as a transcription factor when internalized by hepatocytes to lower MAT1A expression, the major defense against CRLM. This is a novel crosstalk between CRC and hepatocytes that contributes to CRLM growth.

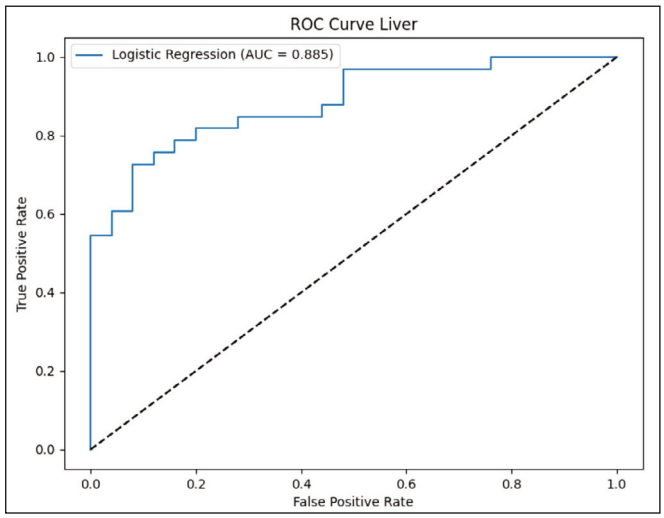
P35. AI Radiomic Analysis Predicts Chemotherapy Response in patients with Colorectal liver metastasis

Teodora C Dumitra[1]; Monica R Justo, MD[2]; Eric Pletcher[3]; Touseef Qureshi[4]; Linda Azab[5]; Lixia Wang[6]; Ashley Wachsman[7]; Jun Gong[8]; Debiao Li[9]; Alexandra Gangi, MD, FSSO[10]

[1]Cedars Sinai Medical Center, Los Angeles, CA, US; [2]Cedars Sinai Medical Center, Los Angeles, CA, US; [3]Hackensack Meridian Health, Edison, NJ, US; [4]Cedars Sinai, Los Angeles, CA, US; [5]Cedars Sinai Medical Center, Los Angeles, CA, US; [6]Cedars Sinai Medical Center, Los Angeles, CA, US; [7]Cedars Sinai Medical Center, Los Angeles, CA, US; [8]Cedars Sinai Medical Center, Los Angeles, CA, US; [9]Cedars Sinai Medical Center, Los Angeles, CA, US; [10]Cedars-Sinai Medical Center, Los Angeles, CA, US

INTRODUCTION: Predicting chemosensitivity of colorectal liver metastasis (CRLM) can optimize treatment strategies and improve disease control. While cross-sectional imaging is the current standard noninvasive tool utilized to evaluate response, critical aspects can be missed. As such, artificial intelligence (AI) may help with better prediction modeling. This study set to evaluate imaging based predictors of treatment response in patients with CRLM. **METHODS:** Radiomic analysis was performed examining the nontumor-bearing liver and CRLM in pre- and post-chemotherapy abdominal CT scans. Response to chemotherapy was measured based on change in tumor size with responders defined as having a significant reduction in tumor size. Radiomic analysis was conducted comparing morphologic, intensity-based, shape and size related features of both the normal liver and CRLM to identify features predictive of treatment response. Statistical significance was determined by t-test and logistic regression, and ROC-AUC curve. **RESULTS:** A total of

32 patients underwent radiomic analysis, 84% of whom were male, with a mean age of 62. Most patients had a colon primary (91%) and metastasis were confined to the liver in most cases. The majority of patients were classified as responders (n=23, 72%) and had significant reduction in tumor size ranging from 27-92%; 9 patients were non-responders. Several textural features of CRLM, including elongation, sphericity, size non-uniformity and grey-level variance, were significantly different between the two groups. The model predicted CRLM response with 72% overall accuracy (ROC-AUC score 0.806). Liver analysis identified multiple liver shape and various texture patterns as significant predictors of liver injury, with an accuracy of 78% (ROC-AUC score 0.885). **CONCLUSIONS:** This study highlights the potential of AI radiomic analysis to predict chemotherapy response of both the non-tumor bearing liver and CRLM. While these features may be difficult to identify by standard radiologic assessment, AI has the potential to identify critical morphologic and textural features which can predict response. Utilizing AI can aid in distinguishing which patients may benefit from therapy and allow for early tailoring of treatment.



P36. Assessing Resolution of Inflammation as a Potential Novel Risk Determinant for Stage 3 Colon Cancer Recurrence: A Translational Study

Megan L Sulciner[1]; Robert Nshimiyimana[2]; Kimmie Ng[3]; Chandrajit Raut[4]; Charles Serhan[5]

[1]Brigham and Women's Hospital, Boston, MA, US; [2]Center for Experimental Therapeutics & Reperfusion Injury, Department of Anesthesiology, Brigham & W, Boston, MA, US; [3]Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, US; [4]Division of Surgical Oncology, Department of Surgery, Brigham & Women's Hospital, Harvard Medical Sc, Boston, MA, US; [5]Center for Experimental Therapeutics & Reperfusion Injury, Department of Anesthesiology, Brigham & W, Boston, MA, US

INTRODUCTION: Resolution of inflammation is the active process of returning to homeostasis after inflammatory insult, mediated by endogenous specialized pro-resolving mediators (SPMs). SPMs are biosynthesized endogenously from polyunsaturated fatty acids, and include several families, namely the resolvins and lipoxins. Failed resolution of inflammation secondary to surgery contributes to tumor recurrence in animal models. We sought to characterize a comprehensive profile to assesses whether it is possible to predict to tumor recurrence in stage 3 colon cancer patients after primary resection based on SPM values. **METHODS:** Plasma collected postoperatively from adult stage 3 colon cancer patients was obtained from an institutional biobank. Levels of pro-inflammatory and pro-resolution mediators were quantified via ELISA and reported as mean. Mediators of interest were identified using solid phase extraction, liquid chromatography with tandem mass spectrometry (LC-MS/MS). Patient characteristics, oncologic outcomes, and surgical outcomes were analyzed. Student t-test was used for comparison analysis. **RESULTS:** A total of 34 patients were included, 17 developed recurrence after primary resection (cohort 1) and 17 patients did not (cohort 2). Median follow-up was 49 months. Recurrence was either local, distant, or local and distant. Plasma levels of acute pro-inflammatory mediators IL-6, C-reactive protein, and leukotriene B_4 were similar between the cohorts, indicating no difference in the state of acute inflammation. Levels for resolvin D2 were significantly higher in cohort 2 at 162.0 pg/ml, compared to 76.9 pg/ml in cohort 1 (p=0.02). Resolvin D1 and lipoxin A4 levels were higher in cohort 2, but were not statistically significant compared to cohort 1. (Table 1) The summation of SPMs was used to provide a quantification of each patient's resolution state. Patients in cohort 2 had a significantly higher summation than cohort 1 (p=0.04). LC-MS/MS data demonstrated the presence of 14-HDHA, 17-HDHA and 18-HEPE, pathway markers for the SPMs, in the plasma samples. This robust method suggests SPMs activity in patients' plasma and supports the ELISA findings. **CONCLUSIONS:** Patients with stage 3 colon cancer that recurred after primary resection had lower plasma levels of resolvin D2 and summation of SPMs. Trends noted with other SPMs need further investigation. Together, these findings hold the potential to shift the paradigm in which failure of the resolution of inflammation contributes to the pathophysiology, prognosis, and treatment of tumor recurrence.

Table 1. Postoperative levels of pro-inflammatory and pro-resolving mediators (n=34)

Mediator	Recurrence (cohort 1, n=17)	No Recurrence (cohort 2, n=17)	p-value
	Mean (SEM)	Mean (SEM)	
Pro-inflammatory			
IL-6 (pg/ml)	4.5 (2.5)	4.9 (1.4)	0.29
C-reactive protein (ug/ml)	3.1 (0.7)	4.4 (6.9)	0.20
Leukotriene B_4 (pg/ml)	50.2 (7.2)	52.6 (7.0)	0.41
Pro-resolving			
Lipoxin A4 (pg/ml)	232.8 (17.9)	252.7 (3.4)	0.29
Resolvin D1 (pg/ml)	61.3 (8.6)	68.9 (12.1)	0.30
Resolvin D2 (pg/ml)	76.9 (7.5)	162.0 (35.1)	0.02
SPM summation	371.0 (24.1)	497.9 (64.9)	0.04

P37. Early Onset Appendiceal Adenocarcinoma: Characteristics of a National Cohort

Amy Y Li, MD[1]; Monique H Gandawidjaja[2]; Belain Eyob[3]; Thuy B. Tran[4]; Michael O'Leary[5]; Oliver S Eng[6]

[1]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [2]University of California, Irvine, Orange, CA, US; [3]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [4]University of California Irvine Department of Surgical Oncology, Irvine, CA, US; [5]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [6]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US

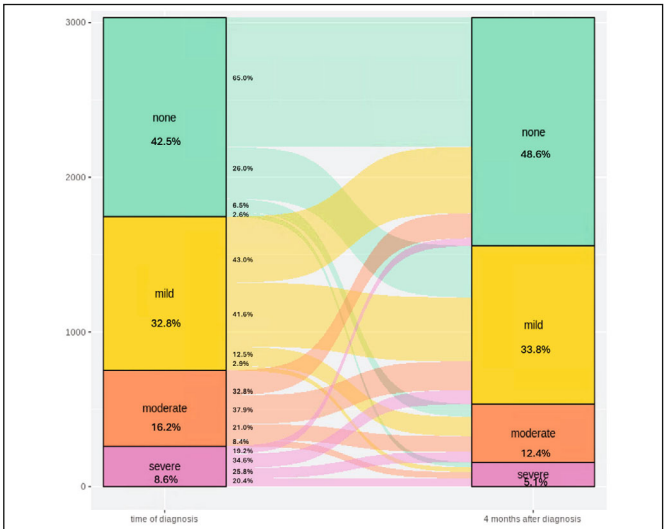
INTRODUCTION: Prior studies have shown an alarming increase in the rate of incidence of appendiceal adenocarcinoma. Yet, unlike in other histologies of malignancies, population-based data on early onset (under age 50) appendiceal adenocarcinoma remains limited and with a relative paucity in the body of literature. This study utilizes a national cohort of patients to characterize the sociodemographic characteristics and factors associated with survival in patients diagnosed with early-onset appendiceal adenocarcinoma. **METHODS:** Adult patients diagnosed with appendiceal adenocarcinoma between 2004-2019 were identified in the National Cancer Database. Early-onset appendiceal adenocarcinoma (EOAA) was defined as diagnosis under the age of 50. Patients without documented staging were excluded. Sociodemographic data associated with survival were evaluated with multivariable analyses. Overall survival was calculated with Kaplan Meier curves. **RESULTS:** There were 11,803 patients identified, of which 28.5% (n=3366) were diagnosed with EOAA, and the remainder 71.5% (n=8437) were diagnosed at 50 years of age or later. In the EOAA cohort, a higher proportion of patients were without comorbidities, had stage I disease, and had private insurance (all $p<0.05$); yet fewer patients underwent definitive surgery of the primary site (67.3% vs 69.9%, p=0.006). Stage 4 disease was seen in 38% of EOAA patients. On multivariable analysis, female sex and Hispanic origin remained significantly associated EOAA (HR<1.0, $p<0.05$). Median overall survival (OS) was not reached for EOAA, although median OS for patients diagnosed after 50 was 57.9 (54.16-61.56) months. On Cox regression analysis, early onset diagnosis, having any insurance, and treatment at an academic center were associated with improved survival (HR<0.05). **CONCLUSIONS:** Approximately 1 in 4 patients are diagnosed with appendiceal adenocarcinoma at under 50 years of age. Approximately half of these patients are diagnosed at Stage I and II. However, almost 40% of EOAA patients that are diagnosed with metastatic disease. Furthermore, fewer EOAA patients underwent definitive surgery. Attention is warranted to better understand potential diagnostic and therapeutic barriers in the management of EOAA.

P38. Identification of patients at risk of higher patient-reported pain after diagnosis of colorectal cancer

Alice Zhu[1]; Adom Bondzi-Simpson[2]; Alyson Mahar, PhD[3]; Amy Hsu[4]; Paul James[5]; Zharmaine Ante[6]; Kayan Ip[7]; Ekaterina Kosyachkova[8]; Julie Hallet, MD[9]; Natalie G Coburn, MD, MPH[10]

[1]University of Toronto, Toronto, ON, CA; [2]University of Toronto, Toronto, ON, CA; [3]Queens University, Kingston, ON, CA; [4]Ottawa Hospital Research Institute, Ottawa, ON, CA; [5]University of Toronto, Toronto, ON, CA; [6]Institute for Clinical Evaluative Sciences, Toronto, ON, CA; [7]Sunnybrook Research Institute, Toronto, ON, CA; [8]University Health Network, Toronto, ON, CA; [9]Sunnybrook Health Sciences Centre, Toronto, ON, CA; [10]University of Toronto, Toronto, ON, CA

INTRODUCTION: Pain is one of the most feared and debilitating symptoms among patients with cancer, with considerable impact quality of life and well-being. Poor pain management can exacerbate psychological distress, limit social engagement, and influence overall survival. This study examined the trajectory of, and factors associated with patient-reported pain after colorectal cancer (CRC). **METHODS:** This retrospective cohort study identified patients with CRC between 2011-2019. Patients treated at regional cancer centers, reporting Edmonton Symptom Assessment System (ESAS) pain scores at diagnosis and 4 months (120-150days) after diagnosis were included. The primary outcome was the highest patient-reported pain score 4 months after diagnosis, categorized as 0 (none), 1-3 (mild), 4-6 (moderate), and 7-10 (severe). Multivariable logistic regression examined factors associated with reporting for moderate-to-severe (ESAS ≥4) pain at 4 months post-diagnosis. **RESULTS:** Of 3,032 patients, 1746 (57.6%) reported pain at diagnosis: 995 (32.8%) mild, 491 (16.2%) moderate, and 260 (8.6%) severe. At 4 months, fewer patients reported pain (51.4%). Of those reporting no pain at diagnosis, only 9% reported moderate-to-severe pain at 4 months, while of those reporting moderate-to-severe and severe pain scores at diagnosis, 64.8% reported lower pain scores at 4 months (Figure1). Multivariable analysis identified baseline pain scores as the factor most strongly associated with patient-reported pain score at 4 months. A baseline reporting of moderate pain presented an OR of 4.08 (95% CI 3.08-5.40), and a score of severe pain had an OR of 8.11 (95% CI 5.88, 11.2). Other factors associated with increased odds of reporting moderate-to-severe pain score at 4 months were stage IV disease (OR 1.89, 95% CI 1.08-3.54), higher material deprivation (OR 1.6, 95% CI 1.02-2.49 for highest quintile, vs lowest), and rectal primary site (OR 1.37, 95% CI 1.11-1.70, vs colon primary). **CONCLUSIONS:** Patient-reported pain score at diagnosis is associated with pain at 4 months after CRC diagnosis. Very few patients with initially no or mild pain scores at reported worsening pain score at 4 months, whereas those initially reporting high pain scores have 4 to 8-fold increase in the odds of reporting moderate-to-severe pain after 4 months. These findings highlight the need for early pain assessment as to provide proactive management strategies and targeted interventions for better symptom management in patients diagnosed with CRC.



Sankey diagram illustrating the proportion of colorectal cancer patients reporting no pain (ESAS = 0), mild pain (ESAS = 1-3), moderate pain (ESAS = 4-6), and severe pain (ESAS ≥ 7) at the time of diagnosis and 4 months post-diagnosis, along with the proportion of patients transitioning between pain categories over time.

Figure 1. Patient-reported pain in colorectal cancer patients at the time of diagnosis and 4 months post-diagnosis.

P39. Identification of Therapeutic Targets for Treatment of Early Onset Colorectal Cancer

Sophia Hernandez, MD[1]; Letizia Todeschini, MD[2]; Tommaso Pollini, MD[3]; Paul Wong[4]; Luis Laurean Aguilar, BS[5]; Guilin Qiao, PhD[6]; Marco Zampese, MD[7]; Shao Tao, PhD[8]; Ajay Maker, MD[9]

[1]University of California, San Francisco, San Francisco, CA, US; [2]University of California, San Francisco, San Francisco, CA, US; [3]University of California, San Francisco, San Francisco, CA, US; [4]University of California, San Francisco, San Francisco, CA, US; [5]University of California, San Francisco, San Francisco, CA, US; [6]University of California, San Francisco, San Francisco, CA, US; [7]University of California, San Francisco, San Francisco, CA, US; [8]University of California, San Francisco, San Francisco, CA, US; [9]University of California, San Francisco, San Francisco, CA, US

INTRODUCTION: Colorectal cancer (CRC) incidence has been rising in individuals under 50 years of age, referred to as early-onset colorectal cancer (EOCRC). Understanding gene expression differences between early and late-onset CRC could provide critical insights into unique biological mechanisms and potential therapeutic targets. **METHODS:** RNA expression profiles were performed on 591 patients with colorectal cancer to assess transcriptomic profiles. Concurrently, DNA alteration profiles were analyzed using Comparative Genomic Hybridization (CGH) Array. Key molecular features, including microsatellite instability (MSI), CpG island methylator phenotype (CIMP), chromosomal instability (CIN), and mutation status of TP53, KRAS, and BRAF, were evaluated. Statistical associations between these variables were assessed using Chi-squared tests. Cox proportional hazards regression was employed to determine median recurrence-free survival (RFS) and overall survival (OS). **RESULTS:** Of 565 patients that were included in this study, 13% had EOCRC. There was no difference in median overall survival or recurrence free survival between patients with Late-onset compared to EOCRC (HR: 0.64 CI 0.3-1.2, p=0.07; HR: 0.69 CI 0.3-1.4, p=0.17, respectively). Intrinsic molecular subtypes of colorectal cancer differed significantly between groups, with a substantial proportion of EOCRC patients exhibiting gene expression patterns linked to reduced immune pathway activation (p<0.05). Late-onset CRC tumors showed increased Wnt pathway expression in 28.9% of cases (p<0.05). There were no significant differences in MSI (p=0.08), KRAS (p=0.32), TP53 (p=0.99), CIMP (p=0.09), or CIN (p=0.52) status between EOCRC and Late-onset CRC patients. None of the EOCRC patients had a BRAF mutation, compared to 11% of Late-onset CRC patients (p<0.05). Additionally, 11% of Late-onset CRC patients with a TP53 mutation harbored a C524G>A mutation. While overall KRAS mutation frequency did not differ significantly between groups (p=0.32), it is critical to note that EOCRC patients had a significantly higher frequency of targetable KRAS mutations (p=0.02). Notably, there was a marked increase in G12D mutations among EOCRC patients (p=0.03), which holds therapeutic implications given the development of targeted therapies for these mutations (Table 1). **CONCLUSIONS:** Our study identifies distinct molecular subtypes in EOCRC, with many patients showing reduced immune pathway activation. While overall KRAS mutation rates were similar, EOCRC had more targetable G12D mutations, highlighting a critical group for targeted therapies and clinical trials.

Table 1. Subset Analysis of KRAS Mutation Target Frequencies

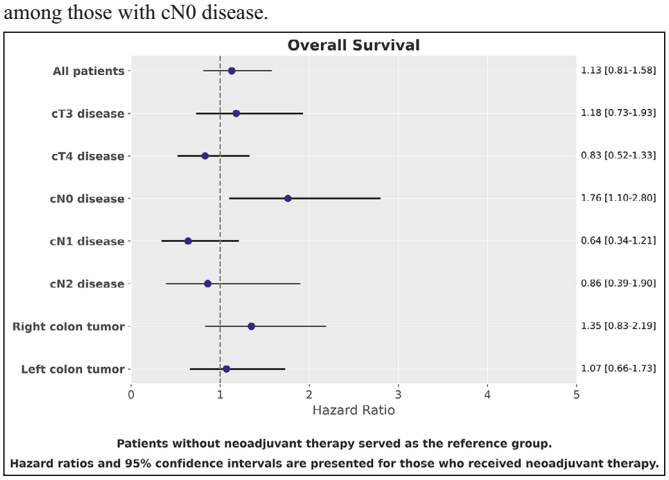
	All patients (n = 213)	Early Onset Colorectal Cancer (n=32)	Late Onset Colorectal Cancer (n=181)	
Variables	*Frequency (%)*	*Frequency (%)*	*Frequency (%)*	*P-Value*
KRAS Mutation				0.32
No	328 (60.3)	39 (54.9)	289 (61.1)	
Yes	216 (39.7)	32 (39.7)	184 (38.9)	
Targetable KRAS mutation frequency				0.02*
G12D (c35G>A)	52 (24.41)	12 (37.5)	40 (22.1)	0.03*
G12R (c35G>C)	7 (3.3)	2 (6.3)	5 (2.9)	0.22
G12C (c35G>T)	22 (10.3)	5 (15.6)	17 (8.8)	0.28
G13D (c38G>A)	27 (12.7)	6 (18.8)	21 (11.1)	0.26

(*) statistically significant

P40. Impact of neoadjuvant chemotherapy on overall survival of patients with early-onset locally advanced colon cancer

Usama Waqar[1]; Courtney L Devin[2]; Terrah J Paul Olson[3]; Patrick Sullivan[4]; Seth A Rosen[5]
[1]Emory University, Atlanta, GA, US; [2]Emory University, Atlanta, GA, US; [3]Emory University, Atlanta, GA, US; [4]Emory University Hospital Midtown, Atlanta, GA, US; [5]Emory University, Atlanta, GA, US

INTRODUCTION: The incidence of early-onset colon cancer is rising. Studies suggest that younger patients with locally advanced colon cancer (LACC) are more likely to receive neoadjuvant chemotherapy (NAC) than those with late-onset disease. However, there is a paucity of evidence on the survival benefit of NAC in this population. This study aims to assess the impact of NAC on overall survival (OS) in patients with young-onset LACC. **METHODS:** Data from the 2006-2021 National Cancer Database were used to identify patients aged ≤49 years diagnosed with cT3-4, N0-2, M0 colon cancer. The exclusion criteria included patients without definitive surgery, those receiving palliative therapy, those with rectosigmoid/ appendiceal tumors, or those who underwent neoadjuvant or adjuvant radiation. Patients who received NAC formed the NAC group, while those who underwent upfront surgery were categorized into the no-NAC group. The primary outcome was OS, with secondary outcomes including R0 resection and 30-day readmission. Kaplan-Meier survival analysis, log-rank test, and multivariable regression were performed to evaluate outcomes overall and within predefined subgroups based on clinical T and N stage and tumor location. **RESULTS:** Of the 8476 patients included, 302 (3.6%) received NAC. NAC use was higher in cT4 vs. cT3 disease (9.5% vs. 1.8%, p<0.001), cN1 vs. cN0 disease (4.9% vs. 2.9%, left vs. right colon cancer (4.1% vs. 2.9%, and clinical stage III vs. stage II disease (4.5% vs. 2.9%, p<0.001). On regression analyses, factors associated with NAC included treatment at academic/research institutions (OR 2.674 [95% CI 1.452-4.922], left colon disease [1.695 [1.243-2.311], cT4 disease (5.320 [4.005-7.066], and cN1 disease (1.730 [1.273-2.352]). Kaplan-Meier analysis showed no significant difference in OS between the NAC and no-NAC groups (p=0.080). Subgroup analysis revealed lower OS in NAC-treated patients with cN0, cT3, or right-sided colon cancer (p<0.005), but improved survival in cT4 patients (p=0.043). Multivariable cox regression showed no significant differences in OS between NAC and non-NAC groups overall or within subgroups (Figure). Patients with cN0 disease managed with NAC had worse OS (HR 1.75 [1.10-2.80]). NAC was not significantly associated with R0 resection or 30-day readmission. **CONCLUSIONS:** NAC may not confer any survival benefit in patients with young-onset LACC. In contrast, NAC may be associated with worse survival among those with cN0 disease.



P41. Incidence and associated factors of neoplastic diagnosis following appendectomy for a clinically abnormal appendix

Tina Gowda[1]; Nicole Aguirre[2]; Karri Hester, MD[3]; Mostafa Mohamed[4]; Philip B. Paty, MD[5]; Martin R. Weiser, MD[6]; Maria Widmar[7]; Jesse Joshua Smith, MD, PhD[8]; Emmanouil P. Pappou, MD, PhD[9]; Iris H. Wei, MD[10]; Julio Garcia-Aguilar, MD, PhD[11]; Andrea Cercek[12]; Michael Foote[13]; Garrett M. Nash, MD[14]; Georgios Karagkounis[15]
[1]Memorial Sloan Kettering Cancer Center, New york, NY, US; [2]Memorial Sloane Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US; [11]Memorial Sloan Kettering Cancer Center, New York, NY, US; [12]Memorial Sloan Kettering Cancer Center, New York, NY, US; [13]Memorial Sloan Kettering Cancer Center, New York, NY, US; [14]Memorial Sloan Kettering Cancer Center, New York, NY, US; [15]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Appendiceal abnormalities, beyond those typical of acute appendicitis, are occasionally detected on imaging or endoscopy, leading to surgical evaluation for a diagnostic appendectomy. How often these reflect an underlying neoplasm, however, remains unclear. This study aimed to determine the incidence and associated findings of neoplastic disease in this setting. **METHODS:** Patients who underwent diagnostic appendectomy following abnormal findings in endoscopy or imaging at a single academic cancer center from 2011 to 2021 were reviewed (IRB#16-134). Patients with preoperative diagnoses of suspected acute appendicitis without associated mass or other "suspicious" lesion, with peritoneal carcinomatosis, or with known malignancy were excluded. Radiographic, biochemical and colonoscopic findings of patients with neoplastic and non-neoplastic appendiceal pathology were compared. **RESULTS:** One hundred thirty-two patients were identified (mean age 68 years, 52% female). Neoplastic disease was found in 68 (52%) cases, including 52 (39%) with low-grade appendiceal mucinous neoplasms (LAMN), 9 (6.8%) adenomas, 4 (3%) neuroendocrine tumors, 2 (1.5%) adenocarcinomas, and 1 (0.7%) spindle cell neoplasm. The remainder (48%) had non-neoplastic pathology. Neoplastic diagnosis was more common in patients with cystic mass (77%, p<0.001), calcifications (75%, p=0.02), or dilated appendix (63%, and less common in patients with thickened wall (28%, p=0.001) or inflammation (6%, p<0.001) on imaging (Figure). Among 104 patients who underwent colonoscopy prior to appendectomy, no findings correlated with the presence of neoplasm. Pre-operative CEA values did not significantly differ between groups. Radiographically occult peritoneal carcinomatosis was not discovered in any case. Following appendectomy, 2 (1.5%) patients with adenocarcinoma required right hemicolectomy and subsequent adjuvant chemotherapy, while the remainder required no additional treatment. **CONCLUSIONS:** Neoplastic pathology is common in patients referred to a cancer center with appendiceal abnormalities on imaging or endoscopy, in particular when a cystic mass, calcifications, and/or a dilated appendix, are present. These findings support the use of diagnostic (and, in most cases, therapeutic) appendectomy in this setting.

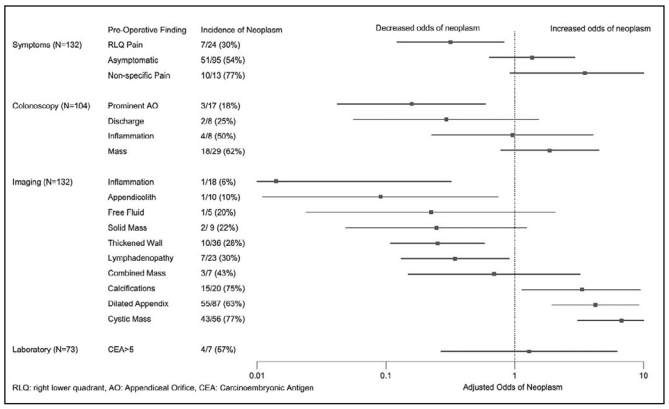


Figure. Association between preoperative findings and incidence of neoplasm in the setting of appendectomy for clinically abnormal appendix.

P42. Institutional experience with total neoadjuvant therapy for locally advanced rectal cancer and proposed role of ctDNA testing

Kristen M Quinn, MD[1]; John C Hulse[2]; Nathaniel P Oberholtzer[3]; Raegan Roy[4]; Colleen Donahue[5]
[1]Medical University of South Carolina, Charleston, SC, US; [2]Medical University of South Carolina, Charleston, SC, US; [3]Medical University of South Carolina, Charleston, SC, US; [4]Medical University of South Carolina, Charleston, SC, US; [5]Medical University of South Carolina, Charleston, SC, US

INTRODUCTION: Improvement in rates of complete clinical response (cCR) after total neoadjuvant therapy (TNT) for locally advanced rectal cancer (LARC) have resulted in widespread utilization of TNT and an increase in

organ preservation. However, regrowth can occur in upwards of 30% of cases requiring strict surveillance, which may be improved with the addition of circulating tumor DNA (ctDNA). The purpose of this study was to share the experience from a single institution's cohort of rectal cancer patients and the utilization of ctDNA in this patient population**. METHODS:** Patients diagnosed with a LARC from 2021 -2024 were reviewed at multidisciplinary tumor board and recommended for TNT if they had cT2/3N+ or cT4Nany, threatened circumferential resection margin and adequate organ function to tolerate therapy. The TNT protocol included a combination of systemic chemotherapy with FOLFOX or XELOX with short- or long-course chemoradiation. Clinical outcomes included clinical response, surgery type, recurrence, and disease-free survival. Patient demographics, tumor characteristics, and laboratory results including ctDNA were analyzed against these outcomes. **RESULTS:** 139/193 patients received TNT. The mean age was 59.3 years, 59.6% of patients were male, and 75.1% of patients were white (19.6% black, 5.2% Hispanic or other). 10.7% had stage 2 disease, 77.7% stage 3, and 11.5% stage 4. Of the patients who went straight to surgery, 97.4% with available ctDNA demonstrated a negative post-operative ctDNA (n= 38/39). For the patients undergoing TNT, after completion, 36.8% demonstrated complete response (CR) or near complete response (nCR), and 50.9% demonstrated incomplete response (IR). After completion of TNT and surgery, 89.5% of patients with available ctDNA demonstrated negative post-operative ctDNA (n=34/38). 21 watch-and-wait approach patients had available ctDNA, and for the 13 without recurrence, 100% of their ctDNA has remained negative. Of the 8 who have developed recurrence, 6/8 demonstrated a positive ctDNA, and 3/6 of those patients were noted to have a positive ctDNA before clinical or imaging evidence of recurrence. **CONCLUSIONS**: TNT for LARC has led to an increase in organ preservation without compromising long term oncologic outcomes. However, the risk of regrowth remains high, thereby requiring strict surveillance. The addition of ctDNA to watch and wait in rectal cancer better allows us to better identify appropriate patients for organ preservation as well as patients at risk of regrowth potentially even earlier than the currently available surveillance modalities.

P43. Investigation of patient-derived organoid models as a system to study individualized therapy for colorectal cancer

Leah Hendrick[1]; Francisca Beato[2]; Rufain Dai[3]; Alexandra Tassielli[4]; Diana Diaz[5]; Esther Jean-Baptiste[6]; Daniel Jeong[7]; Sophie Dessureault[8]; Benjamin Powers[9]; Julian Sanchez, MD[10]; Seth Felder, MD[11]; Kun Jiang[12]; Barbara Centeno[13]; Mokenge Malafa[14]; Jamie K. Teer[15]; Jane Figueiredo[16]; Jennifer B. Permuth[17]; Stephanie L. Schmit[18]; Jason Fleming[19]

[1]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [2]H. Lee Moffit Cancer Center and Research Institute, Tampa, FL, US; [3]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [4]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [5]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [6]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [7]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [8]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [9]University of Maryland School of Medicine-Department of Surgery, Baltimore, MD, US; [10]Moffitt Cancer Center, Tampa, FL, US; [11]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [12]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [13]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [14]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [15]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [16]Samuel Oschin Comprehensive Cancer Institute, Cedars Sinai Medical Center, Los Angeles, CA, US; [17]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [18]Genomic Medicine Institute, Cleveland Clinic, Cleveland, OH, US; [19]UT Southwestern, Dallas, TX, US

INTRODUCTION: Despite advances in screening and early detection, colorectal cancer (CRC) remains a leading cause of morbidity and mortality in the United States. Pre-clinical models to study CRC evolution and sensitivity to systemic therapy are lacking. We sought to develop an experimental platform to study CRC using patient-derived organoids (PDO) from surgically resected specimens to evaluate the viability of these models as a platform to determine tumor-specific sensitivity to systemic therapy. **METHODS:** Tumor specimens were obtained from therapy-naïve patients with non-metastatic tumors of the colorectum. Parallel PDO and PDX models were established, growth rates and time to tumor formation (TTF) were observed, and organoid drug sensitivity assays (ODSA) were performed with standard CRC systemic therapies. Clinical correlation was evaluated between PDO/PDX growth rates, drug sensitivities, and clinical management. **RESULTS:** From January 2020 to November 2023, we obtained tumor tissue samples from 35 patients. The median age was 65 years, 48.6% were female, 62.9% self-identified as non-Hispanic white, and 22.8% had Lynch Syndrome. Stage of disease at harvest was I (11.4%), II (54.3%), or III (31.4%). PDX models were generated for 31/35 (88.6%) samples and PDO models for 25/35 (71%) samples. ODSA was successful for 80.9% of all organoid samples. Five patients undergoing adjuvant chemotherapy had tumors with sensitivity by ODSA to the regimens they received, none of whom had recurrence during the study period. Four patients (25.0%) undergoing adjuvant therapy had disease recurrence, two of whom received an adjuvant regimen with demonstrated tumor resistance by ODSA. **CONCLUSIONS:** This pre-clinical model demonstrates the viability of organoid use for primary tumor sensitivity assessment, and may ultimately allow for development of clinically relevant novel biomarkers and individualized therapies for CRC management.

P44. Patient, provider and institutional factors associated with wait time benchmarks for curative-intent colorectal cancer surgery: a population-based cross sectional study

Adom Bondzi-Simpson, MD, MSc[1]; Tiago Ribeiro, MD, MSc[2]; Alice Zhu, MD, MSc[3]; Andrea Covelli, MD, PhD[4]; Aisha Lofters, MD, PhD[5]; Rinku Sutradhar, PhD[6]; Rebecca A. Snyder, MD, MPH[7]; Callisia Clarke, MD, MS, FSSO[8]; Natalie G Coburn, MD, MPH[9]; Julie Hallet, MD, MSc, FSSO[10]

[1]University of Toronto, Toronto, ON, CA; [2]University of Toronto, Toronto, ON, CA; [3]University of Toronto, Toronto, ON, CA; [4]Sinai Health System - Mount Sinai Hospital, Toronto, ON, CA; [5]University of Toronto, Toronto, ON, CA; [6]University of Toronto, Toronto, ON, CA; [7]MD Anderson Cancer Center, Houston, TX, US; [8]Medical College of Wisconsin, Milwaukee, WI, US; [9]University of Toronto, Toronto, ON, CA; [10]Sunnybrook Health Sciences Centre, Toronto, ON, CA

INTRODUCTION: For quality monitoring, cancer care systems set benchmarks and report wait times (WT) by providers, hospitals, and regions. They are generally reported as a population-level aggregate, potentially overlooking inequalities in achieving benchmarks by sociodemographic or provider factors. We examined WT patterns and factors associated with target benchmarks for colorectal cancer (CRC) surgery. **METHODS:** We conducted a population-based cross-section study of adults undergoing surgery for stage I-IV CRC (2007-2020) using health administrative data in Ontario, Canada. Sociodemographic, provider, and institutional characteristics were examined, adjusting for clinical factors. The primary outcome was "within target wait times", as a benchmark of initiation of treatment within 28 days from date of consent. Hybrid *a priori* and stepwise selection was utilized to select covariates into the model. Multivariable logistic regression accounting for clustering at the surgeon-level assessed the association of each factor with the outcome. **RESULTS:** Of 40,213 patients, 30,693 (76.3%) were operated within target WT. Median WT was 20.2 days (IQR 9-27 days). Among sociodemographic characteristics, increasing age (Odds Ratio, OR 0.80; 95% confidence interval, CI] 0.72-0.89 for age 70-79) was associated with lower odds of within target WT, while rural residence (OR 1.24; 95% CI 1.13-1.36) and neighborhood ethnic diversity (OR 1.22 95% 1.12-1.33 for most diverse) were associated with higher odds of within target WT, after adjusting for cancer site, stage, surgical approach, and receipt of pre-operative therapy. For provider factors, surgery by sub-specialized surgeon (OR 0.84; 95% CI 0.75-0.95), high number of primary care physician visits (OR 0.94; 95% CI 0.89-0.99), and receipt of surgery at a larger institution (OR 0.89; 95% CI 0.83-0.95) were associated with lower odds of surgery within WT target, while surgery by a female surgeon sex (OR 1.12; 95% CI 1.05-1.21) was associated with higher odds of surgery within WT target. **CONCLUSIONS:** Sociodemographic and provider factors associate differently with achieving target WT for CRC surgery. This points towards differences in achieving WT quality target by social determinants of health, and the potential role of providers in doing so. These results outline the need to report WT quality metrics stratified by sociodemographic factors to identify and address inequities. These data also support assessing provider-level practices to improve WT metrics.

Table 1. Patient, provider and hospital factors associated with target wait time benchmarks in multivariable analysis.

Characteristic	Covariate	Multivariable		
		Odds Ratio[1]	95% CI	p-value
Socio-demographic	**Age categories**			
	≤ 50	--	--	--
	51-60	0.881	0.789 - 0.983	**0.023**
	61-70	0.813	0.732 - 0.902	**< 0.001**
	71-80	0.797	0.719 - 0.885	**< 0.001**
	80+	0.813	0.728 - 0.907	**< 0.001**
	Geography			
	Urban	--	--	--
	Rural	1.241	1.134 - 1.357	**< 0.001**
	Neighborhood Ethnic Diversity			
	1st Quintile (Lowest Diversity)	--	--	--
	2nd Quintile	1.073	0.996 - 1.155	0.063
	3rd Quintile	1.099	1.015 - 1.189	**0.019**
	4th Quintile	1.118	1.031 - 1.212	**0.007**
	5th Quintile (Highest Diversity)	1.217	1.117 - 1.325	**< 0.001**
Clinical	**Cancer Site**			
	Colon	--	--	--
	Rectum	0.893	0.839 - 0.952	**< 0.001**
	Stage			
	Stage I	--	--	--
	Stage II	1.446	1.357 - 1.542	**< 0.001**
	Stage III	1.496	1.404 - 1.593	**< 0.001**
	Stage IV	1.715	1.548 - 1.899	**< 0.001**
	Neoadjuvant Therapies			
	Received neoadjuvant chemotherapy	0.751	0.678 - 0.832	**< 0.001**
	Received neoadjuvant radiotherapy	0.581	0.535 - 0.632	**< 0.001**
	Surgical Approach			
	Open surgery	--	--	--
	Laparoscopic	1.084	1.028 - 1.142	**0.003**
Provider	**Surgeon Sex**			
	Male surgeon	--	--	--
	Female surgeon	1.125	1.046 - 1.209	**0.001**
	Surgeon specialty			
	General Surgeon	--	--	--
	Colorectal/Surgical Oncologist	0.843	0.752 - 0.946	**0.004**
	Family doctor			
	< 75th percentile of family doctor visits	--	--	--
	≥ 75th percentile	0.944	0.893 - 0.999	**0.045**
	Hospital bed size			
	< 75th percentile	--	--	--
	≥ 75th percentile	0.888	0.833 - 0.947	**< 0.001**

P45. Right Hemicolectomy vs. Appendectomy for 1.0 – 2.0 cm Appendiceal Neuroendocrine Tumors: A Multi-Center Cohort Experience

Richard M. Miller, BS[1]; Po Hong Tan, MBBS[2]; Hoe Yan Hor[3]; Melody Pi Yin Tu[4]; Arshia Pessaran[5]; Andrew Saleeb[6]; Emily R Thompson[7]; Zhi Ven Fong, MD, MPH, DrPH[8]; Chee-Chee H. Stucky, MD[9]; Sanjay Bagaria, MD[10]; Emmanuel Gabriel[11]; Travis E. Grotz, MD, FSSO[12]; Nabil Wasif, MD, MPH[13]

[1]Mayo Clinic, Phoenix, AZ, US; [2]Mayo Clinic, Phoenix, AZ, US; [3]Mayo Clinic Arizona, Phoenix, AZ, US; [4]Mayo Clinic Arizona, Phoenix, AZ, US; [5]Mayo Clinic Arizona, Phoenix, AZ, US; [6]Mayo Clinic Arizona, Phoenix, AZ, US; [7]Mayo Clinic Arizona, Phoenix, AZ, US; [8]Mayo Clinic Arizona, Phoenix, AZ, US; [9]Mayo Clinic Arizona, Phoenix, AZ, US; [10]Mayo Clinic Florida, Jacksonville, FL, US; [11]Mayo Clinic Florida, Jacksonville, FL, US; [12]Mayo Clinic, Rochester, MN, US; [13]Mayo Clinic, Phoenix, AZ, US

INTRODUCTION: Current NCCN guidelines recommend consideration of right hemicolectomy for appendiceal neuroendocrine tumors (NET) >2 cm and observation for <1 cm. The management of tumors 1-2 cm remains controversial. Our goal was to compare long-term survival and recurrences for patients receiving right hemicolectomy/ileocecectomy versus appendectomy for appendiceal NETs 1-2 cm. **METHODS:** Patients with pathologically confirmed 1.0 - 2.0 cm well-differentiated appendiceal NETs treated across three sites from 1972 to 2024 were included. Primary outcomes examined were tumor recurrence and all-cause mortality post-resection. Predictors of lymph node (LN) metastasis were calculated for patients with LN involvement. **RESULTS:** A total of 53 patients with appendiceal NET 1.0 - 2.0 cm were identified, of which 24 (45.3%) underwent appendectomy only, 28 (52.8%) underwent right hemicolectomy, and one (1.9%) underwent ileocecectomy. Fifteen (28.3%) patients were male, 28 (71.7%) were women, and the median age at diagnosis was 40.1 years. Of patients with known tumor pathology grades, 38 (95.0%) were Grade 1 and two (5.0%) were Grade 2. The median length of follow-up was 6.8 years (IQR 3.3 – 12.5). In patients undergoing hemicolectomy, the rate of nodal positivity was 17.9%. Tumor size >1.5 cm vs <1.5 cm, T3/T4 stage, or LVI were not associated with node positivity. There was no difference in all-cause mortality between patients undergoing appendectomy or right hemicolectomy. Similarly, node positivity was not associated with adverse long-term survival. No recurrence was identified in any patient with a median length of follow up of 6.8 years. **CONCLUSIONS:** Resection with right hemicolectomy/ileocecectomy after appendectomy did not improve survival for patients with 1.0 - 2.0 cm appendiceal NETs. There was no recurrence in patients undergoing appendectomy only, and node positivity was not associated with worse survival. The benefit of right hemicolectomy in this patient population remains unclear.

P46. Risk of Residual Tumor Following Removal of a Malignant Colorectal Polyp with High-Risk Features

Thikhamporn Tawantanakorn, MD[1]; Thikhamporn Tawantanakorn, MD[2]; Ayyuce Begum Bektas, PhD[3]; Matthew Hill[4]; Maria Widmar[5]; Georgios Karagkounis, MD[6]; Iris H. Wei, MD[7]; Jesse Joshua Smith, MD, PhD[8]; Emmanouil P. Pappou, MD, PhD[9]; Garrett M. Nash, MD[10]; Philip B. Paty, MD[11]; Julio Garcia-Aguilar, MD, PhD[12]; Mithat Gonen, PhD[13]; Martin R. Weiser, MD[14]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6], US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US; [11]Memorial Sloan Kettering Cancer Center, New York, NY, US; [12]Memorial Sloan Kettering Cancer Center, New York, NY, US; [13]Memorial Sloan Kettering Cancer Center, New York, NY, US; [14]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: National guidelines recommend surgery when pathology analysis of a malignant colorectal polyp reveals high-risk features: positive margin/piecemeal resection (PM/PR), lymphovascular/perineural invasion (LVI/PNI), poor differentiation (PD), or tumor budding (TB). However, some patients choose to avoid surgery, with its morbidity and quality-of-life implications, despite the risk of residual disease. **METHODS:** This single-center cohort study determined the rates of luminal or lymph node disease and distant metastasis in patients who underwent surgery and patients who underwent observation following removal of a malignant colorectal polyp with high-risk features between 2015 and 2022. **RESULTS:** Of 336 patients who underwent a malignant polypectomy in the colon (n = 226) or rectum (n = 110), 312 had a PM/PR, 96 had LVI/PNI, 47 had PD, and 45 had TB; 208 patients (62%) underwent surgery, and 128 (38%) underwent observation. Patients with a malignant polyp in the rectum were more likely to undergo observation than patients with a malignant polyp in the colon (79 [72%] vs. 49 [22%] patients; $P < 0.01$). In the surgery group, 19 patients (9%) had residual luminal disease, 39 patients (19%) had lymph node disease, and 5 patients (2%) had distant metastasis. In the observation group, disease was identified in 14 patients (11%): regrowth in the lumen, 7 patients (9%); regrowth in lymph nodes, 5 patients (6%); distant metastasis, 1 patient (1%); regrowth with distant metastasis, 1 patient (1%). The 12 cases of regrowth (lumen and lymph node) were salvaged: resection, 4 patients; local excision, 2 patients; chemoradiotherapy, 6 patients. **CONCLUSIONS:** The risk of residual disease following removal of a malignant colorectal polyp with high-risk features is considerable. Patients concerned about the morbidity of surgery and postsurgery quality of life should be counseled about this risk, as well as the availability of effective salvage options.

High-risk features (HRF)	Surgery (n = 208)	Observation (n = 128)	Luminal/LN disease at surgery (n = 51; 25%)	Luminal/LN regrowth during observation (n = 12; 9.4%)	Distant metastasis (n = 7; 2.1%)
PM/PR (n = 312; 93%)	193	119	49 (25%)	12 (10%)	7 (2.2%)
LVI/PNI (n = 96; 29%)	56	40	16 (29%)	3 (7.5%)	3 (3.1%)
PD (n = 47; 14%)	33	14	11 (33%)	0	1 (2.1%)
TB (n = 45; 13%)	20	25	5 (25%)	1 (4.0%)	1 (2.2%)
1 HRF (n = 215; 64%)	141	74	31 (22%)	8 (11%)	4 (1.9%)
2 HRF (n = 78; 23%)	39	39	11 (28%)	4 (10%)	1 (1.3%)
3 HRF (n = 35; 10%)	25	10	8 (32%)	0	2 (5.7%)
4 HRF (n = 6; 1.8%)	2	4	1 (50%)	0	0

P47. Sacral Periosteal Elevation as Alternative Surgical Approach to Sacrectomy in Locally Advanced Primary and Recurrent Rectal Cancer with Posterior Extension

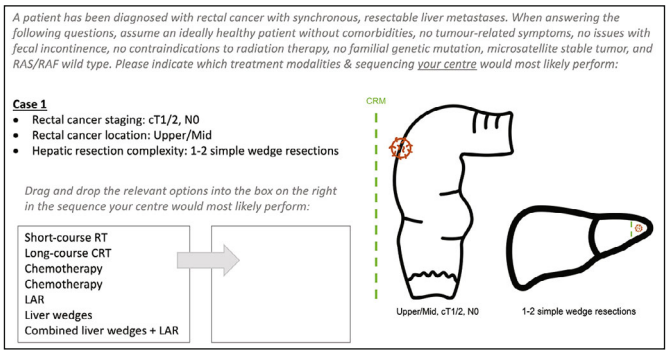
Erika M Schmitz, MD, FRCSC[1]; Raphaele Charest-Morin[2]; Andrew McFadden[3]; Nicolas Dea[4]; Elizaveta Vasilyeva[5]; Jason Park[6]
[1]University of British Columbia, Vancouver, BC, CA; [2]Vancouver General Hospital, Vancouver, BC, CA; [3]Vancouver General Hospital, Vancouver, BC, CA; [4]Vancouver General Hospital, Vancouver, BC, CA; [5]Vancouver General Hospital, Vancouver, BC, CA; [6]Vancouver General Hospital, Vancouver, BC, CA

INTRODUCTION: Pelvic exenteration with en-bloc sacrectomy is performed for locally advanced and recurrent rectal tumors with posterior extension. Sacral periosteal elevation (SPE) is a recently described variation on sacrectomy that involves sacral cortex osteotomy with preservation of bone and uninvolved nerve roots. The procedure allows for extending dissection to otherwise unresectable spinal levels, while minimizing morbidity and preserving completeness of resection. **METHODS:** Patients who underwent SPE for primary and recurrent locally advanced rectal adenocarcinoma with posterior extension were reviewed. The primary outcome is the obtention of negative pathologic margins. Secondary outcomes include intra-operative blood loss, perioperative complications, and survival. **RESULTS:** Nine patients (mean age 59) underwent SPE at a single institution from 2021-2024 for primary rectal adenocarcinoma (n=2) and locally recurrent disease (n= 7). Two patients underwent S5 sacrectomy after SPE (SSPE). Periosteal elevation levels included S2 (n=1), S3 (n=1), S4 (n=6) and S5 (n=1). All patients had negative posterior pathologic margins. Two patients had microscopically positive lateral side wall margins. Median blood loss was 2 L [IQR 1.75-2.80] for SPE patients and 2.7 L (range 0.98 – 4.50 L) for SSPE patients. There were no deaths within 90 days. The median length of stay was 27 days [IQR 16-49.5] for SPE patients, and 63 days (range 57-69) for SSPE patients. One patient had no complications, 3 had minor post-operative complications, and 5 had major post-operative complications owing to flap dehiscence, enteroatmospheric fistula and pelvic abscess. Two patients had local recurrences at 1.8 and 10.5 months, 2 had progression of indeterminate lung nodules at 2 and 6.3 months, and 3 patients had distant recurrences (mean 9.7 months, range 2.9-13.3 months). **CONCLUSIONS:** Sacral periosteal elevation is a novel approach to sacral resection that is associated with complete pathologic resection and acceptable short-term outcomes in select patients.

P48. The contemporary management of rectal cancer with resectable synchronous liver metastases: a national survey of Canadian cancer centres

Ashwin Rao, MD Candidate[1]; Maria Kalyvas[2]; Brooke E Wilson[3]; Sunil Patel[4]; Ameer Farooq[5]; Sean Bennett[6]
[1]Queen's University, School of Medicine, Kingston, ON, CA; [2]Queen's University, Kingston, ON, CA; [3]Queen's University, Kingston, ON, CA; [4]Queen's University, Kingston, ON, CA; [5]Queen's University, Kingston, ON, CA; [6]Queen's University, Kingston, ON, CA

INTRODUCTION: Various multimodal strategies exist for patients with rectal cancer (RC) and synchronous liver metastases (SLM), including surgery, chemotherapy, and radiation. The optimal sequence remains uncertain. This study aimed to examine current standards of management across Canadian cancer centres. **METHODS:** One surgeon from all 27 Canadian centres that deliver comprehensive care for patients with RC with SLM was invited to complete an online survey consisting of 12 clinical case scenarios with varying rectal tumour location, clinical T and N stage, and liver resection complexity. Respondents listed the various treatment options, in sequence, that their centre would typically recommend. Descriptive statistics were calculated to summarize practice patterns. **RESULTS:** A total of 21 centres participated (78% response rate), with 76% having a combined multidisciplinary cancer conference attended by both hepatobiliary and colorectal surgeons. Adjuvant chemotherapy was recommended for all patients by 57%, while 43% recommended selective use for high-risk features. Among all responses where radiation was indicated (85%), chemoradiotherapy (CRT) was chosen in 56% and short course radiotherapy (RT) in 44%. Conversely, RT was preferred (88%) over CRT (12%) for upper rectal, cN0 tumours. In cases requiring low anterior resection (LAR) and wedge resections, 81% favored combined surgeries. For abdominoperineal resection (APR) and wedge resections, 55% preferred combined surgery, while 41% preferred staged, liver first procedures. For cases requiring right hepatectomy, 96% preferred staged operations, with 75% liver first. For patients with complete clinical response to neoadjuvant therapy, 57% have previously offered a non-operative strategy for the rectal primary, and 33% were open to adopting this approach in the future. For cases requiring two-stage hepatectomy, the most common first treatment was chemotherapy (68%). **CONCLUSIONS:** Our study provides a foundation for future guideline development to standardize multimodal treatment. Despite randomized trials demonstrating no overall survival benefit, adjuvant chemotherapy remains widely used, with over half of surgeons favoring its use for all patients. Radiation use is strongly linked to tumour location and nodal status, with CRT generally being preferred over RT. Combined operations were reserved for minor hepatectomies, while staged, liver-first approach preferred for major hepatectomies. Future prospective data is required to investigate outcomes associated with all treatment options.



P49. True Incidence of Appendiceal Neoplasms in Patients Presenting with Complicated Appendicitis: A Call for a Revised Management Algorithm

Laleh Foroutani[1]; Joshua Myszewski[2]; Shreyas Kiran[3]; Han Yin[4]; Suwayda Ali[5]; Amir Ashraf Ganjouei[6]; Jane Wang[7]; Bahaa Aburayya[8]; Yusuf Althawadi[9]; Kenzo Hirose, MD[10]; Eric K. Nakakura, MD, PhD[11]; Carlos U. Corvera, MD[12]; Adnan Alseidi[13]; Mohamed A. Adam, MD[14]
[1]University of California San Francisco, San Francisco, CA, US; [2]University of California, San Francisco, San Francisco, CA, US; [3]University of California, San Francisco, San Francisco, CA, US; [4]University of California San Francisco, San Francisco, CA, US; [5]University of California, San Francisco, San Francisco, CA, US; [6]University of California San Francisco, San Francisco, CA, US; [7]University of California San Francisco, San Francisco, CA, US; [8]UCSF, San Francisco, CA, US; [9]UCSF, San Francisco, CA, US; [10]University of California, San Francisco, San Francisco, CA, US; [11]University of California, San Francisco, San Francisco, CA, US; [12]University of California, San Francisco, San Francisco, CA, US; [13]University of California San Francisco, San Francisco, CA, US; [14]University of California, San Francisco, San Francisco, CA, US

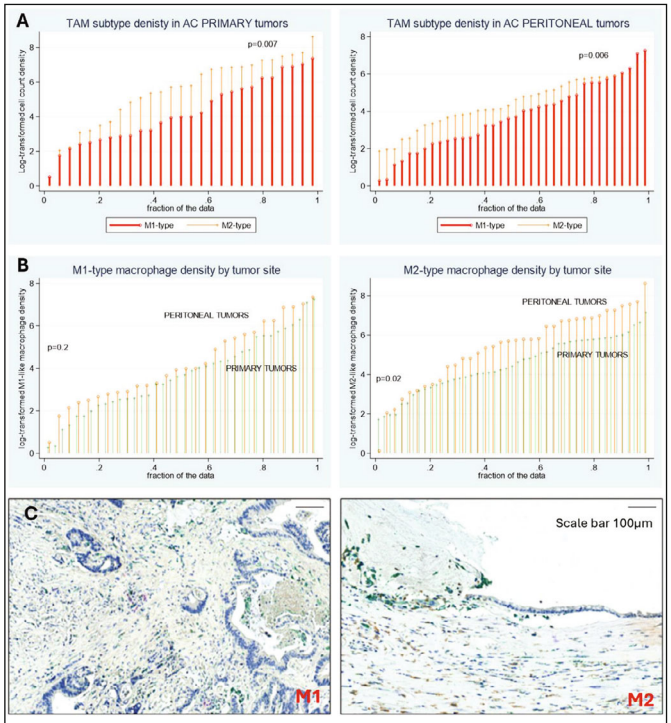
INTRODUCTION: Previous studies have demonstrated a link between complicated appendicitis and underlying appendiceal neoplasms; however, the reported incidence rates of appendiceal neoplasms vary widely (3%-28%). Most published data are limited to surgical cohorts, which may not capture all patients presenting with complicated appendicitis. We aimed to determine the rate of appendiceal neoplasms among patients diagnosed radiologically with complicated appendicitis. **METHODS:** All adults presented with acute appendicitis at a large tertiary center were identified (2010-2014). Of whom, patients diagnosed radiographically with complicated appendicitis (gangrene, abscess, phlegmon, mucocele, or perforation) were included. Patients with a prior history of appendiceal neoplasm were excluded. To ensure diagnostic accuracy, an expert surgeon reviewed radiologic images with uncertain findings. The neoplasm rate was calculated based on subsequent pathology reports. Multinomial logistic regression was performed to evaluate the association between potential risk factors, radiologic findings, and the likelihood of neoplasm. **RESULTS:** A total of 1,690 patients diagnosed with acute appendicitis, with 23% (N=387) presenting with complicated appendicitis. Of the complicated appendicitis cases, 47% had perforated appendicitis, 42% abscess, 5% mucocele, 14% phlegmon, and 2% gangrenous appendicitis. The rate of appendiceal neoplasms among patients with complicated appendicitis was 16%. The most common tumor types included mucinous neoplasms (53%), followed by neuroendocrine tumors (19%) and adenocarcinomas (9%). The incidence of appendiceal neoplasms varied significantly based on radiologic findings, with the highest rate of neoplasms was observed in cases with mucocele (64%), followed by phlegmon (21%), abscess (19%), and perforated appendicitis (9%). Multinomial logistic regression analysis showed that older age, higher BMI, larger appendiceal size, and lymph node involvement were significantly associated with a

higher likelihood of neoplasm. **CONCLUSIONS:** This large study, which included both surgical and non-surgical patients, suggests a concerning rate of appendiceal neoplasms (16%) among those presenting with complicated appendicitis. Given the growing interest in non-operative management of complicated appendicitis, management algorithms should account for the elevated risk of underlying appendiceal neoplasms in these patients.

P50. Tumor-Associated Macrophage Subsets in Appendiceal Cancer

Christopher Sherry, DO[1]; Neda Dadgar[2]; Hyun Park[3]; Chelsea Knotts[4]; Rosie Blodgett[5]; Ali Zaidi[6]; Ashten Omstead[7]; Kunhong Xiao[8]; Erin Grayhack[9]; Vera Donnenberg[10]; Albert Donnenberg[11]; David Bartlett[12]; Patrick Wagner[13]
[1]Allegheny Health Network, Pittsburgh, PA, US; [2]Cleveland Clinic Foundation, Cleveland, OH, US; [3]Allegheny Health Network, Pittsburgh, PA, US; [4]Allegheny Health Network, Pittsburgh, PA, US; [5]Allegheny Health Network, Pittsburgh, PA, US; [6]Allegheny Health Network, Pittsburgh, PA, US; [7]Allegheny Health Network, Pittsburgh, PA, US; [8]Allegheny Health Network, Pittsburgh, PA, US; [9]Allegheny Health Network, Pittsburgh, PA, US; [10]Allegheny Health Network, Pittsburgh, PA, US; [11]Allegheny Health Network, Pittsburgh, PA, US; [12]Allegheny Health Network, Pittsburgh, PA, US; [13]Allegheny Health Network, Pittsburgh, PA, US

INTRODUCTION: The appendiceal cancer (AC) tumor microenvironment (TME) remains understudied due to the rarity of AC and the diversity of AC its histologic subtypes. Insight into the TME could uncover key mechanisms of tumor development and new avenues for targeted therapeutic intervention. Tumor-associated macropahges (TAM) are a key cellular element of the TME across a number of tumor types, and in this study we extended previous work on lymphocyte density in AC by characterizing TAM subsets and their potential association with clinicopathologic features and survival. **METHODS:** We employed immunohistochemistry and automated image analysis software (Bond Aperio) to analyze M1-like (dual CD86+/CD68+ stain) and M2-like (dual CD206+/CD68+ stain) TAMs in 78 archival formalin-fixed, paraffin embedded tissue samples from patients who underwent surgery for AC. Cell densities were tested for association with patient clinical and pathologic variables, including age, sex, grade, tumor site (primary vs. peritoneal metastases), disease extent (peritoneal carcinomatosis index/PCI), and oncologic outcome (progression-free/PFS and overall/OS survival). Subgroup comparisons were performed with log-transformed cell counts using linear regression and Cox regression for survival. **RESULTS:** Both M1- and M2- like macrophages were abundant in AC. TAM densities did not vary significantly with patient age or sex and showed no association with tumor grade. M2-like TAMs were more prevalent at higher concentrations than M1-like TAMs in primary and peritoneal tumors (mean 417 [95%CI 271, 561] vs 178 [95%CI 102, 254] cells/mm2, p<0.0001), and M2 TAM density was higher in peritoneal metastases relative to primary tumors (p=0.02). Both M1 and M2 subtypes were associated with increased disease extent/PCI (p=0.02 and p=0.03 for M1 and M2, respectively). A trend toward improved overall survival was seen in patients with the highest tertile of M2-like macrophage density (HR=0.27, p=0.06), in spite of a higher risk of progression (HR 2.67, p=0.05). **CONCLUSIONS:** TAMs are prevalent in the TME of AC, with M2-type TAMs being more abundant in peritoneal vs. primary tumors, and are associated with increased burden of disease. A subset of high-M2-density was associated with shorter PFS but prolonged OS, raising the possibility that these cells typify a locally aggressive but biologically indolent subset of AC cases. Future research will be needed to validate and mechanistically define these early findings.



(A) M2-like TAMs are more abundant than M1-like TAMs in primary and peritoneal tumors, with significant differences in metastases (p=0.006). (B) M2-like TAM density is higher in peritoneal metastases (p=0.02), while M1-like TAMs show no significant site difference (p=0.2). (C) Immunohistochemical images of M1-like (left) and M2-like (right) TAMs. Scale bar: 100 µm.

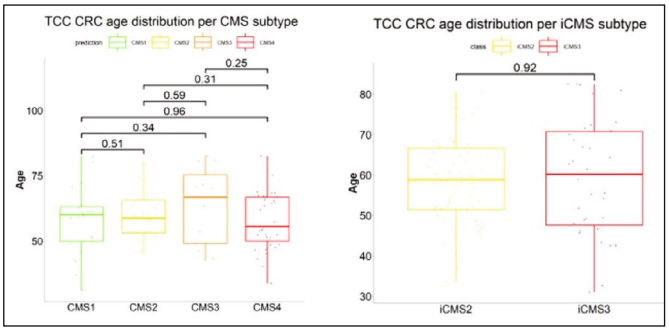
Figure 1. TAM density and distribution in appendiceal cancer.

P51. Unbiased transcriptomic analysis of primary early-onset vs average-onset colorectal cancer.

Ryan T Heslin, MD[1]; Alessandro La Ferlita, Ph.D[2]; Samantha Ruff, MD[3]; Zachary Whitham, MD[4]; Nilesh Verma, MD[5]; Huocong Huang, MD PhD[6]; Alex Kim, MD, PhD[7]
[1]UT Southwestern, Dallas, TX, US; [2]The Ohio State University Medical Center, Columbus, OH, US; [3]University of Virginia, Charlottesville, VA, US; [4]UT Southwestern, Dallas, TX, US; [5]UT Southwestern, Dallas, TX, US; [6]UT Southwestern, Dallas, TX, US; [7]UT Southwestern, Dallas, TX, US

INTRODUCTION: Colorectal cancer is the 2nd leading cause of cancer death in the US. Despite the decline in diagnosed average-onset colorectal cancer (AOCRC) patients over recent decades, the incidence of early onset of colorectal cancer (EOCRC) continues to rise. Previous genomic studies examining the potential germline mutations for EOCRC demonstrate mixed results. However, transcriptomic examination of the EOCRC compared to AOCRC remains limited. We hypothesized that EOCRC may present with enrichment in aggressive molecular signatures consistent with Consensus Molecular Subtype (CMS)4 and iCMS3 subtypes. To understand the molecular mechanism behind EOCRC, we performed an unbiased RNA-Seq analysis across age groups of 32-82 in 95 patients. **METHODS:** We identified 95 patients from the Total Cancer Care network who were diagnosed with colorectal cancer between the ages of 32-82 and underwent RNA-sequencing of their primary tumors. We collected unnormalized raw-count RNA-Seq data from these patients, along with their clinical information. Differences in sequencing depth across samples were scaled using the Reads Per Million (RPM) formula. The scaled reads in RPM were then utilized to assess the CMS classification of each patient through two distinct approaches: the R package CMScaler and a deconvolution analysis using SpatialDecon with the iCMS gene signature. Differences in age at the sample collection across patients with different CMS classifications were assessed by performing two-tailed unpaired T-tests. Additionally, differential expression analysis between EOCRC and AOCRC patients, defined by the upper and lower quartiles of the patients' ages at the sample collection, was conducted using the LIMMA R package. **RESULTS:** Clinicopathologic assessment of the primary tumors

revealed left-sided tumors with poorly differentiated phenotype, consistent with previous reports in EOCRC. Differential gene expression analysis between EOCRC and AOCRC demonstrated no significant differences. Stratification of transcriptomic data by decades also did not reveal any significant differences. Furthermore, there were no differences in CMS or iCMS classifications between different age groups. **CONCLUSIONS:** The RNA-Seq analysis comparing EOCRC and AOCRC did not identify any differential gene expression patterns. Additionally, no differences were observed in CMS or iCMS classifications. These findings suggest that EOCRC and AOCRC share similar tumor biology based on molecular phenotypes implying that environmental factors triggers the same disease process earlier. This underscores the importance of earlier colonoscopy screenings.



P52. Urinary Volatile Organic Compound Metabolites and Colorectal Cancer Incidence: Pilot Results from a Clinical Case-Control Study

Sandy Kavalukas[1]; Allie Jin[2]; Pawel Lorkiewicz[3]; Tatiana Krivokhizhina[4]; Luis Salazar Guzman[5]; Natalie DuPre[6]

[1]University of Louisville School of Medicine, Louisville, KY, US; [2]University of Louisville School of Medicine, Louisville, KY, US; [3]University of Louisville, Louisville, KY, US; [4]University of Louisville, Louisville, KY, US; [5]University of Louisville, Louisville, KY, US; [6]University of Louisville, Louisville, KY, US

INTRODUCTION: Workplace exposure to Volatile Organic Compounds (VOCs) has been shown to have a positive association with Colorectal Cancer (CRC) incidence, but there has been little investigation into the role of ambient exposures to environmental toxins that may contribute to elevated CRC rates. In prior work, we have identified areas with high ambient VOCs that correlate with "hotspots" of high CRC incidence. Until now, the impact of these toxins in individual-level biospecimens and CRC has not been explored. **METHODS:** A clinical case-control pilot study was initiated in August 2023. Patients undergoing procedures related to CRC cancer or screening were enrolled, completing a detailed questionnaire and providing urine samples. Urinary VOC metabolites (VOCm) in 80 participants (49 Controls, 31 CRC Cases) were measured including three Benzene metabolites (MU, PPMA, PMA), three 1,3-Butadiene metabolites (DHBMA, MHBMA1, MHBMA3), and one derived from Toluene (BMA). Four VOCm (PPMA, PMA, MHBMA3) had 36%-61% of the participants below the limit of detection (LOD) and were dichotomized into below or above the LOD. MU, BMA, and DHBMA were creatinine normalized and then compared as "low" or "high" based on the median value. Logistic regression adjusted for age, gender, family history, and smoking was used to estimate Odds Ratios (ORs) of CRC with 95% Confidence Intervals (CI) comparing high vs low VOC exposure. **RESULTS:** Those with high 1,3-Butadiene-derived MHBMA3 levels had 3.75 (95% CI 1.45, 9.67) times higher odds of having CRC compared to those with low levels, that was attenuated after adjusting for covariates (OR=3.06 95% CI 1.06, 8.80; Table 1). Similarly, the adjusted OR of CRC were elevated for Benzene PMA (OR=2.51 95%CI 0.87, 7.30). Toluene BMA, Benzene MU, Benzene PPMA, Butadiene DHBMA, and Butadiene MHBMA1 did not show a strong association with CRC. **CONCLUSIONS:** Our data suggests that Benzene PMA and 1,3-Butadiene MHBMA3 are higher in CRC patients, and patients without cancer in the "hotspots" have higher levels of VOCs, but no analysis was run due to small sample size. While CRC tumors excrete other VOCs, the available data is vague and nonspecific, and our data may capture environmental VOC exposure and/or tumor secretion. Future research comparing tumor and urinary levels will shed light on urinary VOC sources in this population.

Table 1. The Odds Ratios (95% Confidence Intervals) of Colorectal Cancer by binary categories of benzene, toluene and butadiene VOCs

	Controls/Cases	Crude	Model 1[a]
Benzene MU	**49/31**		
Below Median^	25/13	REF	REF
Above Median^	24/18	1.442 (0.582, 3.572)	0.978 (0.344, 2.783)
Benzene PPMA	**49/31**		
Below LOD	32/17	REF	REF
Above LOD	17/14	1.550 (0.618, 3.890)	1.207 (0.387, 3.758)
Benzene PMA	**49/31**		
Below LOD	33/14	REF	REF
Above LOD	16/17	2.504 (0.992, 6.319)	2.51 (0.869, 7.296)
Toluene BMA	**49/31**		
Below Median*	24/14	REF	REF
Above Median*	25/17	1.166 (0.473, 2.874)	1.752 (0.605, 5.074)
Butadiene DHBMA	**49/31**		
Below Median#	24/15	REF	REF
Above Median#	25/16	1.024 (0.416, 2.518)	0.966 (0.349, 2.676)
Butadiene MHBMA1	**49/31**		
Below LOD	17/12	REF	REF
Above LOD	32/19	0.841 (0.331, 2.136)	0.972 (0.334, 2.825)
Butadiene MHBMA3	**49/31**		
Below LOD	33/11	REF	REF
Above LOD	16/20	3.750 (1.454, 9.672)	3.058 (1.062, 8.799)

[a]Model 1 is adjusted for age at diagnosis (years), gender (man, woman), family history of CRC, and ever smoking status (current and past smokers or never smoker).
^Median for MU: 16.8 ng/mg creatinine
*Median for BMA: 16.7 ng/mg creatinine
#Median for DHBMA: 73.0 ng/mg creatinine

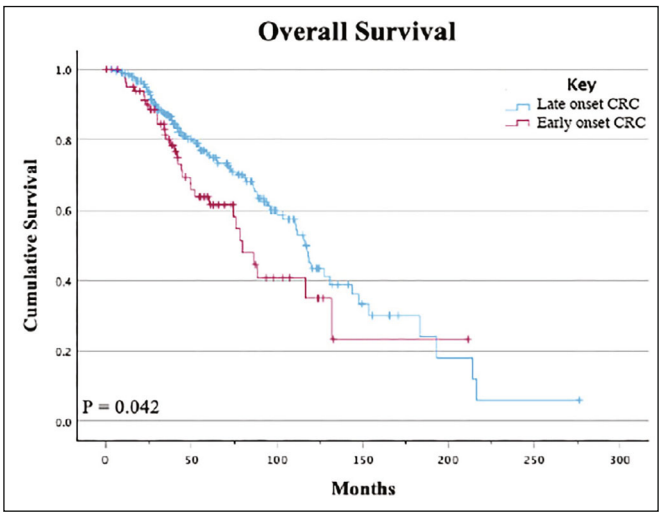
P53. Worse Overall Survival in Early vs Late Onset Colorectal Cancer Patients with Liver Metastases

Judy Li, MD[1]; Giacomo Waller, MD[2]; Yunyun Qin, MBBS[3]; Allen T Yu, MD, PhD[4]; Thomas M Li, MD[5]; Deborah M Li, BA[6]; Rami Srouji, MD[7]; Camilo Correa-Gallego, MD[8]; Spiros Hiotis, MD, PhD[9]; Ganesh Gunasekaran, MD[10]; James O Park, MD[11]; Noah A. Cohen, MD[12]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, US; [2]Icahn School of Medicine at Mount Sinai, New York, NY, US; [3]Icahn School of Medicine at Mount Sinai, New York, NY, US; [4]Icahn School of Medicine at Mount Sinai, New York, NY, US; [5]Icahn School of Medicine at Mount Sinai, New York, NY, US; [6]Stony Brook School of Medicine, Stony Brook, NY, US; [7]Icahn School of Medicine at Mount Sinai, New York, NY, US; [8]Icahn School of Medicine at Mount Sinai, New York, NY, US; [9]Icahn School of Medicine at Mount Sinai, New York, NY, US; [10]Icahn School of Medicine at Mount Sinai, New York, NY, US; [11]Icahn School of Medicine at Mount Sinai, New York, NY, US; [12]Icahn School of Medicine at Mount Sinai, New York, NY, US

INTRODUCTION: Almost 50% of patients with colorectal cancer develop liver metastases (CRLM). The incidence of early onset colorectal cancer (EOCRC), defined as <50 years of age at time of diagnosis, is increasing. In this study, we aim to explore the prognosis of early vs late onset colorectal cancer patients with CRLM who receive curative-intent treatment. **METHODS:** A retrospective study was conducted to assess clinical outcomes in patients with CRLM presenting with EOCRC compared to those with late onset colorectal cancer (LOCRC). All patients underwent surgical resection and/or ablation between 2009 and 2024 at a tertiary care center. Groups were defined by patient age at the time of diagnosis of the primary tumor < 50 years versus ≥ 50 years. Demographics, tumor characteristics, and treatment modalities were compared between groups using Chi-square, independent samples t-test, and Mann-Whitney U-test. Survival outcomes were assessed using Kaplan-Meier. **RESULTS:** 342 patients met inclusion criteria. There were 85 (24.9%) EOCRC patients, with a median age at diagnosis of 44 years versus 63 years in the LOCRC group. EOCRC patients had fewer major medical comorbidities. EOCRC patients had a smaller proportion of right-sided (15.9% vs 29.6%, P=0.049) tumors. Both groups had similar rates of synchronous metastases, median size and number of metastases. EOCRC patients had higher rates of node-positive disease (75.6% vs 58.8%, P=0.010) and Fong Clinical Risk Scores 3-5 (57.0% vs 39.7%, P=0.009). Both underwent similar operative management with no differences in morbidity, but more EOCRC patients received neoadjuvant therapy (82.4% vs 66.1%, P=0.017). There were no significant differences in *RAS/RAF* (37.6% in EOCRC vs 34.2%, P=0.669) or *TP53* (25.9% vs 34.6%, P=0.98) mutational status or microsatellite instability (stable in 74.1% in EOCRC vs 69.3%, P=0.523). Both intra- (46.5% in EOCRC vs 50.6%, P=0.535) and extra-hepatic (47.7% in EOCRC vs 38.1%,

P=0.129) recurrences occurred at similar rates, with no significant differences in post-recurrence treatments received. Patients with CRLM and EOCRC had significantly worse overall survival, with a median time of 80 months versus 116 months (P=0.042). **CONCLUSIONS:** Despite similar clinical, pathologic, and genetic features, fewer comorbidities, and receiving similar medical and surgical treatments, EOCRC patients had worse median overall survival than LOCRC patients. High risk Fong Clinical Risk Scores were more common in the EOCRC group, who also received neoadjuvant therapy at higher rates. Additional research is needed to understand the differences in survival.

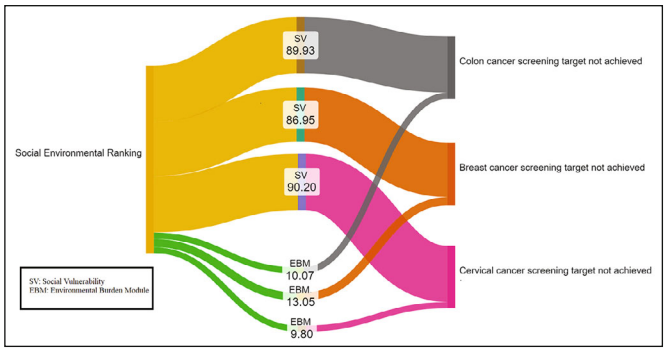


P54. Association of Socio-Environmental Burden and Inequality with Cancer Screening and Mortality

Shahzaib Zindani[1]; Mujtaba Khalil[2]; Zayed Rashid[3]; Abdullah Altaf[4]; Selamawit Woldesenbet[5]; Tim Pawlik[6]

[1]The Ohio State University, Columbus, OH, US; [2]The Ohio State University, Columbus, OH, US; [3]The Ohio State University, Columbus, OH, US; [4]The Ohio State University, Columbus, OH, US; [5]The Ohio State University, Columbus, OH, US; [6]The Ohio State University, Columbus, OH, US

INTRODUCTION: Social and environmental injustice may influence accessibility and utilization of health resources, as well as effect outcomes of patients with cancer. We sought to assess the impact of socio-environmental inequalities on cancer screening rates, screening targets, and mortality rates for breast, colon, and cervical cancer. **METHODS:** Data on national census-tract level cancer screening and environmental justice index social and environmental ranking (SER) was extracted from the Centers for Disease Control and Prevention (CDC) PLACES and Agency for Toxic Substances Disease Registry, respectively. County level data for cancer mortality rates were extracted using CDC WONDER. SER was divided into low, moderate, and high (high denoting poorer conditions). Screening targets were defined by *Healthy People 2030* initiative as 80.3%, 68.3%, and 79.2% for breast, colon, and cervical cancers. Logistic regression analyzed association between SER tertiles and achievement of cancer screening targets. **RESULTS:** Among 59,667 census tracts, 14,659 were classified as 'low', 29,534 as 'moderate', and 15,474 as 'high' relative to SER. Screening targets were achieved by 31.1% (n=18,541), 16.2% (n=9,669), and 88.6% (n=52,839) of tracts for colon, breast, and cervical cancers, respectively. Compared with tracts that were low SER, tracts with higher SER were less likely to meet screening targets for colon (moderate OR: 0.33, 95%CI: 0.32-0.34; high OR: 0.06, 95%CI: 0.05-0.06), breast (moderate, OR: 0.51, 95%CI: 0.48-0.53; high, OR: 0.24, 95%CI: 0.22-0.26), and cervical (moderate, OR:0.19, 95%CI: 0.17-0.22; high, OR: 0.05, 95%CI: 0.04-0.06) cancer (all p<0.001). Moreover, median mortality rates for colon [16.7% (IQR: 13.9-21.0) vs. 21.0 (IQR: 16.7-27.2)], breast [13.4 (IQR: 10.8-16.1) vs. 14.75 (IQR: 12.6-19.9)], and cervical [1.0 (IQR: 0.9-1.0) vs. 1.6 (IQR: 1.3-2.0)] cancers were higher for counties with high versus low SER (all p<0.05). In assessing the different components of SER, failure to achieve screening targets was largely attributable to social vulnerability rather than environmental burden (10.07% vs. 89.93% for colon; 13.05% vs. 86.95% for breast, and 9.80% vs. 90.20% for cervical cancers) (Figure 1). **CONCLUSIONS:** Social and environmental factors adversely impact both cancer screening rates, as well as mortality. There is a need to implement policies to reduce environmental injustice through measures like accessible and equitable cancer screening services to reduce cancer-related mortality among socially vulnerable communities.



P55. Breast Cancer Screening Knowledge and Practice Patterns Amongst Physicians Who Provide Gender Diverse Care

Danielle Brabender, MD[1]; Eloise Stanton, MD[2]; Erin Wolfe, MD[3]; Roberto Travieso, MD[4]; Emily Siegel, MD[5]

[1]Keck Medicine of University of Southern California, Los Angeles General Medical Center,, Los Angeles, CA, US; [2]Keck Medicine of USC, Los Angeles, CA, US; [3]Keck Medicine of USC, Los Angeles, CA, US; [4]Keck Medicine of USC, Los Angeles, CA, US; [5]Keck Medicine of USC, Los Angeles, CA, US

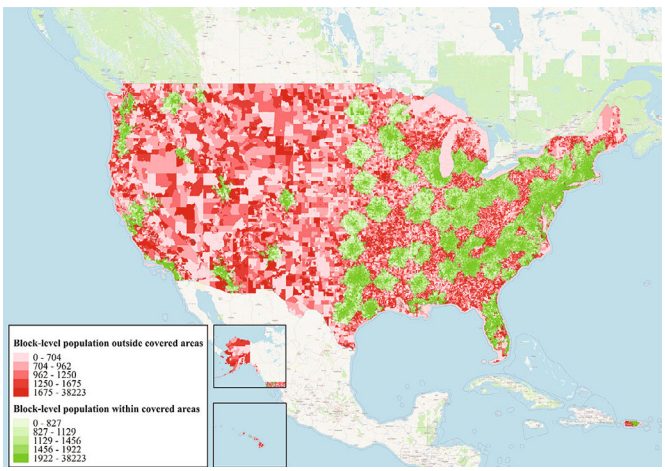
INTRODUCTION: Knowledge of breast cancer screening and treatment for transgender and gender diverse patients (TGD) varies significantly among physicians. Providers may be unaware of the varied guidelines for screening and management, even when delivering gender-affirming care. The aim of this study was to evaluate the familiarity and practice patterns of physicians regarding breast cancer (BC) risk and screening for TGD patients. **METHODS:** An anonymous survey was electronically distributed to a diverse group of physicians committed to the care of LGBTIQA+ patients at a tertiary academic medical center. Survey questions assessed physicians' training and experience with TGD patients, as well as their knowledge/opinions regarding gender-affirming hormones (GAH) cancer risk and BC screening for TGD individuals. **RESULTS:** The survey was distributed to 52 physicians, with a response rate of 52% (n=27). Participants represented a variety of specialties, predominantly Pediatrics/Adolescent (19%) and Family Medicine (19%). Only 36% received formal training in TGD patient care. Among participants, 36% served a patient population that was >25% TGD, and 56% prescribed GAH. Notably, of the total population, 25% were unaware of BC screening recommendations specific to TGD patients, but for those who prescribed GAH 93% were aware. However, 25% of GAH prescribers do not discuss the effects of hormones on BC risk with their patients. Of the total population, 44% were unsure whether to recommend ceasing GAH in patients diagnosed with hormone receptor-positive BC, and 84% believed transgender males who undergo mastectomy require BC screening. Only 39% of physicians believed transgender males receiving gender-affirming care should follow different BC screening guidelines compared to cisgender women, while 61% felt they should have different guidelines than cisgender men. Although 76% felt that the responsibility for ordering cancer screening tests lies with the hormone-prescribing and primary care providers, 40% lacked confidence in performing breast exams on TGD patients. **CONCLUSIONS:** This study highlights significant gaps in physician knowledge and training regarding TGD patients BC screening and treatment. Addressing these disparities through educational initiatives is crucial for increasing provider awareness and ensuring the appropriate management of TGD individuals.

P56. Centralization of pancreatic cancer surgery may restrict access to care for a large portion of the US population: a nationwide analysis based on Medicare beneficiaries

Alessandro Paro, MD[1]; Selamawit Woldesenbet, MS[2]; Adrian Diaz, MD[3]; Ekaterina Baron, MD[4]; Rohit Sharma, MD, FACS[5]; Jessica Wernberg, MS, FACS[6]; Andrea I Ferrer Melendez, MD[7]; Tim M Pawlik, MD, PhD, MPH, MTS, MBA[8]

[1]Marshfield Medical Center, Marshfield, WI, US; [2]The Ohio State University, Columbus, OH, US; [3]University of Chicago, Chicago, IL, US; [4]Marshfield Medical Center, Marshfield, WI, US; [5]Marshfield Medical Center, Marshfield, WI, US; [6]Marshfield Medical Center, Marshfield, WI, US; [7]Marshfield Medical Center, Marshfield, WI, US; [8]The Ohio State University, Columbus, OH, US

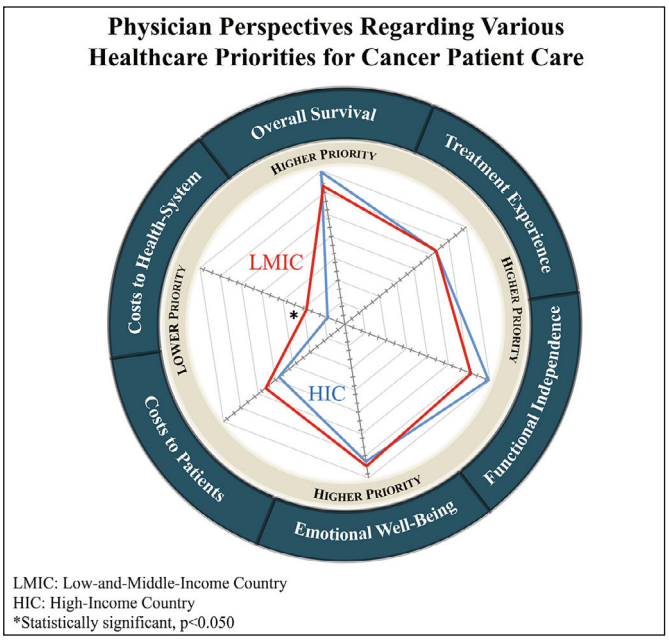
INTRODUCTION: Given the well-established relationship between volume and outcomes for pancreatic cancer surgery, there has been a push towards centralization of these procedures to high-volume centers. The impact of centralization on patient access to surgery remains poorly understood, especially at a national level. **METHODS:** Centers performing pancreatic cancer surgery between 2017-2021 were identified via the Medicare Standard Analytical Files. Centers in the highest-volume quartile were geolocated based on their address as reported in the National Plan and Provider Enumeration System database; service areas representing 90-minute drive-time areas from high-volume centers were defined. Populations within and outside these areas were compared based on their block-level sociodemographic characteristics obtained from the 2021 5-year American Community Survey data. **RESULTS:** Among a total of 832 centers, the 212 centers in the highest-volume quartile performed a median of 37 (27–61) resections for pancreatic cancer over the study period. A total of 74,566,841individuals (22.4% of the population) resided outside the service areas of the highest-volume centers (Figure). These people were more often male (50.2% vs. 49.3%, p<0.01), older (42.3±11.0 vs. 40.3±9.9, White (75.7% vs. 65.8%, veterans (8.2% vs. 6.4%, unemployed (5.8% vs. 5.5%, uninsured (9.9% vs. 8.4%, without higher education (65.0% vs. 55.6%, without internet access (14.0% vs. 9.4%, p<0.01) and had a lower annual household income ($62,315±30,405 vs. $82,146±44,574, p<0.01) compared with individuals within those service areas. On multivariable logistic regression, there was lower odds of being included in the service area of the highest-volume centers among geographic areas consisting of populations that had a higher proportion of individuals who were men (OR 0.89, 95%CI 0.87–90), older (OR 0.95, 95%CI 0.94–0.96), Hispanic (OR 0.87, 95%CI 0.87–0.88), veterans (OR 0.69, 95%CI 0.68–0.71), without a higher education (OR 0.92, 95%CI 0.92–0.93), unemployed (OR 0.95–0.98), uninsured (OR 0.91, 95%CI 0.90–0.92) or without internet access at home (OR 0.80, 95%CI 0.79–0.81). Conversely, geographic areas with a higher percentage of non-White residents (OR 1.23, 95%CI 1.22–1.23) and a higher median income (OR 1.11, 95%CI 1.10–1.11) had higher odds of being included in the service area of the highest-volume centers. **CONCLUSIONS:** Restricting pancreatic cancer surgery to the highest-volume centers in the current environment may limit access to these procedures for a significant portion of the US population and may disproportionately affect socially vulnerable communities.



P57. Comparing Value-Based Cancer Care Through the Lens of Physicians in Diverse Economic Contexts

Edward A Joseph, MBBS[1]; Muhammad Muntazir Mehdi Khan, MBBS[2]; Muhammad Anees Khaliq[3]; Bibek Aryal[4]; David Bartlett[5]; Casey J. Allen, MD[6]
[1]Allegheny Health Network, Pittsburgh, PA, US; [2]Allegheny Health Network, Pittsburgh, PA, US; [3]Aga Khan University, Karachi, Sindh, PK; [4]Allegheny Health Network, Pittsburgh, PA, US; [5]Allegheny Health Network, Pittsburgh, PA, US; [6]Allegheny Health Network, Pittsburgh, PA, US

INTRODUCTION: Physicians play a crucial role in cancer care delivery, helping to shape the frameworks that define "value." We compared perceptions of "value" in cancer care between physicians in high-income countries (HICs) and low- and middle-income countries (LMICs). **METHODS:** A novel survey was disseminated to physicians from HICs (United States) and LMICs (Pakistan and Nepal), assessing the relative importance of healthcare priorities, including overall survival, patient experience, functional and emotional well-being, and costs to patients and the health system. Kendall's coefficient of concordance (W) assessed agreement between groups. **RESULTS:** We received 155 physician responses, of which 62 (40%) were from HICs and 93 (60%) from LMICs. The overall cohort had a mean age of 38.1 ± 12.6 years, was 49% male, and identified primarily as South Asian (n=93, 60%) or White (n=49, 32%). LMIC providers were younger (31.2 ± 6.4 vs. 48.5 ± 12.4, p<0.001) and more likely to work in tertiary hospitals (100% vs. 79%, p<0.001). Both cohorts exhibited moderate consensus (HIC: W=40%; LMIC: W=22%, both p<0.001) regarding the rank order of healthcare priorities. HIC physicians ranked functional independence as most important (2.5 ± 1.3 vs. 3.0 ± 1.6, p=0.096), whereas LMIC physicians ranked emotional well-being as the most important priority (2.8 ± 1.6 vs. 2.9 ± 1.4, p=0.658). Both physician cohorts showed consensus on the rank order of other priorities, including overall survival (2.5 ± 1.0, p=0.221), treatment experience (3.4 ± 1.7 vs. 3.6 ± 1.5, p=0.296), and costs to the patient (4.1 ± 0.9 vs. 3.7 ± 1.6, p=0.077). LMIC physicians reported a higher mean rank priority for costs to the health system (5.1 ± 1.3 vs. 5.6 ± 0.9, p=0.010). **CONCLUSIONS:** Physicians in both HICs and LMICs prioritized patient-centric outcomes. However, LMIC physicians placed greater emphasis on costs to the health system compared to HIC physicians. These findings underscore the importance of developing adaptable value frameworks that are relevant and effective across diverse healthcare settings.



P58. Concordance of Colorectal Cancer Treatment with National Comprehensive Cancer Network Harmonized Guidelines: Analysis of a Large Multicenter Nigerian Cancer Registry

Betel Yibrehu[1]; Julia Jackman[2]; Olujide Arije[3]; Mobolaji Oludara[4]; Olawale A Badejo[5]; Fatima B Abdulkareem[6]; Chukwuma E Okereke[7]; Samuel A Olatoke[8]; Alex Doyle[9]; Erica Mann[10]; Catherine Zivanov[11]; T. Peter Kingham, MD[12]; Isaac Olusegun Alatise[13]
[1]Univeristy of Toronto, Toronto, ON, CA; [2]Kaiser Permanente Bernard J. Tyson School of Medicine, Pasadena, CA, US; [3]Obafemi Awolowo Universit, Ile-Ife, NG; [4]Department of Surgery, Lagos State University Teaching Hospital, Lagos, Nigeria, US; [5]Department of Surgery, National Hospital Abuja, US; [6]Department of Anatomical Pathology, Lagos University Teaching Hospital Lagos, US; [7]Department of Surgery, Federal Medical Center, Owo, Ondo state, US; [8]Department of Surgery, University of Ilorin Teaching Hospital, Ilorin, Kwara State, Nigeria., US; [9]Memorial Sloan Kettering, New York City, NY, US; [10], Lankenau Medical Center, Wynnewood, PA, US; [11]Washington University in St. Louis, St. Louis, MO, US; [12]Memorial Sloan Kettering Cancer Center, New York, NY, US; [13]Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun State, NG

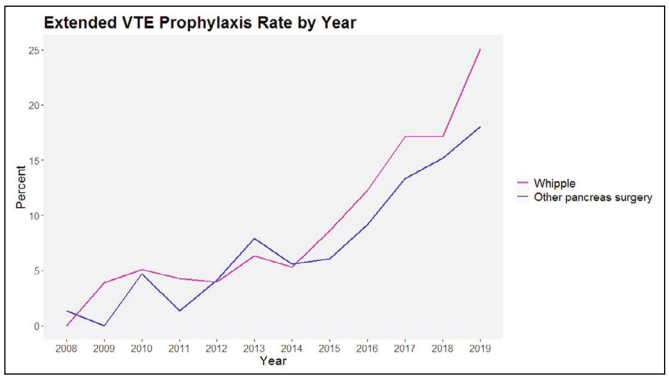
INTRODUCTION: In Nigeria, Africa's most populous country, colorectal cancer (CRC) incidence and mortality are rising. While data have shown improved survival in patients undergoing guideline-concordant treatment,

there are significant barriers to guideline implementation in resource-limited settings. To address this, several cancer guidelines have been adapted for these settings. The adherence to and impact of adapted guidelines in their intended context is not well characterized. Our objective was to examine the concordance of CRC treatment in Nigeria with the National Comprehensive Cancer Network (NCCN) Harmonized Guidelines and evaluate for associations with patient outcomes. **METHODS:** We performed a retrospective analysis of patients diagnosed with CRC between August 2013 and January 2024. Patient information was derived from a prospectively maintained database established by the African Research Group for Oncology which included data from 5 Nigerian tertiary referral centres. The primary outcome was guideline concordance, defined using a stage-dependent evaluation scheme and based on the NCCN Harmonized Guidelines for Colon and Rectal Cancer. The categories of guideline concordance were Standard of Care, Minor Deviation (from standard), Major Deviation, and No Cancer-Directed therapy. Only patients with complete staging data were included in analysis. **RESULTS:** A total of 840 patients met inclusion criteria. The median age at diagnosis was 55 (IQR 44-66), 53.3% of patients were male (448), and 79.4% of patients presented with colon cancer (667). Only 38.0% of patients underwent CT abdomen for staging (294), and less than 2% of patients underwent CT chest (11). Forty percent of patients presented with stage IV disease (337). Of the 477 (56.8%) patients with non-metastatic disease: 41.9% (200) received No Cancer-Directed therapy, 32.76% (156) received care with Major Deviations, 13.8% (66) received care with Minor Deviations, and 5.5% (26) received Standard of Care. Deviations were most commonly due to patient death (16.1%, 135), patient finances (11.3%, 95), or lack of medical resources (7.3%, 61). In both colon and rectal cancer groups, survival analysis showed a higher mortality rate among patients in the No Cancer-Directed therapy group, although it was significant only among colon cancer patients (HR 2.77; 95% CI 1.21-6.36, p = 0.02). Mortality rates between those who received Standard of Care or treatment with Major or Minor Deviations were similar overall with no statistically significant differences. **CONCLUSIONS:** This study analysed concordance of CRC care in Nigeria with resource-stratified guidelines developed specifically for Africa. While guidelines are helpful tools, most patients did not receive guideline-concordant care, largely due to persistent resource constraints. These results highlight the gap between guidelines and the reality of care delivery in resource-limited settings. Focused effort on broadening access to health coverage, early diagnosis and quality improvement are key areas for future improvement.

P59. Disparities in extended venous thromboembolism prophylaxis after pancreatic cancer surgery

Kelly Dong, MD[1]; Ashlynn Fuccello, MS[2]; Mario Schootman, PhD[3]; Bradley C Martin, PharmD, PhD[4]; Michail Mavros, MD, FACS[5]
[1]McMaster University, Hamilton, ON, CA; [2]University of Arkansas for Medical Sciences, Little Rock, AR, US; [3]University of Arkansas for Medical Sciences, Little Rock, AR, US; [4]University of Arkansas for Medical Sciences College of Pharmacy, Little Rock, AR, US; [5]Johns Hopkins University NCR, Washington, DC, US

INTRODUCTION: Current guidelines recommend extended venous thromboembolism (VTE) prophylaxis following pancreas surgery for cancer; however, adherence to these guidelines is low. We aimed to assess existing disparities in receipt of extended VTE prophylaxis. **METHODS:** This is a retrospective analysis of the 2007-2020 SEER-Medicare dataset for patients with primary pancreas cancer. We analyzed patients undergoing pancreas surgery between January 2008 and December 2019 who were continuously enrolled to parts A, B, and D of Medicare without HMO enrollment from 12 months prior to surgery date up to 3 months after the surgery date. Patients with history of VTE or coagulopathy and those who developed VTE or bleeding or were hospitalized for over 4 weeks during the index surgery admission were excluded. The primary outcome was filling of a prescription for extended VTE prophylaxis within 5 days of discharge. The independent variables included patient demographics, social determinants of health, comorbidities, and cancer and treatment characteristics. The association of independent variables with the outcome was assessed using univariate and multivariable logistic regression models. **RESULTS:** Out of 7,118 continuously enrolled patient/operations, we excluded 1,765 with previous history of VTE or coagulopathy and 526 due to development of inpatient VTE, bleeding, or prolonged index hospitalization. The remaining 4,827 eligible operations were mostly comprised of Whipple procedures (3490, 72.3%) and the most common pathology was pancreatic adenocarcinoma (84.8%). The median age was 73 years and 54.7% were female. Extended VTE prophylaxis prescriptions were filled for 469 patients (9.7% of eligible patients), primarily with enoxaparin (96.2% of prescriptions). The number of prescriptions increased over time (0.4% in 2008 to 23.1% in 2019). After risk adjustment, factors independently associated with receipt of extended VTE prophylaxis included younger age (OR 1.02), white race (OR 2.2), rurality (non-metropolitan area vs metropolitan >1million population, OR 1.6), Whipple procedure (vs other pancreas surgery, OR 1.4), higher pancreas surgery hospital volume (OR 2.3 4th vs 1st quartile), surgical oncologist provider speciality (OR 2.3), and surgery period (2016-2019 vs 2008-2011, OR 5.9). **CONCLUSIONS:** Prescription of extended VTE prophylaxis after pancreas cancer surgery has been modest but increasing. We identified demographic, socioeconomic, and healthcare-related factors associated with receipt of extended VTE prophylaxis.



P60. Evaluating Temporal Trends and Surgical Workforce Depth in Complex Cancer Operations at California's Community and Safety Net Hospitals

Amir Ashraf Ganjouei[1]; Mohamed A. Adam, MD[2]; Javid Sadjadi[3]; Adnan Alseidi, MD, MEd[4]; Ajay V. Maker, MD[5]; Lucas W. Thornblade, MD, MPH[6]
[1]University of California San Francisco, San Francisco, CA, US; [2]University of California, San Francisco, San Francisco, CA, US; [3]Loma Linda University, San Francisco, CA, US; [4]University of California, San Francisco, San Francisco, CA, US; [5]University of California San Francisco, San Francisco, CA, US; [6]University of California, San Francisco, San Francisco, CA, US

INTRODUCTION: Most routine cancer surgery (e.g. colon, breast) occurs outside comprehensive cancer centers, the distribution and management of complex cancer operations at non-specialized facilities is less well understood. Despite recommendations to centralize such procedures at high-volume centers, the extent, trends over time, and outcomes at community and safety net hospitals have not been thoroughly investigated. We hypothesized that while academic centers have seen an increase in the volume of complex cancer operations, a substantial portion of these procedures continues to be done in community settings. **METHODS:** A retrospective study of operations for malignancy in three anatomically complex sites (pancreatic, gastric, adrenal) was conducted within the California Cancer registry (1990-2020). Hospitals were categorized as: NCI-designated Comprehensive Cancer Centers (NCICC, n=8), HMOs (n=49), Integrated Delivery Network hospitals (IDN, n=62), Safety net hospitals (SNH n=19, per California Health Care Safety Net Institute), critical access hospitals (CAH, n=35), and community hospitals (CH, n=211). Demographic, clinical variables, and oncological outcomes were analyzed across these different hospital settings using univariate and multivariate models. **RESULTS:** Over three decades, cases performed at CHs have decreased while cases at NCICCs and HMOs rose (Figure 1). Over the same period, we observed no change in rates of complex cancer resections at SNH. Compared to NCICC, patients with gastric cancer at SNHs were significantly younger (mean 60 vs. 67 years at NCICC), more often Hispanic (43% vs. 16%), uninsured (13% vs. 1.5%), and/or metastatic at presentation (21% vs. 11%). After pancreatectomy, median overall survival was 20, 17, 14, 15, 13, and 9 months at NCICC, HMO, IDN, CH, SNH, and CAH, respectively. All NCICC had ≥1 high-volume pancreas surgeon (≥7 cases/year), versus 91% HMO, 41% IDN, 36% CHs, 33% SNHs, and no CAHs. A similar pattern was observed for gastric cancer resections, where all NCICC facilities had at least one high-volume surgeon, while less than half of the surgeons at IDN, CHs, and SNHs met this criterion. **CONCLUSIONS:** These data suggest a migration of complex cancer operations from community to specialty centers, though no migration of patients out of SNHs was observed,

consistent with diminished portability of care. Patients at SNHs present later and sustain poorer survival, even after resection. Most SNHs lack high-volume surgeons, highlighting a disparity in surgical expertise.



Figure 1. Temporal Trends in Complex Cancer Resections by Hospital Category in California (1990-2020)

P61. Forecasting County-Level Cancer Outcomes Based on County Health Metric Changes

Taylor J Jaraczewski, MD, MEng, MS[1]; Adhitya Ramamurthi, MD[2]; Gopika SenthilKumar, PhD[3]; Cindy Li[4]; Eric Elftmann[5]; Yun Xing, PhD[6]; Ugwuji N Maduekwe, MD, MMSc, MPH, FACS, FSSO[7]; Callisia Clarke, MD, MS, FSSO[8]; Anai N Kothari, MD, MS[9]

[1]Medical College of Wisconsin, Milwaukee, WI, US; [2]Medical College of Wisconsin, Milwaukee, WI, US; [3]Medical College of Wisconsin, Milwaukee, WI, US; [4]Medical College of Wisconsin, Milwaukee, WI, US; [5]Medical College of Wisconsin, Milwaukee, WI, US; [6]Medical College of Wisconsin, Milwaukee, WI, US; [7]Medical College of Wisconsin, Milwaukee, WI, US; [8]Medical College of Wisconsin, Milwaukee, WI, US; [9]Division of Surgical Oncology, Department of Surgery, Medical College of Wisconsin, Milwaukee, WI, US

INTRODUCTION: Health metrics in geographic areas are interconnected, with changes in one often triggering or reflecting shifts in others. Cancer outcomes are a critical part of the broader health landscape, influenced by and contributing to the overall health profile of a region. Onco-temp is a measure (ranging 1-100) of aggregated county-level cancer outcomes that accounts for incidence, late-stage diagnosis, and mortality rates for 19 cancers, with lower Onco-temp being associated with better county cancer health. This study aimed to create a model to forecast Onco-temp scores based on health metrics and temporal changes in these metrics using an AI-assisted analytic approach. **METHODS:** County-level health metrics were obtained using the University of Wisconsin's County Health Rankings, capturing early values (2010–2012) and recent values (2019–2020). All variables with early and recent values were included (46 variables). The target variable, Onco-temp, was calculated for United States counties using SEER data from 2020. Regression models tested included linear, ridge, lasso, and random forest. Performance was evaluated using R-squared (R^2), root mean squared error (RMSE), and mean absolute error (MAE). Counties were classified as "low temp" (Onco-temp < 49) or "high temp" (≥ 49), as this was the median value. The ability of the best regression model to classify was assessed with sensitivity, specificity, and area under the curve (AUC). All analysis was conducted using both OpenAI's GPT-4 and verified with R. **RESULTS:** A total of 2,482 counties were included for analysis with a median Onco-temp of 49 (IQR 35.3 - 61). The highest performing model was random forest regression with an R^2 of 0.44, RMSE of 13.1, and MAE of 10.5. For classification, the model achieved 71.0% sensitivity, 75.0% specificity, and an AUC of 0.82. Independent analysis had an R^2 of 0.51, RMSE of 12.32, 80% sensitivity, 75.5% specificity, and AUC of 0.77. Pearson correlation coefficients for observed vs predicted values (Figure 1) were 0.66 for GPT-4 and 0.72 for the R-model. The most influential variables were early value physical inactivity, early value adult obesity rates, and difference in population over time. **CONCLUSIONS:** This study demonstrates the ability for health metrics to predict the overall cancer health of a United States county. Using this model, policymakers could project the magnitude of impact that interventions to improve specific health metrics might have on improving cancer outcomes over time. Additionally, this study showcases the potential for using AI-assisted analytic tools.

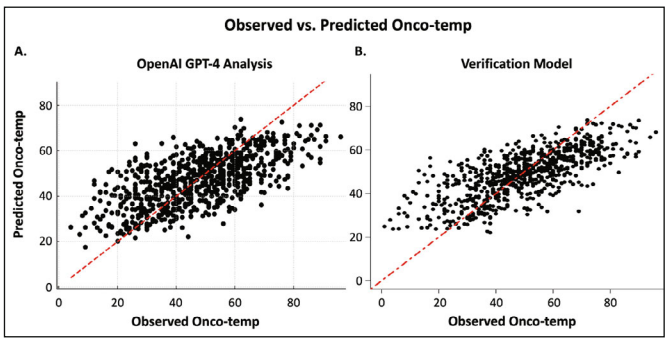


Figure 1. Comparison of observed vs. predicted values in the testing cohorts for the (A) OpenAI's GPT-4 analysis and the (B) Verification analysis in R.

P62. Founding a Native American Surgical Society: A Pathway to Recruit Indigenous Surgical Oncologists

Sydney Aquilina[1]; Joshua Shahbandeh[2]; Lyndsay Kandi[3]; Kirsten Concha-Moore[4]; Vanessa Jensen[5]; Lori Alviso Alvord[6]; Hannah E Woriax, MD[7]

[1], US; [2], US; [3], US; [4], US; [5], US; [6], US; [7]Duke University, Durham, NC, US

INTRODUCTION: Historically, the American Indian/Alaskan Native (AI/AN) population in the United States (US) has been severely underrepresented in medicine, particularly in the field of surgery. In surgical oncology (SO), there is a paucity of AI/AN SOs-a stark contrast to the relative effect of cancer in the AI/AN population. Cancer incidence in AI/AN populations is higher than Non-Hispanic Whites (NHW) for lung, colorectal, kidney, liver, stomach, and cervix. However, beyond incidence, cancers of all types are generally diagnosed at later stage, have worse 5 -year and overall survival in the AI/AN population. Access to high-quality healthcare is a well identified barrier for most AI/AN patients. AI/AN physicians are more likely to return to a tribal territory to practice. Few studies have attempted to determine where to focus efforts that can specifically impact and increase the number of practicing AI/AN surgeons and surgical trainees in this country. We submit that the creation of the Native American Surgical Society will aid in the attraction and recruitment of AI/AN students and surgical residents into the field of SO. **METHODS:** A literature review examining publicly available data, organizational reports,

and published academic literature on diversity and AI/AN representation in surgery was performed. The current landscape of what is known, and potential knowledge gaps and interventions were identified. **RESULTS:** Overall, the proportion of those who identify as AI/AN in the surgical workforce is 0.28%. The severe underrepresentation of this group in medicine has persisted for decades and is particularly true among the surgical subspecialties. The most recent data suggests that only 0.18% of matriculating US medical students, 0.09% of surgical residents, and 0.19% of academic surgical faculty identified as AI/AN. After surveying national society group rolls and the AI/AN surgical community, only two complex general and two breast surgical oncologists have been recognized that identify as AI/AN. **CONCLUSIONS:** The state of AI/AN representation in SO can be considered a crisis. Advocating for policy change, curriculum development, and understanding the political status of AI/ANs is imperative to address the group's lack of representation and health disparities. A group of Native surgeons, surgical residents, and medical students have founded the first organized Native American Surgical Society with the intent to inspire AI/AN trainees to join the surgical workforce and, in turn, aid in decreasing the disparity in SO.

P63. Fragmentation of care and healthcare utilization in pancreatic cancer patients undergoing neoadjuvant therapy

Linda Qu, MD[1]; Anoosh Farooqui[2]; Faelan Jacobson-Davies, MA[3]; Hari Nathan, MD, PhD[4]
[1]Michigan State University, East Lansing, MI, US; [2]University of Michigan, Ann Arbor, MI, US; [3]University of Michigan, Ann Arbor, MI, US; [4]University of Michigan, Ann Arbor, MI, US

INTRODUCTION: Fragmentation of care, defined as healthcare received across multiple institutions, has been associated with increased healthcare utilization (HU). In this analysis, we investigated the implications of fragmented care (FC) on HU in patients with pancreatic ductal adenocarcinoma (PDAC) undergoing neoadjuvant chemotherapy (NCT). We hypothesized that fragmented neoadjuvant care would lead to increased HU. **METHODS:** Using 100% Medicare claims data, we identified patients with PDAC who underwent at least 1 cycle of NCT followed by surgical resection between 2015-2017. Definitions for FC were stratified according to where patients received chemotherapy and surgery: 1) at different hospitals in different healthcare systems (DIFF), 2) at different hospitals within the same system (SAMESYS), and 3) at the same hospital within the same system (SAME). Patient demographics, hospital characteristics, and metrics of HU were compared between groups. **RESULTS:** Of 659 patients with PDAC receiving NCT followed by surgery, 224 (34%) underwent treatment and surgery at DIFF, 96 (15%) at SAMESYS, and 339 (51%) at SAME. Age, sex, race, Elixhauser index, and urban vs rural status did not differ between groups. Hospital pancreatectomy volume and hospital size were highest in the DIFF group compared to SAMESYS and SAME (24.4 vs 13.9 vs 14.7, p=0.0001 and 851 vs 703 vs 749, p=0.0002). Travel distance from home to the hospital performing pancreatectomy was highest in the DIFF group (98.5 vs 69.2 vs 45.7 miles, p=0.0001). In the NCT setting, the number of chemotherapy visits, radiation visits, and endoscopic interventions was similar regardless of FC status (6.2 vs 5.8 vs 5.9, p=0.9; 0.4 vs 0.3 vs 0.4, p=0.29; and 1.7 vs 1.6 vs 1.6, p=0.51). Emergency room utilization and inpatient admissions were similar (1.8 vs 1.8 vs 1.8, p=0.92 and 1.2 vs 1.1 vs 1.3, p=0.29). The DIFF group underwent more preoperative CT imaging (4.5 vs 3.6 vs 4.2, p=0.002), but preoperative MRI use was similar. Postoperative complications (17% vs 18% vs 22%, p=0.25) and readmissions (23% vs 22% vs 21%, p=0.82), and overall costs did not differ. **CONCLUSIONS:** Fragmentation of care does not lead to increased HU or increased healthcare costs in patients with PDAC undergoing NCT followed by surgery. It may be reasonable to keep this population local for treatment when clinically feasible to do so.

P64. Genetic Pathogenic Variants in Asian American/Pacific Islander Women with Breast Cancer: Implications for Surgical and Oncologic Care

Jennifer Tseng[1]; Katharine Schulz-Costello[2]; Veronica Jones[3]
[1]City of Hope, Irvine, CA, US; [2]City of Hope, Duarte, CA, US; [3]City of Hope, Duarte, CA, US

INTRODUCTION: Asian American/Pacific Islander (AAPI) women are an understudied population for genetic testing. Despite a 2024 American Cancer Society report that AAPI women have annual increases in breast cancer incidence for the last 10 years, healthcare providers are less likely to adhere to evidence-based genetic testing guidelines for these patients. Since 2020, the Precision Medicine Initiative at City of Hope has provided germline testing to all patients with breast cancer; implications for surgical and oncologic care were reviewed. **METHODS:** The electronic health record was queried for self-identified AAPI women diagnosed with breast cancer between 2020 and 2024 who had germline testing. Frequency of gene mutations was quantified by age, preferred language, insurance status, molecular subtype, breast surgery type, and associated cancers and diseases. Fisher's exact testing was performed to identify significant interactions. **RESULTS:** Between 2020 and 2024, 835 AAPI women with breast cancer (BC) underwent germline testing. Pathogenic variants (PV) were found in 172 patients (20.6%) (Table 1). Highly penetrant PV (BRCA1, BRCA2, PALB2, TP53, PTEN, CDH1, STK11) were discovered in 44 patients (25.6% PV, 5.3% tested). Thirty-four patients (19.8% PV) had BRCA1/BRCA2. Moderately/low penetrant PV (including ATM, CHEK2, BRIP1, RAD51C, RAD51D) were found in 39 patients (22.7% PV, 4.7% tested). Highly and moderately penetrant PV for BC were associated with bilateral mastectomies over unilateral mastectomy or breast conserving surgery ($p<0.001$). A high number of PV patients were at risk for additional cancers (n=150; 87.2% PV, 18.0% tested). Half were at risk for ≥3 cancers (n=89; 51.7% PV, 10.7% tested). More penetrant PV were associated with additional specialty care for increased risk of other cancers and/or diseases ($p<0.001$). **CONCLUSIONS:** In the largest review to date of Asian American/Pacific Islander women with breast cancer undergoing germline testing, 20% were found to have pathogenic variants. Twenty percent of pathogenic variants were BRCA1/BRCA2, with implications for screening, therapeutic/prophylactic surgery, and systemic treatment options like PARP inhibitors. When a pathogenic variant was found, there was a higher likelihood of needing additional specialty care for screening and treatment of other cancers and diseases. Germline genetic results are a critical part of comprehensive oncologic care for AAPI women, and efforts should be made to improve patient knowledge of and access to testing.

Table 1. Asian American/Pacific Islander Women with Breast Cancer with Pathogenic Variants (n=172)

Characteristics	Highly Penetrant PV	Moderately Penetrant PV	Low Penetrant PV	No Increased Breast Cancer Risk	P-Value
Age					0.082
≤39	5	1	6	2	
40-54	20	5	7	32	
55-75	16	5	13	47	
>75	3	1	1	8	
Language					0.992
English	31	8	22	67	
Chinese (Cantonese/Mandarin)	10	3	3	14	
Other (Burmese/Gujarati/Japanese/Korean/Tagalog/Thai)	3	1	2	8	
Insurance					0.663
Public	8	4	8	21	
Private	29	5	15	45	
Multiple	6	2	4	20	
Other	1	1	0	3	
Molecular Subtype					0.498
DCIS (all)	3	0	3	5	
Luminal A (ER+/PR+/HER2-)	20	7	11	49	
Luminal B (ER+/HER2-/ either high Ki-67 or PR-)	2	0	2	8	
Luminal B- like (ER+/HER2+/any Ki-67 and either PR+ or PR-)	5	2	5	14	
HER2 enriched (ER-/PR-/HER2+)	0	0	1	3	
Basal like/triple negative (ER-/PR-/HER2-)	14	3	5	10	
Surgery					0.007
Breast Conserving Surgery	7	3	7	36	
Unilateral mastectomy	12	3	9	32	
Bilateral mastectomy	24	5	8	16	
No Surgery	1	1	3	5	
Reconstruction					0.025
Yes	25	5	12	22	
No	18	6	12	62	
N/A	1	1	3	5	

P65. Health Literacy and Surgical Treatment of Breast Cancer

Emma Bradley, MD[1]; Palina Woodhouse[2]; Danish Ali, MBBS[3]; Rachel McCaffery, MD[4]; Kamran Idrees, MD, MSCI, MMHC, FACS[5]
[1]Vanderbilt University Medical Center, Nashville, TN, US; [2]Vanderbilt University Medical Center, Nashville, TN, US; [3]Vanderbilt University Medical Center, Nashville, TN, US; [4]Vanderbilt University Medical Center, Nashville, TN, US; [5]Vanderbilt University Medical Center, Nashville, TN, US

INTRODUCTION: Breast cancer treatment is complex, incorporating multimodality treatments that depend on patient understanding, participation and shared decision-making. While health literacy (HL) has been shown to be a key determinant of health in many chronic diseases, its effect on oncologic treatment of breast cancer is less well defined. Here we aim to elucidate the impact of HL on surgical treatment of breast cancer and outcomes. **METHODS:** A cohort of newly diagnosed breast cancer patients from 2005-2022 at a single academic tertiary care center was retrospectively reviewed. Patient health literacy was assessed using a validated Brief Health Literacy Screen (BHLS), with low HL defined as BHLS ≤9. Multivariable logistic regression was used to determine associations between patient health literacy, cancer stage and likelihood of undergoing certain types of surgical intervention. Multivariable Cox proportional hazards model was used to assess the impact of health literacy on overall and disease-free survival. **RESULTS:** Out of a total of 3918 breast cancer patients, mean BHLS was 13.9 (SD 2.1, range 3-15). Patients with low

health literacy were more likely to be older (median age 64 vs 58 years), non-White (21.1% vs 14.3%), and less likely to hold private insurance (26.9% vs 55.3%). Adjusted for patient and oncologic characteristics, patients with low HL presented with later stage disease (OR 1.12, CI [1.09-1.16]). In patients undergoing mastectomy, lower HL was associated with a decreased odds of undergoing prophylactic contralateral mastectomy (OR 0.93 [0.87-0.99]) and reconstruction (OR 0.91 [0.86-0.96]). There was no difference in receipt of breast conservation therapy vs. mastectomy associated with patient HL (OR 0.998 [0.96-1.04]). Controlling for other variables, low HL was associated with an increased risk of all-cause mortality in breast cancer patients (HR 1.11 [1.08-1.14]) and increased risk of breast cancer recurrence (HR 1.07 [1.02, 1.13]). Covariate adjusted survival curves by stage are represented in Figure 1. **CONCLUSIONS:** This study demonstrates that low HL has an impact on stage at presentation, surgical treatment and survival outcomes in breast cancer patients. These findings emphasize the importance and value of assessing and understanding HL in the shared decision-making process of oncologic breast cancer treatment. These findings also help to define areas within breast cancer care that may benefit from implementation of health-literacy sensitive interventions.

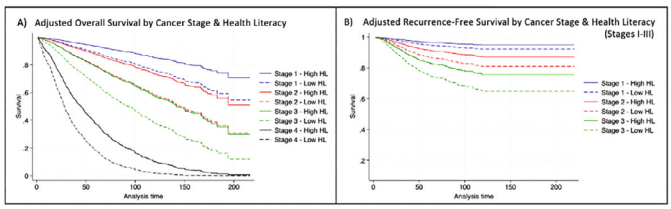


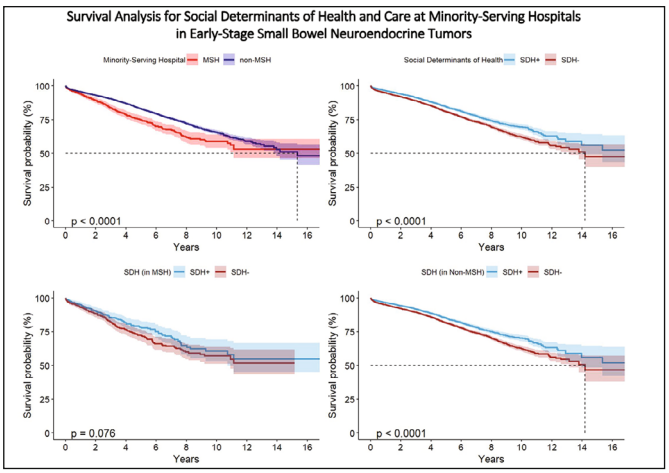
Figure 1. Cox Proportional Hazard Model Adjusted Kaplan-Meier Survival Curves by Cancer Stage and Health Literacy for A) Overall Survival and B) Re-currence-Free Survival

P66. Higher Composite Social Determinants of Health scores predict Worsened Survival for Early-stage Small Bowel Neuroendocrine Tumors

Ahmed Alnajar, MD, MSPH[1]; Amber Collier, MD[2]; Alessia C Cioci, MD[3]; John I Lew, MD, FACS[4]; Tanaz M. Vaghaiwalla, MD, FACS[5]

[1]Division of Endocrine Surgery; DeWitt Daughtry Department of Surgery, University of Miami Health Sys, Miami, FL, US; [2]Division of Endocrine Surgery; DeWitt Daughtry Department of Surgery, University of Miami Health Sys, Miami, FL, US; [3]Division of Endocrine Surgery; DeWitt Daughtry Department of Surgery, University of Miami Health Sys, Miami, FL, US; [4]Division of Endocrine Surgery; DeWitt Daughtry Department of Surgery, University of Miami Health Sys, Miami, FL, US; [5]Division of Endocrine Surgery; DeWitt Daughtry Department of Surgery, University of Miami Health Sys, Miami, FL, US

INTRODUCTION: Early stage I/II well-differentiated small bowel neuroendocrine tumors (sbNETs) typically have favorable overall survival with timely diagnosis and treatment. However, the impact of social determinants of health (SDH) and care at Minority-Serving Hospitals (MSH) on survival in patients with sbNETs has not been previously studied. This study examines the combined impact of SDH factors and hospital type on long-term survival, offering insight into health disparities in patients with sbNETs. **METHODS:** The 2010-2020 National Cancer Database was queried to adult patients with G1 and G2 sbNETs, diagnosed with Stage I or II disease who underwent complete surgical resection. Exclusion criteria included G3 NETs, stage III/IV disease, neuroendocrine carcinoma, duodenal NETs, and patients with incomplete follow-up. The SDH score was developed using a composite of four sociogeographic factors: (1) low income, (2) low education, (3) distance travelled for treatment (>250 miles), and (4) rurality. Patients were categorized into SDH+ (0-1 score) and SDH- (2-4). Hospitals in the top decile of Black and Hispanic patient representation were classified as MSHs. Kaplan-Meir and Cox regression analyses were used to assess outcomes. **RESULTS:** Of 2688 patients with sbNETs, the median age was 64 (54-73) years, 48% female, and 57% classified as SDH-. Overall survival rates at 5, 10, and 15 yrs were 79%, 62%, and 49%. Stratified by SDH and hospital type, SDH+ patients at MSHs had a 5-year survival of 82%, while SDH- patients dropped to 63%. Non-MSH hospitals showed similar results: 82% for SDH+ and 77% for SDH-. Median survival for SDH- patients was 11 yrs at MSHs vs. 12 yrs at non-MSHs, with minimal SDH impact on survival at non-MSHs (Figure). In the regression analysis, SDH score was a significantly associated with worse survival for the SDH- group (HR 1.24, p<0.001). Treatment at non-MSH hospitals was linked to significantly better survival (HR 0.41, p<0.001). Black patients had a 20% higher risk of mortality compared to White patients (HR 1.20, p=0.002), while Hispanic patients showed no significant difference (HR 0.87, p=0.2). Other significant factors included age, sex, and insurance status. **CONCLUSIONS:** A higher composite SDH score and hospital type associated with worsened survival for early stage sbNETs. Addressing SDH factors, such as income, education, and geographic barriers, is crucial in improving cancer outcomes, particularly for populations treated at MSHs. Interventions to reduce disparities may provide additional survival benefit for patients with sbNETs.



P67. Impact of Financial Hardship, Financial Toxicity, and Transportation Issues on Older Patients Undergoing Surgery for Cancer

Sara Myers[1]; Elizabeth S Davis, MSPH[2]; Jeffrey Franks[3]; Teviah Sachs, MD[4]; Kelly Kenzik, MS, PhD[5]

[1]Boston Medical Center/Boston University School of Medicine, Boston, MA, US; [2]Boston Medical Center, Boston, MA, US; [3]University of Alabama, Birmingham, AL, US; [4]Boston Medical Center, Boston, MA, US; [5]Boston Medical Center, Boston, MA, US

INTRODUCTION: Financial hardship (FH), a measure of material and behavioral financial burdens, and financial toxicity (FT), a measure of psychological stress associated with the cost of cancer care, are associated with worse outcomes among cancer patients. Although cost and transportation issues are reasons patients may decline treatment or delay follow-up care, FH, FT, and transportation issues are understudied among older surgical cancer patients. We surveyed patients 50 years and older at the time of cancer diagnosis who underwent surgery. **METHODS:** The University of Alabama at Birmingham tumor registry was used to identify patients diagnosed at ≥50y with breast, colorectal, prostate, and lung cancers who received curative-intent treatment from 2000-2019. Age, sex, race, income, diagnosis, stage, treatment, and comorbidities were collected from survey responses and medical records. FH, FT, and transportation issues were evaluated using validated questions. Multivariable regression models were used to evaluate factors associated with FH, and transportation challenges. **RESULTS:** Surgical patients (n=615) experiencing FH were younger (74y vs 78y, p<0.001), non-White (43% vs 22%, p<0.0001), had annual incomes <$50,000 (40% vs 16%, higher FT (p<0.001), and reported issues with transportation (22% vs 6%, p<0.001). Up to 39% of patients without FH reported FT: 29% worried about finances due to cancer and treatment, 21% were not certain they could afford the cost of treatment, and 7% reported not being able to meet monthly expenses. Compared to patients without FH, patients with FH faced more transportation-related barriers to care; 22% had trouble getting to the doctor (p<0.001), 10% were unable to find a ride to the doctor (p<0.001), 9% could not get to a pharmacy to obtain medications (p<0.001), and 26% traveled more than one hour for care (p=0.024). In multivariable models, age <65, low income, more recent diagnosis, and transportation issues were associated with FH and FT. Non-White patients had higher odds of experiencing transportation issues (OR 3.2, 95% CI 1.7-6.0). **CONCLUSIONS:** Older surgical cancer patients face significant financial hardship, financial toxicity, and transportation issues when accessing cancer care. As FH and FT measure different components of

the financial burden of cancer care, older patients with new cancer diagnoses should be screened early for FH, FT, and transportation issues in order to address barriers to care and offer appropriate interventions.

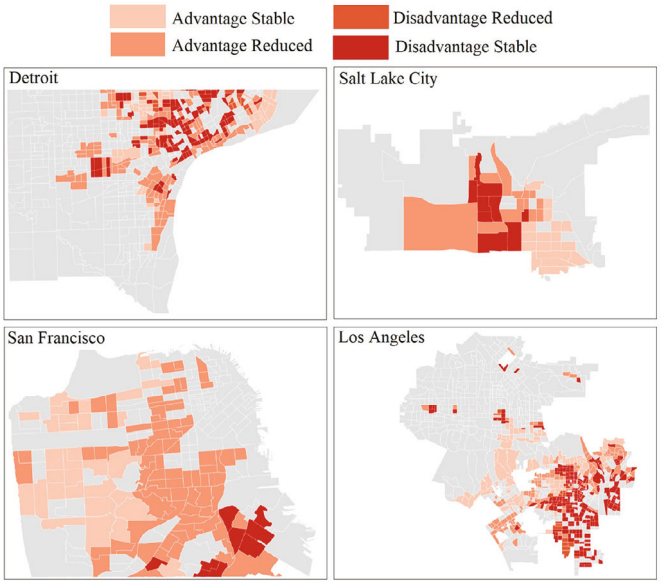
Table. Multivariable regression models for financial toxicity (linear), financial hardship (logistic), and transportation issues (logistic)

Variable	Financial Toxicity	Financial Hardship	Transportation Issues
Demographics	β (95% CI)	OR (95% CI)	OR (95% CI)
Age <65	3.98 (2.37-5.59)	3.1 (1.75-5.51)	1.22 (0.6-2.5)
Sex	-1.15 (-3.09-0.78)	0.62 (0.32-1.18)	0.99 (0.42-2.35)
Race (non-white)	2.27 (0.56- 3.99)	1.19 (0.68-2.09)	3.19 (1.7-5.95)
Comorbidities	0.14 (-2.66-2.94)	0.65 (0.26-1.64)	0.68 (0.21-2.24)
ADI (>median)	-0.95 (-2.24-0.34)	0.91 (0.57-1.44)	1.09 (0.61-1.94)
Low income	6.65 (5.27-8.04)	3.41 (2.06-5.63)	0.6 (0.32-1.12)
Transportation issues	3.98 (2.14-5.82)	2.8 (1.54-5.08)	-
Time since diagnosis	-0.27 (-0.41- -0.15)	0.88 (0.83-0.93)	1.08 (1.02-1.15)
Diagnosis			
CRC (ref. breast)	1.99 (-0.10-4.08)	1.33 (0.65-2.73)	1.14 (0.45-2.85)
Lung	2.15 (0.15- 4.16)	1.19 (0.59-2.4)	1.06 (0.43-2.62)
Prostate	-0.07 (-2.71- 2.56)	0.55 (0.21-1.44)	0.62 (0.18-2.07)
Late stage	-0.74 (-4.08- 2.60)	1.03 (0.34-3.09)	0.46 (0.06-3.73)
Treatment			
Radiation	1.99 (0.62- 3.37)	1.51 (0.91-2.48)	0.89 (0.46-1.7)
Chemotherapy	-0.08 (-1.61- 1.46)	0.96 (0.57-1.64)	0.76 (0.38-1.53)

P68. Impact of Historical Redlining and Neighborhood Trajectories on Gastrointestinal Cancer Care

Mujtaba Khalil[1]; Selamawit Woldesenbet[2]; Shreya Shaw[3]; Shahzaib Zindani[4]; Zayed Rashid[5]; Abdullah Altaf[6]; Syed Husain[7]; Tim Pawlik[8]
[1]The Ohio State University, Columbus, OH, US; [2]The Ohio State University, Columbus, OH, US; [3]The Ohio State University, Columbus, OH, US; [4]The Ohio State University, Columbus, OH, US; [5]The Ohio State University, Columbus, OH, US; [6]The Ohio State University, Columbus, OH, US; [7]The Ohio State University, Columbus, OH, US; [8]The Ohio State University, Columbus, OH, US

INTRODUCTION: Historical discriminatory policies, such as residential redlining, along with current economic and social changes in a neighborhood, may impact gastrointestinal (GI) cancer care. We sought to investigate how evolving neighborhood characteristics impact the diagnosis and treatment of GI cancer. **METHODS:** Individuals who were diagnosed with GI cancer between 2016 and 2020 were identified using the Surveillance, Epidemiology, and End Results database. Neighborhood trajectory was calculated using Social Vulnerability Index and historical redlining grade. Neighborhood trajectories included advantage stable, advantage reduced, disadvantage stable, and disadvantage reduced. Multivariable regression was utilized to examine the association between neighborhood trajectory and stage at diagnosis, cancer directed treatment and surgical outcomes. **RESULTS:** Among 15,118 individuals, 30.5% (n=4,608) resided in advantaged stable neighborhoods, 44.5% (n=6,727) in disadvantaged reduced neighborhoods, 2.96% (n=448) in advantaged reduced neighborhoods, and 22.1% (n=3,335) in disadvantaged stable neighborhoods (Figure). Individuals residing in disadvantaged stable neighborhoods had a higher Charlson Comorbidity Index (CCI >2: 33.1% vs. 26.8%) and were diagnosed at an advanced stage (stage III and IV: 57.2% vs. 52.4%) (both p <0.001). In terms of cancer-directed treatment, individuals living in disadvantaged stable neighborhoods were less likely to undergo surgery (55.8% vs. 59.2%), receive chemotherapy (56.7% vs. 60.3%), and achieve a textbook outcome (TO) following surgery (41.3% vs. 51.3%) (all p <0.001). On multivariable analyses, compared with living in advantaged stable neighborhoods, individuals in disadvantaged stable neighborhoods had 29% (OR 1.29, 95% CI 1.18 – 2.42) higher odds of being diagnosed at an advanced stage, 33% (OR 0.66, 95% CI 0.58 – 0.76) lower odds of receiving chemotherapy, and 32% (OR 0.68, 95% CI 0.59 – 0.77) lower odds of achieving a TO. **CONCLUSIONS:** Individuals living in disadvantaged stable neighborhoods have advanced stages at diagnosis and experience poorer surgical outcomes. There is an urgent need for targeted interventions and policies to address structural inequities to ensure health equity relative to diagnosis and surgical outcomes for patients with GI cancer.



P69. Leveraging community-engaged feedback to identify barriers in research participation for underrepresented populations with rare cancer

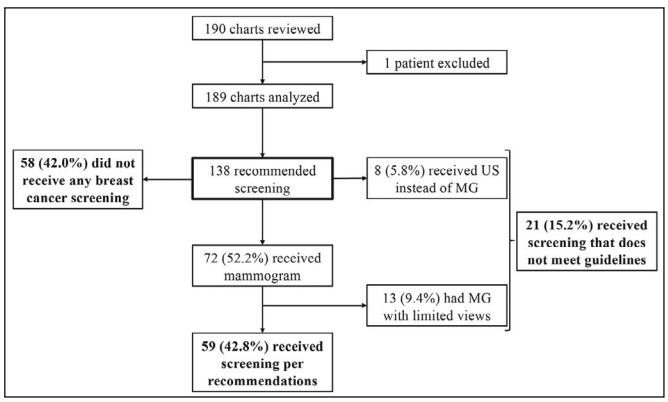
Sophia Williams-Perez, MD[1]; Viola Leal, MPH[2]; Sophia Russell, MPH[3]; Luz Macias Melendez, MSSW[4]; Robert Volk[5]; Mark Zafereo[6]; Mimi Hu[7]; Julie A Sosa[8]; Larkin Strong[9]; Elizabeth Grubbs, MD[10]
[1]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [4]University of Texas Health Science Center Houston, Houston, TX, US; [5], US; [6], US; [7], US; [8], USUS; [10]The University of Texas MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Both rare cancer and underrepresented patient populations face clinical vulnerabilities which lead to increased mortality, limited research participation, and patient distrust in the healthcare system. We manage a multi-institutional registry that facilitates the study of a rare disease, medullary thyroid cancer, (MTCCoRe); however, underrepresented patient enrollment is limited, preventing the real-world representation of this disease. We report using community-based participatory feedback to identify barriers to registry involvement and research participation in the Latino/a community, an underrepresented group in MTCCoRe. **METHODS:** Using a community-based participatory feedback method to identify stakeholders, we worked with the Community Scientist Program (CSP) at The University of Texas MD Anderson Cancer Center, a program joining trained patients with researchers. Two sessions occurred, one with underrepresented English-speaking cancer patients and one with mono- or bi- lingual Spanish-speaking cancer patients. Sessions were 60 minutes with a 15-minute presentation followed by a 45-minute discussion. **RESULTS:** Seventeen community scientists participated across two sessions. Most participants identified as female (n=15). Research presentation material included our previous efforts enrolling patients in MTCCoRe. Questions for each group included perceptions with research participation and barriers towards outreach in underrepresented communities. From the English-speaking session, common cited barriers included desire for privacy surrounding their disease and concerns of unauthorized information sharing. From the Spanish-speaking session, common cited barriers included lack of culturally-adapted education and enrollment materials as well as varying preferences and abilities with electronic communication. Both groups recommended using community health partners, such as local clinics, churches, and “promotores”, to promote research awareness and inclusion. **CONCLUSIONS:** Our current multi-institutional registry for medullary thyroid cancer, a rare cancer, lacks appropriate inclusion of underrepresented patients. Utilizing community-based participatory feedback, we worked with underrepresented cancer patients to identify barriers in research participation including uncertainty around data-sharing and lack of culturally-adapted materials. Next steps include patient co-development of such adapted resources.

P70. Mammogram screening rates and barriers among women with disabilities

Madison S. House, BS[1]; Giles Hamilton-Fletcher, PhD[2]; Connie Lam, MS[3]; John-Ross Rizzo, MD[4]; Kathie-Ann Joseph, MD, MPH[5]
[1]NYU Grossman School of Medicine, New York, NY, US; [2]NYU Langone Health, New York, NY, US; [3]Initiative for Women with Disabilities, NYU Langone Health, New York, NY, US; [4]NYU Grossman School of Medicine, New York, NY, US; [5]NYU Grossman School of Medicine, New York, NY, US

INTRODUCTION: Significant disparities exist in breast cancer screening, detection, and treatment for women with disabilities. The reasons for these disparities have not been studied extensively and are poorly understood, limiting efforts towards equity. We evaluated rates of mammogram screening at a clinic for women with disabilities. **METHODS:** We examined a retrospective cohort of 190 women who received gynecologic care at the NYULH Initiative for Women with Disabilities (IWD) from February 2023 through January 2024. One patient who passed away was excludedx. The primary outcome was rate of adequate breast cancer screening. Secondary outcomes included breast exam rate, barriers to breast cancer screening, and imaging rates by race, ethnicity, and insurance type (Medicaid, Medicare, private, uninsured). **RESULTS:** 138 of 189 (73%) participants met criteria for breast cancer screening per ASBrS guidelines: annually for women over 40 years old or earlier for women with a first-degree family history. Of recommended participants, only 72 (52.2%) received screening mammograms (SMs) within an appropriate time window. Among the 72 participants who received SMs, 13 (18.1%) of mammograms had views that were limited by "wheelchairs" or "patient immobility." Only 52 (42.0%) women met screening guidelines. Among 138 women recommended for a SM, 8 (5.8%) received a breast ultrasound instead of a SM, which is not standard of care. Overall, of the 138 patients recommended for a SM, 59 (42.8%) patients received adequate screening, 58 (42.0%) received no screening, and 21 (15.2%) received inadequate screening. 8% of all women were missing a documented breast exam within the study period. Most patients, 83.1%, had requests for mobility-related accommodations. There were no significant differences in primary or secondary outcomes by race, ethnicity, or insurance type. **CONCLUSIONS:** Low screening rates and inadequate screening persist for women with disabilities. The IWD is a specialized advocacy clinic, leading us to believe that SM disparities may be even more pronounced in general. Further studies should elucidate the structural barriers preventing this group from accessing screening and receiving the necessary accommodations for adequate diagnostic imaging. Ultimately, this work should be used to mitigate perpetuated disparities in care for this vulnerable population.



P71. Medicaid Expansion is Not Associated with the Reduction in Racial Cancer Disparities in the Receipt of Timely Guideline Concordant Cancer Care

Zachary A Whitham, MD[1]; Matthew Porembka, MD[2]; Patricio M. Polanco, MD[3]; Cecilia G Ethun, MD[4]; Alex Kim[5]; Amanda Dann, MD[6]; Amit Singal[7]; Adam Yopp, MD[8]
[1]The University of Texas Southwestern Medical Center, Dallas, TX, US; [2]UT Southwestern Medical Center, Dallas, TX, US; [3]University of Texas Southwestern Medical Center, Dallas, TX, US; [4]UT Southwestern Medical Center, Dallas, TX, US; [5]UT Southwestern Medical Center, Dallas, TX, US; [6]The University of Texas Southwestern Center for Breast Care, Dallas, TX, US; [7]University of Texas Southwestern Medical Center, Dallas, TX, US; [8]UT Southwestern Medical Center, Dallas, TX, US

INTRODUCTION: Although Medicaid expansion (ME) under the Affordable Care Act increased healthcare access, the reduction of racial/ethnic cancer disparities is dependent on both patient- and system-level factors. Receipt of timely, guideline-concordant cancer care (GCC) is associated with the reduction of cancer disparities, but the impact of ME on this cancer quality outcome remains poorly characterized. **METHODS:** Patients aged 40-64 with lung (non-small cell and small cell), colon adenocarcinoma, rectal adenocarcinoma, pancreas adenocarcinoma, and breast cancer within the National Cancer Database were identified. A quasi-experimental, difference-in-difference approach was used to compare receipt of timely (within 30 days of diagnosis) GCC (based on NCCN guidelines) between patients in ME states vs. non-expansion (NE) states before (2009-2013) and after (2015-2019) ME enactment. Adjusted DID estimates stratified by race for timely GCC were calculated using multivariate linear regression. **RESULTS:** 646,410 patients (lung n=108,274; colon n=85,656; rectal n=38,841; pancreatic n=24,367; breast n=388,272) were identified. Examining all cancer subtypes combined, in both White and Black patients, receipt of timely GCC decreased over time in both ME and NE states. (Table) However, declines were smaller in states post-ME and thus were associated with a relative increase in timely GCC in Black compared to White patients (DID=1.5, p=0.03). When examined by cancer subtype, ME was associated with an increase in timely GCC among White patients with lung (DID=1.8, p=0.006), rectum (DID=2.2, p=0.04) and breast (DID=3.4, p<0.001) cancers and among Black patients with pancreas (DID=8.9, p=0.01) or breast (DID=4.7, p<0.001) cancers. Compared with White patients, Black patients only had a significant improvement in receipt of timely GCC associated with ME in pancreas (difference DID=10.0, p=0.007) but not colon, rectum, breast or lung cancers. **CONCLUSIONS:** Among patients with the four highest mortality rates in the United States, ME was associated with receipt of timely GCC. However, only in pancreas cancer was ME associated with a reduction in White-Black disparities in the receipt of timely GCC. Access to healthcare is just one factor that needs to be mitigated to reduce racial cancer care disparities.

Table. Receipt of Timely and Guideline Concordant Cancer Care

	Non-Expansion States		Expansion States					
	Pre-2014	Post-2014	Pre-2014	Post-2014	Adjusted DID (95%CI)[&]	P	Adjusted difference in DID[&*] (95%CI)	P
All sites, combined								
White	64.8	53.3	60.6	51.6	2.6 (2.1, 3.1)	<0.001	Ref	0.034
Black	56.8	48.9	49.0	44.9	4.2 (2.8, 5.5)	<0.001	1.5 (0.1, 3.0)	
Lung								
White	65.6	58.3	63.2	57.2	1.8 (0.1, 3.1)	0.006	Ref	0.674
Black	53.6	49.4	50.1	47.8	2.5 (-0.8, 5.8)	0.143	0.7 (-2.7, 4.2)	
Colon								
White	86.6	79.5	83.4	76.7	3.0 (-0.9, 1.5)	0.630	Ref	0.406
Black	81.4	73.9	74.2	67.8	1.5 (-1.3, 4.3)	0.288	1.2 (-1.6, 4.1)	
Rectum								
White	56.1	41.2	48.2	36.0	2.2 (1.0, 4.4)	0.043	Ref	0.411
Black	42.1	31.8	32.5	27.2	5.0 (-1.0, 11.0)	0.101	2.8 (-3.9, 9.4)	
Pancreas								
White	66.7	64.0	66.1	62.0	-0.7 (-3.6, 2.1)	0.615	Ref	0.007
Black	55.4	49.8	52.5	54.4	8.9 (2.0, 15.8)	0.011	10.0 (2.7, 17.2)	
Breast								
White	60.5	47.0	56.1	46.0	3.4 (2.7, 4.1)	<0.001	Ref	0.147
Black	50.7	42.4	42.3	38.4	4.7 (3.0, 6.5)	<0.001	1.4 (-0.5, 3.2)	

[&] model adjusted for: age at diagnosis, sex, Charlson-Deyo comorbidity score, cancer stage, rural/urban residence, and facility type.
[*] model using White race as reference

P72. Military Insurance and Melanoma Outcomes in the National Cancer Database

Robert Connor Chick, MD[1]; Taylor P Williams, MD[2]; Robert W Krell, MD[3]; Hayley Dunlop, BS[4]; Hayden Raish, BS[5]; Carlo M Contreras, MD[6]; Samilia Obeng-Gyasi, MD MPH[7]; Alex Kim, MD PhD[8]; Tim M Pawlik, MD PhD[9]; Joal D Beane, MD[10]
[1]The Ohio State University Wexner Medical Center, Columbus, OH, US; [2]The Ohio State University Wexner Medical Center, Columbus, OH, US; [3]Uniformed Services University of the Health Sciences, Bethesda, MD, US; [4]The Ohio State University Medical Center, Columbus, OH, US; [5]The Ohio State University Wexner Medical Center, Columbus, OH, US; [6]The Ohio State University Wexner Medical Center, Columbus, OH, US; [7]The Ohio State University Wexner Medical

Center, Columbus, OH, US; [8]UT Southwestern Medical Center, Dallas, TX, US; [9]The Ohio State University Wexner Medical Center, Columbus, OH, US; [10]The Ohio State University Wexner Medical Center, Columbus, OH, US

INTRODUCTION: Melanoma is one of the most common cancers diagnosed among military servicemembers and veterans, who are increasingly pushed to seek cancer care in civilian settings with Tricare or Veterans Affairs (VA) acting as an insurance payor. Outcomes for military beneficiaries (MB) with melanoma who are treated outside VA hospitals have not been reported. The aim of this study is to examine outcomes among MB with melanoma and explore the influence of demographic or treatment differences on outcomes. **METHODS:** Using the National Cancer Database, patients age <65 with stage I-IV cutaneous melanoma from 2010 to 2017 with private (PI) or Other Government insurance (i.e. MB), no prior malignancies, and Charlson-Deyo score <3 were included. Care fragmentation was defined as discrepancy between diagnosing and treating facility, or receiving only a fraction of treatment in the reporting facility. Descriptive analyses were performed using chi-square and Kruskal-Wallis tests. Kaplan-Meier method and Cox proportional hazards models were used to evaluate overall survival (OS). Logistic regression was performed to identify predictors of stage III or IV melanoma at diagnosis. **RESULTS:** A total of 110,246 patients met inclusion criteria, of whom 2,009 were MB. MB were more likely than PI to be male, live in lower median income areas, present at later stages, travel further for care, have fragmented care, and have treatment delay >30 days (all p<0.001). OS was worse for MB compared with PI (98.0 vs. 103.6 months, p<0.001, Figure 1); this difference persisted after stratification by stage (p=0.015). After adjusting for age, sex, race, urban/rural, median income, comorbidities, fragmentation, travel distance, and treatment delay, MB remained an independent predictor of OS (adjusted HR 1.39, p<0.001). MB was an independent predictor of stage III/IV at diagnosis (adjusted OR 1.38, p<0.001). **CONCLUSIONS:** MB with cutaneous melanoma have significantly worse OS compared with PI. While MB have more advanced stage presentation, care fragmentation, distance traveled, and treatment delay, there may be additional barriers to timely access to care in this population. Previous studies have suggested equivalent outcomes between MB and the general population due to universal insurance coverage, but these results suggest MB with melanoma face additional challenges when treated outside federal facilities. Further studies should examine the impact of geographical assignment, timely access to care, and care fragmentation on diagnosis and treatment of melanoma among military beneficiaries.

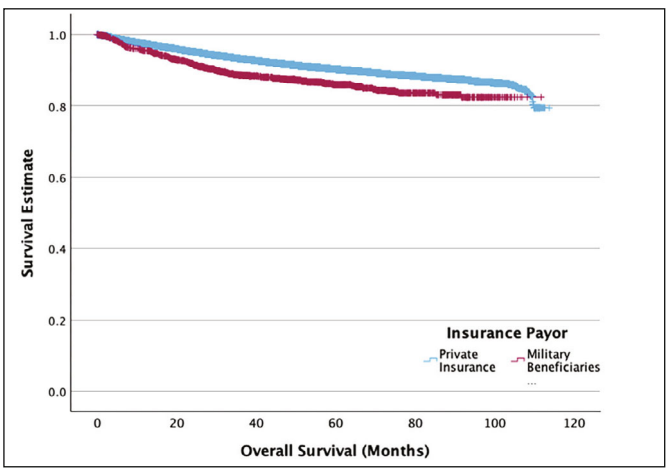


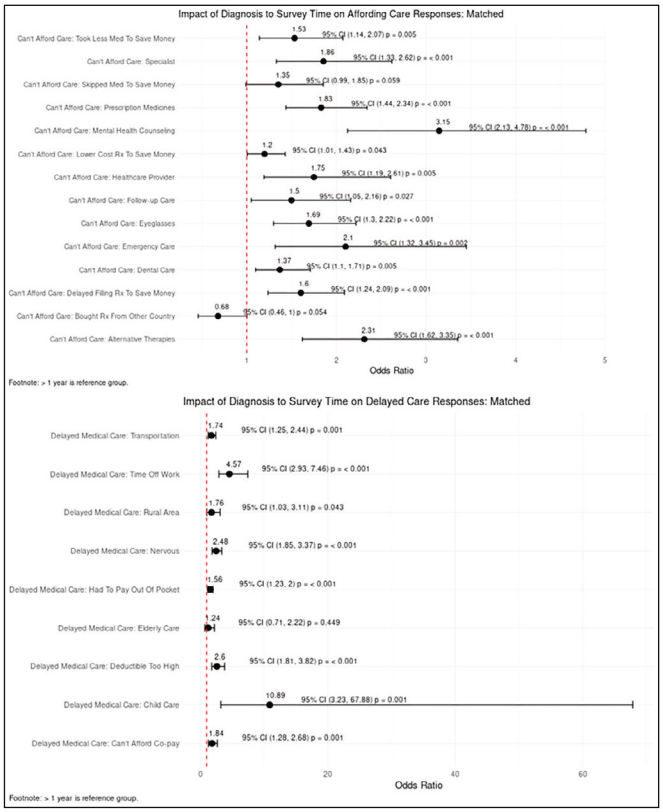
Figure 1. Kaplan-Meier overall survival estimate comparing private insurance (103.6 months) and military beneficiaries (98.0 months, p<0.001).

P73. Self-Perceived Barriers to Healthcare Experienced by Patients with Gastrointestinal Cancers

Samuel D. Butensky, MD[1]; Elizabeth L Godfrey, MD[2]; Jihoon Kim[3]; Daniel Kerekes, MD[4]; David G su, MD[5]; Dina Gamroudi[6]; John W Kunstman, MD[7]; Kelly Olino, MD[8]; Kevin G. Billingsley, MD, MBA[9]; Kiran Turaga, MD, FACS[10]; Nita Ahuja, MD, MBA, FACS[11]; Caroline H. Johnson, PhD[12]; Sajid Khan, MD, FACS[13]

[1]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [2]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [3]Yale University Department of Biomedical Informatics and Data Sciences, New Haven, CT, US; [4]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [5]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [6]Yale University School of Public Health, New Haven, CT, US; [7]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [8]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [9]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [10]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [11]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [12]Yale School of Public Health, New Haven, CT, US; [13]Yale University School of Medicine, Department of Surgery, New Haven, CT, US

INTRODUCTION: Gastrointestinal cancer (GIC) treatment is complex, situating cancer patients at increased vulnerability in multiple facets of healthcare. We hypothesized that a diagnosis of GIC was associated with delays in care and decreased affordability of treatment. **METHODS:** Prospectively collected data from The All of Us database was queried for GIC patients who completed the Healthcare Access and Utilization (HAU) survey. This cohort was separated by those who answered the survey less than 1 year after their diagnosis and those who answered more than 1 year after their diagnosis. These cohorts were propensity-matched based on age, race, sex, deprivation index, income, insurance, employment, and Charlson Deyo comorbidities. Regression was used to analyze the relationship between diagnosis to survey response time and survey scores. **RESULTS:** A total of 9,975 patients were included: 1,804 answered the survey less than 1 year after their cancer diagnosis, and 8,171 answered more than 1 year. Patients were most commonly white (88.5%), female (57.3%), non-Hispanic (99.0%), employed (40.8%), and earning $50,000-100,000 (30.5%). Colon cancer was most represented (75%), followed by anus (12%), rectum (6.2%), stomach (3.2%), and pancreas (0.9%) cancers. The median time between cancer diagnosis and survey response was 3.5 years (IQR 1.5-6.7 years). GIC patients surveyed before 1 year after diagnosis were more likely to have trouble affording healthcare compared to those surveyed after 1 year, including mental health counseling (OR 3.15, [95% CI: 2.13-4.78]), emergency care (OR 2.10, [95% CI: 1.32-3.45]), and prescription medications (OR 1.83, [95% CI: 1.33-2.62]). Patients surveyed before 1 year were more likely to experience delays in care due to inability to get time off work (OR 4.57, [95% CI: 2.93-7.46]), nervousness (OR 2.48, [95% CI: 1.85-3.37]), and childcare (OR 10.89, [95% CI: 3.23-67.9]). Lower income was associated with increased delays in care and decreased affordability. Income < $50,000 (vs. > $50,000) was associated with a lower likelihood of not affording emergency care (OR 0.24, [95% CI: 0.15-0.36]) and mental health counseling (OR 0.20, 95% CI: 0.15-0.28]). Receiving chemotherapy did not affect affordability or delays of care in either group. **CONCLUSIONS:** Newly diagnosed gastrointestinal cancer patients perceive financial barriers to emergency healthcare, mental health counseling, and prescription medications, and work and childcare lead to delays in cancer treatment. Societal and medical reforms following a cancer diagnosis are warranted.



P74. Social vulnerability, but not rurality, is associated with receipt of guideline concordant care for pancreas cancer in North Carolina

Sarah Provencher[1]; KyungSu Kim, MS[2]; Christopher Baggett, PhD[3]; Peter J Allen, MD[4]; Dan G Blazer, MD[5]; Anai N Kothari, MD, MS[6]; Callisia N Clarke, MD, MS, FSSO[7]; Ugwuji N Maduekwe, MD, MMSc, MPH, FACS, FSSO[8]; Allison N Martin, MD, MPH[9]

[1]Department of Surgery, Duke University School of Medicine, Durham, NC, US; [2]Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [3]Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [4]Duke University Medical Center, Durham, NC, US; [5]Duke University Medical Center, Durham, NC, US; [6]Division of Surgical Oncology, Department of Surgery, Medical College of Wisconsin, Milwaukee, WI, US; [7]Medical College of Wisconsin, Milwaukee, WI, US; [8]Medical College of Wisconsin, Milwaukee, WI, US; [9]Department of Surgery, Duke University School of Medicine, Durham, NC, US

INTRODUCTION: Previous studies have shown that patients with pancreatic ductal adenocarcinoma (PDAC) and higher social deprivation index (SDI) scores are less likely to receive guideline concordant care (GCC). This relationship may be influenced by rural geographic location. The relationship between SDI scores and likelihood of receiving GCC amongst rural PDAC patients is under investigated. We hypothesized that SDI and rurality would impact receipt of GCC for patients with PDAC. **METHODS:** The North Carolina Central Cancer Registry, linked to multi-payer claims data was retrospectively queried to identify patients with PDAC (2004-2019). Patients without 12 months of continuous coverage after diagnosis, incomplete staging or missing SDI were excluded. Rural-Urban Commuting Area were used to specify geographic location. GCC was defined by National Cancer Center Network guidelines for PDAC, with staging according to NIH Surveillance, Epidemiology, and End Results: localized disease receiving surgery and chemotherapy, regional disease receiving at least chemotherapy, and distant disease receiving chemotherapy or palliative care. Logistic analysis was performed to assess impact of patient-level factors, SDI, and patient location at the time of diagnosis on GCC receipt. **RESULTS:** The final study cohort included 1,884 PDAC patients. The cohort included urban (n=1360, 72%), suburban (n=425, 23%), and rural dwellers (n=99, 5%). Most patients had regional disease at diagnosis (n=1155, 61%). Most of the cohort was between 65-79 years (n=1098, 58%), female (n=1008, 54%), non-Hispanic white (n=1383, 73%), medium SDI (n=911, 48%), and Charlson Comorbidity Index (CCI) 3+ (n=722, 38%). By stage, GCC was received by 2124 (45%) localized, 1013 (88%) regional, and 290 (64%) distant stage PDAC. Multivariable regression including all stages demonstrated decreased odds of receiving GCC for patients with high SDI (OR = 0.66, 95% confidence interval (CI) [0.48, 0.93]), age 80 or older (OR=0.33, 95%CI [0.24, 0.45]), and with CCI ³1 (see Table 1). Stage-specific multivariable regressions demonstrated significant associations with medium SDI on localized PDAC (OR 0.45, 95% CI [0.24, 0.87]) and high SDI on regional PDAC (OR 0.45, 0.26, 0.78). Patients with distant PDAC had no association with SDI. Across all PDAC stages, there was no association between receipt of GCC and rural location. **CONCLUSIONS:** Social vulnerability, but not rurality, was associated with decreased receipt of guideline concordant care for patients diagnosed with pancreas cancer. Multilevel interventions are needed to better understand barriers and facilitators of receipt of GCC at a state-level.

Table 1. Associations of Patient-Level Characteristics with Receipt of Guideline Concordant Care for Pancreas Cancer (N=1,884)

			95% Confidence Interval		
Parameter		**Odds Ratio**	**Lower**	**Upper**	**p-value**
Sex	Male	(ref)	-	-	-
	Female	1.06	0.85	1.32	0.625
Age	Age 65-79	(ref)	-	-	-
	Age 18-64	1.27	0.91	1.78	0.165
	Age 80 or above	0.33	0.24	0.45	<.0001
Race	Non-Hispanic White	(ref)	-	-	-
	Hispanic or Other	0.83	0.5	1.37	0.461
	Non-Hispanic Black	1.09	0.81	1.46	0.563
Location	Rural	(ref)	-	-	-
	Suburban	0.75	0.43	1.28	0.292
	Urban	0.84	0.5	1.41	0.52
Insurance	Private	(ref)	-	-	-
	Medicaid	0.72	0.49	1.06	0.095
	Medicare	1.35	0.89	2.06	0.157
CCI	0	(ref)	-	-	-
	1	1.62	1.17	2.25	0.004
	2	1.78	1.27	2.51	0.0008
	3+	2	1.48	2.71	<.0001
SDI	Low	(ref)	-	-	-
	High	0.66	0.48	0.93	0.016
	Medium	0.77	0.59	1.01	0.061

SDI: Social Deprivation Index | CCI: Charlson Comorbidity Index

P75. The Impact of Neighborhood Socioeconomic Disadvantage on Treatment and Outcomes for Resectable Gastric Cancer Patients in Florida: An Incidence-Based Retrospective Cohort Study

Anna Zemora, BS[1]; Crystal Li, BS[2]; Jennifer B. Permuth, PhD MS[3]; Susan Vadaparampil, PhD, MPH[4]; Jason Fleming, MD[5]; Jeremy L. Davis, MD[6]; Benjamin Powers, [7]

[1]University of Maryland School of Medicine, Baltimore, MD, US; [2]University of Maryland School of Medicine, Baltimore, MD, US; [3]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [4]Moffitt Cancer Center, Tampa, FL, US; [5]UT Southwestern, Dallas, TX, US; [6]National Cancer Institute, Bethesda, MD, US; [7]University of Maryland School of Medicine- Department of Surgery, Baltimore, MD, US

INTRODUCTION: Patients with resectable gastric cancer are undertreated in the United States. Although socioeconomic status is thought to be associated with disparities, studies have typically used large geographic areas (zip codes or counties) for assessment. A statewide cancer registry was used to assess socioeconomic disadvantage (SED) at the neighborhood level. **METHODS:** Using the incidence-based Florida Cancer Data System, 8,304 gastric adenocarcinoma patients diagnosed from 2008-2015 were identified; 3,622 had resectable gastric cancer (AJCC clinical stage I-III after excluding T1a) and were clinically eligible for surgery (no comorbidity precluded surgery). The Area Deprivation Index (ADI) was used to assess receipt of treatment and overall survival. The national ADI a validated dataset that ranks neighborhoods (census block groups) from 1-100 (higher scores=higher disadvantage) at the national level. Descriptive statistics and survival analysis

with Kaplan-Meier and Cox proportional hazard regression were used. **RESULTS:** The median national SED ranking was 60, interquartile range 38-80. The rates of surgery, chemotherapy, radiation, and multimodal treatment (chemotherapy + surgery) for the cohort were 66.7%, 49.7%, 31%, and 34.4%, respectively. SED was associated with race, ethnicity, insurance status, receipt of chemotherapy, and multimodal treatment, and survival ($p<0.05$) but not associated with age, surgery, gender, and radiation. The median OS for the cohort was 22.6 months and 30.9, 25.8, and 16.3 months for stage I, II and III, respectively. The median OS for surgery and no-surgery cohorts were 31.1 and 10.3 months, respectively ($p<0.05$). The highest SED quartile had a lower OS (19.1 months) compared to the lowest SED quartile (25.8 months). After adjustment for demographic and treatment variables, the highest SED quartile had an increased odds of mortality relative to the lowest SED quartile (HR 1.31; 95% CI, 1.16-1.46). **CONCLUSIONS:** Resectable gastric cancer patients with higher neighborhood SED received less chemotherapy and have worse overall survival than lower SED patients; however, there was no difference in receipt of surgery. The OS disparity for higher SED patients persisted after controlling for demographic and treatment variables. Future studies are needed to identify the drivers of survival disparities, particularly treatment quality, that may contribute to survival disparities.

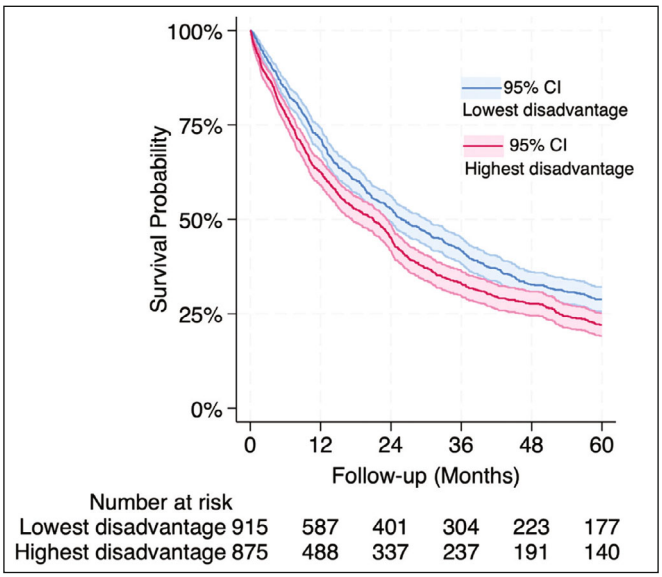


Figure 1. Kaplan Meier Overall Survival Estimates of Resectable Gastric Cancer in Florida by Neighborhood Socioeconomic Deprivation

P76. The Melanoma Divide: Skin-deep Hispanic Health Disparities from Latin America to the United States

Gabriel A De la Cruz Ku[1]; Gonzalo Ziegler Rodriguez[2]; Sheila K Diaz-Mora[3]; Luis Piedra-Delgado[4]; Jiddu A Guart[5]; Alanna Hickey[6]; Kabir A Torres[7]; Jessica J Farzan[8]; Anshumi Desai[9]; Camila Franco[10]; Michael P Mallouh, MSc[11]; Juan C Haro Varas[12]; Sandro Casavilca-Zambrano[13]; Jose M Cotrina Concha[14]; Mecker Moller[15]

[1]University of Massachusetts Medical School, Worcester, MA, US; [2]Instituto Nacional de Enfermedades Neoplasicas, Lima, PE; [3]Instituto Nacional de Enfermedades Neoplasticas, Lima, PE; [4]Universidad Cientifica del Sur, Lima, Peru, Lima, PE; [5]University of Massachusetts Medical School, Worcester, Worcester, MA, US; [6]University of Massachusetts Medical School, Worcester, MA, US; [7]University of Massachusetts Medical School, Worcester, MA, US; [8]University of Massachusetts Medical School, Worcester, MA, US; [9]University of Miami Miller School of Medicine, Miami, FL, US; [10]University of Texas Medical Branch at Galveston, Texas, Galveston, TX, US; [11]University of Massachusetts Medical School, Worcester, MA, US; [12]Instituto Nacional de Enfermedades Neoplasicas, Lima, PE; [13]Instituto Nacional de Enfermedades Neoplasicas, Lima, PE; [14]Instituto Nacional de Enfermedades Neoplasicas, Lima, PE; [15]University of Chicago Pritzker School of Medicine, Chicago, IL, US

INTRODUCTION: Melanoma is a heterogeneous malignancy that has increased by 20% in the Hispanic population over the past two decades. Disparities in healthcare access significantly impact patient outcomes. We aimed to compare the clinical, pathological, and outcome-related characteristics of Hispanic patients with melanoma in Latin America (HPLA) vs The USA (HPUS). **METHODS:** Two retrospective cohorts were evaluated: HPLA diagnosed with melanoma at tertiary institution in Lima-Peru and HPUS with melanoma from the Surveillance, Epidemiology, and End Results Program (SEER) during 2010-2019 period. **RESULTS:** A total of 1136 HPLA and 5302 HPUS were included. HPLA patients were older (61.17 vs. 56.63 years, $p<0.001$), more likely to be male (51.5% vs. 39.6%, and resided in non-metropolitan areas (49.6% vs. 3.5%, $p<0.001$). They also had a higher prevalence of primary lesions in the lower extremities (75.5% vs. 36.9%, $p<0.001$) and ulceration (65.3% vs. 21.3%, $p<0.001$). Histologically, HPLA most commonly presented with acral lentiginous melanoma (38.1%), while HPUS had more superficial spreading melanoma (30.8%, $p<0.001$). HPLA showed greater Breslow depth (mean: 7.66 mm vs. 1.51 mm, $p<0.001$) and mitotic activity (mean: 6.62 vs. 2.12, and were diagnosed at more advanced stages: T3-4 (70.4% vs. 28.8%, N+ (63.1% vs. 16.8%, Stage III (36.5% vs. 15.0%), and Stage IV (23.0% vs. 3.8%, $p<0.001$). In terms of treatment, HPLA had more sentinel lymph node biopsies (74.4% vs. 53.6%, received more systemic chemotherapy (13.6% vs. 8.2%, and radiotherapy (3.7% vs. 2.1%, $p=0.003$). With a median follow-up of 74 months, HPLA exhibited worse 5-year OS rates across all stages vs HPUS: Stage I (84% vs. 93%, $p=0.002$), Stage II (52% vs. 73%, Stage III (25% vs. 56%, and Stage IV (7% vs. 14%, $p=0.001$). **CONCLUSIONS:** HPLA with melanoma exhibit more aggressive pathological features than their HPUS counterparts and are diagnosed at more advanced stages, resulting in poorer overall survival rates across all stages. These findings emphasize the need for further research to deepen our understanding of the molecular factors influencing this diverse biological presentation in Hispanic populations. Additionally, they highlight the critical need to improve early access to cancer care in Latin American countries.

P77. Trends in Compliance with Updated Colorectal Cancer Screening Guidelines

Meredith Gunder[1]; Julie B Siegel, MD[2]; Neal Bhutiani[3]; Sandy Kavalukas[4]; Michael E. Egger, MD, MPH[5]

[1]University of Louisville, Louisville, KY, US; [2]University of Louisville, Louisville, KY, US; [3]University of Louisville, Louisville, KY, US; [4]University of Louisville School of Medicine, Louisville, KY, US; [5]University of Louisville Department of Surgery, Louisville, KY, US

INTRODUCTION: Incidence of colorectal cancer in younger patients is increasing in the United States. In May 2021, the United States Preventative Services Task Force (USPSTF) updated recommendations for colorectal cancer screening to start at age 45. There is limited data on compliance with the new guidelines. **METHODS:** Data from the 2022 and 2023 Behavioral Risk Factor Surveillance System (BRFSS) was reviewed to identify survey respondents aged 45-49 who had any screening test for colorectal cancer within the recommended time period. Statistical analysis was performed to identify predictive factors for compliance with screening guidelines in each year. Cochran-Mantel-Haenszel tests were conducted to analyze the difference in trends in compliance over a two year period. **RESULTS:** In 2022, 26.6% of survey participants aged 45-49 met USPSTF screening guidelines for colorectal cancer. The rate of screening compliance among 45-49 year-olds increased to 35.5% in 2023. In comparison, 70.3% and 72.7% of patients aged 50-79 met screening guidelines in 2022 and 2023, respectively. In 2023, for patients aged 45-49, the rate of colorectal cancer screening was highest in white (40.4%) and multiracial patients(40.4%), compared to Black (30.1%), Hispanic (32.9%), and Asian patients (14.3%). Patients who did comply with screening guidelines were more likely to have health insurance (37.8% vs 12.3%, $p<0.001$), and have a primary care physician (PCP) (38.2% vs 19.5%, $p<0.01$). Patients with higher education level and higher income level were also more likely to be adherent to updated recommendations (39.4% vs 24.6% $p=0.02$, 44.0% vs 26.5%, $p=0.004$, respectively) Over the two year analysis, rates of screening increased more in women compared to men (12.2% vs 5.2%, and those with a PCP (9.4% vs 6.1%, $p<0.001$). Patients with private health insurance had a greater increase in screening compared to those with public health insurance or no health insurance (10.2% vs 6.4% vs 4.2%, $p<0.001$) and patients with higher education level and higher income level had larger increases in screening than their lower education level and lower income level counterparts (10.1% vs 7.7%, $p<0.001$, and 11.3% vs 2.8%, respectively). **CONCLUSIONS:** Compliance with updated colorectal cancer screening guidelines is increasing in patients aged 45-49. A more prompt adoption of new screening guidelines is seen among women, patients with higher education level, higher income level, private insurance, or those with a primary care physician. Additional

work is needed to increase awareness of new recommendations in both the general population and medical community.

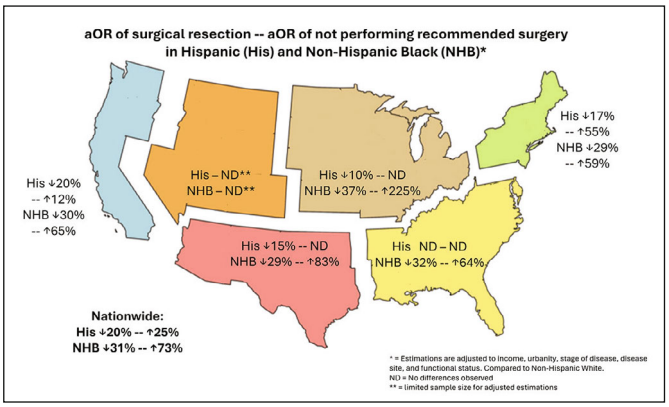
	Met Criteria 2022 (n=524)	Met Criteria 2023 (n=334)	% Change	CMH p-value
Sex				
Male	258 (27.3%)	147 (32.5%)	5.2	<0.001
Female	266 (26%)	187 (38.2%)	12.2	
Race				
White, NH	327 (28.2%)	212 (40.4%)	12.2	<0.001
Black, NH	74 (31.1%)	41 (30.1%)	-1	
Hispanic	79 (23.2%)	46 (32.9%)	9.7	
Asian	10 (11.1%)	8 (14.3%)	3.2	
AI/AN/PI	10 (27.0%)	1 (14.3%)	-12.7	
Multiracial	4 (18.2%)	21 (40.4%)	22.2	
Income				
<$50k	116 (23.7%)	54 (26.5%)	2.8	<0.001
$50k-$100k	113 (26.7%)	73 (33.5%)	6.8	
$100k-$200k	137 (27.7%)	105 (38.3%)	10.6	
>$200k	85 (32.7%)	59 (44.0%)	11.3	
Education Level				
No Degree	25 (16.9%)	15 (24.6%)	7.7	<0.01
HS Degree	196 (25.2%)	131 (32.8%)	7.6	
College Degree	303 (29.3%)	188 (39.4%)	10.1	
Health Insurance Status				
Public Insurance	123 (27.9%)	49 (34.3%)	6.4	<0.01
Private Insurance	378 (28.5%)	251 (38.6%)	10.1	
No Insurance	11 (8.1%)	10 (12.3%)	4.2	
Health Awareness				
Have PCP	487 (28.8%)	304 (38.2%)	9.4	<0.001
Don't Have PCP	37 (13.4%)	26 (19.5%)	6.1	

P78. Two-Decade Trends in Gastrointestinal Neuroendocrine Tumors: Rising Incidence and Unresolved Disparities

Salvador Rodriguez Franco, MD[1]; Paul V Winter[2]; Bianca Bechini[3]; Sumaya Abdul Ghaffar, MD[4]; Andrii Khomiak, MD[5]; Reed Weiss[6]; Mona Hamermesh[7]; Benedetto Mungo[8]; Richard Schulick, MD MBA[9]; Marco Del Chiaro, MD PhD[10]; Ana L. Gleisner, Md, PhD[11]

[1]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [2]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [3]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [4]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [5]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [6]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [7]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [8]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [9]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [10]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [11]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US

INTRODUCTION: Gastrointestinal neuroendocrine tumors (GI NETs) are rare malignancies with evolving treatment strategies over the past two decades. However, most large-scale analyses aggregate GI NETs with lung neuroendocrine tumors (NETs), which have double the incidence, potentially skewing accurate GI NET-specific data. Furthermore, due to this lack of specific data, recent concerns about rising costs, limited healthcare access, and treatment disparities have been inadequately evaluated within the context of GI NETs. **METHODS:** A retrospective analysis was conducted using data from the National Cancer Database (NCDB) and the Surveillance, Epidemiology, and End Results (SEER) program from 2001 to 2021. Age-adjusted incidence rates and average annual percentage change (AAPC) were calculated for GI NETs across various anatomical sites: stomach, liver, pancreas, duodenum, ileum and jejunum, colon, and rectum. Treatment patterns were analyzed over time and stratified by facility type, insurance status, race, age, and functional status. Differences in clinical practices were evaluated across demographic variables. **RESULTS:** A total of 173,000 GI NET cases were analyzed. The age-adjusted incidence of GI NETs in the United States exhibited a consistent upward trend with an AAPC of +5% from 2001 to 2021. The most pronounced increases were observed in the appendix (AAPC +12.5%), pancreas (+8.6%), and duodenum (+5.5%). Compared to the period from 1973 to 2004, the current increase is less steep but remains significant. Surgical resection rates for GI NETs have significantly increased over the years across all settings, aligning with evolving clinical recommendations. However, substantial disparities were identified based on demographic factors. After adjusting for geographic location, urbanity, income, and disease characteristics, Non-Hispanic Black and Hispanic patients had lower odds of undergoing surgical resection (adjusted odds ratios [aOR] 0.69 [95% CI 0.65–0.72] and 0.80 [95% CI 0.76–0.84], respectively) and higher odds of NOT receiving surgery despite clinical indications (aOR 1.73 [95% CI 1.53–1.95] and 1.25 [95% CI 1.10–1.43], respectively). National differences are presented in Figure 1. **CONCLUSIONS:** Over the past two decades, the incidence of GI NETs has steadily risen in the United States. While surgical intervention rates have improved in alignment with clinical guidelines, persistent disparities based on race, ethnicity, and other demographics exist. These disparities are especially troubling given the rarity of GI NETs, suggesting that these inequities can exist in less rare settings and have not been completely addressed.



P79. Age-Associated Alterations in Cytokine and Extracellular Matrix Remodeling in the Papillary Thyroid Cancer Tumor Microenvironment

Grace Thompson[1]; Fahong Yu[2]; Song Han[3]; Steven Hughes[4]; Aditya Shirali[5]

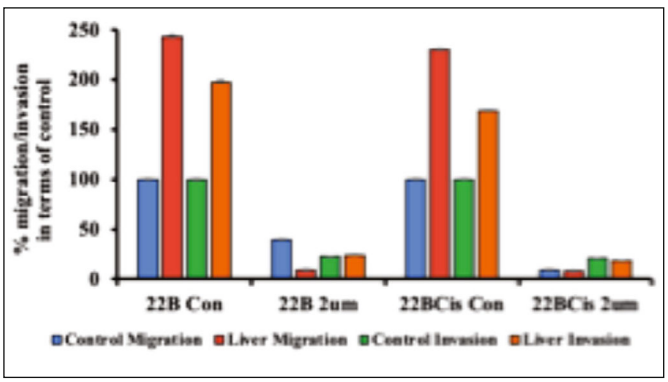
[1]University of Florida College of Medicine, Department of Surgery, Gainesville, FL, US; [2]1. University of Florida, Interdisciplinary Center for Biotechnology Research, Gainesville, FL, US; [3]University of Florida, College of Medicine, Department of Surgery, Gainesville, FL, US; [4]University of Florida College of Medicine, Department of Surgery, Gainesville, FL, US; [5]University of Florida College of Medicine, Department of Surgery, Gainesville, FL, US

INTRODUCTION: Mechanisms underlying the link between cancer and aging are the subject of ongoing investigation. Age related changes in the tumor microenvironment (TME), specifically alterations in cytokine secretion and the extracellular matrix (ECM), are thought to contribute to cancer progression in the older adult. In the context of papillary thyroid cancer (PTC) our group analyzed changes in gene expression with age to identify differences in cytokine activity and the ECM. **METHODS:** RNA sequencing data of PTC samples were obtained from The Cancer Genome Atlas (TCGA). Given the use of 55 years as cutoff by the AJCC 8th edition for PTC, samples were divided into four groups by age: G1 (<55 yrs), G2 (≥55 yrs, ≤64 yrs), G3 (≥65 yrs, ≥74 yrs), and G4 (≥75 yrs). Disease stages were defined as local ($T_{1-2}N_0M_0$), nodal ($T_{1-3}N_{1ab}M_0$), and advanced ($T_4N_XM_{0-1}$). Differentially expressed genes (DEGs) identified from DESeq2 RNA-seq analysis were subjected to Gene set enrichment analysis (GSEA) and ingenuity pathway analysis (IPA) for biological processes and pathways analysis. Significantly activated or inhibited pathways identified by IPA were defined by z-score>2.0 or <-2.0, respectively. **RESULTS:** 498 PTC samples were retrieved from the TCGA portal and divided into age groups: G1 (n=338), G2 (n=84), G3 (n=49) and G4 (n=27). Local and nodal disease were more prominent in younger patients (98% of patients in G1 vs 81% in G4, p<0.0001), but advanced disease increased in older patients (2% of patients in G1 vs 10% in G4, p<0.0001). Comparing G1 vs G2, G1 vs G3, and G1 vs G4 identified 222, 283, and 286 total DEGs respectively (padj<0.01). The number of unique DEGs in G1 vs G2, and G1 vs G4 were 141, 202, and 218 respectively (padj<0.01). GSEA identified the number of DEGs associated with the ECM in G1 vs G2 and G1 vs G4 to be 27 (19 unique) and 22 (14 unique), respectively. The number of DEGs associated with cytokine receptor binding in G1 vs G3 and G1 vs G4 were 17 (all unique) and 10 (all unique), respectively. From G1 to G4, multiple pathways involved in cytokine regulation were found to be dysregulated, including the VDR/RXR activation pathway (z-score=-2.2, p<0.05) and IL33 signaling pathway (z-score=2.3, p<0.05). **CONCLUSIONS:** Transcriptional diversity increases with age in PTC. Expression of genes associated with the ECM and cytokine receptor binding changed significantly with advanced age, supporting the hypothesis that age related changes in the TME may contribute to cancer progression. Further validation studies are needed to elucidate the role of the TME in PTC.

P80. Novel Hsp90 inhibitor PC0 inhibits metastatic spread and overcomes cisplatin resistance in head and neck squamous cancers.

Chitra Subramanian[1]; Kelli McNamara[2]; Myra Kamdar[3]; Michael Depasqale[4]; Daniel Hess[5]; Eva Amatya[6]; Brian Blagg[7]; Mark S Cohen[8]
[1]Carle Illinois College of Medicine, Urbana, IL, US; [2]Carle Illinois College of Medicine, Urbana, IL, US; [3]Carle Illinois College of Medicine, Urbana, IL, US; [4]Carle Illinois College of Medicine, Urbana, IL, US; [5]Carle Illinois College of Medicine, Urbana, IL, US; [6]University of Notre Dame, Notre Dame, IN, US; [7]University of Notre Dame, Notre Dame, IN, US; [8]Carle Illinois College of Medicine, Urbana, IL, US

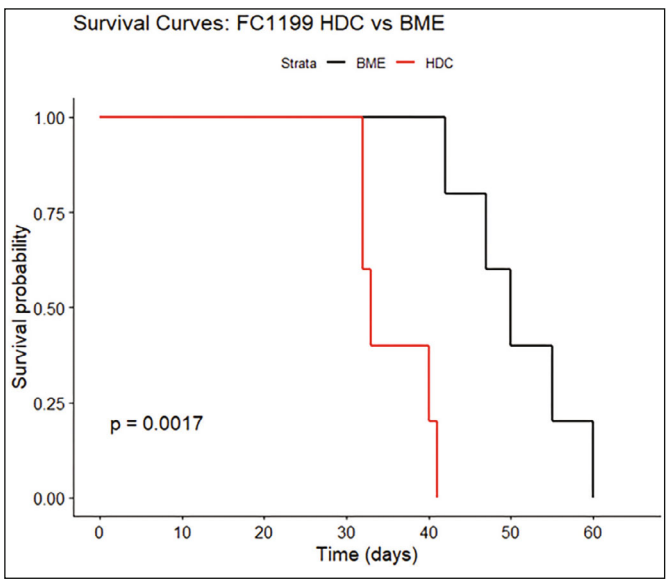
INTRODUCTION: Introduction: The five-year survival rate for head and neck squamous cell carcinoma (HNSCC) remains low at 65%, with first-line cisplatin based regimens having high resistance rates as well as metastatic spread on therapy. Hsp90 is a molecular chaperone whose clients are involved in regulating several cisplatin-resistant pathways. We hypthesize that a novel Hsp90 inhibitor (PC0) targeting the C-terminal binding site, can overcome cisplatin-resistance in HNSCC and block metastatic spread. **METHODS:** Methods: Validated HNSCC cell lines including 2 cisplatin-resistant lines(UMSCC22B, UMSCC22Bcis, UMSCC108, UMSCC108cis, UMSCC47,and UMSCC104) were treated with PC0 over varying concentrations. In vitro studies include cell viability by CellTiter-Glo;RT-PCR and Western blot(WB) analysis to identify the pathways targeted by PC0 after treatment; and transwell migration and invasion assays with and without liver metastatic components(decellularized HNSCC liver metastates from rodent livers). The UALCAN database validated gene expression to assess survival advantages in The Cancer Genome Atlas database. **RESULTS:** Results: CellTiter-GLO viability assay showed PC0 IC50 values were 0.788±0.172uM(22Bcells) and 0.655±0.123uM(22Bcis), and 0.855±0.092uM(108cells) and 1.1±0.26uM(108cis), respectively, indicating potent,effective targeting of both parent and cis-resistant cells at similar concentrations. A dose-dependent decrease in PARP and Akt, as well as an upregulation of p-ERK was seen on WB. RT-PCR analysis using IC50 PC0 concentrations showed a 50-70% downregulation of cell cycle proteins MCM2, CD4, and CD6, and a 70-90% downregulation of the gene AKR1C3(upregulated in cis-resistant tumors),p <0.001 vs. untreated for all. UALCAN and TCGA analysis indicated upregulated AKR1C3 expression levels in HNSCC vs. normal cells, which also associated with significantly worse overall survival (p<0.01). UMSCC22B and 22B-cis cells showed a two-fold increase in migration and invasion in the presence of metastatic ECM components which was reduced by 80% (22B) and 90% (22B-cis) when treated PC0 (p<0.001 each). **CONCLUSIONS:** Our novel Hsp90 inhibitor, PC0, blocks invasion and metastastic spread and induces apoptosis along with inhibiting drug-resistant cell-cycle up-regulation to potently treat cisplatin-resistant HNSCCs. Further in vivo translation is warranted to validate these promising findings for future clinical development.



P81. 3D High-Density Collagen I Improves Modeling of Metastatic Pancreatic Cancer

Kim Nguyen-Ta, MD, MS, MPH[1]; Sural Ranamukhaarachchi, PhD[2]; Jeffrey Turner, BS[3]; Utsav Joshi, PhD[4]; Himangshu Sonowal, PhD[5]; Jorge de la Torre Medina, MD[6]; Herve Tiriac, PhD[7]; Stephanie Fraley, PhD[8]; Rebekah White, MD[9]
[1]University of California San Diego, La Jolla, CA, US; [2]University of California San Diego, La Jolla, CA, US; [3]University of California San Diego, La Jolla, CA, US; [4]University of California San Diego, La Jolla, CA, US; [5]University of California San Diego, La Jolla, CA, US; [6]University of California San Diego, La Jolla, CA, US; [7]University of California, San Diego, La Jolla, CA, US; [8]University of California San Diego, La Jolla, CA, US; [9]University of California San Diego, La Jolla, CA, US

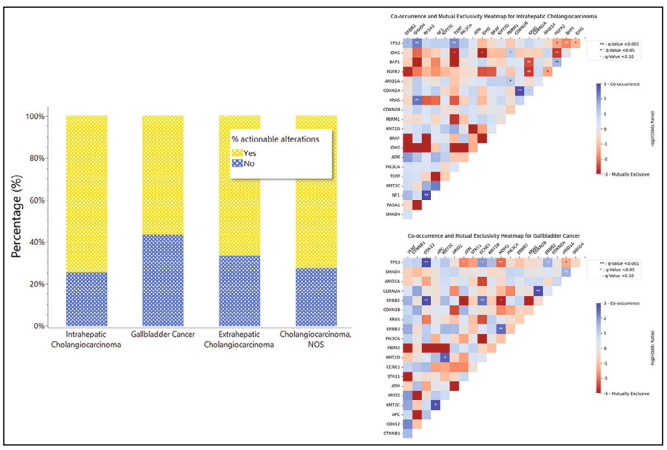
INTRODUCTION: Fibrillar collagen type I constitutes the majority of the extracellular matrix in pancreatic ductal adenocarcinoma (PDAC), yet most *in vivo* murine models involve the use of basement membrane extracts (BME), which instead contain collagen type IV, as matrices to embed PDAC cells. Type I collagen in the PDAC tumor microenvironment has been directly associated with worse prognosis. Our hypothesis is that PDAC cells grown in 3D high-density collagen I (HDC) gels behave more aggressively compared to the same cells grown using conventional BME (Matrigel). **METHODS:** The FC1199 2D cell line was previously generated from a pancreatic tumor that developed in a genetically-engineered (KPC) male mouse. FC1199 cells were cultured *in vitro* in 3D HDC or BME for one week. Orthotopic tumors were established by embedding FC1199 cells in HDC (N=10) or BME (N=10) in the pancreatic tail of syngeneic C57BL/6J mice via laparotomy. Half of the tumors were collected five weeks after tumor implantation, and the other half utilized for a survival study. Collagen was imaged by second harmonic generation (SHG) microscopy. **RESULTS:** *In vitro* imaging of single FC1199 cells grown in HDC revealed an aggressive phenotype with clonal network-like structures compared to a spheroidal, non-aggressive phenotype for cells grown in BME over the course of seven days. SHG imaging confirmed consistent formation and organization of collagen in HDC tumors but minimal to faint collagen formation in BME tumors. Gross examination of HDC mice showed 60% with visible liver metastasis compared with none in the BME mice. Histology results from HDC liver sectioning confirmed multiple areas of metastatic sites within the liver. In the survival study, the entire HDC group died before any of the BME group ($P < 0.01$). Western blot results show increased vimentin (a marker of epithelial-to mesenchymal transition) expression in HDC tumors compared to BME tumors. **CONCLUSIONS:** Our pilot study is the first, to our knowledge, to successfully generate orthotopic PDAC tumors using 3D HDC I in a mouse model. FC1199 cells embedded in HDC showed an aggressive phenotype *in vitro* with resultant tumors demonstrating more robust collagen organization compared to the same cells grown in the BME substrate, which translated to worse survival with confirmed visible and histological liver metastasis formation prior to death from primary tumor burden–this is not typical for most KPC-derived cell lines but is typical for human PDAC patients. Our preliminary findings support our novel approach of using 3D HDC as an alternative substrate for modeling the aggressiveness of pancreatic cancer.



P82. Actionable Targets for Small Molecule Inhibitor Therapy in Biliary Tract Cancers: An Analysis of American Association for Cancer (AACR) Project GENIE

Diamantis I. Tsilimigras, MD, PhD[1]; Hunter Stecko[2]; Tim M. Pawlik[3]
[1]The Ohio State University, Columbus, OH, US; [2]The Ohio State University / NIH, Columbus, OH, US; [3]The Ohio State University, Columbus, OH, US

INTRODUCTION: FDA-approved targeted therapies for biliary tract cancers (BTCs) are currently largely limited to *IDH1* and *FGFR2* inhibitors. With the increasing availability of small molecule inhibitors (SMIs) for solid tumors, these agents represent a growing opportunity to treat BTCs. The exact potential of actionable targets for SMIs in treating BTCs remains unknown. We examined prevalence and co-alteration patterns among genomic loci targeted by 80 FDA-approved SMIs in the AACR Project GENIE BTC cohort. **METHODS:** A list of 80 FDA-approved SMIs as of August 2024 were examined for known genetic targets. A total of 57 genomic loci representing targets of FDA-approved SMI were identified and queried. 3,157 samples from 3,039 patients with BTC who had full genomic information were identified in the AACR Project GENIE database. Prevalence of genomic alterations and patterns of co-occurrence and mutual exclusivity were examined. **RESULTS:** Among 3,157 BTC samples analyzed, 2,199 (69.6%) had an alteration in a target for which there is currently an FDA-approved SMI therapy; intrahepatic cholangiocarcinoma (iCCA): 74.4%; extrahepatic cholangiocarcinoma (eCCA): 66.7%; cholangiocarcinoma NOS (CCA): 72.4%; gallbladder cancer (GBC): 56.3% (Figure 1). Besides *IDH1* and *FGFR2* alterations, the most prevalently altered genomic loci were *KRAS* (n=438, 13.9%) followed by *ERBB2/HER2* (n=208, 7.8%), *ATM* (n=217, 7.1%), *PIK3CA* (n=199, 6.3%), and *BRCA2* (n=130, 4.6%). Collectively, 636 (20.1%) BTC samples harbored actionable alterations in these five targets. While *KRAS* was altered in 438 (13.9%) samples, only 30 (0.9%) harbored the G12C alteration currently targetable by SMI therapies. *IDH1* mutations occurred more frequently among White patients (p<0.001) whereas *ERBB2* alterations were more frequent among African American or Asian individuals (p<0.01). While *IDH1* and *FGFR2* alterations were mutually exclusive among iCCA samples; *FGFR2* gene was frequently co-mutated with *BAP1* (log2OR: 1.55, Q<0.001), while *IDH1* gene was commonly co-mutated with *PBRM1* (log2OR: 1.09, Q<0.001). *ERBB2/HER2* alterations among GBC patients frequently co-occurred with alterations in *CDK12* (log2OR: >3), *CCNE1* (log2OR: 2.43) and *TP53* genes (both Q<0.05). **CONCLUSIONS:** While no single genomic alteration was uniquely prevalent across BTCs, a significant proportion of BTC patients harbor alterations in SMI-targetable genomic loci. These data highlight significant opportunities for (neo)adjuvant SMI therapy for surgical BTC patients emphasizing the need for further clinical trials.



P83. Colorectal liver metastases in young patients: Management patterns and outcomes

Victoria F Peters, BS[1]; Morgan F Pettigrew, MD[2]; Nafeesah Fatimah, MD[3]; Arushii Nadar, BS[4]; Ryan T Heslin, MD[5]; Matthew Porembka, MD[6]; Sam Wang, MD[7]; Alex Kim, MD, PhD[8]; Patricio M. Polanco, MD[9]; John C Mansour, MD[10]; Herbert J Zeh, MD[11]; Adam Yopp, MD[12]; Cecilia G Ethun, MD, MS[13]
[1]UT Southwestern Medical Center, Dallas, TX, US; [2]UT Southwestern Medical Center, Dallas, TX, US; [3]UT Southwestern Medical Center, Dallas, TX, US; [4]UT Southwestern Medical Center, Dallas, TX, US; [5]UT Southwestern Medical Center, Dallas, TX, US; [6]UT Southwestern Medical Center, Dallas, TX, US; [7]UT Southwestern Medical Center, Dallas, TX, US; [8]UT Southwestern Medical Center, Dallas, TX, US; [9]UT Southwestern Medical Center, Dallas, TX, US; [10]UT Southwestern Medical Center, Dallas, TX, US; [11]UT Southwestern Medical Center, Dallas, TX, US; [12]UT Southwestern Medical Center, Dallas, TX, US; [13]UT Southwestern Medical Center, Dallas, TX, US

INTRODUCTION: Primary colorectal cancer in young patients is associated with worse oncologic outcomes compared to average-onset disease. However, the impact of age-of-onset on patients with colorectal liver metastases (CRLM) is less understood. We compared disease patterns, treatment strategies, and outcomes between young-onset versus average-onset patients with CRLM. **METHODS:** All patients diagnosed with CRLM at UT Southwestern and Parkland Memorial Hospital from 2016-2023 were retrospectively identified and included. Young-onset was defined as CRLM diagnosis <50 years of age. Average-onset was defined as CRLM diagnosed >50 years of age. Liver-directed therapy (LDT) was defined as resection, ablation, arterial-based therapies, and/or radiation. Primary outcome was overall survival (OS). **RESULTS:** Of the 830 patients included, 251 (30%) had young-onset CRLM. Young-onset patients were more likely to be Hispanic (35%) and have better performance status (30%) than average-onset patients (both p<0.001). There were no differences in hepatic lobar involvement, number or size of liver lesions, or presence or pattern of extrahepatic disease between groups. Young-onset patients were more likely to receive LDT (44% versus 33%, p<0.001). Median OS was 25.6 months for early-onset patients versus 21.9 months for average-onset (p=0.06). On univariable analysis, Black race, public insurance, poor performance status, bilobar disease, >3 liver lesions, liver tumor size ≥5 cm, and extrahepatic disease were associated with worse OS (all p<0.05). Receipt of LDT was associated with improved OS (p<0.001). Young-onset was not associated with OS. On multivariable analysis, bilobar involvement, and liver tumor size ≥5 cm were associated with worse OS (all p<0.05). Receipt of LDT was associated with improved survival (p<0.001). Among patients with young-onset CRLM, receipt of LDT was associated with improved median OS (51.1 months) compared to no LDT (14.3 months, p<0.001). Among only patients who underwent LDT, young-onset patients had similar OS to those with average-onset (51.1 months versus 52.5 months, p=0.82). **CONCLUSIONS:** Patients with young-onset CRLM have similar metastatic disease burden and survival compared to patients with average-onset despite having better performance status and being more likely to receive LDT. Receipt of LDT had the strongest association with improved survival among both groups. Referral to an oncology-trained liver surgeon for consideration of multimodal management should be offered for all young patients with CRLM.

Table 1. Univariable and multivariable analysis of factors associated with survival in patients with colorectal liver metastases

	Hazard Ratio	95% Confidence Interval	P value	Hazard Ratio	95% Confidence Interval	P value
Age						
Average onset	ref					
Early onset	0.84	0.70 - 1.01	0.60	1.08	0.86 - 1.34	0.52
Race/Ethnicity						
White	ref			ref		
Hispanic	0.90	0.73 - 1.11	0.31	0.88	0.68 - 1.14	0.32
Black	1.54	1.23 - 1.88	**<0.001**	1.30	1.02 - 1.66	**0.03**
Asian	0.86	0.55 - 1.34	0.51	0.74	0.44 - 1.24	0.26
Native American	0.58	0.14 - 2.32	0.44	0.74	0.18 - 3.06	0.68
Primary payor						
Private	ref			ref		
Public	1.52	1.23 - 1.87	**<0.001**	1.21	0.94 - 1.56	0.13
None	1.31	1.06 - 1.62	**0.01**	0.88	0.67 - 1.16	0.36
ECOG Performance Status						
0/1	ref			ref		
2	1.46	1.16 - 1.84	0.001	1.37	1.06 - 1.76	**0.02**
3/4	3.64	2.84 - 4.68	**<0.001**	1.82	1.35 - 2.46	**<0.001**
Lobar involvement						
Unilobar	ref			ref		
Bilobar	2.04	1.67 - 2.49	**<0.001**	1.47	1.18 - 1.84	**<0.001**
Number of Liver Lesions						
≤ 3	ref					
> 3	2.02	1.66 - 2.47	**<0.001**			
Size of Largest Lesion (cm)						
< 5	ref			ref		
≥ 5	1.63	1.36 - 1.97	**<0.001**	1.38	1.12 - 1.69	**0.003**
Extrahepatic disease						
Absent	ref			ref		
Present	1.83	1.54 - 2.18	**<0.001**	1.16	0.94 - 1.42	0.18
Liver Directed Therapy						
No	ref			ref		
Yes	0.20	0.16 - 0.25	**<0.001**	0.24	0.19 - 0.31	**<0.001**

P84. Combined genomic, metabolomic and clinical outcome analysis identifies ATP6V1C1 and thonzonium as a novel target and potential treatment for HCC

Kathryn Tsai[1]; Daniel S Cheah, MSE[2]; Helen J Kemprecos[3]; Fumihiro Kawano, MD, PhD[4]; Chitra Subramanian, PhD[5]; Claudius H Conrad, MD, PhD[6]; Mark S Cohen, MD[7]

[1]Carle Illinois College of Medicine, Urbana, IL, US; [2]Carle Illinois College of Medicine, Urbana, IL, US; [3]Carle Illinois College of Medicine, Urbana, IL, US; [4]Carle Foundation Hospital, Urbana, IL, US; [5]Carle Illinois College of Medicine, Urbana, IL, US; [6]Carle Illinois College of Medicine, Urbana, IL, US; [7]Carle Illinois College of Medicine, Urbana, IL, US

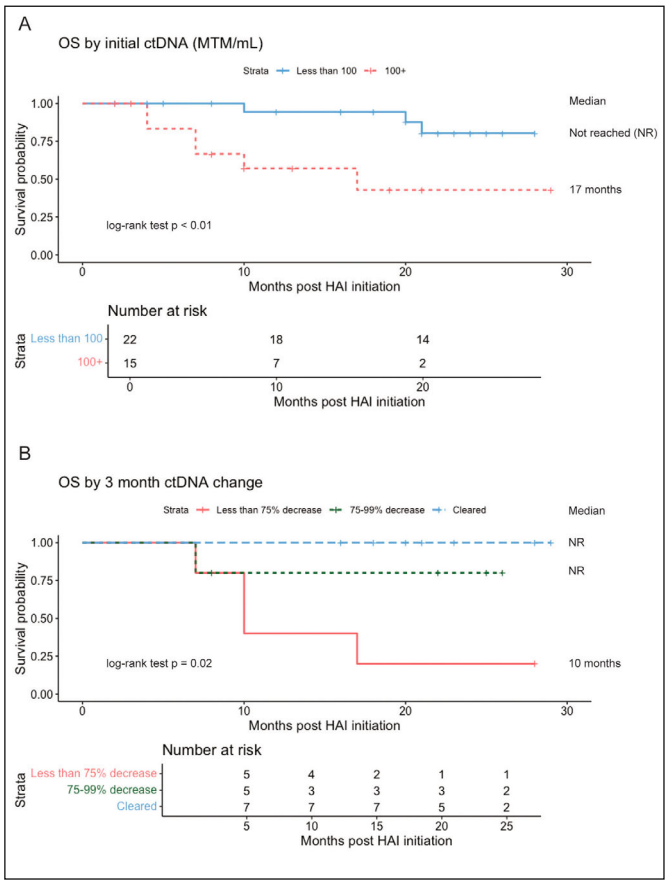
INTRODUCTION: Despite advancements in hepatocellular carcinoma (HCC) treatment, five-year survival remains low at 21%. HCC cells can reprogram their metabolism leading to treatment resistance, recurrence, and poor survival outcomes, necessitating a need for new biomarkers and treatments in HCC. Therefore, we hypothesize that metabolic and lipidomic genes analysis when correlated with survival outcomes may identify novel biomarkers or targets for HCC. **METHODS:** A list of 110 metabolic genes linked to HCC was compiled from RNA-Seq data in TCGA and Genomic Spatial Event databases. Differential expression and survival analyses were conducted using R and University of Alabama at Birmingham Cancer Data Analysis Portal (UALCAN). Gene Ontology and Database for Annotation, Visualization and Integrated Discovery analyses were used to highlight key metabolic and drug pathways, focusing on potential drug repurposing targets. **RESULTS:** Among the 110 metabolic genes evaluated, 18 were upregulated and 23 downregulated >2-fold in HCC tumor tissue compared to normal liver tissue. Of these significantly modulated genes, ATP6V1C1 expression levels highly correlated and increased with tumor stage progression (Figure 1A), with higher expression in males (p=0.0155). Notably, clinical outcome analysis revealed that ATP6V1C1 overexpression was linked to significantly worse overall survival outcomes (p=0.018) (Figure 1B). Further, pathway analysis revealed several key metabolic pathways significantly associated with HCC progression, including metabolism of lipids, steroids, fatty acids, arachidonic acid, retinol, and xenobiotics (p<0.0001 for each vs. controls). Additionally, steroid hormone biosynthesis and gluconeogenesis/glycolysis were among the pathways most enriched in tumor tissues. Finally, UALCAN drug database analysis identified the FDA-approved drug thonzonium as targeting ATP6V1C1 and its pathways. **CONCLUSIONS:** Comparative genomic, metabolomic, lipidomic, and clinical survival database combined analysis of HCC tumors and patients identified a new biomarker gene for HCC, ATP6V1C1, whose increased expression was significantly correlated with decreased overall survival by disease stage. ATP6V1C1 was also identified to be targeted by the FDA-approved drug thonzonium. Further in vitro and in vivo validation and mechanistic studies are warranted to evaluate the role of this new biomarker in HCC as well as potential repurposing of thonzonium clinically in HCC.

P85. ctDNA as a novel biomarker of treatment efficacy in patients with unresectable colorectal liver metastases treated with hepatic arterial infusion

Annie Liu, MD, PhD[1]; Benjamin Wildman-Tobriner, MD[2]; John Strickler, MD[3]; David Hsu, MD, PhD[4]; Julie KM Thacker, MD[5]; Christopher R Mantyh, MD[6]; Billy Lan, MD[7]; Susanna S Hill, MD, MSCI[8]; Ellery H Reason[9]; Brittany Sullivan, MD[10]; Daniel P Nussbaum, MD[11]; Sabino Zani, MD[12]; Peter J Allen, MD[13]; Hope Uronis, MD[14]; Michael E Lidsky, MD[15]

[1]Duke University Medical Center, Durham, NC, US; [2]Duke University Medical Center, Durham, NC, US; [3]Duke University Medical Center, Durham, NC, US; [4]Duke University Medical Center, Durham, NC, US; [5]Duke University Medical Center, Durham, NC, US; [6]Duke University Medical Center, Durham, NC, US; [7]Duke University Medical Center, Durham, NC, US; [8]Duke University Medical Center, Durham, NC, US; [9]Duke University Medical School, Durham, NC, US; [10]Duke University Medical Center, Durham, NC, US; [11]Duke University Medical Center, Durham, NC, US; [12]Duke University Medical Center, Durham, NC, US; [13]Duke University Medical Center, Durham, NC, US; [14]Duke University Medical Center, Durham, NC, US; [15]Duke University Medical Center, Durham, NC, US

INTRODUCTION: Hepatic arterial infusion (HAI) pump chemotherapy is an expanding treatment for patients with unresectable colorectal liver metastases (uCRLM). While the role of HAI in this patient population remains the focus of several randomized trials in the United States and Europe, there is an unmet need to improve patient selection and optimize oncologic outcomes. Here, we examine the role of preoperative quantitative ctDNA and ctDNA dynamics as a novel biomarker to predict oncologic outcomes following HAI. **METHODS:** We analyzed HAI outcomes for patients with uCRLM at Duke University from February 2022- June 2024, where quantitative ctDNA were measured prior to and during their treatment course. Demographics, laboratory values, and oncologic outcomes were assessed. ctDNA values were determined using Signatera as mean tumor molecules per mL (MTM/mL). Overall survival (OS), progression free survival (PFS), and hepatic- and extra-hepatic PFS (hPFS and ehPFS, respectively) were calculated from the date of HAI initiation and compared using Kaplan-Meier and Cox proportional hazards methods. **RESULTS:** Of the 37 patients who had pre-HAI initiation ctDNA collected, 26 had ctDNA collected at approximately 3 months after HAI initiation. 23 (62%) patients were male, with a median age of 51 years (range(R): 37, 79). Median follow-up time was 17 months (range: 2, 29). Median CEA was 47ng/mL (R:1, 644; n=36) and median ctDNA level was 309 MTM/mL (R: undetectable (n=3), 2678; n=37), collected at a median 24 (11, 44) days prior to HAI initiation. Patients with pre-HAI ctDNA ≤ 100 MTM/mL had significantly better OS (hazard ratio (HR): 6; 95% CI, 1.4-25; p=0.01, Fig1A). For patients with decreasing ctDNA on treatment, magnitude of change was associated with OS and PFS. Following 3 months of HAI, patients whose ctDNA decreased by 75% had significantly worse PFS (<75% vs. 75-99% vs. 100% change; log rank test, p<0.01) and OS (< log rank test, p=0.01), Fig1B. While patients with initial CEA <100ng/mL had significantly better OS than those with higher CEA (HR, 2.6; 95% CI, 1.0-6.4; p=0.04), there was no relationship between magnitude of CEA change after 3 months of HAI and OS or PFS. **CONCLUSIONS:** Preoperative ctDNA and ctDNA dynamics are associated with oncologic outcomes in patients with uCRLM treated with HAI. These hypothesis-generating findings require validation before incorporating quantitative ctDNA in patient selection algorithms and using ctDNA dynamics to guide therapy once receiving HAI for uCLRM.



P86. Detection of Volatile Organic Compounds as a Novel Biomarker for Pancreatic Adenocarcinoma

Kyle R. Stephens, MD[1]; Walter Donica[2]; Prejesh Philips, MD[3]; Robert Martin, MD, PhD[4]; Kelly McMasters, MD, PhD[5]; Zhenzhen Xie, PhD[6]; Xiao-An Fu, PhD[7]; Victor Van Berkel, MD, PhD[8]; Michael E. Egger, MD, MPH[9]; Charles Scoggins, MD, MBA[10]

[1]Division of Surgical Oncology, Department of Surgery, University of Louisville School of Medicine, Louisville, KY, US; [2]University of Louisville, Louisville, KY, US; [3]University of Louisville, Louisville, KY, US; [4]University of Louisville, Louisville, KY, US; [5]University of Louisville, Louisville, KY, US; [6]Department of Chemical Engineering, JB Speed School of Engineering, University of Louisville, Louisville, KY, US; [7]Department of Chemical Engineering, JB Speed School of Engineering, University of Louisville, Louisville, KY, US; [8]Department of Cardiovascular and Thoracic Surgery, University of Louisville School of Medicine, Louisville, KY, US; [9]University of Louisville Department of Surgery, Louisville, KY, US; [10]Division of Surgical Oncology, Department of Surgery, University of Louisville School of Medicine, Louisville, KY, US

INTRODUCTION: Exhaled volatile organic compounds (VOC) are being investigated in a variety of malignancies. VOC might be a useful biomarker for patients with pancreatic ductal adenocarcinoma (PDAC). We hypothesized that VOC would be elevated in PDAC patients and might be a novel biomarker for PDAC. **METHODS:** Treatment-naïve patients with biopsy-proven PDAC without metastases were enrolled alongside matched controls (spouse, children, or siblings) to account for similar environmental exposures. Exhaled breath samples were collected and analyzed using a microfabricated silicon microreactor combined with a carbonyl trapping agent, capturing carbonyl compounds through oximation reactions. The captured compounds were quantified using Ultra High-Performance Liquid Chromatography-Mass Spectrometry (UHPLC-MS). Patients with VOC concentrations >75th percentile of the corresponding control IQR were considered elevated. Spearman correlation and univariate analysis were performed on VOC and clinicopathologic factors. **RESULTS:** 25 patients were enrolled, as well as 23 controls. VOC were detected in all patients. 5 unique VOC with median differences of >60% in PDAC relative to controls were evaluated. Significantly elevated levels of heptanone, hexanal, hexanone, MDA, and acetaldehyde were observed in pancreatic cancer patients compared to controls (p-values ranging from 0.001 to 0.019), Figure. Considering all patients, all 5 VOC were associated with lower CA19-9 at diagnosis (p-values <.001), and hexanal and heptanone were associated with smaller tumor size (p-values .001-.016). This trend was consistent in patients with elevated VOC. 65% of patients with elevated VOC were male, while 32% of non-elevated VOC patients were male, which was significantly different (p-value .042). **CONCLUSIONS:** A unique signature of VOC is detectable in the exhaled breath of PDAC patients. These results underscore the need for larger studies to validate the use of VOC in the early detection and monitoring of pancreatic cancer.

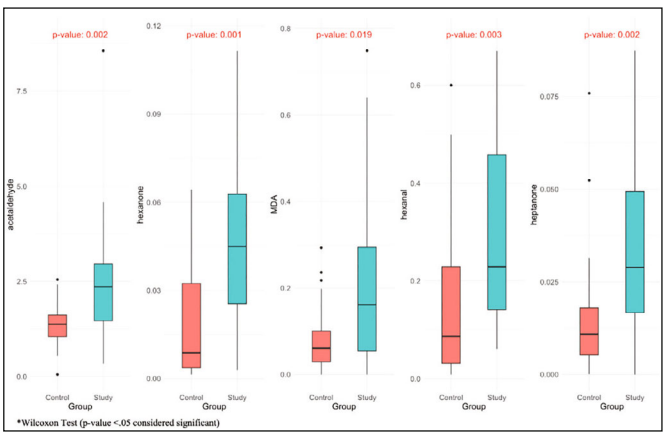


Figure. Comparing VOC (acetaldehyde, hexanone, MDA, hexanal, and heptanone) concentrations between newly diagnosed, biopsy proven, treatment naive pancreatic adenocarcinoma patients vs matched controls on UHPLC-MS.

P87. Developing a predictive model to identify patients with pancreatic cancer who are at risk of non-completion of curative-intent therapy.

Chad E Cragle, MD, PhD[1]; Yun Xing, PhD[2]; Mohammed Aldakkak[3]; Anai N Kothari, MD, MS[4]; Douglas B Evans, MD[5]; Kathleen Christians, MD[6]

[1]Medical College of Wisconsin, Miwaukee, WI, US; [2]Medical College of Wisconsin, Milwaukee, WI, US; [3]Medical College of Wisconsin, Milwaukee, WI, US; [4]Division of Surgical Oncology, Department of Surgery, Medical College of Wisconsin, Milwaukee, WI, US; [5]Medical College of Wisconsin, Milwaukee, WI, US; [6]Medical College of Wisconsin, Milwaukee, WI, US

INTRODUCTION: In treatment of pancreatic cancer, neoadjuvant therapy (NAT) is employed to facilitate receipt of multimodality therapy and improve overall survival. However, not all patients who begin NAT complete curative intent therapy by undergoing surgical resection. Understanding this attrition and developing tools to identify patients at risk represents an opportunity to improve outcomes. **METHODS:** A retrospective analysis was conducted of all patients diagnosed with pancreatic adenocarcinoma and treated with NAT at a single institution. Patients with histologically confirmed resectable, borderline resectable, or locally advanced type-A pancreatic adenocarcinoma were included. Demographics, clinical characteristics, treatment regimens, social determinants of health, and outcomes were extracted from electronic medical records. Multivariable logistic regression was used to assess the independent association between pre-treatment characteristics and non-completion of curative intent therapy. Predictive models were trained using 80% of the cohort and validated using 20%. Three model types were compared (logistic, random forest, XGBoost). **RESULTS:** Included were 651 patients treated from January 2014 to December 2023. There were 257 (40%) with radiographically resectable cancer, 300 (46%) with borderline resectable, and 94 (14%) with locally advanced type-A. Among these, 22.2% with resectable cancers, 30% with borderline resectable cancer, and 25% with locally advanced type-A cancer did not undergo resection. The most common reasons for this were metastatic progression (66%), inadequate performance status (18%), and patient choice (9%). Multivariable analysis identified area deprivation index (ADI)and resectability status as significant predictors of non-completion ($p < 0.05$). Among predictive models, random forest performed best, with F1-macro score of 0.88 (0.86 – 0.89). Applying the model to the validation cohort, 28.9% of patients classified as high-risk did not complete therapy compared to 8.6% and 7.7% the medium and low-risk groups. Of the 10 most important variables determining model predictions, 50% were non-biologic with ADI and all treatment being delivered at our institution highly impacting model output. **CONCLUSIONS:** A subset of patients starting NAT for pancreatic cancer do not undergo curative-intent surgery, underscoring the importance of careful monitoring during treatment. Using predictive modeling, we developed a tool to help identify patients at risk for non-completion of NAT prior to starting therapy.

P88. Development of an APP-led Pancreatic Cyst Surveillance Clinic

Leslie A Shaw, PA-C[1]

[1]University Hospitals of Cleveland, Cleveland, OH, US

INTRODUCTION: Pancreatic cysts are common and often identified incidentally during routine imaging studies. Proactive surveillance for precancerous pancreatic cysts is essential for early detection and intervention. Management of pancreatic cysts can prove challenging due to guideline inconsistencies, long wait times for specialist referrals, and patients being lost to the system. To address these issues, we implemented a Pancreatic Cyst Surveillance Clinic (PCSC) at our regional hospital system led by a single Advanced Practice Provider (APP). **METHODS:** The PCSC started in April 2022 with in-person and virtual appointments to accommodate patients from across the region. The clinic was promoted by outreach to primary care offices, institutional newsletters and community lectures. Referrals were generated via the electronic medical record, direct communication with the lead APP, or through an incidental pancreas radiology findings initiative. Referrals were scheduled by a dedicated medical assistant into two structured APP-led clinics per week. Further testing, surgical referral, or surveillance was managed based on subject-matter expertise, aided by standardized algorithms designed by the multidisciplinary pancreas team. **RESULTS:** From April 2022 to September 2024, 479 patients were seen in the PCSC. The average patient age was 69 years (range 25-93) and 62% were female. Overall, 359 patients had branch duct IPMNs (60% multifocal), 26 had indeterminate presumed mucinous cysts, 23 had serous cystic neoplasms, 22 had pseudocysts, 20 had mixed-type IPMNs, 16 had main-duct IPMNs, 9 had mucinous cystic neoplasms, 6 had solid tumors. Thirty-one patients required endoscopic therapy, including

27 EUS-FNA/FNB and 4 ERCP for incidental choledocholithiasis, recurrent pancreatitis and malignant biliary obstruction. Of the 35 patients referred to a Surgical Oncologist from the PCSC, 24 underwent surgery. Of these, 1 patient had malignant transformation of presumed low-risk IPMN under surveillance, 4 had high-grade dysplasia, and 2 had invasive cancer. **CONCLUSIONS:** The establishment of a PCSC has significantly enhanced patient care at our institution by ensuring timely access to specialists, fostering collaboration between teams, and affording consistent communication and follow-up by a dedicated provider. This effort has bolstered network integrity and we expect to drive program growth, improve quality care and cancer detection, and be foundational for investigational protocols.

P89. Do Plant-based Foods Impact the Risk of Developing Pancreatic Ductal Adenocarcinoma?

Parit T Mavani, MBBS[1]; Caitlin P Sok, MD, PhD[2]; Subir Goyal, PhD[3]; Francesca Castro, RD[4]; David A Kooby, MD[5]; Urvi A Shah, MD[6]; Mihir M. Shah, MD[7]

[1]Emory University, Sandy Springs, GA, US; [2]Emory University, Atlanta, GA, US; [3]Emory University, Atlanta, GA, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Emory University School of Medicine, Atlanta, GA, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Emory University, Atlanta, GA, US

INTRODUCTION: Adopting a plant-based diet positively influences modifiable risk factors associated with pancreatic ductal adenocarcinoma (PDAC). We assessed the impact of plant-based diet Index (PDI) on the incidence of PDAC in a US-based large prospective cohort. **METHODS:** In the National Institute of Health-AARP Diet and Health Study, the dietary habits of AARP members were queried using a food frequency questionnaire (1995-96). Adherence to a plant-based diet was calculated using PDI score (range 18-90), in which 12 plant-based food groups scored positively and 6 animal-based food groups scored negatively. Participants were divided into quartiles. Higher quartile implied higher adherence to a plant-based diet. Exclusion criteria comprised: questionnaires completed by proxy, baseline history of any cancers (except nonmelanoma skin cancer), end-stage renal disease, implausible energy intake (<800/600 or >4200/3500 kcal/day in men/women, respectively) or <1 year of follow-up data. The PDAC incidence was identified using 13 state registries (1995-2019). The Cox proportional hazard regression model was utilized to evaluate the association between PDAC incidence and PDI quartiles after adjusting age at baseline, sex, body mass index (BMI), daily energy intake, education level, smoking status and alcohol consumption. The proportional hazard assumption was tested by including an interaction term between PDI and time. To assess reverse causality, PDAC patients diagnosed within the first 3 years of follow-up were excluded in sensitivity analyses. **RESULTS:** Of 566,398 participants, 57.8% (n=327,338) met our inclusion criteria, with a median age of 62 (50-71) years. During the median follow-up of 22 years, 3,719 (1.1%) participants developed PDAC. Participants who developed PDAC were noted to be older (age>62 years) (54.3 vs. 46%, p<0.001), male (61.2 vs. 56.2%, college graduates (40.9 vs. 38.5%, p=0.002), overweight or obese (BMI≥25) (67.5 vs. 64.5%, p<0.001) and active smokers (14.2 vs. 10.8%, p<0.001) compared to participants who did not develop PDAC. On multivariable analysis, participants in the highest quartile of PDI had a lower incidence of PDAC compared to the lowest quartile ($aHR_{Q4\ vs.\ Q1}$ 0.89, p=0.017). No violation of the proportion hazard assumption was observed (p=0.604). The association between PDI and PDAC persisted with sensitivity analysis, i.e. after excluding participants who developed PDAC within the first three years ($aHR_{Q4\ vs.\ Q1}$ 0.88, p=0.016). **CONCLUSIONS:** Increased consumption of a diet rich in plant-based foods is associated with a significantly lower risk of developing pancreatic ductal adenocarcinoma.

Table 1. Association between plant-based diet index and the risk of pancreatic ductal adenocarcinoma on multivariable Cox proportional hazard regression model analysis

	Incidence of Pancreatic Ductal Adenocarcinoma		
	N	Hazard ratio (95%CI)	HR p value
Plant-based Diet Index			
4th Quartile	77,223	0.89 (0.81-0.98)	**0.017**
3rd Quartile	76,982	0.90 (0.82-0.99)	**0.034**
2nd Quartile	76,760	0.94 (0.86-1.04)	0.232
1st Quartile	76,686	-	-

Bold values indicate statistical significance (p<0.05)
Dash indicates reference.
CI confidence interval

* Number of observations in the original data set = 324,419; Number of observations used = 327,338.
** Adjusted using entry method for age at entry (years, continuous), sex (female and male), education (some college or less and college graduates), body mass index (≥25 and <25), smoking (never smoker, former smoker and active smokers), alcohol consumption (≥3 drinks/day and <3 drinks/day) and energy intake (kcal/day).

P90. Factors Driving Attrition to Pancreatectomy in Patients Undergoing Neoadjuvant Therapy for Localized Pancreatic Cancer

Erin M Dickey, MD, MBS[1]; Lucy Min[2]; Annika Dhawan, BS[3]; Mary Martos[4]; Peter Hosein, MD[5]; Gretel Terrero, MD[6]; Jashodeep Datta, MD[7]; Nipun Merchant, MD[8]; Caitlin A. Hester, MD[9]

[1]University of Miami, Miami, FL, US; [2]University of Miami, Miami, FL, US; [3]University of Miami, Miami, FL, US; [4]University of Miami, Miami, FL, US; [5]University of Miami, Miami, FL, US; [6]University of Miami, Miami, FL, US; [7]University of Miami, Miami, FL, US; [8]University of Miami, Miami, FL, US; [9]University of Miami, Miami, FL, US

INTRODUCTION: Treatment paradigms are shifting toward a neoadjuvant therapy (NAT) approach for localized pancreatic cancer (LPC) based on the rationale of treating occult metastasis, downstaging to resectability and selecting pts with favorable biology. While the benefits of NAT for LPC have been well described, true attrition rates and reasons for failure to proceed to pancreatectomy remain underreported. We present true intent-to-treat attrition data of LPC undergoing NAT at a tertiary referral center. **METHODS:** LPC patients (pts), who underwent ≥ 1 cycle NAT from Jan. 2013-2022, were included. Clinicopathologic data were retrospectively obtained. Multivariable models identified factors associated with odds of attrition. Overall survival (OS) was estimated using the Kaplan-Meier method. **RESULTS:** 427 LPC pts received NAT, including 57 (13%) with resectable (R), 133 (31%) borderline resectable (BR), and 237 (56%) locally advanced (LA) disease. 64% had head tumors with median tumor size of 3.3 cm (IQR 2.7-4.2) and CA 19-9 of 267 U/mL (IQR: 58-766). 60% received FOLFIRINOX and 28% Gemcitabine-Abraxane for a median of 4.2 months (IQR 2.5-5.7). During NAT, 22% switched regimens and 30% received neoadjuvant radiation. 207 pts (48%) underwent attempted resection, and 182 pts (43%) had successful pancreatectomy. The overall rate of attrition during NAT was 52%, of which 20% had disease progression, 18% remained LA, 11% had physiologic decompensation, 2% were lost to follow-up, and 1% declined surgery. Rates of attrition were: 23% for R, 44% for BR, and 73% for LA (p<0.01). Most common reasons for attrition were: progression (5% in R, 18% in BR, 26% in LA), remained inoperable (2% in R, 12% BR, 32% LA), and physiologic decompensation (7% R, 11% BR, 12% LA). Pts undergoing pancreatectomy had a median OS of 30 vs 16 months for those not undergoing pancreatectomy (p<0.01). Median OS inversely correlated with stage – R: 30, BR: 21 and LA: 18 months (p<0.01). There was no difference in OS for those who received NAT and resection – R: 31, BR: 27, and LA: 34 months (p=0.66). **CONCLUSIONS:** At tertiary center with 87% BR and LA pts, 43% of patients proceeded to pancreatectomy following NAT including 27% with LA tumors. No difference in OS was seen in pts receiving all curative-intent treatment regardless of stage. Progression of disease remains a significant issue for pts receiving NAT for LPC even in the setting of resectable PC, highlighting the importance of NAT in the selection of biology and pts most likely to benefit from pancreatectomy.

P91. Flower monoclonal antibody works synergistically with standard of care chemotherapy to attenuate tumor growth and metastasis in pancreatic ductal adenocarcinoma

Vignesh Yudatha[1]; Praveen Bhoopathi[2]; Antonio Palma[3]; Esha Madan[4]; Rajan Gogna[5]; Jose Trevino[6]
[1]VCU Health, Richmond, VA, US; [2]VCU Health, Richmond, VA, US; [3]VCU Health, Richmond, VA, US; [4]VCU Health, Richmond, VA, US; [5]VCU Health, Richmond, VA, US; [6]VCU Health, Richmond, VA, US

INTRODUCTION: Cell competition between cancer cells and the tumor microenvironment (TME) play a large role in tumor growth and metastasis. Variable expression of the cell competition transmembrane protein, Flower, between tumor and TME provides tumor cells a competitive advantage over the surrounding microenvironment. The purpose of this study is to demonstrate the efficacy of targeting this cell competition mechanism in pancreatic ductal adenocarcinoma (PDAC). **METHODS:** Two preclinical PDAC patient derived xenograft (PDX) models were used to evaluate the effectiveness of a Flower protein monoclonal antibody. A solid PDAC PDX (G100) was orthotopically implanted into the pancreas of NSG mice and tumor volumes were tracked via ultrasound. In the second experiment, a metastatic model was utilized by injecting a GFP-tagged PDAC PDX (G46) cell line into the spleen of NSG mice and tracked with IVIS. In each experiment, the mice (n=5 per group) were treated weekly with either no therapy, Flower antibody, FOLFIRINOX, Gemcitabine/Abraxane, or a combination therapy. **RESULTS:** In the orthotopic model, tumor growth was attenuated with the addition of Flower antibody. The group that received both Flower and FOLFIRINOX had final tumor volumes that were significantly lower than the control ($p = 0.033$) and FOLFIRINOX only ($p = 0.022$) groups. The cohort that received both Flower and Gemcitabine/Abraxane had final tumor volumes that were significantly reduced compared to the control ($p = 0.032$), FOLFIRINOX only ($p = 0.022$), and Gemcitabine/Abraxane only ($p = 0.030$) groups. Similarly, in the splenic injection model, the combination groups outperformed the standard of care therapies and demonstrated a decrease in signal over time. The FOLFIRINOX/Flower combination group had significantly reduced signal compared to the Flower only ($p = 0.001$), FOLFIRINOX only ($p = 0.020$), and Gemcitabine/Abraxane only ($p < 0.0001$). The Gemcitabine/Abraxane and Flower group also had reduced tumor burden compared to the Flower only ($p = 0.001$), Gemcitabine/Abraxane only ($p < 0.0001$), and FOLFIRINOX only ($p = 0.0020$) groups. **CONCLUSIONS:** In this study, we present a novel therapy for PDAC that targets the cellular competition between the tumor cells and the surrounding microenvironment. The monoclonal antibody works synergistically with existing standard of care chemotherapy to not only attenuate primary tumor growth, but also reduce metastatic disease.

P92. GATA6 immunohistochemistry is not predictive of tumor subtype in pancreatic ductal adenocarcinoma

Jaewon Lee[1]; Mohammed Aldakkak[2]; Yusha Liu[3]; Naim Rashid[4]; Saryn Doucette[5]; Susan Tsai, MD[6]; Jen Jen Yeh, MD[7]
[1]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [2]Medical College of Wisconsin, Milwaukee, WI, US; [3]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [4]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [5]University of Wisconsin, Madison, WI, US; [6]The Ohio State University, Columbus, OH, US; [7]University of North Carolina Chapel Hill, Chapel Hill, NC, US

INTRODUCTION: Tumor-intrinsic subtypes of pancreatic ductal adenocarcinoma (PDAC), classical and basal-like, have repeatedly been shown to be prognostic and there is interest in developing single-marker classifiers. GATA6, a transcription factor central in pancreatic tissue differentiation, has been identified as a potential marker for classical subtype PDAC. We previously developed PurIST, a single-sample classifier that robustly defines subtypes based on the expression of 8 gene pairs. We sought to benchmark the performance of GATA6 expression against PurIST in determining PDAC subtypes. **METHODS:** We performed RNA-seq on 122 surgical specimens with matched GATA6 and CK5 immunohistochemical (IHC) staining. Tumors were classified as classical or basal-like by PurIST as well as GATA6 and/or CK5 IHC score. Concordance was measured using Cohen's kappa. Overall survival (OS) between subtypes was compared using log-rank test, and hazard ratios (HR) were calculated using Cox proportional hazards model. **RESULTS:** 122 patients with PDAC had results available from RNA-seq and GATA6/CK5 staining. By RNA-seq, 5 samples (4%) were basal-like whereas by GATA6 IHC, 57 (47%) were basal-like. The maxstat R package was used to determine the best GATA6 and CK5 IHC cutoffs. Subtyping by GATA6 level was not prognostic where OS of patients with GATA6-low (scores 0, 1, and 2) was not significantly worse than patients with GATA6-high (scores 3 and 4) tumors (log-rank $P = 0.12$, HR = 1.41). In addition, GATA6 IHC scores did not correlate well with RNA-seq gene expression (Spearman's rho = 0.175, $P = 0.069$). PurIST subtype was prognostic; patients with basal-like tumors had significantly worse OS than those with classical tumors (log-rank $P < 0.0001$, HR = 6.13). Cohen's kappa between PurIST and GATA6 subtypes was 0.058, indicating only slight agreement. The addition of CK5 IHC score improved the Cohen's kappa to 0.465, indicating moderate agreement, but GATA6/CK5 IHC combined subtype was not prognostic of OS (log-rank $P = 0.72$, HR = 1.59). **CONCLUSIONS:** Using matched samples, GATA6 protein expression was not prognostic of OS in patients with PDAC. Neither GATA6 alone nor in combination with CK5 accurately predicted PurIST subtype. Caution should be utilized when performing molecular subtyping of PDAC using single marker genes.

P93. Genomic Profiling Reveals Predictors of Response to Neoadjuvant Chemotherapy in Pancreatic Ductal Adenocarcinoma

Gregor Werba, MD[1]; Jacob C Hodges[2]; Asmita Chopra[3]; Rudy El Asmar[4]; Nikhil Tirukkovalur[5]; Genia Dubrovsky[6]; Kenneth K Lee[7]; Alessandro Paniccia[8]; Aatur D Singhi[9]; Janie Y Zhang, MD[10]; Amer H. Zureikat, MD[11]
[1]UPMC Medical Center, Pittsburgh, PA, US; [2]UPMC Medical Center, Pittsburgh, PA, US; [3]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [4]UPMC Medical Center, Pittsburgh, PA, US; [5]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [6]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [7]UPMC Medical Center, Pittsburgh, PA, US; [8]UPMC Medical Center, Pittsburgh, PA, US; [9]UPMC Medical Center, Pittsburgh, PA, US; [10]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [11]University of Pittsburgh Medical Center, Pittsburgh, PA, US

INTRODUCTION: Pancreatic adenocarcinoma (PDAC) remains a highly treatment-resistant malignancy, with most patients eventually succumbing to their disease even after complete surgical resection. While significant progress has been made over the past decade in understanding the genomic drivers of PDAC, there is limited data on how these genetic alterations influence response to neoadjuvant chemotherapy (NACT) in resected PDAC. **METHODS:** In total, 949 PDAC patients underwent targeted next-generation sequencing (Oncomine), of which n=120 underwent NACT followed by surgical resection between 2017 and 2021. Response to NACT was determined on resection specimens based on the College of American Pathologists (CAP) scores and correlated with patient demographics, clinical parameters, genetic alterations, and survival. **RESULTS:** Among the 120 patients included in our study, n=89 demonstrated a CAP score of 1 or 2 whereas n=31 had a CAP score of 3. Baseline clinical parameters were not statistically different between the cohorts. However, CAP1-2 patients were more likely to have received FOLFIRINOX than gemcitabine/nab-paclitaxel as their primary neoadjuvant chemotherapy regimen (65% versus 25% p=0.029). On pathology, CAP1-2 patients had earlier pathologic stage (p=0.003), with smaller primary tumors (2.1 versus 2.7cm, p<0.001) and a lower number of positive lymph nodes (2.7 versus 3.9, p=0.008). Furthermore, CAP1-2 patients more frequently underwent an R0 resection (62% versus 29%, p<0.001) and exhibited a lower rate of lymphovascular invasion (73% versus 93%, p=0.021). Genomic profiling revealed that CAP3 patients had a higher frequency of alterations in cell cycle regulation (CCR) genes (48% vs. 18%, p=0.002), primarily driven by mutations in CDKN2A and CDKN2B. Multivariate analysis showed that patients with CCR gene alterations had a 3.8-fold higher likelihood of having a CAP3 score (p=0.008). Interestingly, the presence of KRAS G12R or G12V mutations trended towards treatment resistance (OR 3.15, p=0.055). Furthermore, a smaller decrease in preoperative CA19-9 values (OR 1.58, p=0.036), higher TMB (OR 1.99, p=0.025), and a switch in NACT regimen (OR 5.63, p=0.01) were all associated with higher odds of a CAP3 score. CAP3 scores were highly predictive of reduced restricted-mean RFS (15.6 versus 32.1 months, p<0.001) and OS (29.4 versus 62.6 months, p<0.001). **CONCLUSIONS:** Alterations in cell cycle regulation, higher TMB, and potentially KRAS G12R/G12V mutations were more frequently associated with a CAP3 score, indicating a poorer response to NACT. These findings suggest that molecular profiling may help reveal predictors of chemoresponse and resistance in patients undergoing neoadjuvant treatment for PDAC.

Table 1. Logistic Model Predicting CAP Score 3 (vs 1-2)

Predictors		OR (95% CI)	P-Value
CA19-9 Ratio *		1.58 (1.03, 2.42)	0.036
TMB *		1.99 (1.09, 3.62)	0.025
NACT Regimen	FOLFIRINOX	Baseline	
	Gemcitabine/nab-Paclitaxel	2.39 (0.79, 7.22)	0.123
	Both	5.63 (1.52, 20.77)	0.010
Cell Cycle Regulation Pathway		3.80 (1.42, 10.16)	0.008
KRAS G12R/G12V		3.15 (0.98, 10.14)	0.055

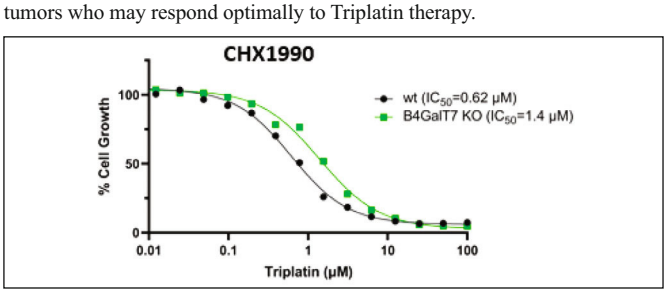
Cross-Validated AUC (95% CI) = 0.676 (0.603, 0.822)

*A natural log transformation was used for the CA19-9 Ratio and TMB variables to correct right skewness.

P94. Glycan-Targeted Therapy with Triplatin for Effective Treatment of Pancreatic & Ovarian Cancer

Vashti Bandy[1]; Nicholas Farrell[2]; Erica Peterson[3]; Praveen Bhoopathi[4]; Vignesh Vudatha[5]; Jose Trevino[6]; Arunima Punjala, MD[7]
[1]Virginia Commonwealth University, Richmond, VA, US; [2]Virginia Commonwealth University, Richmond, VA, US; [3]Virginia Commonwealth University, Richmond, VA, US; [4]VCU Health, Richmond, VA, US; [5]VCU Health, Richmond, VA, US; [6]VCU Health, Richmond, VA, US; [7]VCU Health, Richmod, VA, US

INTRODUCTION: New research surrounding pancreatic ductal adenocarcinoma (PDAC) has demonstrated that overexpression of glycosaminoglycans (GAGs) may contribute to chemotherapeutic treatment resistance. In a prior study, we discovered that expression of an isolated GAG sequence can predict PDAC tumor sensitivity to the polynuclear platinum drug Triplatin (BBR3464). This study aims to evaluate *in vitro* and *in vivo* effects of Triplatin vs. Oxaliplatin on PDAC cellular and patient-derived xenograft (PDX) models with defined levels of GAG expression. **METHODS:** *In vitro*, the cytotoxicity of Triplatin and Oxaliplatin against human PDAC and mouse cell lines were compared. Flow cytometry was used to assess GAG expression in wild-type and GAG-deficient (B4GalT7 KO) mouse cell lines. In *vivo*, mice were injected subcutaneously with CHX1990, a syngeneic PDAC cell line from the established KPC mouse model of pancreatic cancer. Mice with established PDAC tumor burden were randomized into experimental and control groups (n=5). Triplatin was administered intraperitoneally on days 1, 5, and 9. Following treatment, tumor growth and body weight were measured twice weekly. Mice were sacrificed at 30 days and organs and tissues were processed for histological analysis. **RESULTS:** Our results demonstrated that Triplatin had greater cytotoxicity than Oxaliplatin in both human and mouse PDAC cell lines. This was reflected by Triplatin's lower IC50 values and significant decreases in tumor growth kinetics following continuous drug treatment (i.e. in treatment of the CHX1990 cell line, Triplatin IC50= 0.239 mM vs. Oxaliplatin IC50= 7.74 mM). Triplatin had reduced efficacy in treatment of GAG knockout cells, indicating the role of GAGs in drug mechanism of action (see attached figure: "Cytotoxicity of Triplatin in mouse CHX1990 wt and B4GalT7 KO PDAC cell lines; 1h treatment"). Regarding analysis of PDAC PDX mice models, Triplatin again demonstrated significant reduction of tumor kinetics comparable to *in vitro* models. Upon further analysis of PDX models, CHX1990 tumor-bearing mice treated with Triplatin were found to have little to no change in body weight when compared to the untreated control, thus demonstrating Triplatin's potential to avoid toxicity. Additionally, elevated levels of IFN-γ in explanted PDX splenocytes suggested that Triplatin not only had cytotoxic effects as demonstrated by reduction in tumor growth kinetics, but also stimulated an immune response. **CONCLUSIONS:** Triplatin exhibits potent cytotoxicity in PDAC models, with GAGs playing a crucial role in drug mechanism of action and modulation of immune response, making it a promising therapeutic candidate for PDAC. These findings have potential to facilitate personalized medicine by identifying patients with GAG-expressing tumors who may respond optimally to Triplatin therapy.



P95. Identifying Risk Factors for Post-Hepatectomy Liver Failure in Patients with Adequate Liver Remnants: A Single-Center, Retrospective Analysis.

Sumaya Ghaffar, MD[1]; Andrii Khomiak, MD[2]; Aline Hikari Ishida, MD[3]; Salvador Rodriguez Franco, MD[4]; George Zlotchenko, MD[5]; Phillipe Abreu, MD[6]; Richard Schulick, MD MBA[7]; Marco Del Chiaro, MD PhD[8]; Ana L. Gleisner, Md, PhD[9]
[1]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [2]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [3]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [4]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [5]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [6]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [7]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [8]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [9]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US

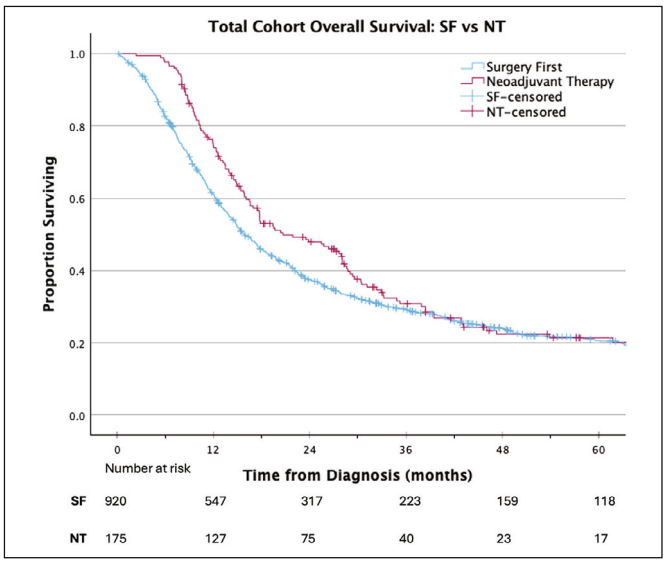
INTRODUCTION: Post-hepatectomy liver failure (PHLF) is typically linked to inadequate liver remnant (LR). However, it can still occur in patients with an adequate LR (those without chronic liver disease, cirrhosis, or those with a satisfactory response to portal vein embolization). This study aims to identify the risk factors for PHLF in this specific patient population. **METHODS:** A retrospective analysis of our surgical oncology database was conducted for patients who underwent right or extended right hepatectomy between January 2012 and February 2024. Exclusion criteria comprised patients with known cirrhosis, insufficient response to portal vein embolization, or incomplete data. Patients were categorized into two groups: those who developed PHLF and those who did not. Categorical variables were assessed using the Chi-Square Test, and continuous variables with the Kolmogorov-Smirnov test. Cox regression analysis was used to calculate Hazard Ratios (HR). **RESULTS:** A total of 224 patients were included, with a majority being female (53.6%), and white (83.5%). PHLF developed in 33 patients (14.7%). Univariate analysis revealed that patients who developed PHLF were older (66.7 vs 58.6 years, p=0.039), more likely female (56.5% vs 36.4%, p = 0.032), had a higher BMI (26.8 kg/m2 vs 25.9, and had lesions near the take-off of the hepatic veins (21.2% vs 5.2%, p = 0.001). They also more frequently showed biliary cholestasis in their preoperative liver background evaluation (6.1% vs 1.0%, p=0.045), underwent preoperative endoscopic retrograde cholangiopancreatography (18.2% vs 6.3%, p=0.020), and had percutaneous transhepatic biliary drainage placement (6.1% vs 0.5%, p=0.011). The conversion to open surgery was more common (6.1% vs 0, p=0.03), and these patients received vascular divestment (15.2% vs 1.0%, p < 0.001), hilar lymphadenectomy (42.4% vs 12.0%, and bile duct resection (21.2% vs 5.2%, p = 0.001) more frequently. Intraoperative complications such as hemorrhage (6.1% vs 0.5%, p=0.011) and the need for blood products (36.4% vs 15.7%, p=0.019) were also more common. In the multivariate analysis, the receipt of hilar lymphadenectomy [HR 3.74 (95%CI 1.02-13.6), p = 0.045] and a BMI > 25 kg/m2 [HR 3.86 (95%CI 1.14-12.9, p = 0.029] were significantly associated with the development of PHLF. **CONCLUSIONS:** A higher BMI and the receipt of hilar lymphadenectomy were independently associated with an increased risk of PHLF in patients with adequate LR. These findings suggest that careful preoperative management is crucial in such patients to mitigate the risk of PHLF. Larger, prospective studies are needed to further validate these risk factors and to better understand the mechanisms underlying PHLF in this patient population.

P96. Impact of neoadjuvant therapy on the outcomes of patients with adenosquameous carcinoma of the pancreas

Amanda Walsh, BS[1]; Diamantis I. Tsilimigras, MD, PhD[2]; Alex Blair, MD[3]; Susan Tsai, MD[4]; Tim Pawlik, MD, PhD, MPH, MBA[5]; Ashish Manne, MBBS[6]; Shafia Rahman, MD[7]; Eric Miller, MD, PhD[8]; Kenneth Pitter, MD, PhD[9]; Jordan M Cloyd, MD[10]
[1]The Ohio State University, Columbus, OH, US; [2]The Ohio State University, Columbus, OH, US; [3]Ohio State University, Columbus, OH, US; [4]The Ohio State University, Columbus, OH, US; [5]The Ohio State University, Columbus, OH, US; [6]The Ohio State University, Columbus, OH, US; [7]The Ohio State University, Columbus, OH, US; [8]The Ohio State University, Columbus, OH, US; [9]The Ohio State University, Columbus, OH, US; [10]The Ohio State University, Columbus, OH, US

INTRODUCTION: Pancreatic adenosquamous carcinoma (PASC) is a rare and aggressive form of pancreatic cancer. Neoadjuvant therapy (NT) is increasingly utilized for pancreatic ductal adenocarcinoma, but its role for patients with PASC has not been thoroughly investigated. **METHODS:**

Patients who underwent pancreatectomy for localized PASC between 2006 and 2020 were identified using the National Cancer Database. Treatment cohort characteristics and overall survival (OS) were compared between those who received neoadjuvant chemotherapy and/or radiation therapy prior to surgery and those who underwent surgery first (SF) **RESULTS:** Among 1191 patients with PASC, 208 (17.4%) received NT, whereas 983 (82.5%) underwent SF. NT consisted of chemotherapy (75.0%), chemotherapy and radiation therapy (23.6%), and radiation therapy alone (1.4%); the median length of NT treatment was 3.9 months. While there were no differences in sex, insurance status, or positivity of surgical margins, patients who received NT were more likely to be younger (p=0.01), to be white (p=0.03), to be diagnosed in a more recent year (p<0.001), to have higher household income (p=0.009), to be treated at an academic/research facility (p=0.002), to live farther from their treatment facility (p<0.001), to have worse Charlson-Deyo comorbidity score(p<.001), to have stage I disease (p<0.001), and were less likely to receive any adjuvant therapy (p<.001) when compared to SF patients. On Kaplan Meier analysis, the receipt of NT was associated with improved OS compared to a SF approach (median 20.7 vs 15.9 months; p=0.03) (Figure 1). On multivariable Cox regression analysis, factors independently associated with improved OS included: treatment at an academic/research facility (HR 0.83 95% CI 0.71-.97, p<0.05), receipt of adjuvant chemotherapy (HR 0.60 95% CI 0.51-0.72, p<0.001) and receipt of NT (HR 0.69 95% CI 0.585- 0.87, p<0.01). Factors associated with decreased OS included black race (HR 1.28 95% CI 1.03-1.6, positive surgical margins (HR 1.30 95% CI 1.06-1.60, p=0.01), and worse Charlson-Deyo comorbidity score (HR 1.34 95% CI 1.07-1.67, p=0.01). **CONCLUSIONS:** Receipt of neoadjuvant therapy prior to surgical resection is associated with improved survival for patients with pancreatic adenosquamous carcinoma.

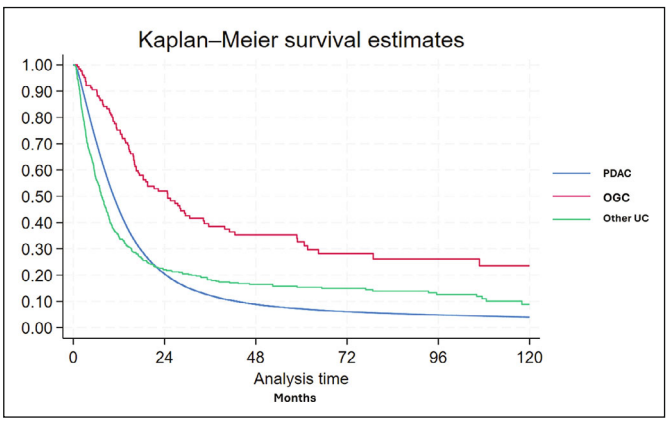


P97. Impact of Reclassification on Osteoclast-like Giant Cell Carcinoma of the Pancreas: A Comparative Analysis

Bianca Bechini[1]; Lindsey M Westbrook[2]; Aline Hikari Ishida, MD[3]; Paul V Winter[4]; Hiroyuki Ishida, MD, PhD[5]; Andrii Khomiak, MD[6]; Benedetto Mungo[7]; Salvador Rodriguez Franco, MD[8]; Ana L. Gleisner, MD, PhD[9]; Richard Schulick, MD, MBA[10]; Marco Del Chiaro, MD PhD[11]

[1]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [2]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [3]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [4]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [5]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [6]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [7]University of Colorado School of Medicine, Aurora, CO, US; [8]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [9]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [10]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [11]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US

INTRODUCTION: Historically, osteoclast-like giant cell carcinoma (OGC) of the pancreas has been grouped with pancreatic ductal adenocarcinoma (PDAC) and undifferentiated carcinomas due to overlapping histological features. However, strong evidence indicates that OGC behaves differently from these entities and may account for a significant proportion of 10-year survivors in pancreatic cancer cohorts. This misclassification could skew survival analysis and affect the accurate interpretation of outcomes in pancreatic cancer. **METHODS:** We conducted a retrospective analysis using data from the National Cancer Database (NCDB) and the Surveillance, Epidemiology, and End Results (SEER) program. Patients diagnosed between 2001 and 2021 with PDAC (histology code 8140), OGC (8035), and undifferentiated carcinomas (8020–8022) were identified. The number of reported OGC cases per year served as a surrogate marker to observe reclassification trends before and after 2014. Demographics, tumor characteristics, treatment modalities, and survival outcomes were extracted and compared among the three groups and time periods. **RESULTS:** A total of 265 OGC cases were reported between 2001 and 2021, with the majority diagnosed in or after 2014 (63.8%), indicating increased recognition and reclassification of OGC. No significant demographic differences were found among the groups. Pathologically, OGC tumors were larger at diagnosis compared to PDAC and undifferentiated carcinomas (>2 cm in 91.7% vs. 77.6% vs. 81.8%; p<0.0001) but were diagnosed at earlier stages (Stage I–II in 60.4% vs. 31.2% vs. 32.2%;0.0001). Regarding practice patterns, surgical resection rates were significantly higher in OGC patients compared to PDAC and undifferentiated carcinoma patients (57.4% vs. 17.5% vs. 31.9%;0.0001). Systemic chemotherapy utilization was similar between OGC and PDAC patients but lower than in undifferentiated carcinoma patients (38.9% vs. 39.3% vs. 48.9%;0.0001). Radiation therapy use was comparable among the three groups (80.0% vs. 81.6% vs. 84.1%; p=0.19). Temporal analysis revealed that reclassification had a significant impact on treatment and survival. For OGC patients, median survival improved from 15.9 months before 2014 to 25.6 months after 2013 (p<0.0001), correlating with increased chemotherapy utilization (from 43.8% to 63.3%). These changes were not observed in PDAC and undifferentiated carcinoma patients despite changes in practice patterns between periods. Notably, the proportion of 10-year survivors was 25% for OGC patients compared to less than 5% in the other two groups. **CONCLUSIONS:** Our findings underscore that osteoclast-like giant cell carcinoma exhibits distinct clinical characteristics and significantly improved survival outcomes compared to pancreatic ductal adenocarcinoma and undifferentiated carcinomas, supporting the benefits of its reclassification as a separate entity. Detailed attention should be placed on accurate histopathological classification of OGC to ensure appropriate treatment strategies, refine prognostic assessments, and improve survival analyses in pancreatic cancer research.



P98. Improving Quality through the Systematic Review of All Abnormal Pancreatic Imaging Findings

Leslie A Shaw, PA-C[1]

[1]University Hospitals of Cleveland, Cleveland, OH, US

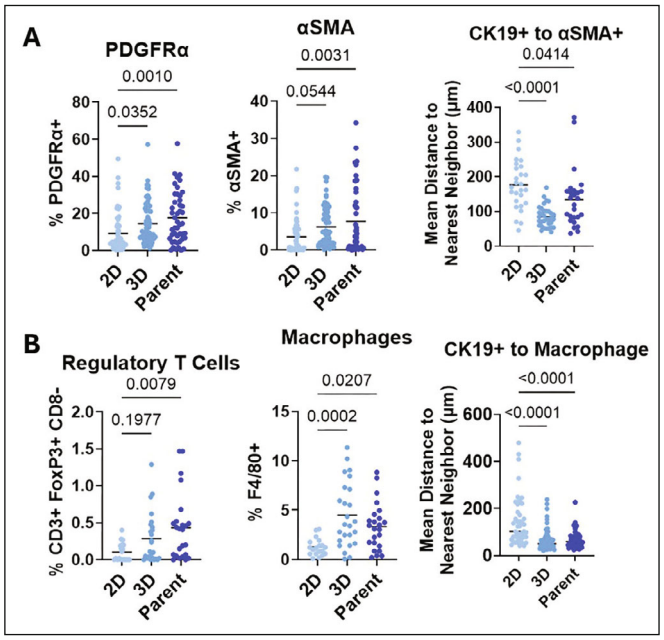
INTRODUCTION: Actionable pancreatic findings (APFs) are common and require interpretation by pancreas-focused specialists, but are often overlooked or misinterpreted due to lack of an operational practice model to capture and manage these findings. We established a program to systematically review all abnormal pancreatic findings noted on radiology reports in a single large health system. **METHODS:** The APFs initiative was implemented at University Hospitals in the Division of Surgical Oncology in March of 2022. APFs were identified using natural language processing of imaging reports and uploaded to a medical database, Thynk Health. A dedicated pancreas-focused Advanced Practice Provider (APP) reviewed the database and discussed

findings in a weekly conference staffed by pancreas-focused radiologists, surgeons, gastroenterologists and medical and radiation oncologists. APFs commonly included pancreatic cysts or masses concerning for cancer. Many were true incidental findings. Findings were communicated by the APP to the ordering provider or patient, and patients were then seen in the APP's specialty clinic as appropriate. **RESULTS:** An average of 40 findings were reviewed daily. Findings were managed by the APP if they met certain criteria (e.g., cyst size ≥1.5 cm), and when the ordering provider or patient were agreeable. A total of 260 patients were offered evaluation, and 157 accepted. Radiographic diagnoses included pancreatic cysts (68%), pancreatitis (5%), pancreatic neuroendocrine tumor (pNET) (5%) and pancreatic (or other) malignancy (22%). Patients with suspected pancreatic ductal adenocarcinoma (n=28) were urgently sent to a pancreatic oncology specialist and seen within an average of 14 days. Sixteen patients in this group underwent resection; the remaining 12 initiated chemotherapy. Less urgent referrals included patients with pNET; 7 underwent resection and 1 received systemic therapy. Eight patients underwent resection of pancreatic cysts including branch duct IPMN with worrisome features, mucinous cystic neoplasms and solid pseudopapillary neoplasms. Five patients underwent resection for main duct IPMN. Two patients underwent resection of non-pancreatic abdominal masses; the remaining patients were surveilled in the specialty clinic. **CONCLUSIONS:** Implementation of a systematically executed PAF Initiative led by a pancreas-focused APP has positively impacted our health system through expert care, patient education, and timely management.

P99. Investigation of the tumor microenvironment of orthotopically implanted tumor organoids and its utility as a preclinical model of pancreatic cancer

Brian D Griffith[1]; Padma Kadiyala[2]; Alberto Olivei[3]; Lei Sun[4]; Aadith Kumar[5]; Yaqing Zhang[6]; Kyoung Lee[7]; Marina Pasca di Magliano[8]; Timothy L Frankel[9]
[1]University of Michigan, Ann Arbor, MI, US; [2]University of Michigan, Ann Arbor, MI, US; [3]University of Michigan, Ann Arbor, MI, US; [4]University of Michigan, Ann Arbor, MI, US; [5]University of Michigan, Ann Arbor, MI, US; [6]University of Michigan, Ann Arbor, MI, US; [7]University of Michigan, Ann Arbor, MI, US; [8]University of Michigan, Ann Arbor, MI, US; [9]University of Michigan, Ann Arbor, MI, US

INTRODUCTION: Genetically engineered mouse models (GEMMs), like KPC mice bearing *Kras* and *Trp53* mutations, mimic the progression of human pancreatic ductal adenocarcinoma (PDAC) and reflect the characteristic desmoplastic stromal reaction, but are limited by high cost and time. Conversely, preclinical models of PDAC utilizing the orthotopic implantation of immortalized 2D tumor cell lines, while offering high throughput, show variable degree of desmoplasia and relative lack of immune infiltration. We asked whether orthotopic implantation of tumor organoids would more accurately reflect the tumor stromal reaction and immune infiltration of GEMMs relative to 2D cell lines. **METHODS:** Spontaneous pancreatic tumors from KPC mice (KrasLSL-G12D/+; Trp53LSL-R172H/+; Pdx1-Cre) were harvested, and these parent tumors were processed for histology, and to generate 2D tumor cell lines or 3D tumor organoid lines. The 2D and 3D lines were then orthotopically implanted into pancreata of wild-type mice, and after 30 days, harvested for histology. Fibroblast and immune infiltration was quantified with multiplex fluorescent immunohistochemistry from parent, 2D and 3D tumors. 3D tumor organoids were implanted into lineage tracing β-actin-GFP mice or wild-type mice, and fibroblast and immune cell infiltration similarly quantified. **RESULTS:** 3D and parent tumors had a higher proportion of cells positive for the fibroblast markers PDGFRα and αSMA, and a shorter distance from CK19+ epithelial cells to αSMA+ cells, relative to 2D tumors (Fig 1A). Similarly, 3D and parent tumors showed a higher infiltration of macrophages, and a trend towards increased regulatory T cell infiltration, relative to 2D tumors, both characteristic of the immunosuppressive PDAC tumor microenvironment (TME). 3D and parent tumors showed shorted distance form epithelial cells to nearest macrophage (Fig 1B). Orthotopic tumors in lineage tracing mice showed epithelial cells originated from the tumor organoids, yet fibroblasts and immune cells in the TME originated from the host mouse, suggesting local interactions between TME and host mouse contribute to the differences observed. **CONCLUSIONS:** The TME of orthotopically implanted of tumor organoids more closely resembled the that of spontaneous tumors in GEMMs relative to 2D orthotopic tumors. These findings suggest that orthotopic implantation of organoids may offer a preclinical model with high throughput that more closely recapitulates the desmoplastic and immunosuppressive TME of GEMMs.



P100. Leveraging the functional specialization of neutrophillic myeloid derived suppresor cells as a predictive biomarker in pancreatic cancer

Manan Patel, MBBS[1]; Da Yin, [2]; Haleh Amirian, MS, MD[3]; Luis Nivelo, MS[4]; Andrew Adams, MS[5]; Karthik Rajkumar, Ph.D[6]; Harper Marsh, BS[7]; Erin M Dickey, MD[8]; Nipun Merchant, MD[9]; Dmitry Gabrilovich, MD, Ph.D[10]; Anna Bianchi, Ph.D[11]; Jashodeep Datta, MD[12]
[1]University of Miami, Miami, FL, US; [2]Johnson And Johnson, New Brunswick, NJ, US; [3]University of Miami, Miami, FL, US; [4]University of Miami, Miami, FL, US; [5]University of Miami, Miami, FL, US; [6]University of Miami, Miami, FL, US; [7]University of Miami, Miami, FL, US; [8]University of Miami, Miami, FL, US; [9]University of Miami, Miami, FL, US; [10]AstraZeneca, Gaithersburg, MD, US; [11]University of Miami, Miami, FL, US; [12]University of Miami, Miami, FL, US

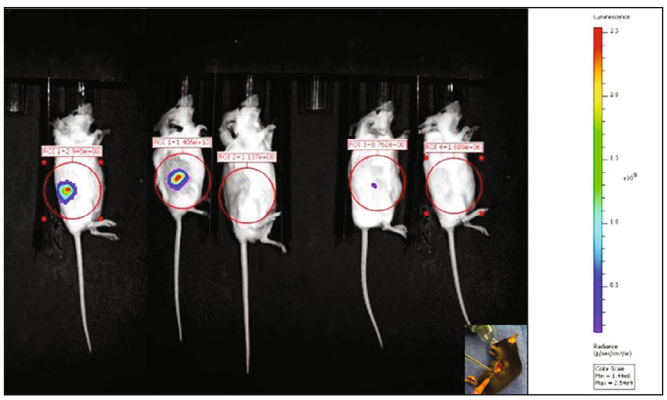
INTRODUCTION: Circulating polymorphonuclear neutrophils (PMN) traffic to pancreatic cancer (PDAC)-derived cues, where they acquire functional specialization as myeloid-derived suppressor cells (MDSC) to orchestrate immunosuppressive networks in the tumor microenvironment and promote therapeutic resistance. We sought to correlate the functional specialization of these PMN/MDSCs during PDAC tumorigenesis with oncologic outcomes in patients with PDAC. **METHODS:** Tumors and spleens from *Ptf1a*Cre/+;LSL-*Kras*G12D/+;*Tgfbr2*fl/fl (PKT) mice at 4 and 6 weeks of age, along with pancreata/spleens from age-matched littermates, were subjected to single-cell RNA sequencing (scRNAseq). Ingenuity Pathway Analysis (IPA) nominated unique surface markers for each subset. Functional studies were performed in sorted PMNs. To validate these observations in human PDAC patients, we utilized the Human Tumor Atlas Network (HTAN) scRNAseq data comprising 72 biospecimens from 32 patients (n=655,076 cells), annotated with clinical data, e.g, chemotherapy regimen, and treatment response. **RESULTS:** scRNAseq of PKT tumors/spleens revealed striking temporal heterogeneity in PMN subclusters with PDAC tumorigenesis. Single-cell trajectory inference identified distinct terminal-state (TS) populations in tumors and circulation. The intratumoral-TS PMNs resembled MDSC-like specialization, with enrichment of programs indicating suppressive function (*Tnf,Il1b,Arg1*). Conversely, spleen-TS PMNs showed imprinting of trafficking programs (*Cxcr2,Il1rap,Gab2*). A discrete PMN cluster in both spleen and tumors displayed upregulated MHC-II and co-stimulatory molecule genes (*H2-Ab,Cd79a,Cd80*). IPA of differentially expressed genes with transmembrane localization nominated *Cd170*, *Cd162*, and MHC-II as surface markers for intratumoral, splenic, and MHC-II PMN subsets respectively, which were validated by flow cytometry. *Ex vivo* co-culture of T-cells with sorted PMNs showed marked reduction in T-cell proliferation and functional activity with Cd170+ MDSCs, but not Cd162+ and MHC-II+ PMNs. In the HTAN dataset, relative dosage of *CD170*:MHC-II-expressing single-cell PMNs was significantly associated with resistance to FOLFIRINOX chemotherapy (p=0.01) in PDAC patients. **CONCLUSIONS:** Phenotypic plasticity of PMNs during PDAC progression drive functional specialization in distinct tissue niches, which may have predictive value in determining

chemosensitivity in PDAC patients. Strategies to titrate the balance between CD170+ or MHCII+ PMNs may mitigate therapeutic resistance in PDAC

P101. Lighting Up PNET: Creating a Murine Model with a Novel Bioluminescent Cell Line

Rachel Nation, MD, MPH[1]; Matthew Moccia, MD[2]; Zena Saleh, MD[3]; T Hess, MD[4]; Young K Hong, MD, MPH[5]; Tao Gao, PhD[6]
[1]Cooper University Hospital, Camden, NJ, US; [2]Cooper University Hospital, Camden, NJ, US; [3]Cooper University Hospital, Camden, NJ, US; [4]Cooper University Hospital, Camden, NJ, US; [5]Cooper University Hosptial, Camden, NJ, US; [6]Cooper University Hospital, Camden, NJ, US

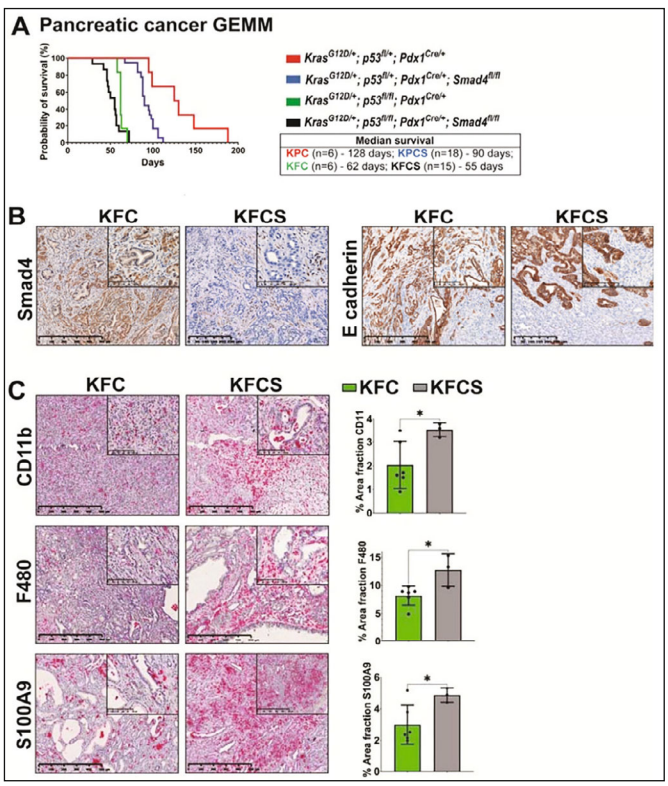
INTRODUCTION: Pancreatic neuroendocrine tumors (PNETs) are characterized by dysregulated signaling pathways that play a critical role in tumor development and progression. Current therapeutic strategies demonstrate limited efficacy, especially in advanced-stage PNETs. To facilitate further evaluation of novel therapies, especially immunotherapies, against PNETs, we aimed to develop a fluorescent/bioluminescent murine neuroendocrine tumor cell line for use in congenic in vivo models of PNETs. **METHODS:** The Intestinal secretin tumor cell line-1 (STC-1) were transduced with Green Fluorescent protein coded lentivirus. The stably-transduced luciferase-labeled cells were then injected into both immunocompromised and immunocompetent mice to evaluate tumor growth using a noninvasive in vivo imaging system (IVIS). **RESULTS:** Murine-derived STC-1 cells were plated at a density of 1.5 × 105 cells per well in a 6-well plate and cultured until reaching approximately 80% confluence before transduction. Cells were transduced using lentivirus encoding eGFP and firefly luciferase in the presence of 4 µg/mL polybrene for 10 hours. Five days post-transduction, cells were exposed to a puromycin concentration established by a killing curve. Following a one-month growth period, the cells underwent fluorescence-activated cell sorting (FACS) and were subsequently cultured in medium without a selection agent. The transduction of STC-1 cells was successful, despite the cell line demonstrating significant intrinsic resistance to puromycin. Post-transduction, cell morphology and growth characteristics remained unaltered. Cells were then injected successfully via subcutaneous inoculation into five SCID mice (1.5 million cells in DMSO) and via orthotopic pancreatic implantation (5x105 cells in 50ug of matrigel) into four immunocompetent mice (IACUC 03-022). Bioluminescence imaging revealed detectable tumor signals in three immunocompromised mice one week post-injection (Figure 1); however, rapid weight loss in these mice necessitated early euthanasia. Weight loss for the immunocompetent mice averaged 0.92g/week (SD .788). **CONCLUSIONS:** The generation of a stably transduced murine neuroendocrine tumor cell line with bioluminescent capability was successfully implanted and visualized in mice under IVIS. Tumors that derived from the luciferase-labeled STC1 cells can be imaged non-invasively in vivo following either subcutaneous or orthotopic pancreatic injection, providing a valuable tool for real-time, monitoring of PNET progression and facilitating the study of immunotherapeutic interventions.



P102. Loss of Smad4 in Genetically Engineered Mouse Models of Pancreatic Cancer Impairs Survival and Alters the Tumor Microenvironment

Gilbert Z Murimwa, MD[1]; Natalie Williams, MD[2]; Dina Alzhanova, PhD[3]; Jill Westcott, PhD[4]; Huocong Huang, MD PhD[5]; Jason Fleming, MD[6]; Rolf Brekken, PhD[7]
[1]UTSouthwestern Medical Center, Dallas, TX, US; [2]UTSouthwestern Medical Center, Dallas, TX, US; [3]UTSouthwestern Medical Center, Dallas, TX, US; [4]UTSouthwestern Medical Center, Dallas, TX, US; [5]UTSouthwestern Medical Center, Dallas, TX, US; [6]UT Southwestern Medical Center, Dallas, TX, US; [7]UTSouthwestern Medical Center, Dallas, TX, US

INTRODUCTION: SMAD4 mutations occur in 25% of pancreatic cancers and are associated with worse outcomes. The biology underlying their poor prognosis is poorly understood, however. We sought to generate a novel genetically engineered mouse model (GEMM) to better delineate the biological mechanisms at play. **METHODS:** 4 murine models were generated on a Black 6 background: KrasLSL-G12D/+; Trp53fl/+; Pdx1Cre/+ (KPC), KrasLSL-G12D/+; Pdx1Cre/+;Smad4fl/fl (KPCS), KrasLSL-G12D/+; Trp53fl/fl; Pdx1Cre/+ (KFC), and KrasLSL-G12D/+;Smad4fl/fl (KFCS). Mice were prospectively enrolled in a survival study and culled when moribund. Murine tissues were collected for analysis of both the tumor and associated microenvironment (TME) using immunohistochemistry and in vitro studies of the derived cell lines. **RESULTS:** Comparing between the wildtype models (KFC &KPC) and the Smad4-deficient models (KFCS & KPCS), the Smad4 deficient GEMMs had worse median overall survival (KPC 127.5d, KPCS 90d, KFC 62d, KFCS 55d; Figure 1A). Immunohistochemistry confirmed genetic ablation of Smad4 as well as formation of E-cadherin positive epithelial tumors (Figure 1B). KFCS tumors showed a myeloid predominant TME with CD11b+ cells, F4/80+ macrophages, and S100A9+ neutrophils (Figure 1C). In matrigel invasion assays, only cell lines from the SMAD4 deficient GEMMs were effective in invading and remodeling the extracellular matrix. **CONCLUSIONS:** Pancreatic cancer GEMMs recapitulate the aggressive nature of disease seen in human patients. In two separate models the loss of SMAD4 translated to impaired survival. Changes in the tumor microenvironment including a myeloid polarization with neutrophil predominance may contribute to the aggressive, metastatic, and treatment resistant phenotype seen in patients.



P103. Minimally Invasive Hepatectomy for Colorectal Liver Metastasis: Comparative Study of Laparoscopic vs Robotic Approach In A Large Multicenter Cohort of Patients

Samy Castillo-Flores[1]; Ricardo E. Nunez-Rocha[2]; Zachary Whitham[3]; Amr I. Al Abbas, MD[4]; Mihir M. Shah, MD[5]; David Iannitti[6]; Melissa Hogg, MD, FSSO[7]; Scott Helton[8]; David Geller[9]; Kerri Simo[10]; Pablo Serrano[11]; Kevin El-Hayak[12]; Hallbera Gudmundsdottir[13]; Ashwin Kamath[14]; Sharona Ross[15]; Peter Kingham[16]; Susanne G Warner[17]; Sean Clear[18]; Adnan Alseidi[19]; Edwin Onkendi[20]; Patricio M. Polanco, MD[21]

[1]University of Texas Southwestern, Dallas, TX, US; [2]University of Texas Southwestern Medical Center, DALLAS, TX, US; [3]The University of Texas Southwestern Medical Center, Dallas, TX, US; [4]UT Southwestern Medical Center, Dallas, TX, US; [5]Emory University, Atlanta, GA, US; [6]CarolinasHealthcare, Charlotte North Carolina, NC, US; [7]Northshore University Health System, Evanston, IL, US; [8]Virginia Mason Franciscan Health, Seattle, WA, US; [9]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [10]ProMedica, Toledo, OH, US; [11]George Washington Medical Faculty Associates, Washington DC, US; [12]Metrohealth, Cleveland, OH, US; [13]Mayo Clinic, Rochester, MN, US; [14]Allina Health, Mineapolis, MN, US; [15]AdventHealth Tampa, TAMPA, FL, US; [16]Memorial Sloan Kettering Cancer Center, New York, NY, US; [17]Mayo Clinic Rochester, Rochester, MN, US; [18]University of Toronto, Toronto, ON, CA; [19]University of California San Francisco, San Francisco, CA, US; [20]Texas Tech University, Lubbock, TX, US; [21]University of Texas Southwestern Medical Center, Dallas, TX, US

INTRODUCTION: The use of minimally invasive hepatic resections have increased in the US. There is limited multicenter data comparing the outcomes of robotic (RLR) versus laparoscopic liver resections (LLR). This study aims to compare these approaches using the composite Textbook Outcomes (TO) of patients with colorectal liver metastasis (CRLM). **METHODS:** A retrospective review of the Americas Minimally Invasive Liver Resection (AMILES) database was conducted on patients with CRLM undergoing minimally invasive liver resections from 15 North American institutions. Continuous and categorical variables were analyzed with appropriate tests, and multivariate logistic regression identified predictors of composite TO (LOS <75th percentile, no major complication (Clavien-Dindo>2), no grade B/C bile leaks, no 30-day reoperation/readmission/mortality and R0 resections). **RESULTS:** A total of 841 patients with CRLM were included, 212 patients underwent RLR and 629 underwent LLR. Overall morbidity was 15% and 20% for RLR and LLR respectively. The multivariate regression analysis identified Child-Pugh score > 5 (OR =0.11, p=0.003), concurrent ablation (OR=3.20, p=0.04) and any concurrent major surgery (OR=0.33, p= 0.02), as independent factors associated with composite TO. RLR was not associated with increased TO in univariate analysis and was not an independent predictor after controlling for cofounders (OR: 1.72, p=0.24); however, the robotic approach was associated with decreased chances of conversion (OR: 0.11, p= 0.01). **CONCLUSIONS:** RLR were not associated with improved TO when compared with laparoscopic approach. Yet, robotic approach was associated with decreased rate of conversions. The study identified Child-Pugh score, concurrent ablation, and concurrent major surgery as factors associated with textbook outcomes. While the robotic approach did not affect TO, it significantly reduced the risk of conversion, highlighting its benefit in reducing intraoperative challenges.

Table. Multivariate analysis Parameters Associated with Textbook Outcomes after Robotic and Laparoscopic Liver Surgery in Colorectal liver metastasis

Variables assessed	Multivariate analysis	
	OR (95% CI)	p value
Age ≥ 65 years (ref: <65 years)	0.75 (0.329- 1.734)	0.509
Operative time > 4 hours (ref: < 4 hours)	0.490 (0.214- 1.120)	0.091
Child-Pugh > 5 (ref: Child-Pugh = 5)	0.114 (0.027 - 0.483)	**0.003**
ASA > 3 (ref: ≤ 3)	0.783 (0.349- 1.756)	0.554
Conversion, yes (ref: no)	0.560 (0.183 - 1.711)	0.309
Pringle maneuver, yes (ref: no)	1.384 (0.523 - 3.661)	0.512
Past abdominal surgery, yes (ref: no)	0.486 (0.230-1.025)	0.058
Total lesions > 1 (ref: 1)	0.583 (0.254-1.337)	0.203
Major Hepatectomy performed (ref: no performed)	1.033 (0.375 - 2.845)	0.949
Robotic surgical approach (ref: laparoscopic approach)	1.720 (0.691 – 4.279)	0.243
concurrent ablation therapy use (ref: no concurrent ablation therapy)	3.207 (1.078 - 9.539)	**0.036**
High surgical difficulty (ref: moderate/low difficulty)	0.460 (0.133 - 1.595)	0.221
Location of largest incision		
Ref: Midline	-	-
Subcostal and right lateral abdomen	0.258 (0.060 - 1.104)	0.068
Suprapubic	0.561 (0.167 - 1.879)	0.349
Other	1.216 (0.427 - 3.461)	0.713
Lymph node dissection, yes (ref: no)	0.253 (0.033- 1.908)	0.183
Proximity to Major vessel, yes (ref: no)	1.00 (0.379- 2.641)	0.999
Portal vein embolization, yes (ref: no)	0.908 (0.065 - 12.642)	0.943
Tumor Size ≥ 5cm (ref: size < 5cm)	1.020 (0.320 - 3.250)	0.972
Concurrent Major surgery, yes (ref: no)	0.335 (0.138 -0.811)	**0.015**

P104. Neoadjuvant Chemotherapy in Pancreatic Ductal Adenocarcinoma: Reassessing Survival and Recurrence After Adjusting for Immortal Time Bias

Jane Wang[1]; Amir Ashraf Ganjouei[2]; Laleh Foroutani[3]; Han Yin[4]; Fernanda Romero Hernandez[5]; Lucas W. Thornblade, MD, MPH[6]; Adnan Alseidi[7]; Mohamed A. Adam, MD[8]

[1]University of California San Francisco, San Francisco, CA, US; [2]University of California San Francisco, San Francisco, CA, US; [3]University of California San Francisco, San Francisco, CA, US; [4]University of California San Francisco, San Francisco, CA, US; [5]University of California San Francisco, San Francisco, CA, US; [6]University of California, San Francisco, San Francisco, CA, US; [7]University of California San Francisco, San Francisco, CA, US; [8]University of California, San Francisco, San Francisco, CA, US

INTRODUCTION: Neoadjuvant chemotherapy (NAC) for resectable pancreatic ductal adenocarcinoma (PDAC) remains controversial. Data supporting the use of NAC over upfront surgery have largely stemmed from retrospective analyses that did not account for immortal time bias (ITB). ITB is a methodological error that occurs when the period during which a patient must remain alive to receive treatment, such as NAC, is not appropriately accounted for in the analysis. This study aims to evaluate the impact of NAC versus upfront surgery on overall survival (OS) and disease-free survival (DFS) for patients with resectable PDAC after accounting for ITB. **METHODS:** Adult patients with early (stage I/II) PDAC who underwent pancreatectomy with or without NAC were identified from the California Cancer Registry (2010-2020). The adjusted association of NAC vs. upfront pancreatectomy with OS and DFS was examined using the Kaplan-Meier estimator and multivariate Cox regression. ITB was adjusted for using landmark analysis and time-varying Cox regression. **RESULTS:** Among 4,791 patients with early-stage PDAC, 18% received NAC and 82% underwent upfront pancreatectomy. Most patients in the NAC and upfront surgery groups had tumors in the pancreatic head (75% vs. 70%) and underwent pancreaticoduodenectomy (79% vs. 73%). Median OS was longer for the NAC group compared to the upfront pancreatectomy group (27 months vs. 22 months; adjusted HR 0.89, p=0.030). After adjusting for ITB, OS (HR 1.12, p=0.063) and DFS (HR 1.06, p=0.300) were no longer statistically significant between groups. **CONCLUSIONS:** NAC for early-stage PDAC is associated

with improved survival; however, after adjustment for ITB, there is no longer a difference in OS or DFS. Our results underscore the importance of accounting for ITB in determining the role and optimal sequence of systemic therapy in the management of PDAC.

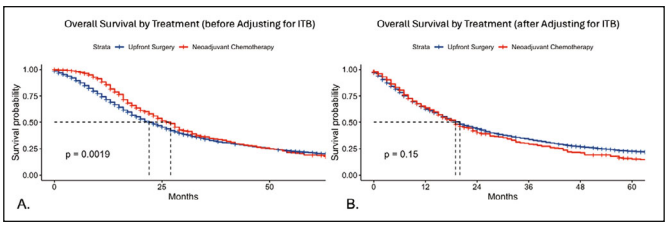


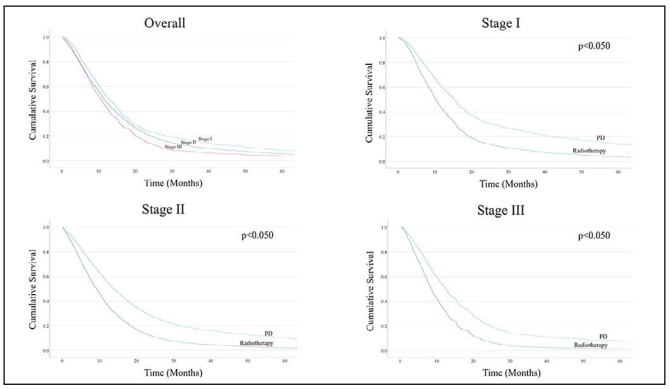
Figure 1. Kaplan-Meier survival curves for NAC vs. upfront surgery before adjusting for 1TB (A) and after adjusting for 1TB (B)

P105. Octogenarians Undergoing Pancreaticoduodenectomy versus Definitive Radiotherapy for Locoregional Therapy of Pancreatic Ductal Adenocarcinoma

Muhammad Muntazir Mehdi Khan, MBBS[1]; Edward A Joseph, MBBS[2]; Ruchita Dunung, MS, BDS[3]; Sricharan Chalikonda, MD[4]; David Bartlett[5]; Casey J. Allen, MD[6]

[1]Allegheny Health Network, Pittsburgh, PA, US; [2]Allegheny Health Network, Pittsburgh, PA, US; [3]Allegheny Health Network, Pittsburgh, PA, US; [4]Allegheny Health Network, Pittsburgh, PA, US; [5]Allegheny Health Network, Pittsburgh, PA, US; [6]Allegheny Health Network, Pittsburgh, PA, US

INTRODUCTION: Pancreaticoduodenectomy (PD) remains the standard for locoregional therapy of pancreatic ductal adenocarcinoma (PDAC) in the head of the pancreas. However, octogenarians have reduced life expectancy, potentially negating benefit of aggressive intervention. Radiotherapy provides an alternative for definitive locoregional therapy, but comparative data on these treatment modalities among octogenarians are limited. We compared survival outcomes of PD versus radiotherapy in octogenarians with non-metastatic PDAC. **METHODS:** We queried the National Cancer Database to identify patients aged 80 and above diagnosed with resectable or borderline-resectable PDAC in the head of the pancreas between 2004 and 2019. Patients with stage IV disease were excluded. Patients were categorized based on the treatment received: PD or radiotherapy. The primary outcome was overall survival from the time of diagnosis. **RESULTS:** A total of 7,910 patients diagnosed with PDAC were included in the analysis. The mean age was 83.1 ± 2.6 years, with 44.8% male (n=3,564), 85.9% non-Hispanic White (n=6,795), and 10.7% (n=850) having a Charlson-Deyo score ≥2. Of these, 23.3% (n=1,842) had stage I, 56.3% (n=4,456) had stage II, and 13.9% (n=1,101) had stage III disease at presentation. The median survival of the overall cohort was 11.5 (5.9-21.8) months. Overall, 55.3% (n=4,373) of patients underwent PD alone, while 44.7% (n=3,537) underwent definitive radiotherapy. Patients in the PD cohort were more likely to be younger (82.7 ± 2.4 vs. 83.6 ± 2.7), non-Hispanic White (86.8% vs. 84.8%), have a Charlson-Deyo score of 1 (26.0% vs. 23.0%), have stage II disease (73.7% vs. 34.9%), and were less likely to have received chemotherapy (34.4% vs. 67.2%), all p<0.050. Patients who underwent PD had better overall survival (median 14.0 [6.0-30.7] vs. 9.9 [5.8-15.9] months, p<0.001) compared to patients who underwent definitive radiotherapy (Figure). On multivariable Cox proportional hazards analysis, after controlling for covariables, radiotherapy (hazard ratio [HR] 1.86, 95% CI 1.74-1.98, p<0.001) and advanced stage of disease (stage III: HR 1.43, 95% CI 1.30-1.56, p<0.001) were predictors of long-term mortality. **CONCLUSIONS:** Octogenarians with non-metastatic PDAC have a poor long-term prognosis. Although of marginal benefit, PD offers higher odds of long-term survival compared to definitive radiotherapy. As PD in the elderly population may pose quality-of-life impairments, these findings highlight the need for individualized treatment strategies for octogenarians with PDAC.



P106. Optimizing Clinical Trial Design May Mitigate Racial Disparities in Pancreatic Cancer Clinical Trial Enrollment

Tracey Pu, MD[1]; Alexandra Gustafson, MD[2]; Kendra N Coleman, BS[3]; Nicole Russell, BA[4]; Oliver S Eng[3]; Rebecca A. Snyder, MD, MPH[6]

[1]National Cancer Institutes/National Institutes of Health, Bethesda, MD, US; [2]National Cancer Institute, Bethesda, MD, US; [3]NCI/NIH, Bethesda, MD, US; [4]National Cancer Institute/National Institutes of Health, Bethesda, MD, US; [5]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [6]MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Participation in pancreatic ductal adenocarcinoma (PDAC) clinical trials remains dismal among patients from minoritized groups. This study aimed to investigate if clinical trial design, including eligibility criteria, affects representation of minoritized populations. **METHODS:** United States Phase I-IV PDAC clinical trials between 2000-2020 were extracted from the ClinicalTrials.gov database. The Surveillance, Epidemiology, and End Results (SEER) database was used to determine cancer incidence linked with years of trial enrollment. Enrollment fraction (EF) was defined as the number of trial participants divided by the incidence of PDAC in each racial and ethnic group. Representation Quotient (RQ) was defined as the proportion of trial participants divided by proportion of PDAC incidence for each subgroup, where underrepresentation was RQ <1.0. **RESULTS:** 8451 patients from 228 unique PDAC clinical trials were analyzed. 55.7% (n=128) and 44.3% (n=102) trials reported racial and ethnic demographic data, respectively. Non-Hispanic Black (NHB), Non-Hispanic Asian/Pacific Islander (NHAPI), Non-Hispanic American Indian/Alaskan Native (NHAIAN), and Hispanic patients were underrepresented (Table 1). NHB patients were more likely to be underrepresented in trials for metastatic PDAC disease (89.4% vs. 73.8% of trials, p=0.035). NHB patients demonstrated an increase in median RQ (0.28 vs. 0.48) in trials from 2000-2010 vs. 2011-2020, while Hispanic patients had a decreased median RQ (0.36 vs. 0.25). Trials with renal insufficiency exclusion criteria without cutoffs or explicit methodology were more likely to accrue NHB patients (RQ 0.88 vs. 0.46, p=0.02), whereas trials that used a creatinine cutoff or the modified Cockcroft-Gault (CG) formula did not significantly affect RQ. Other eligibility criteria including cardiac history, HIV, Hepatitis B/C, and receipt of neoadjuvant therapy did not significantly affect RQ for any racial or ethnic group. Trial location and funding source did not affect RQ for any group. **CONCLUSIONS:** Systemic barriers persist in minority enrollment in PDAC clinical trials. Clinical trial design optimizing inclusive eligibility requirements is a first feasible step in increasing minority clinical trial enrollment.

Table. Enrollment Fraction and Representation Quotient Stratified by Race and Ethnicity for United States Pancreatic Cancer Clinical Trials 2000-2020

	Enrollment Fraction (Median %, IQR)	Representation Quotient (Median, IQR)
NHW	0.28 (0.12-0.62)	1.17 (1.09-1.24)
NHB	0.15 (0-0.33)	0.47 (0-0.87)
NHAPI	0 (0-0.23)	0 (0-0.45)
NHAIAN	0 (0-0)	0 (0-0)
Hispanic	0.07 (0-0.21)	0.26 (0-0.68)

P107. Pancreaticoduodenectomy with Intraoperative Radiation Therapy for Borderline and Locally Advanced Pancreatic Cancer: A Propensity Score Matched Survival Analysis

Alfredo Verastegui, MD[1]; Katherine E Poruk, MD[2]; Mary P Tice, PA[3]; Byron May, MD[4]; Michael Rutenberg, MD PhD[5]; John A Stauffer, MD[6]
[1]Mayo Clinic, Jacksonville, FL, US; [2]Mayo Clinic Florida, Jacksonville, FL, US; [3]Mayo Clinic, Jacksonville, FL, US; [4]Mayo Clinic, Jacksonville, FL, US; [5]Mayo Clinic, Jacksonville, FL, US; [6]Mayo Clinic, Jacksonville, FL, US

INTRODUCTION: Intraoperative Radiation Therapy (IORT) has emerged as an innovative approach in cancer treatment, demonstrating significant efficacy in certain malignancies such as breast cancer. However, its effectiveness in other cancer types remains debated. In pancreatic cancer, particularly pancreatic ductal adenocarcinoma (PDAC), IORT is not routinely indicated, and literature comparing its efficacy in borderline and locally advanced cases is limited. This study aims to evaluate the outcomes of undergoing pancreaticoduodenectomy with adjunctive IORT for PDAC in the context of modern neoadjuvant treatment approaches. **METHODS:** This single-center, case-control study analyzed patients with borderline and locally advanced PDAC who underwent pancreaticoduodenectomy between 2010 and 2023. Patients were categorized into two groups: those who received IORT and those who did not. Propensity score analysis was employed to control for comorbidities and neoadjuvant therapy. Survival analysis was conducted using Kaplan-Meier curves and Cox proportional hazard models, while logistic regression was utilized for additional outcome assessments. **RESULTS:** Out of 147 patients with borderline and locally advanced PDAC, 100 were propensity-matched (50 IORT, 50 non-IORT) based on comorbidities, family history, age, gender, BMI, and neoadjuvant therapy. The median age was 67.9 years (IQR: 60.7-73.9), with 51% male. IORT patients had a longer median survival of 1141 days (IQR: 341-937) compared to 757 days (IQR: 347-1450) in non-IORT patients. Three-year survival rates were 68.75% for IORT vs. 43.75% for non-IORT. Cox regression showed no significant survival benefit with IORT (HR = 0.91, P = 0.8051), while recurrence was a strong predictor of mortality (HR=10.14, P < 0.001). **CONCLUSIONS:** This study suggests potential benefits of IORT in borderline and locally advanced PDAC when combined with neoadjuvant chemotherapy, though the results were not statistically significant. The findings emphasize the impact of recurrence on mortality, and larger studies are needed to confirm the role of IORT in PDAC treatment.

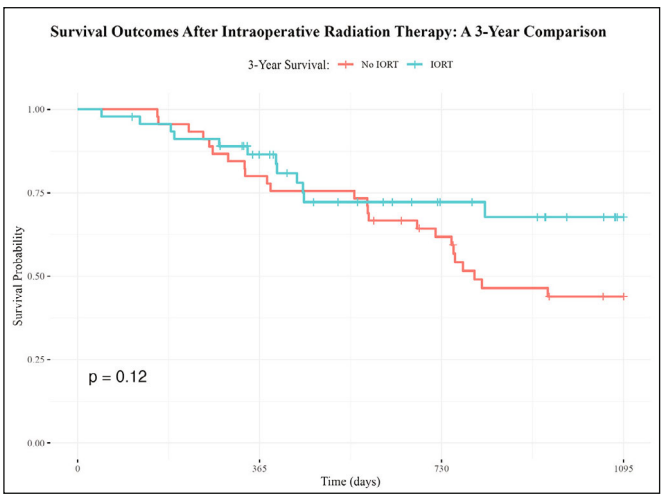


Figure 1. Kaplan-Meier survival curves comparing patients who underwent IORT versus those who did not, over a 3-year follow-up period.

P108. Perioperative Outcomes and Technical Feasibility of A Phase II Trial of Hepatic Artery Infusional Floxuridine with Systemic Chemotherapy in Treatment of Pancreatic Cancer Liver Metastases

Jason M. Aubrey, MD[1]; Mariam Khan[2]; Kathrine Kelly, DO[3]; Hordur M Kolbeinsson, MD[4]; Hannah Liefeld[5]; Jesse Kelley[6]; Mathew Chung, MD[7]; M. Mura Assifi, MD[8]; G. Paul Wright, MD[9]
[1]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [2]Corewell Health West, Grand Rapids, MI, US; [3]Universtiy of Pittsburgh Medical Center, Pittsburgh, PA, US; [4]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [5]Corewell Health West/Michigan State University, Grand Rapids, MI, US; [6]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [7]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [8]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [9]Corewell Health West - Michigan State University, Grand Rapids, MI, US

INTRODUCTION: Pancreatic ductal adenocarcinoma (PDAC) often metastasizes to the liver, leading to hepatic failure and limited survival. Hepatic artery infusion (HAI) chemotherapy with floxuridine (FUDR) has shown survival benefits in other liver malignancies but has not been applied to PDAC liver metastases. We hypothesize that combining HAI FUDR with systemic chemotherapy will improve survival in PDAC with liver metastases. **METHODS:** Single-center, non-blinded, single-arm phase II clinical trial was conducted involving patients with synchronous PDAC liver metastases (NCT03856658). Patients underwent surgical placement of an HAI pump for FUDR delivery in 28-day cycles, combined with systemic chemotherapy selected by their oncologist. Management of the primary tumor included resection or irreversible electroporation during pump placement. The primary endpoint was 1-year hepatic progression-free survival, assessed using RECIST criteria (>20% growth in target lesions or new lesions). Secondary endpoint was overall survival. **RESULTS:** A total of 13 patients were enrolled, with a mean age of 64 years (SD 9.5), 10 male (77%), and a mean BMI of 28 (SD 5.5). The primary tumor was resectable in 9 (69%) and locally advanced in 4 (31%). All patients received at least six cycles of neoadjuvant chemotherapy: 9 (69%) received FOLFIRINOX, and 4 (31%) Gemcitabine-Abraxane. Of the resectable tumors, 7 patients underwent distal pancreatectomy, 1 had pancreaticoduodenectomy, and 1 declined surgery. Irreversible electroporation was performed in 3 (75%) patients with locally advanced tumors. All patients received a Medtronic SynchroMed II pump. Average operative time was 268 minutes (SD 55) and length of stay was 5.8 days (SD 2.8). No in-hospital mortalities occurred. No patients showed extra-hepatic perfusion. The most common complication was chemical hepatitis and was seen in all patients, necessitating adjustments in FUDR dosing or scheduling. One patient required pump removal due to catheter dislodgement (8%). The median number of FUDR cycles received was five (range 1–6), with a mean dosage of 55% of the intended amount (range 20%–92%). At one year, 8 (62%) had hepatic progression-free survival, 2 (15%) had progressive disease, 2 (15%) were deceased, and 1 (8%) enrolled in hospice. Currently, 10 of 13 patients are deceased, with a mean survival time of 466 days. The three surviving patients have been followed for a mean of 665 days with stable disease. **CONCLUSIONS:** HAI FUDR combined with systemic chemotherapy shows potential to improve survival in PDAC patients with liver metastases. Further studies are needed to identify which patients may benefit from this therapy.

P109. Phospho-Mass Spectrometry Reveals Translatable Therapeutic Targets in Metastatic Tumors Without Targetable Mutations

Tracey Pu, MD[1]; Brian A. Joughin, PhD[2]; Priyanka Desai, PhD[3]; Steven D. Forsythe, MS, PhD.[4]; Ronald Holewinski, PhD[5]; Thorkell Andresson[6]; Kendra N Coleman, BS[7]; Timothy Leach, MD[8]; Allan Johansen, PhD[9]; Anirudh Sattiraju, PhD[10]; Ashley Rainey, BS[11]; Carolina Larrain, MD[12]; Jeremy L. Davis, MD[13]; Andrew M Blakely, MD[14]; David Kleiner, MD, PhD[15]; Naris Nilubol, MD[16]; Samira Sadowski[17]; Jaydira del Rivero, MD[18]; Michael B Yaffe, MD, PhD[19]; Jonathan M Hernandez, MD[20]
[1]National Cancer Institutes/National Institutes of Health, Bethesda, MD, US; [2]Koch Institute for Integrative Cancer Research/MIT, Cambridge, MA, US; [3]National Institutes of Health, Bethesda, MD, US; [4]Center for Cancer Research, National Institutes of Health, Bethesda, MD, US; [5]National Cancer Institutes - Frederick, Frederick, MD, US; [6]National Cancer Institutes - Frederick, Frederick, MD, US; [7]NCI/NIH, Bethesda, MD, US; [8]Wake Forest Institute for Regenerative Medicine, Winston-Salem, NC, US; [9]Wake Forest School of Medicine, Winston-Salem, NC, US; [10]Icahn School of Medicine at Mount Sinai, New York, NY, US; [11]National Institutes of Health, Bethesda, MD, US; [12]National Institutes of Health, Bethesda, MD, US; [13]National Cancer Institute, Bethesda, MD, US; [14]National Institutes of Health, Bethesda, MD, US; [15]National Institutes of Health, Bethesda, MD, US; [16]National Institutes of Health, National Cancer Institute, Bethesda, MD, US; [17]National Cancer Institute/National Institutes of Health, Bethesda, MD, US; [18]National Cancer Institute/National Institutes of Health, Bethesda, MD, US; [19]Koch Institute for Integrative Cancer Research, MIT, Cambridge, MA, US; [20]National Institutes of Health, Bethesda, MD, US

INTRODUCTION: Although next-generation sequencing has rapidly transformed oncology, many tumors lack targetable mutations. Tumor proteomics as measured by mass spectrometry (MS) holds promise as a

complementary means to stratify cancers, but analysis of this data for actionable targets is extremely limited. Gastrointestinal neuroendocrine tumors (GEP-NETs) and adrenocortical carcinoma (ACC) lack actionable genetic mutations and were therefore the focus of our investigation. **METHODS:** 105 liver metastases and normal liver patient samples (16 small bowel NET (SBNET),12 pancreatic NET (PNET), 4 ACC) were analyzed by phosphoproteomic mass spectrometry (MS). Data were evaluated using our novel computational motif methodology to identify up- and downregulated kinases based upon biochemical substrate specificity. Approved or investigational drugs to the identified target kinases were then tested and validated using patient-derived organoids (PDOs) from 37 SBNET, 28 PNET, and 5 ACC tumors. Immunoblotting was completed with drug-treated *ex-vivo* patient-matched tumor slice cultures. **RESULTS:** Phospho-MS results were obtained from the following liver metastases: 45 SBNET, 55 PNET, and 5 ACC. A total of 2300 phosphopeptides were identified for SBNET patients, 2517 for PNETs, and 125 for ACC. Our motif analysis method identified upregulation of CK2 (NETs), FAM20C (NETs), TTK (ACC), and regulators of MAPK and TGFβ signaling (NETs). Drug screening in metastasis-matched PDOs identified growth inhibition by silmitasertib (CK2 inhibitor) for NETs (median IC_{50} SBNET = 9.27 uM, PNET =5 μM) and luvixasertib (TTK inhibitor) for ACC (median IC_{50}=4.00 μM). NFκB has previously been implicated in NET pathogenesis, and both CK2 and TTK target the NFκB p65 subunit. Analysis of silmitasertib-treated tumor slice cultures from patient-matched SBNETs and PNETs demonstrate that CK2 inhibition is associated with reduction in expression of phosphorylated NFKB p65 (S529) for all tumors (n=6) predicted to have CK2 activation and none (n=6) of tumors not predicted to have high CK2 activity. Analysis of luvixasertib-treated tumor slice cultures of patient-matched ACC show that TTK inhibition was associated with reduction in expression of phosphorylated NFKB p65 (S529) for two tumors predicted to have high TTK activity. **CONCLUSIONS:** Using low mutation cancers (NETs and ACC), we demonstrate the utility of phospho-MS data to unveil actionable targets for clinical translation. These results carry broad implications for the use of proteomic data to help guide personalized therapies in solid tumors.

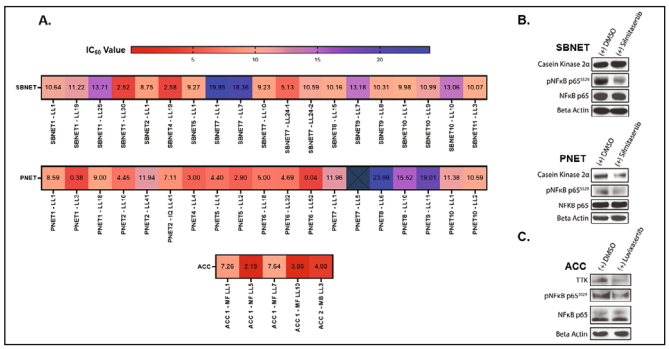


Figure. A. Kinase Screen Using Casein Kinase II Inhibitor, Silmitasertib, for SBNET and PNET Patient Derived Organoids and TTK inhibitor, Luvixasertib, for ACC Patient Derived Organoids. Scale reported as IC50 . B. CK2 Inhibition abrogates phosphorylation of NFKB p65 in SBNET/PNET liver metastases C. TTK inhibition abrogates phosphorylation of NFKB p65 in ACC liver metastases

P110. Postoperative Decision Regret is Higher in Patients with Pancreatic Ductal Adenocarcinoma who are Non-English Primary Speakers or with Poor Health Literacy

Judy Li[1]; Thomas M Li, MD[2]; Adam Geffner, BA[3]; Sophie Neugarten, BA[4]; Camilo Correa-Gallego, MD[5]; Umut Sarpel, MD, MSc[6]; Daniel Labow, MD[7]; Ganesh Gunasekaran, MD[8]; Myron Schwartz, MD[9]; Parissa Tabrizian, MD[10]; Spiros Hiotis, MD, PhD[11]; James O Park, MD[12]; Noah A. Cohen, MD[13]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, US; [2]Icahn School of Medicine at Mount Sinai, New York, NY, US; [3]Icahn School of Medicine at Mount Sinai, New York, NY, US; [4]Icahn School of Medicine at Mount Sinai, New York, NY, US; [5]Icahn School of Medicine at Mount Sinai, New York, NY, US; [6]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, US; [7]Nuvance Health, Danbury, CT, US; [8]Icahn School of Medicine at Mount Sinai, New York, NY, US; [9]Icahn School of Medicine at Mount Sinai, New York, NY, US; [10]Icahn School of Medicine at Mount Sinai, New York, NY, US; [11]Icahn School of Medicine at Mount Sinai, New York, NY, US; [12]Icahn School of Medicine at Mount Sinai, New York, NY, US; [13]Icahn School of Medicine at Mount Sinai, New York, NY, US

INTRODUCTION: Patient communication barriers are associated with worse quality of care and clinical outcomes. However there are limited data exploring their impact on shared decision-making (SDM) in the preoperative setting, especially for pancreatic ductal adenocarcinoma (PDAC). This study investigates the impact of patient communication barriers on patient-physician communication surrounding the decision to pursue pancreatectomy. **METHODS:** This cross-sectional study investigates the impact of communication barriers on the degree of decisional regret (DR) in patients with PDAC who have undergone curative-intent resection at least 6 months prior to study recruitment. Patients completed validated surveys assessing communication preferences, SDM participation, and DR. Health literacy was assessed by the BRIEF Health Literacy survey. Groups were stratified by presence or absence of DR, assessed by the Decisional Regret Scale (DRS). Characteristics and survey scores were compared by chi-square and independent t-test. **RESULTS:** 45 patients met inclusion criteria and completed all questionnaires. 19 (42.2%) patients expressed regret about their decision to pursue surgery with 5 patients expressing moderate to severe regret (DRS ≥ 25). Baseline characteristics were similar between groups. There were no significant differences in neoadjuvant or adjuvant treatments, or operative characteristics. Both groups reported high participation in preoperative SDM (average score 34.47 ± 9.67 in DR group vs 36.08 ± 8.88, P=0.567). Despite similar levels of education between groups, those expressing regret had a lower level of health literacy (14.68 ± 4.10 vs 17.35 ± 2.07, P=0.016). Fewer patients also identified English as their primary language in the DR group (78.9% vs 100%, P=0.026). While most patients preferred an active role in the final decision making process, fewer patients in the DR group reported this happening in actuality (Cohen's kappa= 0.635 vs Cohen's kappa=0.934). **CONCLUSIONS:** Almost half of patients expressed some regret pursuing surgery for PDAC. Despite similar educational backgrounds, a higher proportion of those expressing regret did not identify English as their primary language and had lower health literacy. While there was high participation in SDM, there was greater discordance between preferred and actual roles in the final decision making process. This identifies an important disparity to address in future preoperative discussions.

Table 1. Assessment of Communication Barriers Impacting Shared Decision-Making and Postoperative Decisional Regret

	DR Absent N=26 (%)	DR Present N=19 (%)	Overall N=45 (%)	P-value
Gender				
Male	12 (46.2)	9 (47.4)	21 (46.7)	0.936
Female	14 (53.8)	10 (52.6)	24 (53.3)	
Race				
White	20 (76.9)	13 (68.4)	33 (73.3)	0.483
African American/Black	5 (19.2)	5 (26.3)	10 (22.2)	
Asian	0 (0)	1 (5.3)	1 (2.2)	
Other/unknown	1 (3.8)	0 (0)	1 (2.2)	
Ethnicity				
Hispanic/Latino	1 (3.8)	4 (21.1)	5 (11.1)	0.144
Age at diagnosis (mean, SD)	64.38 ± 8.23	64.68 ± 9.60	64.51 ± 8.73	0.911
Preoperative treatment				
Neoadjuvant chemotherapy	17 (65.4)	13 (68.4)	30 (66.7)	0.831
Upfront surgery	9 (34.6)	6 (31.6)	15 (33.3)	
Surgical Procedure				
Pancreaticoduodenectomy	18 (69.2)	14 (73.7)	32 (71.1)	0.502
Distal pancreatectomy	7 (26.9)	3 (15.8)	10 (22.2)	
Other	1 (3.8)	2 (10.5)	3 (6.7)	
Postoperative chemotherapy	20 (76.9)	17 (89.5)	37 (82.2)	0.435
English as primary language?	26 (100.0)	15 (78.9)	41 (91.1)	**0.026**
Advanced educational degree?[A]				
Yes	19 (73.1)	10 (52.6)	29 (64.4)	0.212
No	7 (26.9)	9 (47.4)	16 (35.6)	
SDMQ9 score[B] (mean, SD)	36.08 + 8.88	34.47 + 9.67	35.40 + 9.15	0.567
BRIEF Health Literacy Score[C] (mean, SD)	17.35 ± 2.07	14.68 ± 4.10	16.22 ± 3.33	**0.016**
Decision Making Preference[D]				
Active role	14 (53.8)	10 (52.6)	24 (53.3)	0.986
Collaborative role	9 (34.6)	7 (36.8)	16 (35.6)	
Passive role	3 (11.5)	2 (10.5)	5 (11.1)	
Decision Making Actuality				
Active role	13 (50.0)	10 (52.6)	23 (51.1)	0.984
Collaborative role	10 (38.5)	7 (36.8)	17 (37.8)	
Passive role	3 (11.5)	2 (10.5)	5 (11.1)	
Cohen's kappa [95% CI]	0.934 [0.807-1.061]	0.635 [0.333-0.937]	0.809 [0.651-0.965]	

[A] Advanced educational degree includes bachelor's degree, graduate degree, or professional degree.

[B] The Shared Decision Making Questionnaire is scored from 0-45, with 45 indicating full participation in shared decision making.

[C] The BRIEF Health Literacy survey is scored from 0-20, with higher scores indicating greater health literacy.

[D] Active role indicates a primarily patient-driven decision. Collaborative role indicates mutual responsibility between the patient and physician in the decision. Passive role indicates a primarily physician-driven decision.

P111. Postoperative Pancreatic Fistula after Pancreatoduodenectomy: can radiomics improve clinical risk scores?

Ankur P Choubey, MD MPH[1]; Josephine Magnin[2]; Johan Gagniere[3]; Abhishek Midya[4]; John Steinharter[5]; Richard Do[6]; Kevin Soares, MD[7]; Mithat Gonen, PhD[8]; Jeffrey Drebin, MD PhD[9]; T. Peter Kingham, MD[10]; Vinod Balachandran[11]; Michael D'Angelica, MD[12]; Peter J Allen, MD[13]; Alice C Wei, MD MSc[14]; Amber Simpson[15]; Jayasree Chakraborty, PhD[16]; William R Jarnagin, MD[17]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US; [11]Memorial Sloan Kettering Cancer Center, New York, NY, US; [12]Memorial Sloan Kettering Cancer Center, New York, NY, US; [13]Duke University Medical Center, DURHAM, NC, US; [14]Memorial Sloan Kettering Cancer Center, New York, NY, US; [15]Queen's University, Kingston, ON, US; [16]Memorial Sloan Kettering Cancer Center, New York, NY, US; [17]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Postoperative pancreatic fistula (POPF) after pancreatoduodenectomy (PD) is associated with high morbidity and mortality. This study examined the potential added benefit of radiomic data to clinical models to predict POPF after PD. **METHODS:** All patients with preoperative CT scan before PD at one center from 2009-2021 were included. Random sampling was used to create a balanced cohort, which was split into training (70%) and test (30%) groups. Manually segmented remnant pancreas was used to extract 254 established radiomic features that reflect heterogeneity in enhancement patterns. Outcomes of interest were all POPF and clinically relevant (grade B/C) POPF (CR-POPF). Using the training cohort, five predictive models were designed with random forest classifier for each endpoint: preoperative (Preop), intraoperative (Intraop), radiomics alone, Preop with radiomics, and Intraop with radiomics. Preop model used pathology and main pancreatic duct (MPD) size, while the Intraop model used pathology, MPD, pancreas texture, and blood loss. Model performance was tested using area under receiver operating characteristic curve (AUC), sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. **RESULTS:** From 1855 patients who underwent PD in the study period, 234 with POPF and 250 without POPF were included after random sampling. POPF group included fewer pancreatic adenocarcinomas ($p<0.001$), fewer pancreata with firm texture ($p<0.001$), fewer dilated MPD ($p<0.001$), with longer operative time ($p<0.001$) and higher blood loss ($p<0.001$). After training, predictive models were evaluated on an independent test sample, 30% of the original cohort. Prediction for all POPF was similar using Intraop and radiomics alone models with AUC=0.81 and AUC=0.82, respectively. Combining Intraop data with radiomics further improved performance with AUC=0.88. Similar trends were observed in predictive modeling for CR-POPF with AUC=0.75 for both Intraop and radiomics alone models. The combined model again performed better with AUC=0.81. **CONCLUSIONS:** Radiomics compared favorably with clinical risk scores for POPF after PD, and further improved predictive modeling when combined with clinical data. This approach has the potential to better identify high risk patients and inform clinical decision making, such as the decision to leave abdominal drains.

Table 1. Predictive performance of each model for all postoperative pancreatic fistula and clinically relevant postoperative pancreatic fistula.

Model	AUC
All POPF	
Preoperative	0.77 [0.69-0.84]
Intraoperative	0.81 [0.74-0.88]
Radiomics	0.82 [0.76-0.89]
Preop with Radiomics	0.87 [0.81-0.92]
Intraop with Radiomics	0.88 [0.83-0.93]
CR POPF	
Preoperative	0.71 [0.63-0.79]
Intraoperative	0.75 [0.67-0.83]
Radiomics	0.75 [0.67-0.83]
Preop with Radiomics	0.79 [0.72-0.86]
Intraop with Radiomics	0.81 [0.75-0.88]

AUC: area under receiver operating characteristic curve; POPF: postoperative pancreatic fistula; CR- POPF: clinically relevant POPF (grade B/C).

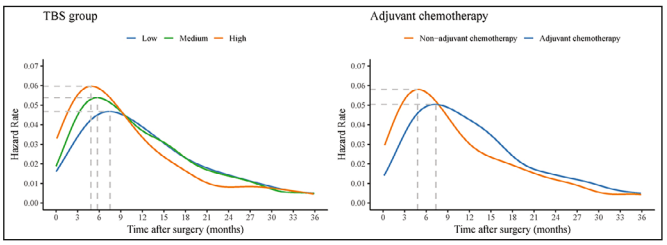
P112. Recurrence Timing and Risk Following Curative Resection of Colorectal Liver Metastases: Insights from a Hazard Function Analysis

Diamantis I. Tsilimigras, MD, PhD[1]; Jun Kawashima[2]; Miho Akabane[3]; Selamawit Woldesenbet[4]; Odysseas P. Chatzipanagiotou[5]; Zayed Rashid[6]; Mujtaba Khalil[7]; Abdullah Altaf[8]; Shahzaib Zindani[9]; Andrea Ruzzente[10]; Irinel Popescu[11]; Minoru Kitago[12]; George Poultsides, MD[13]; Kazunari Sasaki[14]; Federico Aucejo[15]; Itaru Endo[16]; Tim Pawlik[17]

[1]The Ohio State University, Columbus, OH, US; [2]The Ohio State University, Columbus, OH, US; [3]The Ohio State University, Columbus, OH, US; [4]The Ohio State University, Columbus, OH, US; [5]The Ohio State University, Columbus, OH, US; [6]The Ohio State University, Columbus, OH, US; [7]The Ohio State University, Columbus, OH, US; [8]The Ohio State University, Columbus, OH, US; [9]The Ohio State University, Columbus, OH, US; [10]University of Verona, Verona, IT; [11]Institutul Clinic Fundeni, Bucharest, RO; [12]Keio University, Tokyo, JP; [13]Stanford University, Stanford, CA, US; [14]Stanford University, Stanford, CA, US; [15]Cleveland Clinic Foundation, Cleveland, OH, US; [16]Yokohama City University, Yokohama, JP; [17]The Ohio State University, Columbus, OH, US

INTRODUCTION: Different guidelines recommend various postoperative surveillance strategies for patients following resection of colorectal liver metastases (CRLM). To date, data to support these recommendations have been scarce. We sought to assess the timing and risk of recurrence following curative-intent resection of CRLM using recurrence-free survival (RFS) hazard function to inform surveillance strategies. **METHODS:** Patients with CRLM who underwent curative-intent resection between 2000 and 2023 were identified from an international multi-institutional database. Tumor burden score (TBS), which combines tumor size and number, was utilized to define hepatic tumor burden. The RFS hazard function was used to plot hazard rates and identify the peak timing of recurrence over time using the kernel smoothing method. **RESULTS:** Among 1,804 patients who met inclusion criteria, median RFS was 19.9 months. In the overall cohort, the RFS hazard peaked at 5.9 months with a hazard rate of 0.054 and gradually declined, indicating that a subset of patients experienced early recurrence. In subgroup analyses, patients with medium and high TBS had RFS hazard peaks at 5.8 months (peak hazard rate: 0.054) and 4.9 months (peak hazard rate: 0.060), respectively. In contrast, patients with low TBS had a later peak at 7.5 months, with the lowest peak hazard rate of 0.047 (Figure). Patients who did not receive adjuvant chemotherapy (AC) had an earlier recurrence peak at 4.8 months, with a higher peak rate of 0.058 compared with individuals who received AC (recurrence peak: 7.3 months, peak rate: 0.050) . Notably, patients with medium and high TBS who did not receive had earlier and higher recurrence peaks, while patients with low TBS demonstrated similar hazard functions regardless of AC receipt. **CONCLUSIONS:** The recurrence peak for CRLM patients occurred approximately 6 months post-surgery, highlighting the importance of early postoperative surveillance. Patients

with high TBS and individuals who did not receive AC experienced earlier recurrence, underscoring the importance of close monitoring, particularly during the first 6 months after surgery.



P113. Redefining Upfront Resectable Pancreatic Ductal Adenocarcinoma:Does Vein Abutment Matter?

Po Hong Tan, MBBS[1]; Katherine E Poruk[2]; Cornelius Thiels[3]; Chee-Chee H. Stucky, MD[4]; Richard M Miller, BS[5]; Nabil Wasif, MD, MPH[6]; Rick J Bold[7]; Hoe Yan Hor[8]; Melody Pi Yin Tu[9]; Rory L Smoot[10]; Patrick P Starlinger[11]; Susanne G Warner[12]; Michale Kendrick[13]; John A Stauffer[14]; Mark Truty[15]; Zhi Ven Fong, MD, MPH, DrPH[16]

[1]Mayo Clinic, Phoenix, AZ, US; [2]Mayo Clinic Florida, Jacksonville, FL, US; [3]Mayo Clinic, Rochester, MN, US; [4]Mayo Clinic Arizona, Phoenix, AZ, US; [5]Mayo Clinic, Phoenix, AZ, US; [6]Mayo Clinic Arizona, Phoenix, AZ, US; [7]Mayo Clinic Arizona, Phoenix, AZ, US; [8]Mayo Clinic Arizona, Phoenix, AZ, US; [9]Mayo Clinic Arizona, Phoenix, AZ, US; [10]Mayo Clinic Rochester, Rochester, MN, US; [11]Mayo Clinic Rochester, Rochester, MN, US; [12]Mayo Clinic Rochester, Rochester, MN, US; [13]Mayo, Rochester, MN, US; [14]Mayo Clinic, Jacksonville, FL, US; [15]Mayo, Rochester, MN, US; [16]Mayo Clinic Arizona, Phoenix, AZ, US

INTRODUCTION: The National Comprehensive Cancer Network (NCCN) classifies pancreatic ductal adenocarcinoma (PDAC) with ≤180° portomesenteric venous (PMV) abutment as upfront resectable. It is unclear if PMV abutment influences survival outcomes in upfront resectable PDAC. This study aims to determine the association of PMV abutment with overall survival in patients with upfront resectable PDAC. **METHODS:** This multicenter study included patients who underwent pancreatoduodenectomy (PD) for NCCN-defined upfront resectable head and uncinate PDAC from 2002 to 2023 across the Mayo Clinic Enterprise's sites. Patients with PDAC with ≤180° PMV abutment were compared to those without. Overall survival was evaluated using log-rank tests and Cox proportional hazard models, and stratified on whether patients underwent upfront surgery or neoadjuvant therapy (NAT). **RESULTS:** Among 1,446 patients, 521 (36.0%) had PDACs with PMV abutment and 925 (64.0%) had no PMV abutment. Patient's demographics were similar across both groups. There were no significant differences in lymphovascular invasion, perineural invasion, and node positive rates in tumors with or without PMV abutment in both upfront surgery and NAT groups. The median overall survival for patients with PMV abutment was 28.8 months vs 31.2 months for those without (p=0.17). In stratified analysis of patients who underwent upfront surgery, patients with PMV abutment had worse median overall survival when compared to those without (19.2 vs. 27.6 months, p<0.05). However, in patients who underwent NAT, there were no significant differences in median overall survival (42.5 months in the PMV abutment group vs. 51.6 months in the no PMV abutment group, p=0.48, Figure). R0 resection rates were lower in patients with PMV abutment who underwent upfront surgery when compared to those without (63.1% vs. 87.2%, p<0.05). The difference in R0 resection rates was not observed in patients who underwent NAT (91.4% in the PMV abutment group vs 94.0% in the no PMV abutment group, p=0.27). **CONCLUSIONS:** In this largest cohort of patients with upfront resectable PDAC to date, PMV abutment was associated with worse overall survival when compared to those without abutment when upfront resection strategy was used. This was primarily due to lower R0 resection rates rather than differences in tumor biology. The use of NAT in patients with PMV abutment increased R0 resection rates and mitigated this survival difference. These findings suggest that patients with "upfront resectable" PDAC as currently defined with PMV abutment benefit from a NAT approach for optimal survival outcomes.

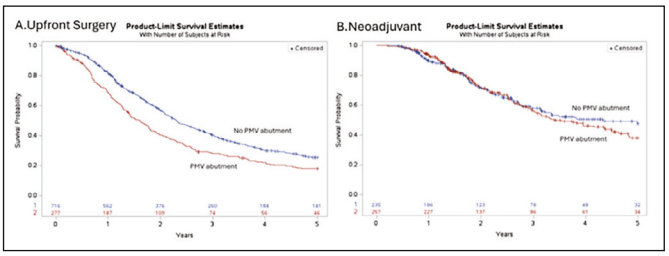


Figure. Kaplan Meier survival curves comparing patients with pancreatic ductal adenocarcinoma with portomesenteric vein abutment vs no abutment, stratified by (Al upfront surgery and (B) neoadjuvant therapy treatment approaches.

P114. Reduced hepatotoxicity and equivalent survival with a lower hepatic arterial floxuridine starting dose in the adjuvant treatment of colorectal cancer liver metastases

Kevin P Labadie[1]; Dana Dominguez[2]; Paul Wong[3]; Darrell Fan[4]; Elizabeth Meshkin[5]; Peter Vien[6]; Cecilia Lau[7]; Jonathan Kessler[8]; Lawrence Wagman[9]; Yuman Fong[10]; Laleh Melstrom, MD[11]

[1]City of Hope, Duarte, CA, US; [2]City of Hope, Duarte, CA, US; [3]University of California, San Francisco, San Francisco, CA, US; [4]City of Hope National Medical Center, Duarte, CA, US; [5]City of Hope National Medical Center, Duarte, CA, US; [6]City of Hope National Medical Center, Duarte, CA, US; [7]City of Hope National Medical Center, Duarte, CA, US; [8]City of Hope National Medical Center, Duarte, CA, US; [9]City of Hope National Medical Center, Duarte, CA, US; [10]City of Hope National Medical Center, Duarte, CA, US; [11]City of Hope Medical Center, Duarte, CA, US

INTRODUCTION: Hepatic arterial infusion (HAI) of floxuridine (FUDR) is an adjuvant therapy used after resection of colorectal cancer liver metastases (CRLM) in patients who are at high risk for hepatic recurrence. Its use is associated with hepatotoxicity leading to dose reductions. The objective of this study is to describe FUDR dosing practices, characterize dose reductions and their risks factors, and examine the impact on oncologic outcomes. **METHODS:** A single institution, retrospective analysis of all patients from 2015-2024 who received adjuvant HAI FUDR after complete resection of CRLM was performed. Selection of either a high (0.12 or 0.10 mg/kg/d) or low (0.08 or 0.06mg/kg/d) starting FUDR dose was based on published reports and provider discretion. HAI FUDR and dexamethasone was administered monthly while systemic chemotherapy was administered every two weeks. Dose modifications were based on published algorithms and at discretion of treating provider. Hepatic recurrence free survival (H-RFS) was defined as time from resection to first radiologic liver recurrence and overall survival (OS) was defined as time from resection to death of any cause. **RESULTS:** 71 patients received adjuvant HAI FUDR treatment. All patients had normal liver function pre-operatively. 88% (n=63) of patients had a left-sided primary tumor, 37% (n=26) were KRAS mutant, and 89% (n=63) had ≥4 liver metastases at presentation. Dosing information was available for 69 patients. A dose reduction occurred in 70% (n=48) of patients due to elevated liver function tests, most commonly after two cycles of treatment. Dose reductions were more common in patients receiving a high compared to a low starting dose of FUDR (80% (n=32/40) vs 55% (n=16/29) p=0.03). Three patients required a biliary stent for biliary sclerosis after starting treatment with 0.12mg/kg/d. On univariate analysis, diabetes was found to be associated with fewer dose alterations during treatment (Table 1). The higher starting dose of FUDR was less frequently used over the time course of the study period. 92% (n=31/34) compared to 26% (n=9/35) of patients were started on a high FUDR dose in the 1st and 2nd half of study period, respectively (p=<0.0001). At a median follow up of 35 months, the median OS rate was not met. The median H-RFS was 47 months. There was no difference in H-RFS or OS between patients started on a high or low FUDR dose (log rank, p = 0.13). **CONCLUSIONS:** In the adjuvant treatment of CRLM, FUDR dose reductions were more common in patients treated with a high compared to low starting dose. Over time, a lower starting dose of FUDR was more commonly used and associated with equivalent oncological outcomes.

P115. SMAD4 Alterations Are a Predictive Biomarker to Guide First-line Chemotherapy Selection for the Neoadjuvant Treatment of Localized Pancreatic Cancer

Julia Button, MD[1]; Elishama Kanu, MD[2]; Erin M Dickey, MD[3]; Brian Diskin, MD[4]; Akshat Sarkari[5]; Unaiza Zaman, MD[6]; David Brauer, MD[7]; Jashodeep Datta, MD[8]; Brock Hewitt, MD[9]; Mchael E. Lidsky, MD[10]; Emil Lou, MD[11]; Nipun Merchant, MD[12]; Daniel P Nussbaum, MD[13]; Susanna Ulahannan, MD[14]; Caitlin A. Hester, MD[15]; Brett L. Ecker, MD[16]

[1]Duke University, Durham, NC, US; [2]Duke University, Durham, NC, US; [3]University of Miami, Miami, FL, US; [4]New York University, New York, NY, US; [5]Masonic Cancer Center, University of Minnesota, Minneapolis, MN, US; [6]University of Oklahoma, Department of Medicine/Section of Hematology/Oncology, Oklahoma City, OK, US; [7]University of Minnesota, Minneapolis, MN, US; [8]university of miami, miami, FL, US; [9]NYU Langone, New York, NY, US; [10]Duke University Medical Center, Durham, NC, US; [11]Masonic Cancer Center, University of Minnesota, Minneapolis, MN, US; [12]university of miami, miami, FL, US; [13]Duke University Medical Center, Durham, NC, US; [14]University of Oklahoma, Department of Medicine/Section of Hematology/Oncology, Okalahoma City, OK, US; [15]university of miami, miami, FL, US; [16]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, US

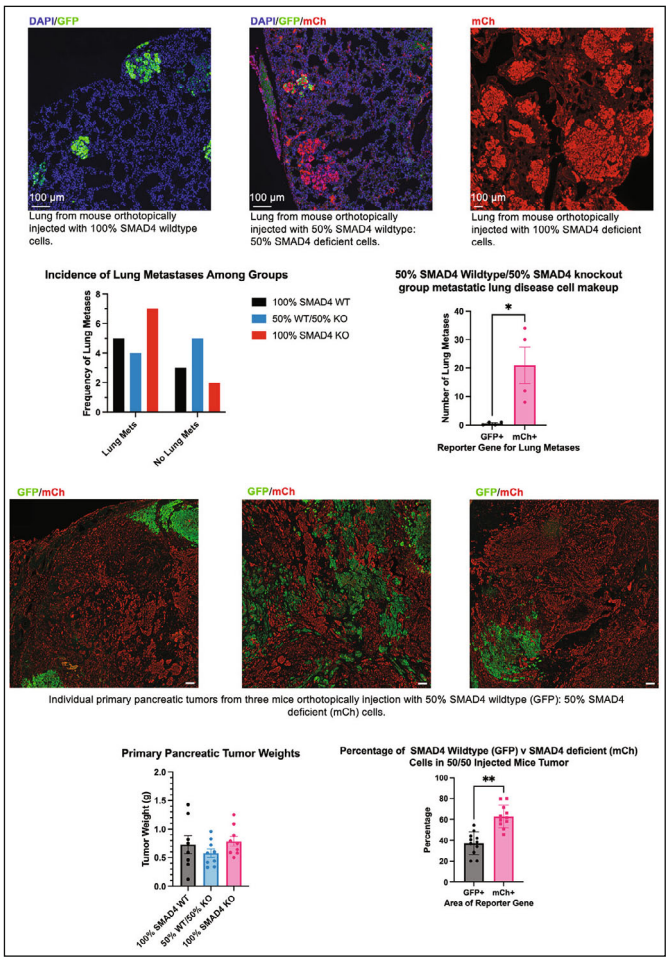
INTRODUCTION: Neoadjuvant chemotherapy is increasingly utilized in the management of localized pancreas ductal adenocarcinoma (PDAC). In biologically unselected patients, FOLFIRINOX and gemcitabine + albumin-bound paclitaxel (gem/nab-p) may be equivalent induction regimens. Previous single-institution studies have identified alterations in SMAD4 as a predictive biomarker of resistance to FOLFIRINOX treatment. Confirmation in a larger, diverse patient cohort is indicated. **METHODS:** A multicenter, retrospective cohort study was conducted of patients with localized PDAC who received at least one cycle of FOLFIRINOX or gem/nab-p as initial therapy. Somatic alterations in SMAD4 were assessed by targeted next-generation sequencing. The impact of SMAD4 alterations on rates of surgical resection were assessed in multivariable logistic regressions accounting for NCCN resectability status and tumor location. **RESULTS:** A total of 309 patients from six academic institutions were identified. The overall rate of SMAD4 alterations was 28%. FOLFIRINOX was the preferred initial treatment (n= 224; 72.5% vs. gem/nab-p: n=85; 27.5%) and more commonly used in younger patients (median: 62 vs 72 years; p<0.001). A total of 173 (62%) patients underwent surgical resection. There was no difference in rates of surgical resection between the two treatment groups (62% vs 64%; p=0.688). However, among patients who received FOLFIRINOX, SMAD4 alterations were associated with a decreased odds of surgical resection (OR 0.40, 95% CI 0.21-0.78; p=0.007). In contrast, in patients who received gem/nab-p, SMAD4 alterations were not associated with odds of resection (OR 1.16, 95% CI 0.35-3.80; p=0.81). **CONCLUSIONS:** Alterations in SMAD4 were associated with a lower probability of achieving surgical resection uniquely for those patients receiving neoadjuvant FOLFIRINOX, but not gem/nab-p. These data warrant prospective evaluation and support future trial designs incorporating SMAD4 as a predictive genomic biomarker.

P116. SMAD4 Intratumoral Heterogeneity in Pancreatic Cancer and its Biological Implications for Standard Therapeutic Agents

Natalie E Williams, MD[1]; Gilbert Z Murimwa, MD[2]; Jill Westcott, PhD[3]; Dina Alzhanova, PhD[4]; Zeynep Yazgan, BS[5]; Jason E Toombs, BS[6]; Huocong Huang, MD PhD[7]; Rolf Brekken, PhD[8]

[1]UTSouthwestern Medical Center, Dallas, TX, US; [2]UTSouthwestern Medical Center, Dallas, TX, US; [3]UTSouthwestern Medical Center, Dallas, TX, US; [4]UTSouthwestern Medical Center, Dallas, TX, US; [5]University of Texas Southwestern Medical Center, Dallas, TX, US; [6]University of Texas Southwestern Medical Center, Dallas, TX, US; [7]UTSouthwestern Medical Center, Dallas, TX, US; [8]UTSouthwestern Medical Center, Dallas, TX, US

INTRODUCTION: More than 85% of newly diagnosed pancreatic cancer cases are locally advanced or metastatic, emphasizing the importance of systemic therapy. Despite therapeutic advancements in other abdominal cancers, the five-year overall survival rate for pancreatic cancer remains ~13%, which emphasizes the need for novel treatments. Mutations in SMAD4, an effector in the canonical TGFβ signaling pathway, are identified in ~25% of pancreatic cancers, and retrospective studies show this is associated with worse disease-free survival, response to chemotherapy, and metastatic propensity. In human samples, we observed intratumoral heterogeneity in SMAD4 expression based on immunohistochemical staining. We utilized murine models to study the biologic mechanisms leading to the increased metastatic potential and differential chemosensitivity of SMAD4 mutant tumors. **METHODS:** To understand this phenotype and recapitulate human SMAD4 mosaicism, we created an admixture, orthotopic model of SMAD4-deficient cells and their parental, wildtype cells. Immunocompetent mice were orthotopically injected with SMAD4-deficient cells, SMAD4 wildtype cells or SMAD4-deficient: wildtype mixes (25:75, 50:50, 75:25). Immunofluorescence (IF) staining was performed to evaluate the tumor microenvironment and the metastatic potential of this mosaic pattern. Response to Gemcitabine/Abraxane and FOLFIRINOX were also studied. **RESULTS:** Mice with higher concentrations of SMAD4-deficient tumor cells showed increased metastatic burden and increased metastases to the lungs. Based on ICC staining, there was no statistical difference in incidence of lung metastases among the groups, but in the 50:50 group, metastases were derived predominantly from SMAD4 deficient primary cells (p=0.019). However, at time of death, primary tumors with increased SMAD4 percentage had no difference in tumor weights (p=0.595). The proportion of SMAD4 deficient cells was also found to impact chemosensitivity to Gem/Abraxane and FOLFIRINOX. **CONCLUSIONS:** Our murine model of SMAD4 mosaicism successfully recapitulates the human condition, and sheds light on SMAD4's potential as a therapeutic biomarker.



P117. Subasumstat Synergizes with 5-Fluorouracil and Irinotecan to Enhance Cytotoxicity in Pancreatic Cancer In Vivo

Asimina Courelli[1]; Leonie Ren[2]; Herve Tiriac[3]; Yuan Chen[4]; Andrew M. Lowy[5]

[1]University of California, San Diego, La Jolla, CA, US; [2]University of California, San Diego, La Jolla, CA, US; [3]University of California, San Diego, La Jolla, CA, US; [4]University of California, San Diego, La Jolla, CA, US; [5]University of california san diego, San Diego, CA, US

INTRODUCTION: Pancreatic cancer (PDAC) has a modest response to multi-agent chemotherapy regimens and identifying synergistic therapies is key to improving patient outcomes. Protein sumoylation affects nuclear localization and DNA binding affinity and sumoylation inhibition (SUMOi) has been linked to cell cycle arrest and mitotic failure. Our previous *in vitro* drug screening using patient derived organoids demonstrated synergy between subasumstat (S), a SUMO inhibitor, and 5- Fluorouracil(5-FU) and Irinotecan (I). We hypothesize that SUMOi can increase *in vivo* the efficacy of 5-FU and I by augmenting their interference with DNA replication. **METHODS:** *In Vitro Synergy:* KPC 46 cells were treated with combinations S and I or 5-FU between 1nM- 500nM for 24 hours. Viability was assessed using cell titer glo. *Mouse Experiments:* NSG mice underwent orthotopic injection of 3000 KPC 46 cells; IP injections with either S 15mg/kg q48 h, I 25mg/kg qweekly, 5-FU 25mg/kg qweekly, S 15 mg/kg+ 5-FU 25 mg/kg, or S15mg/kg+ I 25mg/kg were initiated when

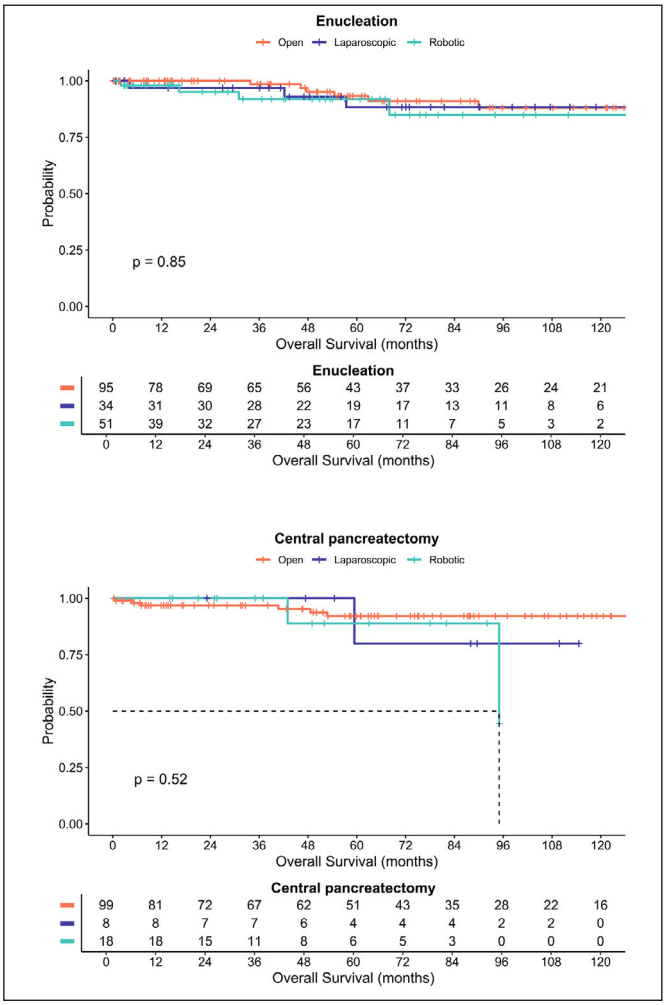
tumors reached 3-5 mm (assessed by ultrasound). Tumor size was evaluated weekly. *Western Blot (WB):* KPC46 cells were treated with S and/or I (50nM or 100nM) for 24 hours. Blots were probed for γ-H2AX and cleaved caspase 3. *Flow Cytometry (FC):* KPC46 cells were treated with either 50nM or 100nM of S, I, and 5-FU and stained using PI. FlowJo Cell cycle function was used to quantify cell cycle phases. **RESULTS:** *In vitro* screening using KPC 46 cells revealed synergy between S and 5-FU/I at concentrations as low as 20 nM. *In vivo*, dual treatments resulted in improved survival compared to monotherapies (5-FU: p= 0.045, I p= 0.039). Tumor growth reduction was observed in the dual treatment groups after 1 week and 2 weeks of treatment. At the time of death, mice with S+I had significantly smaller tumors than I only (I: 1.5g, T+I: 0.9g, p =0.003). *In vitro*, KPC 46 cells were incubated with S, I, and 5-FU and experiments assessing cell cycle arrest and DNA damage were conducted. WB of KPC 46 cells exposed to S and I showed an increase in ϒ- H2AX and cleaved caspase 3. FC showed an increase in the percentage of cells in S phase in 5-FU and Irinotecan monotherapy and combination groups compared to untreated and S only treated cells. **CONCLUSIONS:** Subasumstat synergizes with 5-FU and I by increasing the amount of double stranded DNA breaks and promoting apoptosis with irinotecan, while promoting S phase arrest with 5-FU. Clinically, subasumstat could potentially serve as an adjunct to FOLFIRINOX.

P118. Surgical and Oncologic Outcomes of Open vs Laparoscopic vs Robotic Parenchyma-sparing Operations for Pancreatic Neuroendocrine Tumors: A Multi-Institutional Analysis

Marco Ventin[1]; Martina Nebbia[2]; Alice C Wei, MD MSc[3]; Carlos Fernandez-del Castillo, MD[4]; Alexandra Gangi, MD, FSSO[5]; Motaz Qadan, MD, PhD[6]; Ammar Javed[7]; Jurgis Alvikas[8]; Liti Zhang, MD[9]; Brady Campbell[10]; Pratik Chandra, MD[11]; Nicholas Nissen, MD[12]; Keith D. Lillemoe, MD[13]; Amer H. Zureikat, MD[14]; Jin He, MD, PhD[15]; Cristina R. Ferrone, MD, MS, FSSO[16]

[1]Cedars-Sinai Medical Center, Los Angeles, CA, US; [2]Massachusetts General Hospital, Boston, MA, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Massachusetts General Hospital, Harvard Medical School, Boston, MA, US; [5]Cedars-Sinai Medical Center, Los Angeles, CA, US; [6]Massachusetts General Hospital, Harvard Medical School, Boston, MA, US; [7]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [8]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [9]Cedars-Sinai Medical Center, Los Angeles, CA, US; [10]Johns Hopkins Hospital, Baltimore, MD, US; [11]Memorial Sloan Kettering Cancer Center, New York, NY, US; [12]Cedars-Sinai Medical Center, Los Angeles, CA, US; [13]Massachusetts General Hospital, Harvard Medical School, Boston, MA, US; [14]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [15]Johns Hopkins School of Medicine, Baltimore, MD, US; [16]Cedars-Sinai Medical Center, Los Angeles, CA, US

INTRODUCTION: Low grade and well differentiated pancreatic neuroendocrine tumors (PNETs) have an indolent biology. Parenchyma-sparing resections of PNETs are being increasingly adopted to preserve pancreatic exocrine function and mitigate surgical morbidity, with comparable oncologic outcomes to formal oncologic resections. The preferred surgical approach when evaluating postoperative surgical and long-term oncologic outcomes is still not defined. **METHODS:** Retrospective analysis of pancreatectomies for PNETs performed at five high volume institutions in the United States between 2000 and 2023. Demographic, clinicopathologic, 30-day surgical, and survival outcomes were compared between open (OR), laparoscopic (LR), and robotic (RR) parenchyma-sparing operations (central pancreatectomy or enucleation) only. Group comparisons were performed by chi-square or Mann-Whitney U test, as appropriate. Survival outcomes were analyzed by proportional hazards cox regression and Kaplan-Meier method with log-rank test. **RESULTS:** Of the 2024 patients undergoing pancreatectomy for PNET, 305 (15.1%) had parenchyma-sparing operations, (180 (59.0%) enucleations and 125 (41.0%) central pancreatectomies). The median age was 58.7y and half were females (50.8%), with a median follow-up of 61.0 months. The median tumor size on imaging was 1.8 (IQR, 2.5) cm, and 39 (12.8%) patients had tumors ≥3cm. The median pathologic tumor size distribution was equal between enucleations (1.6 cm, IQR, 1.4) and central pancreatectomies (1.5 cm, IQR 0.9), P=0.248. Open surgery was the most frequent surgical approach for both enucleations and central pancreatectomies (n=95, 52.8% vs n=99, 79.2%, P<0.001), followed by robotic (n=51, 28.3% vs n=18, 14.4%, and laparoscopic resections (n=34, 18.9% vs n=8, 6.4%, P<0.001). Among enucleations, a robotic approach was associated with the longest median operative time (OR: 168.0 vs LR: 146.0 vs RR: 202.0 minutes, P=0.006), and lowest median EBL (OR: 200 vs LR: 100 vs RR: 100 mL, P=0.016). Operative time for central pancreatectomies was also longer with a minimally invasive approach (OR: 202.0 vs LR: 342.0 vs RR: 268.5 minutes, P<.001) but associated with lower blood loss (OR: 200 vs LR: 150 vs RR: 100 mL, P=0.088). Conversion was higher during laparoscopy for both enucleations (LR: 10.5% vs 0.0%, P=0.041) and central pancreatectomies (LR: 20.0% vs 0.0, P=0.067). Median length of hospital stay differed by surgical approach only for enucleations (OR: 6.0 vs LR: 3.0 vs RR: 5.0 days, p=0.001). Severe (Clavien-Dindo ³ grade 3) 30-day morbidity and mortality were equal, however, robotic central pancreatectomies were associated with a significantly higher rate of clinically relevant POPF (OR: 12.1% vs LR: 25.0% vs RR: 44.4%, P=0.004. Other pancreas-specific complications including grade B/C POPF, and hemorrhage, were comparable between groups for enucleations and central pancreatectomies. Tumor recurrence rates was not influenced by the surgical approach and operation type. The 5-year overall survival rates of enucleations were 93.3% (OR), 88.3% (LR), and 91.9% (RR) (P=0.85); The 5-year overall survival rates of central pancreatectomies were 92.1% (OR), 80.3% (LR), and 88.9% (RR) (P=0.52) (Figure 1). **CONCLUSIONS:** Robotic and laparoscopic approaches are associated with improved perioperative surgical outcomes for parenchyma-sparing operations for PNETs and comparable oncologic outcomes to open resections. Minimally invasive central pancreatectomies may be technically more demanding and associated with a higher CR-POPF rate. A minimally invasive enucleation is preferred if technically feasible.



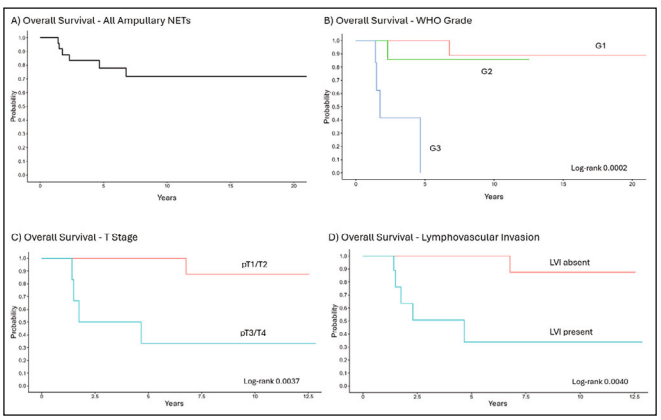
P119. Surgical Management of Ampullary Neuroendocrine Tumors: A 20+ Year Single Institutional Experience

Dylan S Soukup, MD, MBA[1]; Jennifer L Tomlinson, MD[2]; Cornelius A Thiels, DO, MBA[3]; Rory L Smoot, [4]; Mark J Truty, MD, MS[5]; Michael L Kendrick, MD[6]; David M Nagorney, MD[7]; Thor R Halfdanarson, MD[8]; Susanne G Warner, MD[9]

[1]Mayo Clinic, Rochester, MN, US; [2]Mayo Clinic, Rochester, MN, US; [3]Mayo Clinic, Rochester, MN, US; [4]Mayo Clinic, Rochester, MN, US; [5]Mayo Clinic, Rochester, MN, US; [6]Mayo Clinic, Rochester, MN, US; [7]Mayo Clinic, Rochester, MN, US; [8]Mayo Clinic, Rochester, MN, US; [9]Mayo Clinic, Rochester, MN, US

INTRODUCTION: Ampullary neuroendocrine tumors (aNETs) are a rare

pathologic entity with unique biologic features when compared to duodenal and pancreatic NETs. Delineation of prognostic variables and outcomes of aNETs remains confined to small institutional series or larger database studies with inherent data limitations. Herein we report on the outcomes and prognostic pathologic factors for patients undergoing surgical resection. **METHODS:** We retrospectively reviewed our institutional cancer registry. Adult patients who underwent surgical intervention from 2000 to 2023 for intestinal-subtype NETs located at the ampulla of Vater were included. Patients with endoscopic management only were excluded. Demographic, pathologic, and outcome variables were assessed and further studied with Kaplan-Meier survival and Cox regression analyses. **RESULTS:** The 26 included patients were 58% female with a median age of 60 (33-80 years). Pancreatoduodenectomy was performed in 25 (96%) patients and transduodenal ampullectomy with lymphadenectomy was performed in 1 (4%) patient. Median tumor size was 1.8 (0.5-4.0) cm. Eleven (42%) patients had WHO grade 1 tumors, 7 (27%) had grade 2, 7 (27%) had grade 3, and 1 (4%) had unknown grade. Regional lymph node (LN) metastases were present in 21 (81%) patients with a median of 20 (3-49) LNs examined and 16% (0-40%) of examined LNs positive for disease. Three (12%) patients had isolated hepatic metastases at diagnosis and were treated with segmental hepatectomy, transarterial chemoembolization, and liver ablation. Overall survival (OS) was high and tumor grade correlated with survival as expected (Figure 1). Age at diagnosis (HR 1.10, p = 0.03), WHO grade 3 (HR 40.25, p < 0.01), tumor size (HR 1.13, lymphovascular invasion (HR 12.33, p = 0.02), pT3/T4 stage (HR 12.57, and chemotherapy at any point (HR 15.98, p = 0.01) all correlated with worse OS on univariable regression. Regional LN and distant metastases both failed to demonstrate correlation with OS. Multivariable analysis was not performed due to low number of events. **CONCLUSIONS:** This large single-institution series of ampullary NETs supports prior studies suggesting a more aggressive biology in this NET subtype. A high rate of regional LN metastases highlights the ongoing importance of preoperative nodal investigations. Significantly worse OS with high-grade tumors, lymphovascular invasion, and increased depth of invasion and tumor size suggest that definitive surgical resection should be strongly considered if any of these features are present.

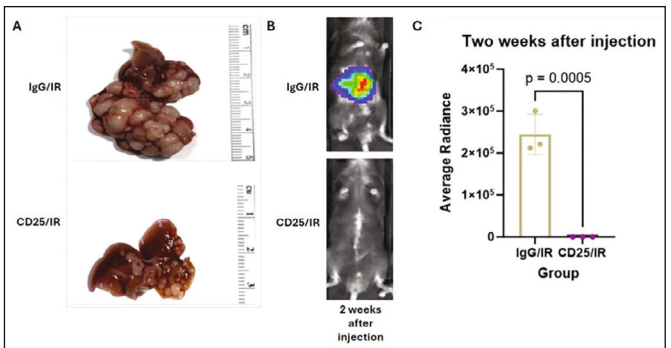


P120. Surgical stress promotes development of colorectal liver metastases via modulation of hepatic regulatory T cells

Grace Wu, MD[1]; Xiaorong Guo, MD, PhD[2]; Ameilia Solan, BS[3]; Danielle DePeralta, MD[4]; Matthew John Weiss, MD[5]; Meihong Deng, MD[6]; Ping Wang, MD[7]; Hai Huang, MD[8]; Sepideh Gholami, MD[9]

[1]Northwell Health, New Hyde Park, NY, US; [2]The Feinstein Institutes for Medical Research, Manhasset, NY, US; [3]The Feinstein Institutes for Medical Research, Manhasset, NY, US; [4]Northwell Health, Hofstra School of Medicine, New Hyde Park, NY, US; [5]Northwell Health, Manhasset, NY, US; [6]The Feinstein Institutes for Medical Research, Manhasset, NY, US; [7]The Feinstein Institutes for Medical Research, Manhasset, NY, US; [8]Feinstein Institute for Medical Sciences, Manhasset, NY, US; [9]Northwell Health, New Hyde Park, NY, US

INTRODUCTION: Complete surgical excision remains central to curative treatment of colorectal liver metastases (CRLM), yet up to 75% of patients undergoing liver resection subsequently recur. One proposed mechanism driving recurrence is the reshaping of the hepatic immune microenvironment during surgical stress [i.e., ischemia/reperfusion (I/R) injury]. Regulatory T cells (Tregs) promote wound healing and repair in injured tissues after surgery but are also known to play a potent immunosuppressive role during tumor development. However, whether surgical stress promotes liver metastases via recruitment of Tregs to the liver remains unknown. We hypothesize that Tregs increase in the liver after I/R injury and foster an immune background conducive to seeding of circulating tumor cells and development of metastases. **METHODS:** Murine MC38 colon carcinoma cells expressing firefly luciferase were injected into wild type mice via the portal vein. 70% hepatic I/R was performed after tumor injection. CD25 neutralizing antibody was used to deplete Tregs prior to surgery and during tumor growth. Treg numbers were confirmed by flow cytometry. Tumor growth was quantified by bioluminescence and number of macroscopic nodules. **RESULTS:** An increased number of hepatic Tregs was demonstrated one week after hepatic IR (5.0% (6 hours) vs. 8.1% (1 week); p=0.001). Hepatic I/R significantly increased Tregs in both hepatic parenchyma (5.9% (I/R) vs. 9.7% (MC38/I/R); p=0.01) and circulation (8.1% (I/R) vs. 13.0% (MC38/I/R); p=0.002) in tumor bearing mice. Compared to sham (SH) mice, liver I/R promoted greater tumor growth one week after I/R and significantly augmented tumor growth 2-weeks post-surgery, indicated by bioluminescence (2.4x10^4 (SH) vs. 4.0x10^4 (I/R), p=0.19 at 1 week; 1.1x10^5 (SH) vs. 2.4x10^5 (IR), p=0.01 at 2 weeks). This was consistent with tumor volume at time of harvest. Depletion of Tregs slowed tumor growth at 1 week post-surgery (4.0x10^4 (IgG) vs. 2.4x10^4 (CD25), p=0.19). Bioluminescent signal was completely abrogated 2 weeks after surgery in Treg-depleted mice (2.4x10^5 (IgG) vs. 0.00 (CD25), p=0.0005). **CONCLUSIONS:** Hepatic I/R injury boosts hepatic infiltration of Tregs, promoting growth of CRLM. Depletion of Tregs before I/R and during tumor development hinders this process. Further studies are needed to identify the mechanism by which liver I/R modulates phenotypic changes of hepatic Tregs in the hepatic tumor microenvironment.



A) Representative photographs of macroscopic nodules and tumor volume. B, C) MC38-luciferase cells allowed in vivo tracking of tumor growth, measured in average radiance.

Figure. Treg depletion via CD25 neutralizing antibody reduces tumor growth after 1/R injury.

P121. The Impact of Hospital Volume on Patient Outcomes after Surgery for Gallbladder Adenocarcinoma

Sasha L Lightfoot, DO[1]

[1]Roger Williams Medical Center, Providence, RI, US

INTRODUCTION: Hepatobiliary surgeries are becoming centralized to high volume centers (HVC) supported by studies showing improved surgical outcomes when patients undergo pancreatectomy and hepatectomy at HVC. However, there is limited data on surgical outcomes at HVC after surgery specifically for gallbladder adenocarcinoma. This study aims to solidify whether mortality and overall survival (OS) for patients undergoing resection for gallbladder adenocarcinoma is altered by hospital volume and to evaluate differences in patient factors by hospital volume. **METHODS:** A retrospective analysis of the National Cancer Database (NCDB), queried from 2004 to 2021 for patients with nonmetastatic gallbladder adenocarcinoma who underwent surgical resection. Patients were then stratified by hospital volume which was divided into tertiles based on annual surgical volume: low volume centers (LVC) 1-9 cases; medium volume centers (MVC) 10-24 cases; HVCs 25-79 cases. Multivariable Cox proportional hazards models were used to evaluate survival in relationship to and hospital volume and patient factors. **RESULTS:** 10,299 patients were evaluated. Patients treated at HVC/MVCs were more likely to be Asian/Pacific Islander (6.8%/5.8% in HVC/MVCs vs 3.8% LVC, p<0.01), Hispanic (15.6%/15.2% in HVC/MVCs vs 8.3% in LVC, p<0.01), and higher income group (38.4%/35.2% in HVC/MVCs vs 33% in LVC p<0.01).

Patients who underwent resection at HVC had lower 30-day (3.2% HVCs vs 7.5% LVC, p<0.01) and 90-day mortality (10.3% HVCs versus 17.0% LVC, p<0.01) than LVCs. Multivariable Cox proportional hazards demonstrated a lower risk of death at a HVC (OR 0.81, 95% CI 0.59-0.85). Patients with higher income (OR 0.83, 95% CI 0.67-0.99), female (OR 0.83, 95% CI 0.77-0.96), Asian/pacific islander (OR 0.45, 95% CI 0.36-0.59), and Hispanic/Latino (OR 0.63, 95% CI 0.50-0.71) were associated with an lower risk of death in those undergoing resection for gallbladder adenocarcinoma. **CONCLUSIONS:** The 30-day, 90-day mortality, and OS are all improved when surgery for gallbladder adenocarcinoma is performed at HVC. However, there are important differences in patient populations between HVC and LVC that may contribute to improved OS, and are overlooked in these comparisons.

P122. Title: Pancreatic cancer shows clinical signs far earlier than previously suspected

Parnian Naji[1]
[1]University Hospitals Cleveland, Cleveland, OH, US

INTRODUCTION: Pancreatic cancer (PC) is fatal in most cases, yet has limited early detection options. There are no routinely used screening tests and presenting signs and symptoms have been offered as early tip-offs, but those studies focus on the year prior to presentation. Genetic studies indicate that PC develops over multiple decades. Yet, to date, there are no data that suggest the disease may be clinically apparent with sufficient lead time beyond one year to affect cure rates. To explore the possibility of earlier detection, we conducted a large-scale retrospective analysis of 189,436 patients and investigated the potential for detectable physiological changes years prior to PC diagnosis. **METHODS:** The TrinetX database is a real-world, health care database with more than 300 million patient records and 189,436 pancreatic cancer patients. Patients with and without pancreatic cancer were matched based on age, sex, race, and ethnicity using the propensity score approach. We examined trends in variables known to be associated with cancer over time as an indirect measure of clinical evidence of occult malignancy. Variables included body mass index (BMI), serum albumin, serum total protein, and serum glucose levels, collected in the 10 years prior to PC diagnosis. Data were analyzed and visualized using GraphPad Prism and linear regressions were calculated. Note, data from each year represent population averages over time, as opposed to changes in a given individual over time. **RESULTS:** Significant changes in BMI, albumin, total protein, and glucose levels were observed in the pancreatic cancer group compared to the control group and were detectable as perturbed as early as 5 years prior to the clinical diagnosis of PC. Slopes for each of the four variables tested over the 5 preceding years were: BMI, -0.3657(meaning each year the mean BMI decreased by 0.36); albumin=-0.08829; total protein=-0.04771; and glucose: 2.571 (see Figure). In contrast, these variables were roughly flat in the five years prior to these changes (10 to 5 years before a PC diagnosis), as well as throughout the entire 10-year period in matched controls. **CONCLUSIONS:** These findings suggest for the very first time that clinical changes are perceptible many years prior to the diagnosis of pancreatic cancer, underscoring the real-world potential for flagging patients at greatest risk for pancreatic and possibly other cancers, through frequent and high-intensity biometric tracking.

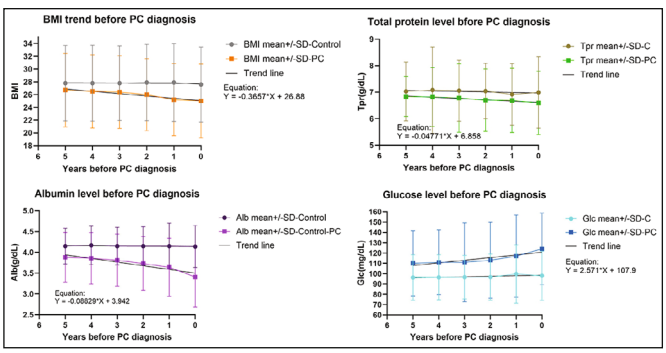


Figure. Pancreatic cancer shows clinical signs far earlier than previously suspected

P123. Utility of Next Generation Sequencing for Prediction of Prognosis in Transplant Patients with Multinodular HCC

Michael Mallouh[1]; Emma Cammann[2]; Lloyd Hutchinson[3]; Xiuling Meng[4]; Samantha Kaliszewski[5]; Nicholas Jarostchuk[6]; Karen Dresser[7]; Xiaoqin Zhu[8]; Babak Movahedi[9]; Amr Tashtoush[10]; Vijay Vanguri[11]; Giles Whalen[12]
[1]University of Massachusetts Chan Medical School, Worcester, MA, US; [2]Maine Medical Center, Portland, ME, US; [3]University of Massachusetts Chan Medical School, Worcester, MA, US; [4]University of Massachusetts Chan Medical School, Worcester, MA, US; [5]University of Massachusetts Chan Medical School, Worcester, MA, US; [6]University of Massachusetts Chan Medical School, Worcester, MA, US; [7]University of Massachusetts Chan Medical School, Worcester, MA, US; [8]University of Massachusetts Chan Medical School, Worcester, MA, US; [9]University of Massachusetts Chan Medical School, Worcester, MA, US; [10]University of Massachusetts Chan Medical School, Worcester, MA, US; [11]University of Massachusetts Chan Medical School, Worcester, MA, US; [12]University of Massachusetts Chan Medical School, Worcester, MA, US

INTRODUCTION: Liver transplantation is an effective treatment for selected patients with cirrhosis and Hepatocellular Carcinoma (HCC). Because donor livers are a relatively scarce resource, parameters exist (e.g. Milan Criteria) for their use in HCC patients. We have hypothesized that removal of a carcinogenic cirrhotic liver and transplantation of a new one would result in much better survival for those patients with multiple new primary tumors than for patients whose index tumor has already metastasized within the liver. **METHODS:** A retrospective cohort of explants from patients with more than one HCC tumor who underwent liver transplantation from January 1998 to December 2018 was studied. DNA was extracted and sequenced from each tumor nodule and we determined if the tumor nodules represented new primaries or metastases in each liver by determining their clonality utilizing a clinically validated, targeted 50 gene next-generation sequencing panel. **RESULTS:** Uniclonal tumors in the same liver specimen were counted as metastases and multiclonal tumors that were genetically distinct were interpreted as separate new primaries. Specimens from 30 of the 68 livers originally included in the study yielded enough genetic material for a reliable genetic analysis to determine clonal status (16 patients in multiclonal group, and 14 in the uniclonal group). For patients that the pre-transplant hepatitis C status was known, hepatitis C was more prevalent in the multiclonal group (78.5%) than the uniclonal group (30.7%). For patients that tumor grade was known, there was a similar proportion of patients in each group that were tumor grade G2 or higher (83.33% in multiclonal group versus 100% in uniclonal group). Uniclonal patient group had better post-transplant overall and disease free survival than the multiclonal group, though the difference was not statistically significant (Fig. 1A and 1B), as assessed by log-rank test. **CONCLUSIONS:** We were able to use next generation sequencing on formalin fixed explanted liver specimens to differentiate clonal status of tumors in multinodular HCC patients, and it appeared that patients in the uniclonal group (presumptive metastasis) had better overall and disease-free survival than those in the multiclonal group (presumptive separate primaries). Although this was not statistically significant, we had expected a large effect size in the reverse direction. There were no clear-cut explanations for this data when looking at hepatitis C status, tumor grade, or cancer stage, and potential explanations are the subject of ongoing study.

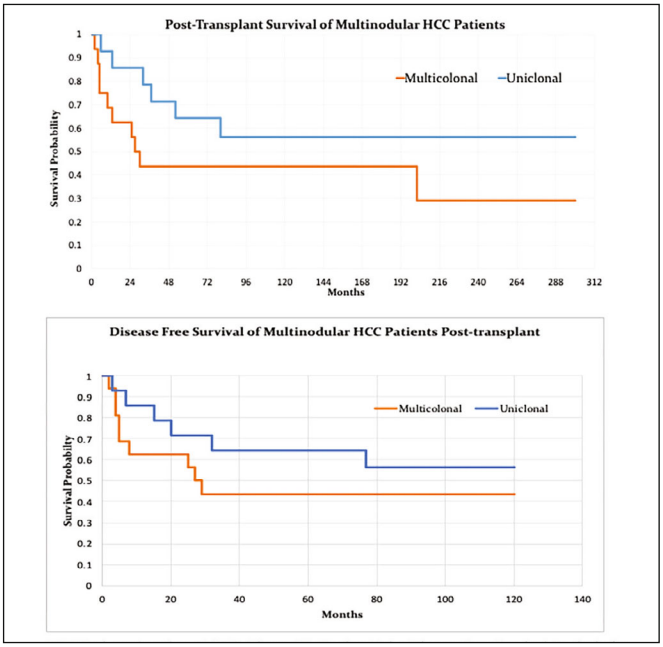
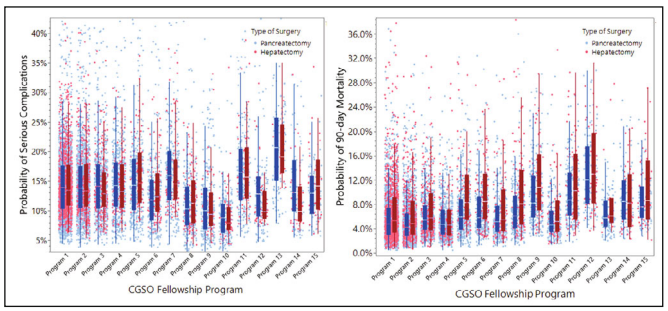


Figure IA. Kaplan Meier Survivorship Analysis for Multiclonal versus Uniclonal Multinodular HCC Patients (p-value= 0.219). Figure 1B. Kaplan Meier Disease-Free Survival Analysis for Multiclonal versus Uniclonal Multinodular HCC Patients (p-value=0.397).

P124. Variations in Outcomes of Surgical Oncology Fellowship Graduates Performing Hepatopancreatic Surgery in the United States Based on Fellowship Training Program

Diamantis I. Tsilimigras, MD, PhD[1]; Odysseas P. Chatzipanagiotou[2]; Selamawit Woldesenbet[3]; Tim M Pawlik[4]
[1]The Ohio State University, Columbus, OH, US; [2]The Ohio State University, Columbus, OH, US; [3]The Ohio State University, Columbus, OH, US; [4]The Ohio State University, Columbus, OH, US

INTRODUCTION: In North America, 28 Complex General Surgical Oncology (CGSO) fellowship programs exist that prepare surgeons for independent practice, yet exposure in hepatopancreatic (HP) surgery can vary among graduates. Real-world outcomes of CGSO fellowship graduates performing HP surgery have not been previously examined. We sought to assess trends and variations in outcomes of CGSO fellowship graduates performing HP surgery in the United States according to their fellowship training. **METHODS:** Medicare claims were used to identify patients who underwent HP surgery for cancer between 2016-2021. Surgeon NPI numbers associated with each surgical procedure were manually screened and a novel database was created that identified all surgeons who had formally completed a CGSO fellowship in the United States or Canada. Surgeon-level data, including fellowship training information, were linked to patient-level Medicare data. Trends and variations in peri-operative outcomes (i.e. severe complications [complications coupled with prolonged length of stay] and 90-day mortality) according to fellowship training were examined. **RESULTS:** Overall, 9,954 HP cancer operations (pancreatectomy: 7,566, 76.0%; hepatectomy: 2,388, 24.0%) were performed between 2016-2021. A total of 609 CGSO fellowship graduates trained at 42 different CGSO programs in the USA or Canada were identified. Most cases (93.2%) were performed by surgeons who had completed an ACGME-accredited CGSO program. Almost half of HP operations were performed by graduates of two specific CGSO programs (n=4,769, 47.9%) although only 698 (7.0%) HP operations were performed at these two centers; 92.1% (n=9,166) of HP operations were performed by graduates of 15 CGSO programs. After adjusting for patient, procedural, hospital and surgeon related factors, the risk-adjusted incidence of severe complications was 9.7% among graduates of CGSO program #10 versus 21.7% (%difference 12.0%) among graduates of CGSO program #13 following HP surgery (p=0.001). Similarly, the risk-adjusted incidence of 90-day mortality was 5.5% among graduates of CGSO program #7 versus 12.1% (% difference 5.1%) among graduates of CGSO program #12 following HP surgery (p=0.002). Marked variations in outcomes by CGSO fellowship program were noted following both hepatectomy and pancreatectomy (Figure). When trends in outcomes over time were assessed, the adjusted risk of serious complications decreased from 2016 to 2021 (16.4% vs. 12.9%; p<0.05), yet the likelihood of 90-day mortality remained relatively stable during the study period (2016: 6.4% vs. 2021: 5.3%; p = 0.19). **CONCLUSIONS:** While outcomes of CGSO graduates improved over time, a marked variation in outcomes of graduates performing HP surgery was noted based on their fellowship training. Further efforts should be made to enhance and standardize HP surgery exposure and training in CGSO programs for fellows intending to perform HP surgery in practice.



P125. Circulating Tumor DNA in High-Risk Stage II/III Melanoma: A Feasibility Study

Kristen E Rhodin, MD, MHS[1]; Margaret O'Connor, MD, PhD[2]; Aaron Therien, BS[3]; Shayna Hollander, BA[4]; Viviana Geron, BA[5]; Riddishkumar Shah, MD[6]; April KS Salama, MD[7]; Douglas Tyler[8]; Georgia M Beasley, MD, MHS[9]
[1]Duke University, Durham, NC, US; [2]Duke University, Durham, NC, US; [3]Duke University, Durham, NC, US; [4]Duke University, Durham, NC, US; [5]Duke University, Durham, NC, US; [6]Duke University, Durham, NC, US; [7]Duke University, Durham, NC, US; [8]University of Texas Medical Branch - Galveston, TX, Galveston, TX, US; [9]Duke University, Durham, NC, US

INTRODUCTION: Adjuvant therapies reduce recurrence in patients with clinical stage IIB/IIC/III melanoma; however, these therapies can result in significant toxicities and are not effective in all patients. Accordingly, there is a need to improve patient selection for adjuvant therapy. Circulating tumor DNA (ctDNA) as a marker of micrometastatic residual disease after surgery is being explored for such purposes in other malignancies. Herein, we aimed to explore the feasibility of serial ctDNA monitoring in patients with stage II/III melanoma, as well as the association of ctDNA elevation with disease burden and outcomes. **METHODS:** A single-institution prospective study was conducted on patients with clinical stage IIB/IIC/III melanoma. Primary tumor was sent to Natera™ for generation of a tumor-informed mPCR-NGS assay (Signatera™) for each individual patient. Peripheral blood was collected for analysis at pre-specified timepoints: pre-operative, within one-month post-operative, three-months post-operative, and then every six months for up to three years. Patients were stratified by ctDNA elevations both pre- and post-operatively to compare tumor characteristics and recurrence-free survival (RFS). **RESULTS:** Overall, 30 patients were enrolled from July 2021 to June 2024. The median age of diagnosis was 66 years (IQR 57, 73) and 47% (N=14) were female. The median Breslow depth was 4.4 mm (IQR 3.0, 6.5) and 70% (N=21) were ulcerated. Final pathologic staging of patients was 33% (N=10) stage IIB, 13% (N=4) stage IIC, 7% (N=2) stage IIIB, and 47% (N=14) stage IIIC. Signatera™ assays were successfully created for all 30 patients. Patients with elevated ctDNA preoperatively had significantly greater Breslow depth (median 6.5 vs. 3.3 mm, p<0.01). Median follow-up from the time of surgery was 16 months (IQR 6.7, 23.7) with a median of 4 timepoints (IQR 3, 6) for analysis. 13 patients have recurred with median RFS of 19 months. Eight of these 13 patients (62%) had elevated ctDNA levels predating their clinical or radiographic recurrence. Elevated ctDNA at the first post-operative timepoint was associated with worse RFS (log-rank p<0.01; Figure). **CONCLUSIONS:** ctDNA monitoring is feasible for patients with high-risk cutaneous melanoma. Our preliminary findings suggest that elevation in ctDNA may indicate greater disease burden pre-operatively and be associated with worse outcomes post-operatively. Elevations during surveillance may predict subsequent clinical recurrence; however, its role in adjuvant therapy decision making and surveillance is not yet ready for broad application.

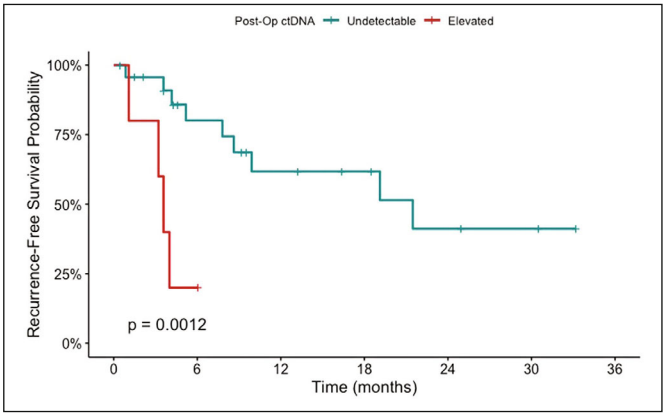


Figure. Recurrence-Free Survival stratified by elevations in ctDNA at the first post-operative timepoint.

P126. Compliance with Nodal Basin Ultrasound Surveillance after Positive Sentinel Lymph Node Biopsy

Natalie N Chakraborty, MD[1]; Maira A Bhatty[2]; Kevin G. Zablonski, MD[3]; Hailey Seibert[4]; Adam Wade[5]; Jarred M. Boone, MD[6]; Trisha Lal[7]; Richard Hoehn, MD[8]; Iris Y. Sheng[9]; Luke D. Rothermel, MD, MPH[10]

[1]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [2]Case Western Reserve University School of Medicine, Cleveland, OH, US; [3]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [4]Case Western Reserve University School of Medicine, Cleveland, OH, US; [5]Case Western Reserve University School of Medicine, Cleveland, OH, US; [6]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [7]Case Western Reserve/University Hospitals, Cleveland, OH, US; [8]University Hospitals, Cleveland Medical Center, Cleveland, OH, US; [9]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [10]University Hosptials Cleveland, Cleveland, OH, US

INTRODUCTION: The Second Multicenter Selective Lymphadenectomy Trial (MSLT-II) demonstrated that completion lymph node dissection (CLND) does not prolong disease-specific survival in patients with sentinel lymph node metastasis. The trial introduced active surveillance protocols with nodal basin ultrasound (US) in patients with positive sentinel lymph node biopsy (SLNB) to avoid the morbidity of immediate CLND. We aimed to identify the rates of compliance with nodal basin US surveillance and its impact on clinical care in a large regional health system. **METHODS:** We retrospectively identified patients with stage III melanoma diagnosed at our institution between 2017 and 2022. We calculated rates of active surveillance and analyzed biopsy data to determine the rate of negative biopsies resulting from imaging. Multivariable logistic regression identified factors independently associated with receipt of US surveillance. Patients who had upfront axillary lymph node dissection or in transit disease without sentinel node metastasis (N1c disease) were excluded from regression analysis, as they did not meet US surveillance criteria. **RESULTS:** Among 205 patients with stage III melanoma, 92.7% received cross-sectional imaging surveillance. Of the 165 patients eligible for nodal basin US surveillance, 62.4% underwent any US surveillance. 6.3% of patients had no surveillance imaging. Age ≥75 (OR 0.14; 95% CI: 0.04-0.44) and N2 stage (OR 0.35; 95% CI: 0.15-0.80) were associated with lower odds of US surveillance, while female sex was associated with higher odds (OR 2.49; 95% CI 1.16-5.33). Socioeconomic status and the Charlson Comorbidity Index were not significant predictors. 20.9% of biopsies obtained due to surveillance imaging were benign. US surveillance led to higher rates of negative biopsies than other imaging modalities: 18 biopsies were obtained due to findings on US, of which 13 (72%) were negative. Conversely, 36 biopsies were obtained due to findings on cross-sectional imaging, but only four (11%) were negative. **CONCLUSIONS:** Cross-sectional imaging was more consistently performed than nodal basin US for melanoma patients eligible for active surveillance. US surveillance prompted more negative biopsies than cross sectional imaging, raising questions about its utility. This data calls for further investigation into the value of US surveillance in melanoma care, as well as into the barriers to receipt of guideline-concordant surveillance imaging in our patient population if US is proven beneficial.

Table 1. Odds of Receiving Nodal Basin US by Clinical Characteristic

Covariate	No. *(%)*	OR (95% CI)	p-value
Age at Diagnosis			
18-59	67 *(40.6%)*	*Ref.*	
60-74	71 *(43.0%)*	0.48 (0.20-1.21)	0.089
75+	27 *(16.4%)*	0.14 (0.04-0.44)	0.001
Sex			
Male	89 *(53.9%)*	*Ref.*	
Female	76 *(46.1%)*	2.49 (1.16-5.33)	0.019
Charlson Comorbidity Index			
0-1	115 *(69.7%)*	*Ref.*	
2-3	39 *(23.6%)*	0.92 (0.38-2.23)	0.855
4+	11 *(6.7%)*	0.59 (0.13-2.59)	0.481
N Stage Group			
N1	110 *(66.7%)*	*Ref.*	
N2	47 *(28.5%)*	0.35 (0.15-0.80)	0.013
N3	8 *(4.8%)*	0.47 (0.06-3.52)	0.463
Size of Largest Nodal Metastasis			
Micrometastatic (≤ 1mm)	107 *(64.8%)*	*Ref.*	
>1mm	58 *(35.2%)*	0.45 (0.20-1.03)	0.058
Receipt of Adjuvant Immunotherapy			
No Therapy Received	32 *(19.4%)*	*Ref.*	
Received Therapy	133 *(80.6%)*	1.28 (0.48-3.43)	0.626

P127. Contemporary survivorship care patterns and management of treatment-related toxicities for melanoma patients

Valerie A Francescutti, MD[1]; Anastasia Gayowsky, PhD[2]; Greg Pond, PhD[3]; Hsien Seow, PhD[4]; Frances C Wright, MD, MSc[5]; Linda Lee, MD[6]; Elaine McWhirter, MD[7]; Elie Isenberg-Grzeda, MD[8]; Nicole J Look Hong, MD[9]

[1]McMaster University/Hamilton Health Sciences, Hamilton, ON, CA; [2]ICES McMaster, Hamilton, ON, CA; [3]McMaster University, Hamilton, ON, CA; [4]ICES McMaster, Hamilton, ON, CA; [5]Sunnybrook Health Sciences Center, Toronto, ON, CA; [6]Walker Family Cancer Center, St. Catharines, ON, CA; [7]Juravinski Cancer Center / McMaster University, Hamilton, ON, CA; [8]Sunnybrook Health Sciences Center, Toronto, ON, CA; [9]Sunnybrook Health Sciences Center, Toronto, ON, CA

INTRODUCTION: Survivorship includes surveillance for detection of cancer recurrence and assessment of ongoing treatment-related side effects; for melanoma patients little is known about this period. We evaluated contemporary patterns of melanoma survivorship care related to treatments received, based on physician visits, imaging studies, symptom assessment, and medications. **METHODS:** Patients with stage I-III melanoma diagnosed from 2007-2019 were retrospectively identified from the Ontario Cancer Registry. Linked administrative databases were used to identify patient characteristics, physician visits, treatments, and patient-reported symptom scores. Descriptive data was analyzed based on the receipt of surgery-only (SO) or surgery + adjuvant therapy (SAT). The survivorship phase was defined as > 6 months following diagnosis in the SO group, and > 18 months following diagnosis in the SAT group. **RESULTS:** 30,553 patients were identified with a median follow up of 8.4 years (Figure 1); 26,446 underwent SO, followed by surgeons, dermatologists, and family physicians. Patients in the SAT group (n=4,107) were additionally followed by medical oncologists. At 5-years post-diagnosis, 50% of all patients had no dermatologist visits. Imaging (CT) was used more frequently in the first 3 years following diagnosis in the SAT group (30 % quarterly CT rate, compared with 3 % in the SO group). 31% of patients in the SAT group reported high pain scores compared with 18% in the SO group in the 18-36 months post-diagnosis. A high proportion of patients at all time points required some form of palliative care services (SO=51%, SAT=82%). SAT patients were more likely to require prescription antidepressants at any time (31%) compared with the SO group (27%). Double the number of patients in the SAT group (82 %) had a specialist consultation related to toxicity (cardiology, respirology, ophthalmology, rheumatology, endocrinology, gastroenterology) within the treatment window compared with the SO group (43%), and remained consistently higher through survivorship. **CONCLUSIONS:** This study identifies delivery of survivorship care in a large cohort of melanoma patients including involvement of various provider groups. Areas for improvement include ongoing dermatology surveillance, and management of chronic pain symptoms. Future qualitative work engaging patients and providers will compliment these results in the development of a comprehensive program, inclusive of all contemporary survivorship needs. This is timely given increasing numbers of melanoma survivors.

Variable	Subgroup	N (%) Surgery Only	N (%) Surgery + Adjuvant Therapy	P Value
N		26,446	4,107	
Sex	F	12,373 (46.8%)	1,577 (38.4%)	<.0001
Age group (years)	18-29	709 (2.7%)	99 (2.4%)	
	30-49	4,655 (17.6%)	657 (16.0%)	
	50-69	11,415 (43.2%)	1,787 (43.5%)	0.0083
	70-89	9,050 (34.2%)	1,487 (36.2%)	
	90+	617 (2.3%)	77 (1.9%)	
Cancer stage at diagnosis	I	7,866 (29.7%)	410 (10.0%)	
	II	3,172 (12.0%)	857 (20.9%)	<.0001
	III	934 (3.5%)	1,321 (32.2%)	
	Missing	14,474 (54.7%)	1,519 (37.0%)	
Melanoma anatomic site	Extremities	12,537 (47.4%)	1,641 (40.0%)	
	Head/neck	4,766 (18.0%)	859 (20.9%)	<.0001
	Other	374 (1.4%)	217 (5.3%)	
	Trunk - n (%)	8,769 (33.2%)	1,390 (33.8%)	
Systemic therapy	Yes	0 (0.0%)	3,071 (74.8%)	<.0001
Radiation therapy	Yes	0 (0.0%)	1,913 (46.6%)	<.0001
Systemic and radiation therapy	Yes	0 (0.0%)	877 (21.4%)	<.0001
Healthcare utilization, physician visits, 1 year following diagnosis[1]	Medical Oncology	1,789 (6.9%)	2,040 (55.1%)	
	Surgery	5,355 (20.7%)	1,190 (32.1%)	
	Radiation Oncology	208 (0.80%)	736 (19.9%)	
	Dermatology	7,795 (30.1%)	1,138 (30.7%)	
	Family Medicine	14,981 (57.9%)	2,438 (65.9%)	
Healthcare utilization, imaging use, 1 year following diagnosis[1]	CT Chest, Abdomen, Pelvis	721 (2.8%)	1,164 (31.4%)	
	CT or MRI brain	781 (3.0%)	750 (20.3%)	
	Nodal Ultrasound	1,353 (5.2%)	386 (10.4 %)	
Median follow-up	Median (IQR) years	8.4 (5.9-11.6)	7.9 (5.5-11.5)	
Death in follow-up	Yes	6,595 (24.9%)	2,233 (54.4%)	<.0001
Access of any palliative care service any time following diagnosis	Yes	13,619 (51.5%)	3,361 (81.8%)	
Access of any mental health care any time following diagnosis	Yes	21,365 (80.8%)	3,790 (92.3%)	

[1]1 year post diagnosis, in first quarter, surgery cohort N=25,863, surgery and adjuvant therapy cohort N=3,702

Figure 1. Survivorship care patterns based on treatments received

P128. Discordant PD-L1 Expression on Primary Tumor versus Circulating Tumor Cells in Cutaneous Melanoma

Jennifer Chen[1]; Vanessa N. Sarli[2]; Salyna Meas[3]; Joshua Upshaw[4]; Merrick I Ross, MD[5]; Anthony Lucci, MD[6]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [4]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [5]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [6]UT-MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: PD-L1 expression in the tumor microenvironment is a dynamic process and may not be accurately defined by traditional IHC assays. We sought to characterize PD-L1 expression on circulating tumor cells (CTCs) and compare expression with primary tumor PD-L1 status in cutaneous melanoma. **METHODS:** Patients were enrolled in a prospective registry from 2008-2023 and underwent serial blood draws at baseline and q6-12 months intervals. Tumor PD-L1 positivity was defined as membranous PD-L1 staining in ≥ 1% of tumor cells via IHC 22C3 assay. CTCs were enumerated using CellSearchTM where ≥ 1 CTCs was considered positive. PD-L1 expression on CTCs was detected using a FITC-conjugated anti-PD-L1 mAb (BioLegend) and immunofluorescence signals were graded on a scale from 0-3 (0 = negative, 3+ = strongly positive). Major pathologic response was defined as ≤ 10% viable tumor on surgical pathology. Chi-square and Fisher's exact tests were used to compare group differences. **RESULTS:** In total, 31 patients with known tumor PD-L1 status and positive CTCs were included. Patients were predominantly White (30, 96.8%) with median age of 60 (IQR 49-69.5) and BMI ≥ 30 kg/m2 (19, 61.3%). Clinical stage ranged from 45.2% (14) stage I-II, 48.4% (15) stage III, and 6.5% (2) stage IV. Up to 29.0% (9) were BRAF-positive (V600E). All patients underwent primary tumor resection and majority (28, 90.3%) underwent nodal dissection (45.2% SLNB, 16.1% CLND, 29.0% SLNB + CLND). Tumor PD-L1 status was 64.5% (20) negative and 35.5% (11) positive. Almost all patients received ICB (29, 93.5%) – 64.5% (20) in the adjuvant setting, 12.9% (4) in neoadjuvant setting, and 16.1% (5) in both. Major pathologic response after neoadjuvant ICB was 40% (2/5) in PD-L1 negative tumors vs. 33.3% (1/3) in PD-L1 positive tumors (p = 0.85). Among PD-L1 positive tumors, PD-L1 expression on CTCs was 100% (11/11), with a total of 22 PD-L1+ CTCs detected across all timepoints. For PD-L1 negative tumors, PD-L1 expression on CTCs was similarly high at 94.4% (17/18, p = 0.63), with a total of 55 PD-L1+ CTCs detected. PD-L1 grade distributions on CMCs were comparable regardless of tumor PD-L status (p = 0.26, Table 1). Subgroup analyses using PD-L1 staining cutoff of ≥ 10% and inclusion of only PD-L1 3+ CTCs yielded similar PD-L1 CTC detection rates irrespective of tumor PD-L1 status. **CONCLUSIONS:** Among patients with detectable CTCs, almost all expressed PD-L1+ CTCs despite lack of PD-L1 expression in the primary tumor. This study supports further investigation into the role of PD-L1 expression on CTCs and its potential use as a predictive biomarker for response to immunotherapy.

Table 1. PD-L1 Grade Distributions on Circulating Melanoma Cells by Primary Tumor PD-L1 Status

PD-L1 Grade	PD-L1 Negative Tumor (N=55 CMCs)	PD-L1 Positive Tumor (N=22 CMCs)	p-value
1+	24 (43.6%)	6 (27.3%)	0.26
2+	14 (25.5%)	5 (22.7%)	
3+	17 (30.9%)	11 (50.0%)	

P129. Does Therapy Duration Matter for Stage III Melanoma Patients Receiving Adjuvant Immunotherapy?

Natalie N Chakraborty, MD[1]; Maira A Bhatty[2]; Kevin G. Zablonski, MD[3]; Hailey Seibert[4]; Adam Wade[5]; Jarred M. Boone, MD[6]; Trisha Lal[7]; Richard Hoehn, MD[8]; Iris Y. Sheng[9]; Luke D. Rothermel, MD, MPH[10]

[1]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [2]Case Western Reserve University School of Medicine, Cleveland, OH, US; [3]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [4]Case Western Reserve University School of Medicine, Cleveland, OH, US; [5]Case Western Reserve University School of Medicine, Cleveland, OH, US; [6]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [7]Case Western Reserve/University Hospitals, Cleveland, OH, US; [8]University Hospitals, Cleveland Medical Center, Cleveland, OH, US; [9]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [10]University Hosptials Cleveland, Cleveland, OH, US

INTRODUCTION: Adjuvant immunotherapy is recommended for 12-month courses or until dose-limiting toxicity in patients with stage III melanoma. Prior studies have demonstrated improved recurrence-free survival (RFS) in patients who receive 12-month regimens, but alternative treatment durations have not been investigated. We hypothesized that receipt of <12 months of immunotherapy would confer similar RFS benefits to completing a 12-month course. **METHODS:** We retrospectively identified patients diagnosed with stage IIIA-IIIC melanoma at our institution from 2015-2022 who were treated with adjuvant immunotherapy. Patients who initiated therapy more than 90 days after surgery were excluded. To account for residual treatment effects beyond the last date of immunotherapy, patients were included in the 12-month cohort if they received at least 316 days of therapy. All included patients had follow up data for more than 316 days, aside from two patients who died of melanoma recurrence before that time. A Cox proportional hazards model was constructed to identify patient and tumor characteristics independently associated with RFS. Recurrence was defined as biopsy-proven local, in transit, or nodal recurrence or distant recurrence identified radiographically, with or without tissue diagnosis. **RESULTS:** A total of 125 patients with stage III melanoma who received adjuvant immunotherapy were identified, including 31 with stage IIIA disease. 51 patients (41%) received <12 months of therapy, while 74 (59%) received at least 12 months. Treatment duration in the <12 months cohort ranged from 18-315 days with a median duration of 203 days. 119 patients (95%) received anti-PD-1 monotherapy (pembrolizumab or nivolumab). Receipt of therapy for at least 12 months was associated with improved RFS compared to shorter treatment durations (HR 0.39; 95% CI: 0.16-0.97). Factors associated with inferior RFS included age 60-79 (HR 2.61; 95% CI: 1.09-6.24), low socioeconomic status (HR 2.42; 95% CI: 1.15-5.10), nodal deposits >1mm (HR

3.10; 95% CI: 1.29-7.45), thick tumors (HR 2.93; 95% CI: 1.15-7.43), and N3 stage (HR 7.18; 95% CI: 1.96-26.29). **CONCLUSIONS:** In this cohort, receipt of at least 12 months of adjuvant immunotherapy conferred improved RFS compared to shorter therapy durations. Further studies are needed to determine if all patients will benefit similarly from the full 12 months of treatment. Ongoing research will explore the relationship between lower socioeconomic status and RFS disparities in our population.

Table 1. Adjusted Hazard Ratios for Recurrence Free Survival among Patients with Stage III Melanoma Who Received Adjuvant Immunotherapy

Covariate	No. *(%)*	Adjusted HR (95% CI)	p-value
Therapy Duration			
< 12 months	51 *(41%)*	*Ref.*	
At least 12 months	74 *(59%)*	0.39 (0.16-0.97)	0.042
Age at Diagnosis			
18-59	55 *(44%)*	*Ref.*	
60-79	63 *(50%)*	2.61 (1.09-6.24)	0.031
80+	7 *(6%)*	0.92 (0.21-4.10)	0.916
Sex			
Male	66 *(53%)*	*Ref.*	
Female	59 *(47%)*	0.55 (0.27-1.13)	0.104
Area Deprivation Index			
1-75 Percentile	95 *(76%)*	*Ref.*	
76-100 Percentile	29 *(23%)*	2.42 (1.15-5.10)	0.020
Unknown	1 *(1%)*	2.98 (0.30-29.90)	0.353
Charlson Comorbidity Index			
0	66 *(53%)*	*Ref.*	
1-2	43 *(34%)*	0.47 (0.16-1.41)	0.176
3	16 *(13%)*	2.36 (0.90-6.17)	0.081
T Stage			
T1-T2	38 *(31%)*	*Ref.*	
T3	48 *(40%)*	0.79 (0.28-2.25)	0.658
T4	35 *(29%)*	2.93 (1.15-7.43)	0.024
N Stage			
N1	80 *(64%)*	*Ref.*	
N2	37 *(30%)*	1.57 (0.70-3.51)	0.271
N3	8 *(6%)*	7.18 (1.96-26.30)	0.003
Size of Largest Nodal Deposit			
Micrometastatic (≤1mm)	64 *(51%)*	*Ref.*	
> 1mm	49 *(39%)*	3.10 (1.29-7.45)	0.012
No Nodal Metastasis (N1c)	6 *(5%)*	3.29 (0.62-17.52)	0.162
Unknown	6 *(5%)*	1.11 (0.20-6.17)	0.899
Type of Immunotherapy			
Anti-PD-1 Monotherapy (Nivolumab/ Pembrolizumab)	119 *(95%)*	*Ref.*	
Ipilimumab + Nivolumab	2 *(2%)*	3.34 (0.35-32.07)	0.297
Other, Including Trial Drug	4 *(3%)*	0.36 (0.04-3.32)	0.368

P130. Enhanced sensitivity of indocyanine green versus isosulfan blue for sentinel lymph node biopsy in melanoma

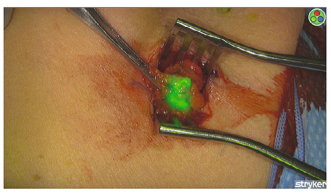
Tannaz Ranjbarian, MD, Surgery Research Fellow[1]; Michael Bouvet, MD, FACS, Professor of Surgery, Director of Endocrine Surgery[2]; Joel M. Baumgartner, MD, MAS, FACS, Professor of Surgery, Surgery 401 Clerkship Director[3]
[1]University of California, San Diego, San Diego, CA, US; [2]University of california san diego, San Diego, CA, US; [3]University of california san diego, San Diego, CA, US

INTRODUCTION: Sentinel lymph node biopsy (SLNB) is critical for assessing lymph node status and prognosis in cutaneous melanoma. Dual tracer lymphatic mapping using blue dye, such as isosulfan blue (IB), and Technetium-99m radioisotope (RI) is the standard for SLNB. Indocyanine green (ICG) is increasingly used in fluorescence-guided surgery but has only recently been considered for SLN mapping in melanoma. This study aims to compare the effectiveness of ICG and IB in SLNB. **METHODS:** A retrospective review was conducted on 375 melanoma patients (median age: 62 years, range 15–91) who underwent SLNB using Tc99m Lymphoseek RI and either IB or ICG at a single institution from 2012-2024. SLNs were identified as positive by RI and/or IB/ICG. Breslow thickness, ulceration, and mitotic rate were recorded, with the sensitivity of ICG versus IB analyzed using the chi-square test, with RI as the gold standard. **RESULTS:** A total of 890 sentinel lymph nodes were identified and removed from 375 patients with stage Ia-IV melanoma (figure 1A). All patients (n=375) received RI; 215 patients received IB, 170 patients received ICG (figure 1B). No anaphylaxis or allergic reactions were reported. ICG demonstrated significantly higher sensitivity for SLN detection compared to IB (100% vs. 54.38%, P < 0.0001). Among SLNs with metastasis, ICG sensitivity was also superior to IB (100% vs. 54.45%, P < 0.0003). Additionally, 0.1% of SLNs were detected by IB and were RI-negative, compared to 0.4% by ICG. Sensitivity by melanoma site showed ICG had higher sensitivity in axilla (100% vs. 52.77%) and inguinal (100 vs. 57.14%) regions. **CONCLUSIONS:** ICG is safe and demonstrates superior sensitivity compared to IB for SLNB when used with RI. Transitioning from IB to ICG may enhance sentinel lymph node detection and staging accuracy, ultimately improving the management of patients with melanoma.

A: Overview of Patient Characteristics and Clinical Parameters with Cutaneous Melanoma.

	Total number of patients (n = 375)	Group ICG (n = 170)	Group IB (n = 215)	P value
Median age, years (range) :	62 (range: 15 - 91)	65 (range: 15 - 90)	60 (range: 19 - 91)	0.00970
Age (95% CI, yo)	61-63	63-67	58-62	
Sex, n (%) :				
Male	200 (54%)	91 (24%)	113 (30%)	
Female	175 (48%)	78 (21%)	102 (27%)	
Primary site of melanoma :				0.50479
Head and neck	1	0	1	
Head and neck + Trunk	1	0	1	
Trunk	159	78	86	
Trunk + Extremity	3	1	2	
Extremity	211	90	125	
Mean Breslow thickness, mm (SD) :	2.0 (2.2)	1.9 (2.0)	2.1 (2.2)	0.25288
Breslow thickness (95% CI, mm)	1.94 - 2.23	1.74 - 2.18	1.94 - 2.32	
Ulceration, n (%) :	90 (24%)	41 (11%)	49 (13%)	1
Ulceration (95% CI)	20%-28%	18% - 31%	17% - 28%	
Mitosis, n (%) :				0.62803
< 1 mm2	97 (25.8%)	40 (10.6%)	57 (15.2%)	
≥ 1 mm2	278 (74.1%)	128 (34.1%)	150 (40%)	
Final Pathologic Stage, n (%) :				0.10331
Stage 0 (in situ)	5 (1.3%)	4 (1%)	1 (0.3%)	
Stage I	190 (50.6%)	84 (22.4%)	114 (28.2%)	
Stage II	81 (21.6%)	34 (9%)	47 (12.6%)	
Stage III	97 (25.8%)	48 (12.8%)	51 (13%)	
Stage IV	2 (0.5%)	0	2 (0.5%)	

B: ICG avid SLN

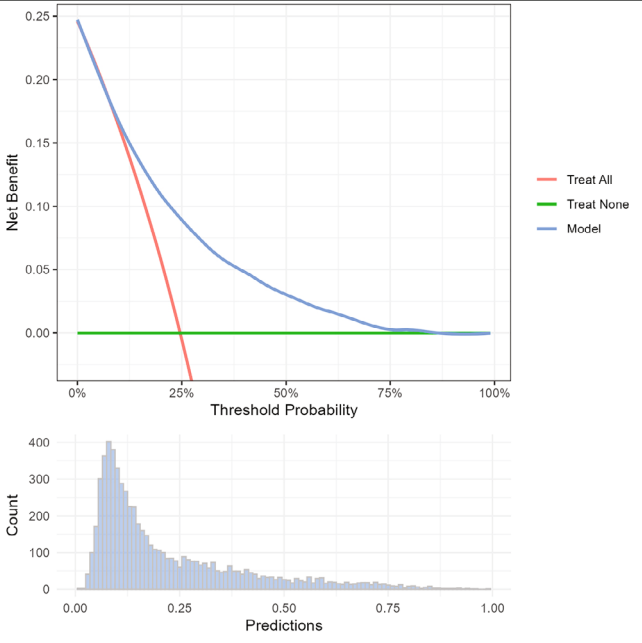


P131. External validation of a model to predict recurrence-free and melanoma-specific survival for patients with melanoma after sentinel node biopsy.

Robert Charles Stassen, MD[1]; Carolien CHM Maas[2]; Stanley P Leong, MD[3]; Mohammed Kashani-Sabet, MD[4]; Richard White, MD[5]; Barbara A Pockaj, MD[6]; Jonathan S. Zager, MD[7]; Schlomo Schneebaum, MD[8]; John T. Vetto, MD[9]; Eli Avisar, MD[10]; J Harrison Howard, MD[11]; Cristina O'Donoghue, MD[12]; Heidi E Kosiorek, MS[13]; Alexander C.J. Van Akkooi, MD, PhD[14]; Cornelis Verhoef, MD, PhD[15]; David van Klaveren, PhD[16]; Roger Olofsson Bagge, MD, PhD[17]; Dirk J. Grunhagen, MD, PhD[18]
[1]Erasmus Medical Centre, Cancer Institure, Rotterdam, NL; [2]Erasmus Universtiy Medical Centre, Rotterdam, NL; [3]California Pacific Medical Center, San Francisco, CA, US; [4]California Pacific Medical Center, San Francisco, CA, US; [5]Atrium Health Levine Cancer Center, Charlotte, NC, US; [6]Mayo Clinic Arizona, Phoenix, AZ, US; [7]Moffitt Cancer Center, Tampa, FL, US; [8]Tel Aviv Sourasky Medical Center, Tel Aviv, IL; [9]Oregon Health and Science University, Portland, OR, US; [10]Sylvester Comprehensive Cancer Center, Miami, FL, US; [11]University of South Alabama, Mobile, AL, US; [12]Rush University Medical Center, Department of Surgery, Chicago, IL, US; [13]Mayo Clinic, Rochester, MN, US; [14]Melanoma Institute Australia, Sydney, AU; [15]Erasmus Medical Center, Rotterdam, NL; [16]Erasmus Universtiy Medical Centre, Rotterdam, NL; [17]Department of Surgery, Sahlgrenska University Hospital, Gothenburg, Sweden, Gothenburg, SE; [18]Erasmus MC, Rotterdam, NL

INTRODUCTION: Recently a model to predict 5-year recurrence-free survival (RFS) and melanoma-specific survival (MSS) after sentinel lymph node biopsy (SLNB) was published. This study aimed to externally validate this model in a large international cohort. **METHODS:** We analyzed the database of the Sentinel Lymph Node Working Group (SLNWG) for patients with melanoma who underwent SLNB. Patients with clinical stage III, a history of other malignancies or those receiving concomitant systemic therapies were excluded. Tumor burden in the SLNWG data was available as a categorical variable (<0.1mm, 0.1-1.0mm, >1.0mm). To account for this, mean values of each category (respectively, 0.05mm, 0.51mm and 3.93mm) were derived from the development cohort and used as proxies for these categories. The model's predictive performance was evaluated using discrimination and calibration metrics in the eligible cohort. Decision curve analysis (DCA) was performed

to assess the clinical utility of the model. The probability threshold of interest was set at 45% (Bajaj, 2020), reflecting the average 5-year composite outcome of recurrence or death (composite outcome = 1 – '5-year RFS') for patients with stage IIB, the minimum eligibility criterion for adjuvant therapy. **RESULTS:** The external validation cohort consisted of 6174 patients from different hospitals in United States, Europe and Israel. A positive sentinel lymph node (SLN) was found in 788 (12.8%) of patients. The area under the time-dependent receiver operating characteristic curve of the external validation was 0.76 (95% CI: 0.74-0.77) for RFS and 0.79 (95% CI: 0.76-0.81) for MSS. The model was well calibrated as the observed 5-year survival rates aligned closely to the predicted survival rates (calibrations slope 1.01 for RFS, 1.02 for MSS). The prediction model provided higher net benefit versus the 'treat all' strategy at the predetermined probability threshold of 45% and higher (Figure 1). At a probability threshold of 45%, the model's net benefit is 0.04. This means that for every 100 patients, the model correctly identifies 4 patients who will experience the composite outcome, after accounting for incorrect identifications. **CONCLUSIONS:** In this external validation study, conducted on a large heterogeneous cohort, the model demonstrated good performance, even in the absence of SLN tumor burden as continuous variable. This consistent performance emphasizes the model's robustness. Additionally, DCA revealed a clear net benefit of the model over a treat all strategy, highlighting its potential for clinical use.



Top figure: The Y-axis represents the net benefit at each probability threshold, reflecting the proportion of patients with the composite outcome correctly identified by the treatment strategy, adjusted for the penalty of incorrectly identifying patients without the composite outcome. X-axis represents the continuum of threshold probabilities for experiencing the composite outcome within 5 years. The green line represents net benefit of treating no individuals with adjuvant therapy ('treat none' approach). The red line represents net benefit of treating all individuals with adjuvant therapy ('treat all' approach). The blue line represents net benefit of treating patients according to the individualized predictions of experiencing the composite outcome resulting from the model across the continuous of threshold probabilities ('model' approach). Note that above the predetermined threshold of 45% (dashed line), the model shows a sustained net benefit over the 'treat all' strategy. Bottom figure: Displays the distribution of predicted probabilities for the composite outcome of recurrence or death.

Figure 1. Decision curve analysis on the full validation cohort of patients with melanoma who underwent a sentinel node procedure in the United States of America, Sweden, Israel, Italy, and Netherlands.

P132. IDH1 modulation sensitizes NRAS mutant melanoma to MEK inhibition

Alexander Loftus[1]; Mehrdad Zarei[2]; Christina S Boutros[3]; Hallie Graor[4]; Jordan Winter[5]; Luke D. Rothermel, MD, MPH[6]
[1]University Hospitals Cleveland Medical Center, Cleveland, OH, US; [2]Case Western Reserve University, Cleveland, OH, US; [3]Univerisity Hospitals Cleveland Medical Center, Cleveland, OH, US; [4]Case Western Reserve University, Cleveland, OH, US; [5]University Hospitals Cleveland Medical Center, Cleveland, OH, US; [6]University Hosptials Cleveland, Cleveland, OH, US

INTRODUCTION: NRAS mutant melanoma represents 10-15% of newly diagnosed cases of melanoma and treatment options are limited for this molecular subtype. Targeted therapies against MEK, such as trametinib, create variable responses. Our lab has recently reported that isocitrate dehydrogenase 1 (IDH1), a cytosolic enzyme that has important roles in detoxification of reactive oxygen species (ROS) and mitochondrial metabolism, and also show that the enzyme is involved the stress response to BRAF inhibitor therapy in BRAF mutant melanoma. We hypothesize that trametinib stress will induce an adaptive upregulation of IDH1 expression in NRAS mutant melanoma to overcome MEK inhibition, and offering a rationale for a novel targeted therapeutic approach. **METHODS:** The human HS852T melanoma cell line with NRAS G12 mutation, wild type BRAF, and wild type IDH1 was utilized for all experiments. Immunoblotting was performed for p-ERK 1/2, ERK 1/2, and IDH1 after treatment with indicated agents. Cell viability was assessed after 4 days of treatment using PicoGreen dsDNA measurement, and the Bliss Independence model was used to calculate pharmacologic synergy. Bioenergetic analyses were performed using the Seahorse assay to measure oxygen consumption rate (OCR) under nutrient and therapeutic stress. Relative ROS levels were measured using DCFDA assay. ROS and Seahorse assays were normalized to cell count using PicoGreen. **RESULTS:** IDH1 expression increased after MEK inhibition with trametinib in HS852T melanoma cells at both 24- and 48-hour time points under low glucose conditions, reflective of the tumor microenvironment. Compared to treatment with trametinib alone, combination therapy with trametinib plus the IDH1 inhibitor, ivosidenib, disrupts ERK signaling leading to significantly decreased p-ERK levels. Cell viability substantially decreases with combination trametinib and ivosidenib, with mean Bliss score of 2.41. The OCR was not changed as a result of exposure to either trametinib or ivosidenib. However, ROS levels were significantly increased in cells treated with trametinib and ivosidenib versus trametinib alone. **CONCLUSIONS:** This suggests that 1) IDH1 expression induction is an acute stress response of NRAS mutant melanoma to MEK inhibition with trametinib; 2) combination of IDH1 inhibition (ivosidenib) and MEK inhibition (trametinib) demonstrated synergy; and 3) the increase in cell death observed when adding ivosidenib to trametinib is likely driven by increased ROS in the combination treatment group. These findings provide a rationale for further investigation into the role of combination wild-type IDH1 and MEK inhibition in NRAS mutant melanoma.

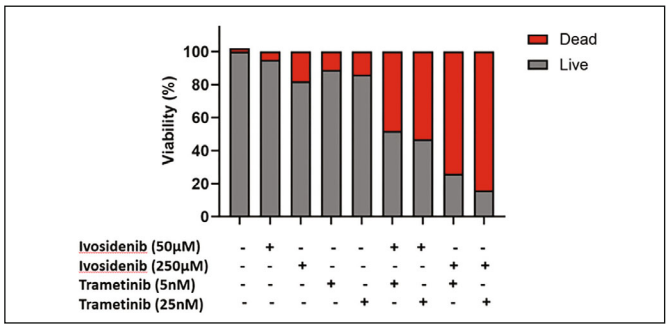


Figure 1. HS852T Melanolma Cell Viability after Exposure to Indicated Concentrations of Ivosidenib and Trametinib.

P133. Impact of sentinel lymph node biopsy on recurrence and survival for Merkel cell carcinoma

Michelle M. Dugan, MD[1]; Caitlyn Balsay-Patel, MD[2]; Nicholas Chin, BS[3]; Jacob Israeli, BS[4]; Kimberly R. Ward[5]; Matthew Nichols, BS[6]; Wenyi Fan, MSPH[7]; C. Wayne Cruse, MD[8]; Michael Harrington, MD[9]; Rogerio I Neves, MD, PhD[10]; Ricardo J. Gonzalez, MD[11]; Matthew C Perez, MD[12]; Amod A Sarnaik, MD[13]; Vernon K Sondak, MD[14]; Jane L Messina, MD[15]; Ahmad A. Tarhini, MD, PhD[16]; Nikhil Khushalani, MD[17]; Andrew S. Brohl, MD[18]; Joseph Markowitz, MD, PhD[19]; Zeynep Eroglu, MD[20]; Lilit Karapetyan, MD, MS[21]; Kenneth Y. Tsai, MD, PhD[22]; Jonathan S. Zager, MD[23]
[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]University of South Florida Morsani College of Medicine, Tampa, FL, US; [4]University of South Florida Morsani College of Medicine, Tampa, FL, US; [5]Moffitt Cancer Center, Tampa, FL, US; [6]Moffitt Cancer Center, Tampa, FL, US; [7]Moffitt Cancer Center, Tampa, FL, US; [8]Moffitt Cancer Center, Tampa, FL, US; [9]Moffitt Cancer Center, Tampa, FL, US; [10]Moffitt Cancer Center, Tampa, FL, US; [11]Moffitt Cancer Center, Tampa, FL, US; [12]Moffitt Cancer Center, Tampa, FL, US; [13]Moffitt Cancer Center, Tampa, FL, US; [14]Moffitt Cancer Center, Tampa, FL, US; [15]Moffitt Cancer Center, Tampa, FL, US;

[16]Moffitt Cancer Center, Tampa, FL, US; [17]Moffitt Cancer Center, Tampa, FL, US; [18]Moffitt Cancer Center, Tampa, FL, US; [19]Moffitt Cancer Center, Tampa, FL, US; [20]Moffitt Cancer Center, Tampa, FL, US; [21]Moffitt Cancer Center, Tampa, FL, US; [22]Moffitt Cancer Center, Tampa, FL, US; [23]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Merkel cell carcinoma (MCC) is a rare disease that carries a poor prognosis in advanced stages. Sentinel lymph node biopsy (SLNB) at the time of excision is standard of care, but the impact of SLNB on survival is unclear. This study examines the impact of SLNB on recurrence and overall survival outcomes for patients with MCC. **METHODS:** A retrospective review included patients from 1999-2024 with clinical N0, resectable MCC. **RESULTS:** 696 patients were identified, with a median age of 76 (69-81) years and 68% males. Primary tumors were located on the head/neck in 48%, upper extremity in 28%, lower extremity in 16%, and trunk in 8%. Staging on pre-operative biopsy was T1 in 80%, T2 in 16%, T3 in 0.7%, T4 in 0.3%, and unknown in 2.9%. Median follow-up from excision was 3 years. 75% of patients underwent SLNB (n=524), with a median of 3 nodes retrieved, 35% positive (n=182) and 65% negative (n=339) nodal status. Reasons for omission of SLNB included comorbidities (34%), provider/patient choice at an outside institution (31%), lack of nodal drainage on lymphoscintigraphy (18%), other (11%), and unknown (6%). Patients who did not have a SLNB were older (79 vs 75 years, p<.001) and more likely to experience recurrence (58% vs 30%, p<.001) than those who had a SLNB; 45.3% of patients who did not have a SLNB developed regional recurrence, compared to 19.8% of those who had a SLNB. On Kaplan-Meier (KM) analysis, median recurrence-free survival (RFS) (4.2 years vs 8.8 months, p<.0001), disease-specific survival (DSS) (5.3 vs 3.2 years, and overall survival (OS) (6.8 vs 3.6 years, p<.0001) were higher for patients who underwent SLNB compared to those who did not. On multivariable analysis (MVA), RFS (HR 2, p<.001), DSS (HR 1.7, p=.01), and OS (HR 1.3, p=.04) remained significantly higher for patients who underwent SLNB. On KM, RFS (5.5 vs 1.4 years, DSS (3.2 vs 1.9 years, and OS (7.4 vs 4.9 years, p=.03) were higher for patients with a negative SLNB compared to those with a positive SLNB. On MVA, RFS (HR 1.6, p<.001) and DSS (HR 3.2, p<.001) remained significantly higher for patients with a negative SLNB. Patients with Merkel cell polyomavirus (MCV) had a significantly higher rate of negative SLNB (87% vs 44%, p=.013) compared to those without MCV. On KM, patients with MCV had higher OS (9.6 vs 2.9 years, p<.001) and DSS (9.6 vs 3.5 years, p=.007) than those without MCV. **CONCLUSIONS:** Patients with MCC who underwent SLNB had significantly better RFS, DSS, and OS than those who did not. SLNB positivity was associated with lower RFS and DSS compared to a negative SLNB. This study emphasizes the importance of SLNB for MCC, with utility in staging as well as a potentially positive impact on recurrence-free and overall survival.

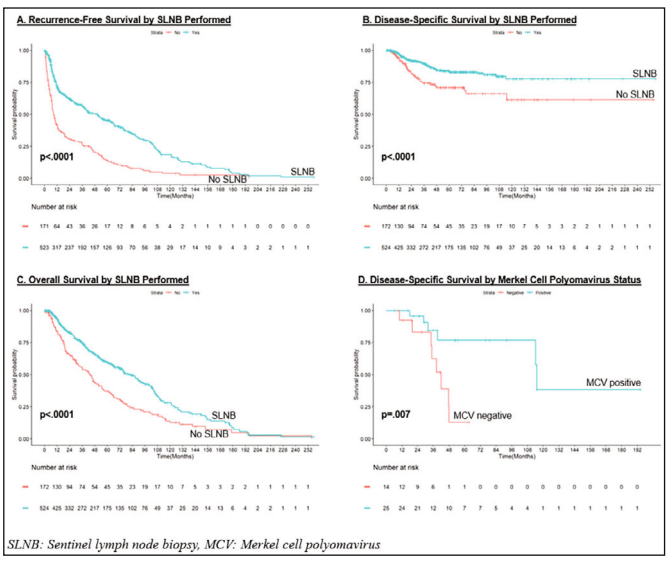


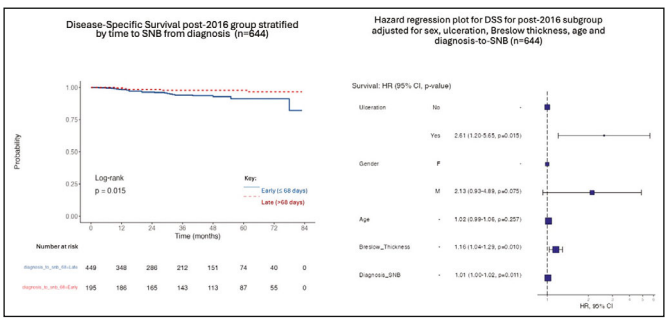
Figure 1. Recurrence-free survival (A), disease-specific survival (B), and overall survival (C) based on whether or not a sentinel lymph node biopsy (SLNB) was performed at the time of primary Merkel cell carcinoma resection, and disease-specific survival based on Merkel cell polyomavirus (MCV) status (D).

P134. Impact of Timing of Sentinel Node Biopsy After Diagnosis on Disease Progression, Metastatic Tumor Burden and Survival Outcomes in Melanoma: Implications for Adjuvant Systemic Therapy

Marc D Moncrieff, MD FRCS(Plast.)[1]; Sofia O. Breeze, M.Res[2]; Martin J Heaton, MD FCRS(Plast.)[3]; Andrew P Snelling, FRCS(Plast.)[4]; Jennifer J Garioch, MD FRCP[5]; Jenny P Nobes, FRCR[6]

[1]Department of Plastic & Reconstructive Surgery, Norfolk and Norwich University Hospitals NHS Foundat, Norwich, GB; [2]Norwich Medical School, University of East Anglia, Norwich, GB; [3]Department of Plastic & Reconstructive Surgery, Norfolk and Norwich University Hospitals NHS Foundat, Norwich, GB; [4]Department of Plastic & Reconstructive Surgery, Norfolk and Norwich University Hospitals NHS Foundat, Norwich, GB; [5]Department of Dermatology, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, GB; [6]Department of Oncology, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, GB

INTRODUCTION: Sentinel node biopsy (SNB) is critical for staging melanoma and guiding adjuvant systemic therapy (AST) decisions. Evidence suggests that patients with low-burden micrometastases may avoid AST, raising concerns about SNB timing and treatment delays. **METHODS:** We investigated whether time from primary melanoma diagnosis to SNB affects key outcomes: (1) rate of macroscopic disease progression, (2) micrometastatic burden, and (3) survival. Micrometastatic burden was assessed by maximum tumor deposit size. Disease-specific survival (DSS), disease-free survival (DFS), and distant metastasis-free survival (DMFS) were primary survival measures. A cohort study included 1,625 melanoma patients treated with SNB at an academic cancer centre between 2010-2023, using a prospective institutional database. SNB waiting times following diagnosis (date of pathology reporting) were analyzed continuously and as early (≤90 days) or late (>90 days), with subgroup analyses for patients post-2016 (when systemic therapy was introduced). Optimal surgery timing was identified via maximally selected rank statistics. **RESULTS:** Median time to SNB from diagnosis was 68 days (IQR 51-95), with a SN positivity rate of 19.2% (n=290). Median time to reporting from diagnostic excision biopsy was 10 days (IQR 6-14). Median follow-up was 75 months (IQR 35-115). Delay to SNB following diagnosis beyond 90 days was associated with higher rates of disease progression prior to surgery (0.3% versus 1.5%; adjusted OR 1.02, 95% CI 1.01-1.03; p<0.001), larger micrometastatic deposits (1.4 mm vs. 2.95 mm: OR 1.10, 95% CI 1.04-1.18; p=0.001) and a higher incidence of high-risk deposits >1mm diameter (44.8% vs. 69%; OR 2.05, 95% CI 1.16-3.71; p=0.016), leading to worse survival outcomes (DSS, DFS, DMFS; log-rank p<0.05). Patients treated after 2015 had an improved DSS (HR 0.92, 95% CI 0.78-0.97; p=0.001). In the post-2016 subgroup, longer wait times following diagnosis correlated with worse DSS (HR 1.01, 95% CI 1.00-1.02; p=0.011), and worse DSS for increasing delay from excision biopsy to SNB (HR 1.01, 95% CI 1.00-1.02; p=0.016). Optimal timing was 68 days from diagnosis to SNB (HR 1.01, 95% CI 1.00-1.02; p=0.013) and 82 days from excision date to SNB (HR 1.01, 95% CI 1.00-1.02; p=0.025). **CONCLUSIONS:** Our data suggests that delays in surgery beyond 90 days from diagnosis to SNB are associated with harm; including increased risk of disease progression, increased micrometastatic burden in positive SNBs, and worse survival. Further validation is needed, but the data identifies 10 weeks to SNB from diagnosis and 12 weeks from excision biopsy as key thresholds for minimizing SN micrometastatic tumor burden and improving survival outcomes.



P135. Isolated limb infusion/perfusion for unresectable acral versus non-acral melanoma in-transit metastases

Michelle M. Dugan, MD[1]; Jacob Israeli, BS[2]; Nicholas Chin, BS[3]; Caitlyn Balsay-Patel, MD[4]; Anne Huibers, MD, PhD[5]; Wenyi Fan, MSPH[6]; Roger Olofsson Bagge, MD, PhD[7]; Jonathan S. Zager, MD[8]

[1]Moffitt Cancer Center, Tampa, FL, US; [2]University of South Florida Morsani College of Medicine, Tampa, FL, US; [3]University of South Florida Morsani College of Medicine, Tampa, FL, US; [4]Moffitt Cancer Center, Tampa, FL, US; [5]Sahlgrenska University Hospital, Gothenburg, SE; [6]Moffitt Cancer Center, Tampa, FL, US; [7]Sahlgrenska University Hospital, Gothenburg, SE; [8]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Acral lentiginous melanoma (ALM) has a worse prognosis compared to non-ALM cutaneous melanoma and a poorly understood tumor genetic profile, limiting therapy options. This is the first study to directly compare outcomes of isolated limb infusion or perfusion (ILI/ILP) for unresectable in-transit metastases (ITM) arising after the treatment of ALM vs non-ALM primary tumors. **METHODS:** An international multi-institution retrospective review included patients with unresectable melanoma ITM with known histologic subtype who underwent ILI/ILP from 2002-2023. In-field progression was defined as new or enlarging lesion(s) within the treated portion of the extremity. Out-of-field progression was defined as new lesion(s) in the regional nodal basin or other distant sites. **RESULTS:** 385 patients were identified, including 55% females, with a median age of 71 (63-78) years; 89 patients had ALM (93% foot), 296 patients had non-ALM melanoma subtypes. Median primary tumor Breslow thickness was 3.0 mm for ALM vs 2.7 mm for non-ALM. Ulceration was present in 38% of patients with ALM vs 26% non-ALM. ILI/ILP was used as first-line therapy in 87% of patients with ALM and 88% non-ALM. There were no differences in complete response (CR) rates (51% for ALM vs 54% for non-ALM) or overall response rates (ORR) (80% for ALM vs 83% for non-ALM). Median follow-up time was 34 months after ILI/ILP. Median overall survival (OS) was 32.5 months for ALM vs 54.2 months for non-ALM (p=0.05). Median disease-specific survival (DSS) was 42.3 months for ALM vs 89.1 months for non-ALM (p=0.01). Median progression-free survival (PFS) was 5.2 months for ALM vs 7.8 months for non-ALM (p=0.04). Median in-field PFS was 9.4 months for ALM vs 10.8 months for non-ALM (p=0.07). Median out-of-field PFS was 10 months for ALM vs 15.6 months for non-ALM (p=0.04). **CONCLUSIONS:** ILI/ILP offers similar response rates and locoregional disease control (in-field PFS) for patients with ALM and non-ALM. OS, DSS, and out-of-field PFS were significantly lower with ALM, correlating to the thought that ALM is a more aggressive histology, and may highlight a potential opportunity to introduce systemic therapies prior to ILI/ILP or sequence therapies in order to optimize local as well as distant disease control.

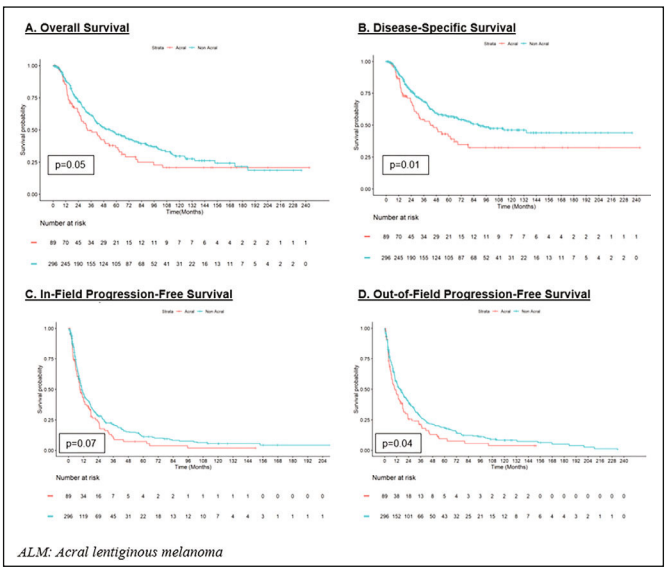


Figure 1. Survival outcomes after isolated limb infusion for acral lentiginous melanorna (ALM) versus non-ALM unresectable in-transit metastases.

P136. Local recurrence and survival in patients with melanoma >2 mm in thickness at critical structures treated with 10-mm versus 20-mm margins

Bianca Taglione[1]; Andrea Maurichi[2]; Francesco Barretta[3]; Roberto Patuzzo[4]; Gianfrancesco Gallino[5]; Ilaria Mattavelli[6]; Michal Shimonovitz Moore[7]; Eran Nizri[8]; Matteo Matteucci[9]; Valeria Summo[10]; Mara Cossa[11]; Barbara Valeri[12]; Umberto Cortinovis[13]; Rosalba Miceli[14]; Mario Santinami[15]

[1]Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milano, IT; [2]Istituto Nazionale dei Tumori, Milano, IT; [3]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [4]Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milano, IT; [5]Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milano, Mi, IT; [6]Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milano, IT; [7]Souraski Tel Aviv Medical Center, Tel Aviv, IL; [8]Souraski Tel Aviv Medical Center, Tel Aviv, IL; [9]Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milano, IT; [10]Fondazione IRCCS Istituto Nazionale dei Tumori di Milano, Milano, IT; [11]Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, IT; [12]Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, IT; [13]Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, IT; [14]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [15]Istituto Nazionale dei Tumori, Milano, IT

INTRODUCTION: Melanoma guidelines recommend surgical excision with 2-cm margins for melanomas >2 mm in thickness. However, this procedure may be problematic at critical anatomical sites. We aimed to compare the outcomes of wide (2 cm) versus narrow (1 cm) excision margins in patients with melanoma >2 mm in thickness near critical structures. **METHODS:** We retrospectively examined 736 patients undergoing excision with wide versus narrow margins at the National Cancer Institute, Milan, Italy between 2001 and 2015. **RESULTS:** Two hundred sixty-five patients (36.0%) received a wide local excision, 82 (30.9%) with linear repair and 183 (69.1%) with flap or graft reconstruction; 471 (64.0%) patients received a narrow excision, 320 (67.9%) with linear repair and 151 (32.1%) with flap or graft reconstruction (P<0.001). Ten-year overall survival was 69.5% (95% CI, 63.3–76.2%) in the wide and 68.7% (95% CI 63.8–74.0%) in the narrow group (P=0.462); 10-year crude cumulative incidence (CCI) of local recurrence was 5.4% (95% CI 3.2–9.2%) in the wide and 8.8% (95% CI 6.4–12.1%) in the narrow group (P=0.150). Multivariable Fine-Gray modeling of the CCI of local recurrence showed that Breslow thickness (P=0.010) was the only statistically significant parameter. Multivariable Cox models for overall survival showed that age (P<0.001), Breslow thickness (P<0.001) and sentinel lymph node status (P=0.019) were statistically significant covariates. Excision margin was not a significant parameter affecting patients' outcome. **CONCLUSIONS:** Wide local excision with 1-cm margins for melanoma >2 mm in thickness was not associated with an increased risk of local recurrence and did not affect overall survival.

P137. Melanoma in Peru: 1000 patients and 10 years of experience

Gonzalo Ziegler Rodriguez[1]; Gabriel A De la Cruz Ku[2]; Sheyla K Diaz-Mora[3]; Luis Piedra-Delgado[4]; Jiddu A Guart[5]; Jessica J Farzan[6]; Anshumi Desai[7]; Camila Franco[8]; Sheila Vilchez-Santillan[9]; Jorge Dunstan Yataco[10]; Juan C Haro Varas[11]; Jose A Galarreta Zegarra[12]; Sandro Casavilca-Zambrano[13]; Jose M Cotrina Concha[14]

[1]Instituto Nacional de Enfermedades Neoplasicas, Lima, PE; [2]University of Massachusetts Medical School, Worcester, MA, US; [3]Instituto Nacional de Enfermedades Neoplasticas, Lima, PE; [4]Universidad Cientifica del Sur, Lima, Peru, Lima, PE; [5]University of Massachusetts Medical School, Worcester, Worcester, MA, US; [6]University of Massachusetts Medical School, Worcester, MA, US; [7]University of Miami Miller School of Medicine, Miami, FL, US; [8]University of Texas Medical Branch at Galveston, Texas, Galveston, TX, US; [9]Instituto Nacional de Enfermedades Neoplasicas, Lima, PE; [10]Instituto Nacional de Enfermedades Neoplasicas, Lima, PE; [11]Instituto Nacional de Enfermedades Neoplasicas, Lima, PE; [12]Instituto Nacional de Enfermedades Neoplasicas, Lima, PE; [13]Instituto Nacional de Enfermedades Neoplasicas, Lima, PE; [14]Instituto Nacional de Enfermedades Neoplasicas, Lima, PE

INTRODUCTION: Epidemiological studies identified distinct characteristics of melanoma based on race and ethnicity. Previous reports have revealed that Hispanic/Latino population with melanoma has different characteristics compared to other races. Our aim was to describe the sociodemographic, clinicopathological features, and long-term outcomes — event-free survival (EFS) and overall survival (OS)—of the Peruvian population diagnosed with melanoma. **METHODS:** We reviewed medical records of new cases diagnosed and treated at a single tertiary institution in the period 2010-2019. Survival analysis included patients with stages I-IV. Multivariate Cox Regression analysis was used to assess prognostic factors of EFS and OS. **RESULTS:** A total of 1136 patients were included, the median age at diagnosis was 63 years (range: 6-97 years), with a slight male predominance (51.5%). Most patients (50.4%) resided in metropolitan areas, the lower extremities were the most common primary tumor location (72%), and ulceration was present in 52.4%. Acral lentiginous melanoma was the most frequent histological subtype (38.1%), followed by melanoma NOS in the vertical growth phase/

nodular melanoma (13.9%). The mean Breslow thickness was 7.66 mm, with a mean mitotic rate of 6.61/mm². Stage T3-4 was present in 58.9%, and 36% has stage N2-3, while Stage III was the most frequent AJCC Stage (36.5%), followed by Stage II (23.9%) and IV (23.0%). In regards to adjuvant therapy, 13.4% received chemotherapy, 3.6% radiotherapy, and 13.6% interferon. No patients received immunotherapy. The median follow up was 117 months. At 3, 5, and 10 years follow up, the EFS was 31%, 20%, and 5%; while the OS was 51%, 38%, and 27% respectively. Prognostic factors of worse EFS were greater age (HR=1.01), male sex (HR=1.34), ulceration (HR=1.73), positive lymph nodes (HR=2.38), histologic subtypes other than acral lentiginous and nodular (HR=1.28), while primary site in upper extremities (HR=0.60) and interferon therapy (HR=0.72) were associated to better EFS. Furthermore, prognostic factors of worse OS were greater age (HR=1.01), of ulceration (HR=1.80), and positive lymph nodes (HR=2.99). **CONCLUSIONS:** Peruvian patients with melanoma display distinct sociodemographic characteristics and are often diagnosed at more advanced stages compared to other populations. The lack of access to immunotherapy likely contributes to the poorer EFS and OS outcomes. Although prognostic factors were consistent with international findings, urgent healthcare policy changes are needed to enable earlier diagnosis and improve access to immunotherapy.

P138. Nodal imaging concordance with pathologic findings after neoadjuvant immunotherapy in patients with Stage III melanoma

Joshua Herb, MD, MSCI[1]; Carlos A Torres-Cabala, MD[2]; Victor G Prieto, MD PhD[3]; Rami Eldaya, MD[4]; Sapna P Patel, MD[5]; Ashley M. Holder, MD[6]; Sarah B. Fisher, MD[7]; Anthony Lucci, MD[8]; Jennifer Wargo, MD MMSC[9]; Rodabe N Amaria, MD[10]; Jeffrey E Gershenwald, MD[11]; Merrick I Ross, MD[12]; Roi Weiser, MD[13]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [4]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [5]University of Colorado Cancer Center, Aurora, CO, US; [6]University of Texas MD Anderson Cancer Center, Houston, TX, US; [7]MD Anderson Cancer Center, Houston, TX, US; [8]UT-MD Anderson Cancer Center, Houston, TX, US; [9]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [10]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [11]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [12]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [13]The University of Texas MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Neoadjuvant immunotherapy (nIO) for clinically node-positive Stage III melanoma is recommended by national guidelines. Real world data correlating pre-nIO nodal imaging and response on post-nIO with pathologic findings are lacking, and could help select patients for de-escalation of nodal surgery after nIO. We assessed correlation of (1) the number of radiographically abnormal lymph nodes (LN) before nIO with the number of involved LN in therapeutic lymph node dissection (TLND) specimens, and (2) response to nIO on post-nIO imaging with response in TLND pathology, **METHODS:** Patients receiving nIO for clinically node positive melanoma followed by TLND at a large academic institution from 2016-2024 were included. The number of abnormal LN (1 or >1) on either US, CT, MRI, or PET/CT was compared to number of involved LN (1 or >1) on pathology. Involved nodes included those with viable or treated tumor, including those with a complete response (pCR). Next, response on post-nIO imaging (defined as decrease in size or activity) was compared to pathologic response (pCR, near-pCR, or partial response vs. no response). **RESULTS:** We included 154 patients. Median (IQR) age was 61(49-69) years, 73% were male, and nodal locations included cervical (40%), axilla (31%), groin (26%) and multiple basins (4%). 72% of patients received combination nIO and 23% single agent. 58% were assessed with >1 imaging modality: 65% US, 65% CT/MRI, and 30% PET/CT. On pre-nIO imaging, 31% of patients had 1 abnormal LN and 69% had >1. Pre-nIO imaging was concordant with the number of involved nodes (1 vs. >1) on final pathology in 62% of cases. It overestimated nodal involvement in 28% and underestimated in 10% of patients. Concordance did not vary by single vs multi-modality imaging (61.5% vs 61.8%, respectively). Post-nIO imaging accurately predicted pathologic response in 80% of cases. Preoperative imaging was 95% accurate when demonstrating response and only 56% when showing no response (P<0.001). **CONCLUSIONS:** In patients with clinically node positive melanoma receiving nIO, pre-nIO imaging was only moderately accurate in estimating 1 vs >1 involved nodes on pathology. Nevertheless, a response on imaging accurately predicted a pathological response in the nodal basin in 95% of cases, consistent with clinical trial data. These findings can help guide patient selection for prospective trials investigating de-escalation of nodal basin surgery in this patient population.

P139. Optimizing Surgical Approaches in Melanoma: The Role of Pre-Operative Imaging in Reducing Deep Inguinal Lymph Node Dissection

Michal Shimonovitz Moore[1]; Eran Nizri[2]; Andrea Maurichi[3]; Mario Santinami[4]

[1]Souraski Tel Aviv Medical Center, Tel Aviv, IL; [2]Tel-Aviv Sourasky Medical Center, Tel-Aviv, IL; [3]Istituto Nazionale dei Tumori, Milano, IT; [4]Istituto Nazionale dei tumori, Milano, IT

INTRODUCTION: The role of surgical lymph node dissection (LND) in melanoma is now limited to macroscopically positive disease. Traditionally, both superficial and deep inguinal lymph nodes are resected when LN in the inguinal region are involved, however this approach may be associated with higher morbidity and costs. This study evaluates whether deep inguinal lymph node dissection can be omitted based on pre-operative imaging findings, potentially reducing surgical intervention. **METHODS:** We conducted a retrospective study of 311 patients with cutaneous melanoma who underwent inguino-pelvic LND in a single institution from 2000 to 2022. Patients were stratified into two groups based on pre-operative imaging (CT or PET/CT): those with suspected positive deep inguinal lymph nodes (PDILN) and those with suspected negative deep inguinal lymph nodes (NDILN). We assessed the correlation between imaging predictions and final pathological outcomes, calculating sensitivity, specificity, and predictive values for each imaging modality. **RESULTS:** Among the 311 patients, 106 had pathologically confirmed PDILN and 205 had NDILN. Patients with PDILN presented with ulcerated (56.7% vs. 38.5%, p=0.004) and tended to have thicker lesions (2.6 (1.1-4.5) mm vs. 1.9 (0.6-4) mm, p=0.06). The number of superficial nodes resected did not differ significantly between groups (10.39±0.45 vs. 10.9±0.29, p=0.32), but the number of positive LNs in the superficial dissection was notably higher in the PDILN group (1.5±0.12 vs. 3.38±0.31, p<0.001). Imaging demonstrated high accuracy in predicting deep node involvement, with a sensitivity of 94%, specificity of 99%, positive predictive value of 98%, and negative predictive value of 97%. Based on imaging results, 66% of patients could have avoided deep inguinal LND without compromising diagnostic accuracy. Melanoma-specific survival (MSS) was significantly lower in the PDILN group compared to the NDILN group before the routine introduction of adjuvant therapy (median MSS: 23 months [95% CI: 15.2-30.7] vs. 94 months; p=0.002), but no significant difference was observed post-adjuvant therapy (p=0.097). **CONCLUSIONS:** Pre-operative imaging, CT or PETCT, is highly effective in predicting deep inguinal lymph node involvement in melanoma patients. Incorporating imaging results into surgical planning could potentially reduce the need for deep inguinal dissection, thereby decreasing surgical morbidity. These findings support a more selective approach to deep inguinal LND based on imaging evidence, aligning with contemporary shifts towards minimizing invasive procedures in melanoma management.

Optimizing Surgical Approaches in Melanoma: The Role of Pre Operative Imaging in Reducing Deep Inguinal Lymph Node Dissection

Table 1. Patient's clinical and pathological characteristics

	All patients (n=311)	Positive deep Inguinal nodes in the pathology (n=106)	Negative deep inguinal nodes in the pathology (n=205)	p- value
Sex, F/M, n (%)	174/137 (55.9/44.1)	58/48 (54.7/45.3)	116/89 (56.6/43.4)	0.75
Age, median (IQR)	62 (49-71)	64 (50.8-74.2)	61 (49-71)	0.3
Breslow mm median (IQR)	2.05 (0.8-4.15)	2.6 (1.1-4.5)	1.9 (0.6-4)	0.06
Regression, n (%)	47 (27.5)	14 (21.9)	33 (30.8)	0.2
Ulceration, n (%)	130 (44.1)	51 (56.7)	79 (38.5)	0.004
Clark, n (%)				0.73
II	10 (3.2)	4 (3.8)	6 (2.9)	
III	33 (10.6)	9 (8.5)	24 (11.7)	
IV	131 (42.1)	49 (46.2)	82 (40)	
V	19 (6.1)	7 (6.6)	12 (5.9)	
missing	118 (37.9)	37 (34.9)	81 (39.5)	
Imaging modality, n (%)				
CT	190 (61.1)	57 (53.8)	133 (64.9)	0.07
PETCT	120 (38.6)	48 (45.3)	72 (35.1)	
Time to Dx, months (IQR)	14 (2-47)	17 (2-51.5)	13 (2-47)	0.48

Table 2. Pathological parameters of resected LN.

	Negative deep final pathology (n=205)	Positive deep final pathology (n=106)	p-value
Superficial positive	1.5±0.12	3.38±0.31	<0.001
Total superficial LN	10.9±0.29	10.39±0.45	0.32
LN ratio	0.13	0.32	
Extracapsular invasion, n (%)	68 (33.2)	50 (47.2)	0.016

Table 3. Imaging accuracy for deep inguinal LN involvement

	NDILN	PDILN	Total
Negative involvement of deep inguinal nodes per imaging	203	6	209
Positive involvement of deep inguinal nodes per imaging	2	100	102
Total	205	106	311

P140. Outcomes of In-Transit Melanoma (ITM) Treated with Checkpoint Inhibitors (CPI) In The Modern Era

Shanie Shemla, MD[1]; Aparna Vancheswaran, MD[2]; Cristian Mantilla-Rosa[3]; Edmund K. Bartlett, MD[4]; Mary Brady[5]; Charlotte Ariyan[6]; Danielle Bello[7]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center,

New York, NY, US; [5]Memorial slaon kettering Cancer Center, New York, NY, US; [6]Memorial Sloan kettering Cancer Center, New York, NY, US; [7]Memorial Slaon Kettering Cancer Center, New York, NY, US

INTRODUCTION: In-transit melanoma (ITM) is a unique form of metastatic melanoma that occurs between the primary tumor site and the nearest lymph node basin. While there many treatment options, we do not yet know which therapies are most appropriate for individual patients. Checkpoint inhibitors (CPI) have demonstrated a 50% 10 year survival for patients with metastatic melanoma. However, ITM is poorly represented in these trials. This study aims to present clinical characteristics of patients with ITM, who often receive multi-modality treatment, in the era of CPI, with long term follow up. **METHODS:** Single institution retrospective cohort study of patients diagnosed with ITM between 2010-2021. All patients received CPI as first-line treatment at time of initial in-transit recurrence, with at least 6 months follow-up. Clinicopathologic data was collected, descriptive statistics were analyzed. **RESULTS:** Of 212 patients, most were male (63%) and AJCC stage III (46%) at diagnosis with median age of 63 years. At time of treatment, 52% of patients (n=111) had a solitary IT lesion and 47% had multiple lesions. Median follow-up was 6 years. Median overall survival (OS) was 101 months. 35% of patients died of disease during follow-up and 93 patients had no evidence of disease (NED, 44%). Overall response rate (ORR) to 1st line treatment with CPI was 56% - 45% had complete response (CR), 4% had stable disease (SD), 7% partial response (PR) and 44% no response (NR). During follow-up 15% of the cohort developed additional IT recurrences after the initial recurrence, 66% developed nodal disease and 55% developed metastatic disease. We divided the cohort to 3 treatment groups - CPI alone, CPI + surgery and CPI + local therapy (radiation, limb infusion, intra-tumoral therapy). Patients who received CPI alone had OS of 63 months and ORR of 49%. For the CPI + surgery group OS was 130 months and ORR was 59%. The CPI + local group had the longest OS (162 months) and ORR of 67%. Overall survival differed significantly between the groups (P=0.008). The CPI + surgery group was divided further to patients who received neo-adjuvant CPI (n=10, OS 99 months, ORR 80%) vs adjuvant (n=70, OS 130 months, ORR 55%). **CONCLUSIONS:** This study adds to the literature demonstrating improved outcomes for patients with ITM who receive CPI in the modern era, especially in the setting of multi-modality therapy. Response rates were promising with almost half achieving long-term survival free of disease. Identification of predictive biomarkers correlating with positive outcomes after CPI could make a significant impact towards advancing care in this heterogeneous group of patients.

Patient variable	Total patient population (n=212)	CPI Only (n=99)	CPI + local (n=33)	CPI + surgery (n=80)
Age at diagnosis, median	63.3	69.3	63.7	60.2
Median Overall Survival (motnhs)	101	63	162	130
Gender				
Female, n (%)	78 (37%)	40 (40%)	14 (42%)	24 (30%)
Male, n (%)	134 (63%)	59 (60%)	19 (58%)	56 (60%)
Genomic mutations				
BRAF, n (%)	58 (27%)	33 (33%)	7 (21%)	18 (23%)
NRAS, n (%)	69 (33%)	23 (23%)	15 (45%)	31 (39%)
cKIT, n (%)	7 (3%)	2 (2%)	1 (3%)	4 (5%)
AJCC Stage at time of diagnosis				
In Situ, n (%)	6 (3%)	3 (3%)	0	3 (4%)
Stage I, n (%)	40 (20%)	14 (14%)	5 (15%)	21 (26%)
Stage II, n (%)	54 (25%)	26 (26%)	9 (27%)	19 (24%)
Stage III, n (%)	98 (46%)	51 (52%)	17 (52%)	30 (38%)
Stage IV, n (%)	7 (3%)	3 (3%)	2 (6%)	2 (2%)
Unknown, n (%)	7 (3%)	2 (2%)	0	5 (6%)
Histologic type				
Superficial Spreading, n (%)	34 (16%)	17 (17%)	6 (18%)	11 (14%)
Acral Lentiginous, n (%)	29 (14%)	15 (15%)	4 (12%)	10 (13%)
Nodular, n (%)	34 (16%)	10 (10%)	6 (18%)	18 (22%)
Others, n (%)	115 (54%)	57 (58%)	17 (52%)	41 (51%)
Melanoma type				
cutaneous, n (%)	172 (81%)	80 (81%)	25 (76%)	67 (83%)
Acral, n (%)	29 (14%)	15 (15%)	4 (12%)	10 (13%)
Unknown primary, n (%)	11 (5%)	4 (4%)	4 (12%)	3 (4%)
First recurrence				
IT only, n (%)	95 (45%)	37 (38%)	22 (67%)	36 (45%)
IT + nodal, n (%)	59 (28%)	29 (29%)	4 (12%)	26 (33%)
IT + distant, n (%)	58 (27%)	33 (33%)	7 (21%)	18 (22%)
IT disease burden				
Solitary, n (%)	111 (52%)	41 (41%)	11 (33%)	59 (74%)
Multiple, n (%)	99 (47%)	57 (58%)	22 (67%)	20 (25%)
Unknown, n (%)	2 (1%)	1 (1%)	0	1 (1%)
Disease progression				
Nodal disease, n (%)	140 (66%)	66 (66%)	19 (58%)	55 (69%)
Distant disease, n (%)	117 (55%)	60 (60%)	11 (33%)	46 (58%)
Additional recurrences				
1 recurrence, n (%)	26 (12%)	10 (10%)	2 (6%)	14 (18%)
2 or more recurrences, n (%)	5 (2%)	2 (2%)	0	3 (4%)
Treatment response				
CR, n (%)	96 (45%)	37 (38%)	19 (58%)	40 (50%)
SD, n (%)	8 (4%)	4 (4%)	1 (3%)	3 (4%)
PR, n (%)	14 (7%)	8 (8%)	2 (6%)	4 (5%)
NR / POD, n (%)	94 (44%)	50 (51%)	11 (33%)	33 (41%)
ORR, n (%)	118 (56%)	49 (49%)	22 (67%)	47 (59%)
Disease status				
NED, n (%)	93 (44%)	35 (35%)	20 (61%)	38 (48%)
AWD, n (%)	20 (9%)	12 (12%)	2 (6%)	6 (7%)
DOD, n (%)	74 (35%)	39 (40%)	5 (15%)	30 (38%)
DOO, n (%)	25 (12%)	13 (13%)	6 (18%)	6 (7%)

P141. Melanoma Screening May Not Lead to Improved Outcomes: A Cross-Sectional Study

Weichuan Dong[1]; Trisha Lal[2]; Uriel Kim[3]; Brock Montgomery[4]; Hanna Kakish[5]; Johnie Rose[6]; Siran Koroukian[7]; Jeremy Bordeaux[8]; Luke Rothermel, MD, MPH[9]; Richard Hoehn, MD[10]

[1]Case Western Reserve University, Cleveland, OH, US; [2]Case Western Reserve/ University Hospitals, Cleveland, OH, US; [3]Case Western Reserve University, Cleveland, OH, US; [4]Case Western Reserve University, Cleveland, OH, US; [5]Johns Hopkins, Baltimore, MD, US; [6]Case Western Reserve University, Cleveland, OH, US; [7]Case Western Reserve University, Cleveland, OH, US; [8]University Hospitals Cleveland Medical Center, Cleveland, OH, US; [9]University Hospitals Cleveland Medical Center, Cleveland, OH, US; [10]University Hospitals Cleveland Medical Center, Cleveland, OH, US

INTRODUCTION: Survival for early-stage melanoma is far superior to that for late-stage disease. Dermatology outreach and screening programs are designed to improve melanoma diagnosis and survival by addressing travel and access barriers. However, the effectiveness of these programs remains uncertain. **METHODS:** We analyzed data from the Ohio Cancer Incidence Surveillance System (2011-2020) to capture all patients diagnosed with cutaneous melanoma. We calculated neighborhood-level incidence rates of early-stage (localized) and late-stage (regional, distant) melanoma and used spatial clustering methods to identify patterns. We also used bivariate mapping to explore associations between socioeconomic status (SES, using the Area Deprivation Index), healthcare accessibility, and early-stage vs late-stage melanoma incidence. **RESULTS:** : Between 2011 and 2020, 24,562 patients were diagnosed with invasive melanoma in Ohio (81.4% early stage, 18.6% late stage). Significant clustering of neighborhoods with high/low incidence of early-stage melanoma (Moran's index 0.305, $p<0.001$) was observed, while late-stage incidence was randomly distributed. Across neighborhoods in Ohio, early-stage melanoma incidence correlated significantly with SES, dermatologist accessibility, and primary care accessibility (all $p<0.001$). Late-stage incidence showed no significant correlation with these factors. High-incidence early-stage neighborhoods were observed primarily in affluent suburbs, whereas low-incidence early-stage clusters were found in disadvantaged inner cities and rural areas. Bivariate maps revealed that neighborhoods with high SES and high access had the highest incidence of early-stage melanoma, with decreasing incidence observed in lower SES areas regardless of access. No correlation was found between SES-access characteristics and late-stage melanoma incidence (Figure 1). **CONCLUSIONS:** SES, dermatologist accessibility, and differences in early-stage melanoma incidence are not associated with the incidence of late-stage melanoma. To improve equity in melanoma outcomes, resources may be better spent increasing access to and receipt of effective systemic therapies for patients with advanced melanoma rather than try to "catch it early" with screening and outreach programs.

P142. Patterns of Melanoma Care in a Rural State

Phoebe Bruffett[1]; Ashlynn Fuccello, MS[2]; Phillip Farmer[3]; Austin Porter, DrPH, MPH[4]; Michail Mavros, MD[5]; Hanna Jensen, MD PhD[6]; Sonia T. Orcutt, MD[7]; Nicholas Callais, MD[8]

[1]University of Arkansas for Medical Sciences, Little Rock, AR, US; [2]University of Arkansas for Medical Sciences, Little Rock, AR, US; [3]University of Arkansas for Medical Sciences, Little Rock, AR, US; [4]University of Arkansas for Medical Sciences, Little Rock, AR, US; [5]University of Arkansas for Medical Sciences, Little Rock, AR, US; [6]University of Arkansas for Medical Sciences, Little Rock, AR, US; [7]University of Arkansas for Medical Sciences, Little Rock, AR, US; [8]University of Arkansas for Medical Sciences, Little Rock, AR, US

INTRODUCTION: Previous studies have shown that melanoma mortality is higher in rural populations compared to urban populations. This study aims to investigate melanoma incidence and treatment outcomes in Arkansas, one of the most rural states in America. **METHODS:** Data were collected from the Arkansas Statewide Cancer Registry. Altogether, 9,790 patients were diagnosed with melanoma in Arkansas between 2014 - 2020. Those without complete staging and rurality were excluded, resulting in a population of 7,860 patients. Patients were stratified by both year of diagnosis (2014-2017 or 2018-2020) and rurality (metropolitan, suburban, or rural). Descriptive statistics and bivariate analyses were performed to compare stage at diagnosis (local, regional, or distant), treatment types (none, surgery alone, surgery and additional treatments, additional treatments only), and 2-year survival rates across rurality and year. Multivariate logistic regression was used to compare rates of survival by year and rurality while adjusting for demographics. **RESULTS:** The mean age at diagnosis was 65.7 years (SD 14.8). Most patients were white (99.1%) and

male (62.3%). More patients presented with regional and distant disease in 2018-2020 as compared to 2014-2017 (regional - 7.8% vs. 5.6% and distant - 3.9% vs. 3.1%, p<0.001). In addition, in 2018-2020, patients were more likely to receive surgery with additional treatments (8.1% vs 3.9%) vs. surgery alone (1.6% vs 1.0%), p <0.001. Patients in metropolitan areas were more likely to present with local disease (91.2% vs. 87.9% in suburban areas and 89.3% in rural areas, p=0.004). Patients in metropolitan areas similarly had higher rates of standalone surgery (96.4% vs. 95.8% in suburban areas and 95.3% in rural areas, p=0.002). Survival was improved in metropolitan areas (2-year survival 92.5% vs. 89.3% in suburban areas and 88.4% in rural areas, p <0.001). On logistic regression analysis, when controlling for age, race, sex, and stage, the survival difference persisted. Compared to those in metropolitan areas, those in suburban areas and rural areas had increased odds of death at 2 years (1.30, p=0.004 and 1.48, p=0.027). **CONCLUSIONS:** There are significant disparities in melanoma treatment and outcomes based on rurality in Arkansas. Patients from rural areas are more likely to present with advanced-stage disease and have worse survival. These findings highlight the need for targeted interventions and improved access to care for rural populations to enhance early diagnosis and treatment of melanoma.

Table 1. Risk-adjusted association of rurality and year with 2 year survival via logistic regression (n = 7626, AUC = 0.819)

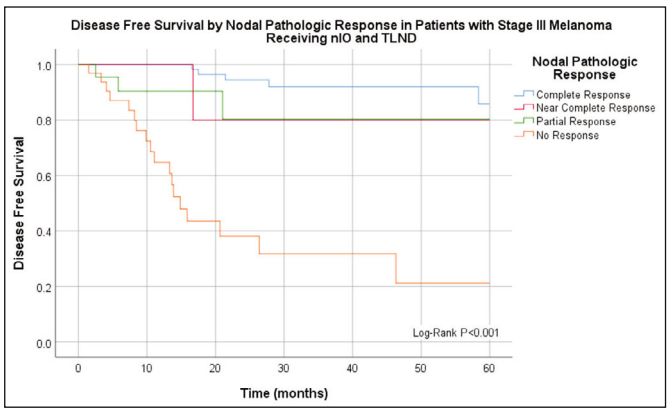
Variable	Odds Ratio	95% CI	P value
Age (10-year increment)	1.97	1.79-2.16	<0.001
Female Sex	0.72	0.59-0.88	0.001
Race (Reference: White)			
Black	0.89	0.20-2.73	0.862
Other	0.83	0.10-4.33	0.840
Stage (Reference: Local)			
Regional	5.33	4.14-6.83	<0.001
Distant	29.84	22.24-40.28	<0.001
Time period (Reference: 2014-2017)			
2018-2020	1.03	0.86-1.22	0.757
Rurality (Reference: Metropolitan)			
Suburban	1.30	1.09-1.56	0.004
Rural	1.48	1.04-2.07	0.027

P143. Real-world outcomes of patients with clinically node positive melanoma undergoing neoadjuvant immunotherapy and nodal dissection

Joshua Herb, MD, MSCI[1]; Carlos A Torres-Cabala, MD[2]; Victor G. Prieto, MD PhD[3]; Sapna P Patel, MD[4]; Ashley M. Holder, MD[5]; Sarah B. Fisher, MD[6]; Anthony Lucci, MD[7]; Jennifer Wargo, MD MMSC[8]; Rodabe N Amaria, MD[9]; Jeffrey E Gershenwald, MD[10]; Merrick I. Ross, MD[11]; Roi Weiser, MD[12]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [4]University of Colorado Cancer Center, Aurora, CO, US; [5]University of Texas MD Anderson Cancer Center, Houston, TX, US; [6]MD Anderson Cancer Center, Houston, TX, US; [7]UT-MD Anderson Cancer Center, Houston, TX, US; [8]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [9]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [10]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [11]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [12]The University of Texas MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Neoadjuvant immunotherapy (nIO) followed by therapeutic lymph node dissection (TLND) for patients (pts) with clinically node positive Stage III melanoma is supported by level 1 evidence. Few studies have assessed real-world outcomes with this treatment strategy. We assessed the association of pathologic response (PR) and nIO regimen with survival among patients with clinical Stage III melanoma undergoing nIO and TLND. **METHODS:** We included pts receiving nIO for clinically node positive melanoma followed by TLND from a large academic institution from 2016-2024. Demographic, clinical, treatment, and outcomes data were collected. Pathologic response was assessed using standard categories (complete PR (pCR) = 0% viable tumor, near-complete PR (pnCR) = 1%-<10%, partial PR (pPR) = 10%-50%, and non-response (pNR) = >50%). Differences in pCR rate by nIO regimen were examined. Kaplan-Mier method was used to assess disease free survival (DFS) by PR and nIO regimen (single vs combination). Multivariable (MV) analysis was used to assess the association of PR and nIO regimen with DFS while controlling for demographic, tumor and treatment factors. **RESULTS:** We included 154 pts. Median (IQR) age was 61(49-69) years, 73% were male, 71% had an ECOG score of 0, and 37% had a BRAF mutation. Lymph node basins included cervical (40%), axillary (31%), groin (26%), or multiple (4%). 73% had combination nIO (ipilimumab/nivolumab (57%), nivolumab/relatlimab (16%)) and 23% had single agent anti-PD-1. Median (IQR) number of nIO cycles was 2 (2-3). The pCR rate was 52.6%, pnCR rate was 4.8%, pPR rate was 13.6%, pNR rate was 22.7%, and PR was not quantified in 6.3%. pCR rate for combination nIO was 57.7% and 38.9% for single agent anti PD-1 (P=0.05). Survival was significantly differed based on pathologic response (Log-Rank P<0.001, Figure). Pts with a pCR had a 5-year DFS rate of 76% compared to 24% DFS among pts with pNR. In univariate analysis, pts, with combination nIO had longer 5y DFS than patients with single-agent anti-PD-1 (Log-Rank P=0.039, 67% vs 50% respectively). On MV analysis, only pathological nodal response was associated with DFS, while nIO regimen was not. **CONCLUSIONS:** Consistent with clinical trial data, our real-world data from a large cohort of pts undergoing nIO+TLND for clinical Stage III melanoma demonstrates that PR is a strong predictor of DFS. Though single vs combination nIO impacted cPR rates, it was not independently associated with longer DFS in this retrospective cohort, as PR seems to be the driver of survival.



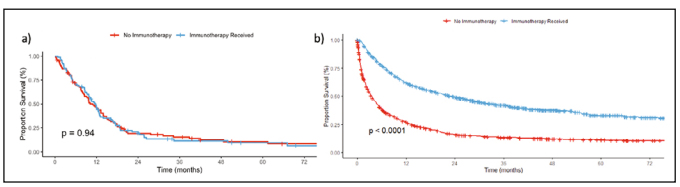
P144. Stagnant Survival Rates in Uveal Melanoma Liver Metastases: The Paradox of Escalating Immunotherapy

Paul Wong, BS[1]; Tommaso Pollini, MD[2]; Sophia Hernandez, MD[3]; Letizia Todeschini, MD[4]; Marco Zampese, MD[5]; Shao Tao, PhD[6]; Luis Laurean Aguilar, BS[7]; Michael Alvarado, MD[8]; James Lee, MD[9]; Katy K Tsai, MD[10]; Adil I. Daud, MD[11]; June S. Peng, MD[12]; Lucas W. Thornblade, MD, MPH[13]; Mohamed A. Adam, MD[14]; Adnan Alseidi, MD, MEd[15]; Carlos U. Corvera, MD[16]; Kenzo Hirose, MD[17]; Kimberly S. Kirkwood, MD[18]; Eric K. Nakakura, MD, PhD[19]; Ajay V. Maker, MD[20]

[1]University of California, San Francisco, San Francisco, CA, US; [2]University of California, San Francisco, San Francisco, CA, US; [3]University of California, San Francisco, San Francisco, CA, US; [4]University of California, San Francisco, San Francisco, CA, US; [5]University of California, San Francisco, San Francisco, CA, US; [6]University of California, San Francisco, San Francisco, CA, US; [7]University of California, San Francisco, San Francisco, CA, US; [8]University of California, San Francisco, San Francisco, CA, US; [9]University of California, San Francisco, San Francisco, CA, US; [10]University of California, San Francisco, San Francisco, CA, US; [11]University of California, San Francisco, San Francisco, CA, US; [12]University of California, San Francisco, San Francisco, CA, US; [13]University of California, San Francisco,

San Francisco, CA, US; [14]University of California, San Francisco, San Francisco, CA, US; [15]University of California, San Francisco, San Francisco, CA, US; [16]University of California, San Francisco, San Francisco, CA, US; [17]University of California, San Francisco, San Francisco, CA, US; [18]University of California, San Francisco, San Francisco, CA, US; [19]University of California, San Francisco, San Francisco, CA, US; [20]University of California, San Francisco, San Francisco, CA, US

INTRODUCTION: Metastatic uveal melanoma portends a poor prognosis, with the liver being the most common site of spread. While immunotherapy and checkpoint inhibitors have revolutionized the treatment armamentarium for cutaneous melanoma, these options have largely failed to accomplish a similar shift in the management of uveal melanoma. In this study, we aimed to understand trends in immunotherapy receipt for uveal melanoma patients presenting with isolated liver metastases and to evaluate its impact on survival. **METHODS:** The National Cancer Database (2010-2020) was queried to identify all patients diagnosed with uveal melanoma, and specifically those that simultaneously presented with isolated liver metastases. A separate cohort of cutaneous melanoma patients with liver-only metastases was generated for comparison of survival outcomes with immunotherapy receipt. Chi-squared tests were conducted for descriptive analyses of patient demographic and clinicopathologic variables. Kaplan Meier and Cox proportional hazard models were created to assess univariable and multivariable mortality risk, respectively. **RESULTS:** Of 17,039 patients with uveal melanoma, 280 (1.6%) presented with distant metastases at the time of initial diagnosis, and 65.7% of these individuals (n=184) had isolated liver metastases. In the cohort of patients with isolated liver metastases, the use of immunotherapy significantly increased from 2010-2015 to 2016-2020 (21.9% to 59.2%, p<0.001). The median overall survival (OS) of patients with liver-only metastases was 11.2 months (1- and 3-year OS: 45.6%, 13.0%, respectively). Metastasectomy was not associated with a difference in mortality risk (HR 0.59 [95% CI 0.289-1.200]; p=0.145), whereas only radiation therapy corresponded with a decreased risk of death (HR 0.52 [0.374-0.734]; p<0.001). Notably, immunotherapy receipt was not associated with overall survival in uveal melanoma patients with isolated liver metastases (median OS: 11.5 vs. 10.2 months, p=0.943) (Figure 1). In primary cutaneous melanoma with isolated liver metastases treated in the same time period, the use of immunotherapy increased from 16.8% to 83.2% (p<0.001), and its receipt was associated with improved median OS (4.2 vs. 26.8 months, p<0.001). **CONCLUSIONS:** The use of immunotherapy for uveal melanoma patients with isolated liver metastases at diagnosis has indeed increased. This shift reflects a growing reliance on immune checkpoint inhibitors, particularly for cutaneous melanoma. Despite the rise in immunotherapy, survival outcomes for these patients have not improved as they have for cutaneous melanoma. More targeted approaches, including liver-directed therapies, novel T-cell-based therapies, and combination strategies should be studied for uveal melanoma patients with liver metastases rather than the use of traditional immune checkpoint blockade.



P145. Survival Outcomes of Acral Lentiginous Melanoma in the Era of Modern Immune Checkpoint Inhibitor and Targeted Therapy

Adrienne B Shannon, MD[1]; Una Milovanovic, BS[2]; Jane L Messina, MD[3]; Amod A Sarnaik, MD[4]; Vernon K Sondak, MD[5]; Rogerio I Neves, MD PhD[6]; Jonathan S Zager, MD[7]; Matthew C Perez, MD[8]

[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4]Moffitt Cancer Center, Tampa, FL, US; [5]Moffitt Cancer Center, Tampa, FL, US; [6]Moffitt Cancer Center, Tampa, FL, US; [7]Moffitt Cancer Center, Tampa, FL, US; [8]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Patients with acral lentiginous melanoma (ALM) have higher rates of recurrence and worse survival compared to those with non-ALM but are underrepresented in trials due to ALM's lower incidence. While conventional melanoma outcomes have improved in the era of immune checkpoint inhibitor (ICI) and targeted therapies (post-2011), whether this has translated to ALM is less understood. **METHODS:** Consecutive adult patients diagnosed and managed for stage I-III ALM 2000-2023 at a high-volume cancer center were identified. Clinical and treatment characteristics were analyzed using univariate analyses. Kaplan-Meier survival analyses of recurrence-free (RFS) and melanoma-specific (MSS) survival were performed, comparing outcomes pre-2011 to those after 2011 in order to account for adoption of ICI adoption. **RESULTS:** Median age of ALM patients (N=338) was 67 (interquartile range [IQR] 55-76) years. Two patients received neoadjuvant ICI, and 2 patients received neoadjuvant targeted therapy for clinical stage III disease at presentation. For definitive surgical management, 245 (72.5%) patients underwent wide excision, 93 (27.5%) patients underwent digital amputation, and 258 (76.3%) patients underwent sentinel lymph node biopsy with 91 (26.9%) having micrometastatic disease in sentinel lymph nodes. The median tumor thickness was 2.1 (IQR 1.1-4) mm, and 126 (37.3%), 110 (32.5%), and 102 (30.2%) patients had pathologic stage I, II, and III, respectively. Among patients diagnosed pre-2011, 1.5% received adjuvant ICI, and among patients diagnosed post-2011, 9% of patients received ICI. Following recurrence, 8.9% and 22.4% of patients diagnosed in the pre-2011 and post-2011 groups, respectively, received ICI. In the pre-2011 and post-2011 groups, 1.5% and 4.5% of patients received targeted therapies. When comparing patients diagnosed pre-2011 to patients diagnosed post-2011, 5-year MSS (56.2% vs 55.6%; p 0.11) and RFS (43.2% vs 34.6%; p 0.19) were not statistically different. Additionally, there was no difference in MSS and RFS when comparing pre- and post-2011 diagnosed patients when stratified by stage I/II (p 0.053 and p 0.054, respectively) and stage III (p 0.46 and p 0.41, respectively). Patients diagnosed post-2011 had similar rates of all-site (53.9% vs 62%, p 0.16) and distant (55.7% vs 60.3%, p 0.51) recurrence compared to pre-2011 patients. Among patients who received adjuvant ICI, there was no difference in all-site (5.8% vs 6%, p 0.94) or distant (3.3% vs 6.5%, p 0.34) recurrence. **CONCLUSIONS:** While survival outcomes have improved for non-acral cutaneous melanoma with the adoption of modern systemic therapies, the prognosis for ALM appears relatively unchanged when comparing the most recent decade with the decade prior. There was no difference observed in MSS and RFS despite increased utilization of more effective systemic therapies.

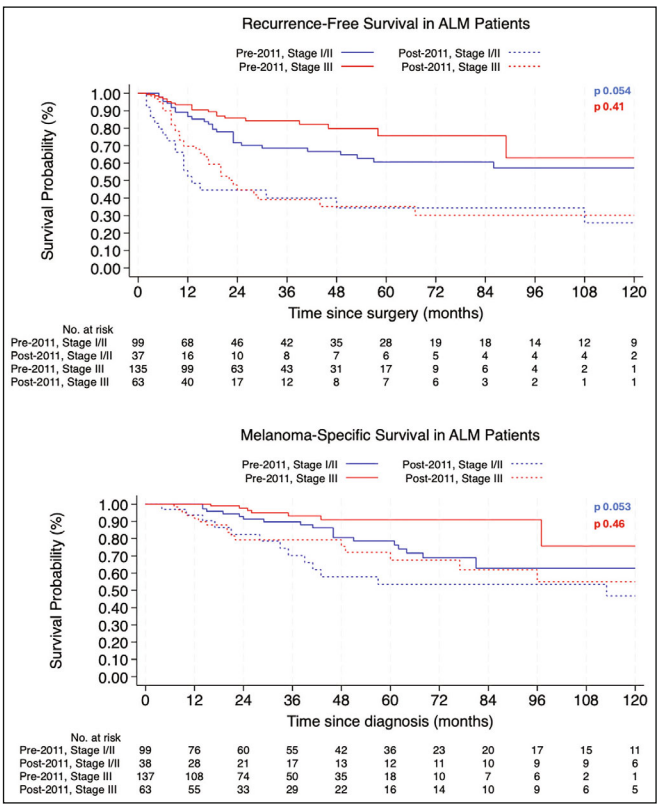


Figure. Recurrence-free survival (A) and melanoma-specific survival (B) in acral lentiginous melanoma patients diagnosed pre-2011 and post-2011 stratified by stage 1/11 and III disease.

P146. Systemic immunotherapy promotes equivalent survival between pathologic stage III cutaneous melanoma subtypes

Avia D Wilkerson, MD, PhD[1]; Justin Bauzon, MD[2]; Jenny Chang, MD[3]; Samer A Naffouje, MD[4]
[1]Cleveland Clinic - Cleveland, OH, Cleveland, OH, US; [2]Cleveland Clinic - Cleveland, OH, Cleveland, OH, US; [3]Cleveland Clinic - Cleveland, OH, Cleveland, OH, US; [4]Cleveland Clinic - Cleveland, OH, Cleveland, OH, US

INTRODUCTION: Different cutaneous melanoma subtypes are suggested to exhibit varying rates of overall survival (OS) as well as differential degrees of treatment response following treatment with immunotherapy (IO). We sought to establish these patterns in the context of nodal disease (Stage III). **METHODS:** NCDB data for cutaneous melanoma treated from 2018-2021 was used. Only patients with cutaneous melanoma of Superficial Spreading (SSM) or nodular (NM) subtypes with confirmed pathologic stage III disease who underwent excision of the primary lesion, proper histologic nodal staging, and received IO as part of their multidisciplinary therapy were included. SSM and NM patients were propensity matched 1:1. The Kaplan-Meier method was used to estimate OS and log-rank tests were used to compare OS outcomes. **RESULTS:** 8,892 patients were selected: 6,163 (69.3%) had SSM and 2,729 (30.7%) had NM. 7,909 (88.9%) had sentinel lymph node biopsy, while 888 (10.0%) had nodal excision and 95 (1.1%) had needle biopsies for nodal staging. 1,140 (12.8%) proceeded to have nodal dissections during their treatment. 8,722 (98.1%) received IO in the adjuvant setting, 71 (0.8%) received neoadjuvant IO, and 99 (1.1%) received both neoadjuvant and adjuvant IO. We matched 2,697 pairs between SSM and NM, for exact pathologic stage (IIIA-D). 5-year OS was not different between matched groups (66% vs 65%; p=0.668). Subgroup OS analysis for the matched groups showed no difference in OS when analyzed stage-for-stage (IIIA-IIID). **CONCLUSIONS:** Despite the more aggressive biologic behavior of NM and overall later stage at presentation, OS was comparable for stage III SSM and NM treated with IO, suggesting that the immune milieu of NM may propagate improved responsiveness to immunotherapy which permits survival outcomes similar to SSM.

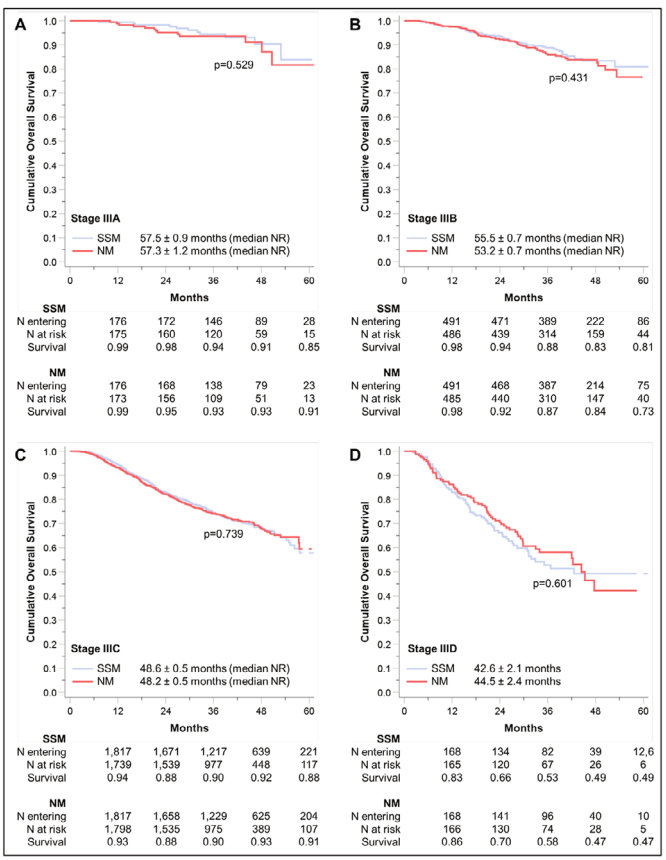


Figure 1. Kaplan Meier survival analysis of SSM vs NM dataset matched by stage

P147. The economic impact of regional communities of practice to improve quality of melanoma care

Laura E. Kerr, MD, FRCSC[1]; Katie Aw[2]; Rebecca Lau[3]; Kednapa Thavorn[4]; Karine Riad[5]; Boaz Wong[6]; Carolyn Nessim, MD, MSc[7]
[1]University of Ottawa, Ottawa, ON, CA; [2], US; [3], US; [4], US; [5], US; [6], US; [7]The Ottawa Hospital (General Campus), Ottawa, ON, CA

INTRODUCTION: Many current best practice guidelines suggest that routine preoperative imaging may not be warranted in patients with early-stage melanoma without clinically palpable lymph nodes. A Communities of Practice (CoP) collaborative on melanoma care for the region of Eastern Ontario set guidelines supporting the restricted use of staging imaging in 2017. This study assesses the practice changes and resultant economic impact after the implementation and dissemination of the CoP guidelines for preoperative imaging in patients with ≤T3b melanoma who are clinically node negative. **METHODS:** Retrospectively collected data from patients with biopsy-proven primary melanoma who underwent wide local excision and sentinel lymph node biopsy surgery were included for analysis. Patients with biopsy dates before and after May 24, 2018, were grouped into the pre- and post-guideline cohorts, respectively. Frequency, type, and positivity rate of preoperative imaging were collected and analyzed. Patient baseline demographics and tumour histological characteristics were collected for multivariable analysis. An economic analysis was performed based on the use of diagnostic work up pre- and post- guideline dissemination. **RESULTS:** A total of 645 patients were included for analysis [pre-guideline (n=339), post-guideline (n=306)]. Patients in the post-guideline cohort had significantly lower rates of pre-operative imaging when compared with the pre-guideline cohort (p<0.0001). This reduction in imaging remained significant when regrouping the post-guideline cohort as 1-, 3-, and 5- months of dissemination after initial guideline announcement. On multivariable analysis, guideline dissemination was associated with lower odds of receiving preoperative imaging [OR, 0.23 (95% CI, 0.13-0.39), p<0.0001]. Breslow thickness [1.75 (1.15-2.71), p=0.0091] and microsatellitosis [9.15 (2.58-33.37), p=0.0006] were independently associated with the use of preoperative imaging. On economic analysis, a total cost savings of $9,641.50 was demonstrated (p<0.01) with most significant cost savings noted in reduction of the use of CT scans of the chest ($3,034.00, p<0.01) and CT scans of the abdomen/pelvis ($6,825.00, p<0.01). **CONCLUSIONS:** These results demonstrated a reduction in inappropriate pre-operative imaging following CoP guideline dissemination, with favourable economic outcomes as a result. These findings support the importance of quality improvement programs such as a CoP to advance melanoma care and resource stewardship initiatives.

P148. The Impact of Second Pathologic Review in the Management of Patients with Malignant Melanoma

Angelina Wang[1]; Yingjoy Li[2]; Lily Rajaee[3]; Tu Tran[4]; James Jakowatz[5]; Kenneth Linden[6]; Bonnie Lee[7]; Linda T. Doan[8]; Maki Yamamoto[9]; Thuy B. Tran[10]
[1]University of California Irvine Department of Surgical Oncology, Orange, CA, US; [2]University of California, Irvine School of Medicine, Irvine, CA, US; [3]Loyola University Chicago Stritch School Of Medicine, Maywood, IL, US; [4]University of California Irvine Department of Surgical Oncology, Orange, CA, US; [5]University of Irvine Department of Surgical Oncology, Irvine, CA, US; [6]University of California, Irvine - Dermatology, Orange, CA, US; [7]University of California, Irvine Department of Dermatology, Orange, CA, US; [8]University of California, Irvine Department of Dermatology, Orange, CA, US; [9]University of California Irvine Department of Surgical Oncology, Orange, CA, US; [10]University of California Irvine Department of Surgical Oncology, Orange, CA, US

INTRODUCTION: The accurate diagnosis and staging of melanoma depend heavily on accurate interpretation of biopsy specimens. Malignant melanoma treated in community centers often do not require pathologic review from an academic center prior to definitive management. The objective of this study is to evaluate predictors of pathology discordance and the impact of pathologic review on patients referred to an academic melanoma center for treatment of malignant melanoma. **METHODS:** Patients referred to an academic center who underwent second pathology review of the initial biopsy by an academic dermatopathologist were identified using a retrospective IRB-approved database. Demographics and pathologic characteristics were evaluated. Pathology was stratified based on discordance between outside community pathology report and academic pathology review in breslow thickness, T-stage, histology, and ulceration. Clinical significance discordance is defined as pathology discrepancy that can alter clinical management. Logistic regression

was used to identify predictors of clinically significant pathologic discordance. **RESULTS:** A total of 404 patients who initially underwent biopsy in the community underwent pathology review at an academic center. The median age was 67 years, and the majority of patients were male (63%). Clinically significant discordance was identified in 26% (n=107): 10.1% (n = 41) had change in Breslow thickness/T-stage, 14% (n=56) had major change in histology, and 3.5 % (n = 14) had a change in ulceration status. There was no significant differences in rates of discordance based on age, race, and skin type. However, those with Medicare tended to have lower rates of pathology discrepancy (42.8 vs. 34%) while those with HMO insurance have higher rates of pathology discordance (3.7% vs. 14.2%)(P=0.005). Patients with prior history of other non-melanoma skin cancers had higher rates of pathology discordance with melanoma (26.2% vs. 14.1%, P=0.005). Patients diagnosed with lentigo maligna (P=<0.001) and desmoplastic melanoma (P=0.001) tended to have higher rates of discordance, while superficial spreading histology tended to have higher rates of pathology concordance (P=0.031). On multivariate logistic regression, predictors of clinically significant pathologic discordance are younger age(OR 0.97, P=0.021), HMO insurance status (OR 4.82, P=0.002), and lentigo maligna histology (OR 4.85, P<0.001). **CONCLUSIONS:** Pathology review by an expert dermatopathologist at an academic center is crucial to ensure the appropriate management of melanoma. The second pathology review before definitive management can impact clinical decisions significantly for melanoma.

P149. The Impact of Talimogene Laherparepvec (T-VEC) on Survival in In-Transit Disease From Acral Lentiginous Melanoma

Adrienne B Shannon, MD[1]; Jonathan S Zager, MD[2]; Amod A Sarnaik, MD[3]; Vernon K Sondak, MD[4]; Matthew C Perez, MD[5]

[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4]Moffitt Cancer Center, Tampa, FL, US; [5]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Talimogene laherparepvec (T-VEC) is an intralesional oncolytic virus approved for treatment of metastatic melanoma to cutaneous, subcutaneous, and nodal sites. T-VEC is proven to result in high local response rates, but less is known about response to T-VEC injection in metastases from less common melanoma subtypes. **METHODS:** Patients who underwent T-VEC intralesional injection for melanoma with metastasis to cutaneous, subcutaneous, and nodal sites 2015-2023 at a high-volume cancer center were identified. Objective in-field treatment response was assessed by univariate analyses and multivariate logistic regression. In-field progression-free survival (PFS) was analyzed using multivariate Cox proportional hazards model. PFS and melanoma-specific survival (MSS) analyses were performed using Kaplan-Meier survival estimates. **RESULTS:** Eighty-two patients with advanced melanoma underwent treatment with T-VEC; the median age at T-VEC initiation was 74.5 (interquartile range [IQR] 65-81) years. Overall, median largest ITM was 10 (IQR 6-20) mm, and the median number of ITM lesions was 8 (4-12) with 38 (47.5%) patients defined as having high-burden of disease. Twelve (14.6%) patients had acral lentiginous (ALM); ALM patients more often had progressed beyond first-line immune checkpoint inhibitor (ICI) therapy (33.3% vs 8.6%, p 0.02) and were more likely to have undergone prior regional therapies (41.7% vs 12.9%, p 0.01) compared to other histology patients. ALM patients had lower objective response rates (ORR) compared to other histology patients (33.3% vs 78.6%, p 0.001). When stratified by clinical and treatment factors, including prior immunotherapy and regional therapies, sequence of therapies, and number of T-VEC injections, ALM patients had significantly worse in-field PFS (hazard ratio [HR] 3.60, p 0.02). When comparing non-responders (NR) to responders (PR/CR), there was no difference between ALM and non-ALM patients in out-of-field PFS (p 0.23 between NR; p 0.44 between PR/CR). MSS was significantly improved for non-ALM PR/CR as compared to non-ALM NR and ALM NR and PR/CR (p 0.003). **CONCLUSIONS:** While T-VEC has a high ORR among non-ALM patients, ALM patients have a lower ORR response to T-VEC and subsequent worse both in-field and out-of-field PFS. Even when ALM patients respond to T-VEC, MSS continues to be poor.

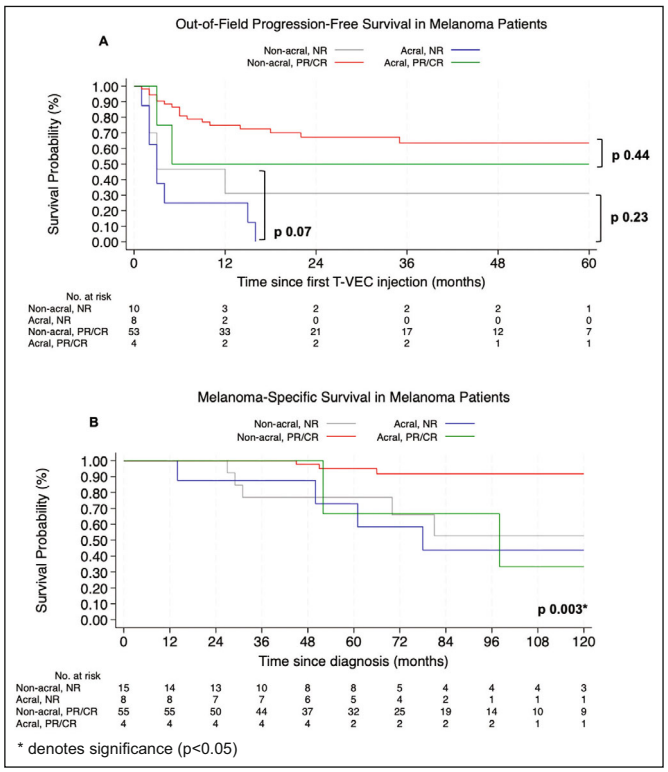


Figure. Kaplan-Meier survival estimates for out-of-field progression-free survival (A) and melanoma-specific survival (B) stratified by acral (ALM) and non-acral histology subtype and treatment response (NR, non-responder; PR/CR, partial or complete response).

P150. The use of radar-guided localization to identify metastatic melanoma after neoadjuvant therapy

Michelle M. Dugan, MD[1]; Kate E. Beekman, BS[2]; Danielle K. DePalo, MD[3]; Lily M. Parker, BS[4]; Kelly M. Elleson, MD[5]; John E. Mullinax, MD[6]; Amod A Sarnaik, MD[7]; Vernon K Sondak, MD[8]; Matthew C. Perez, MD[9]; Jonathan S. Zager, MD[10]

[1]Moffitt Cancer Center, Tampa, FL, US; [2]University of South Florida Morsani College of Medicine, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4]University of South Florida Morsani College of Medicine, Tampa, FL, US; [5]Moffitt Cancer Center, Tampa, FL, US; [6]Moffitt Cancer Center, Tampa, FL, US; [7]Moffitt Cancer Center, Tampa, FL, US; [8]Moffitt Cancer Center, Tampa, FL, US; [9]Moffitt Cancer Center, Tampa, FL, US; [10]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Radar-guided localization (RGL) is a nonradioactive, wireless technique to localize target lesions for resection using a small percutaneously placed reflector and a handheld probe intraoperatively. RGL can play a critical role in the setting of non-palpable or anatomically obscure lesions. This study describes RGL for patients undergoing neoadjuvant therapy (NEO) for metastatic melanoma. **METHODS:** A retrospective review of a prospectively collected database was conducted, including all stage III-IV melanoma patients who underwent NEO followed by metastatectomy with RGL. **RESULTS:** A total of 21 patients underwent RGL reflector placement and NEO. Median age was 66 years, and 8 (38%) were females. One patient is still on NEO, and 1 patient declined clinically while on NEO and was transferred to hospice. Of the 19 patients who underwent resection, reflectors were successfully retrieved in all 19 patients (100%) at a median of 112 days (range 7-282 days) after RGL placement. Operations included 15 index lymph node resections (78.9%), 2 therapeutic lymph node dissection (10.5%), and 2 soft tissue nodule resections (10.5%). Seventeen (89.5%) patients had a measurable response to NEO in the target lesion on imaging, and two patients (10.5%) demonstrated progression on NEO. Eleven lesions were palpable prior to NEO, with only 4 (36%) remaining palpable after NEO. Fifteen of 17 patients had a pathologic response to NEO: 14 patients (82.4%) had a major pathologic response (0 to <10% viable tumor) and 1 patient (5.9%) had a partial response (10-50% viable tumor); 2 patients (11.8 %) had a pathologic non-response; 2 patients had inconclusive surgical pathology. **CONCLUSIONS:**

RGL is an effective tool to ensure successful intraoperative localization and guided resection of target lesions after NEO. Two thirds of the index lesions became non-palpable after NEO and RGL allowed for accurate intraoperative identification and retrieval at any interval (days to months). Specific target lesion marking with fiduciary markers, and intraoperative identification and targeted resection allows the treating team to possibly de-escalate surgery, examine pathologic response, and dictate further therapy on an individualized basis.

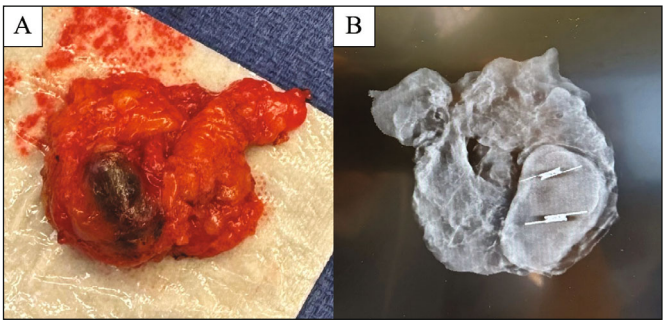


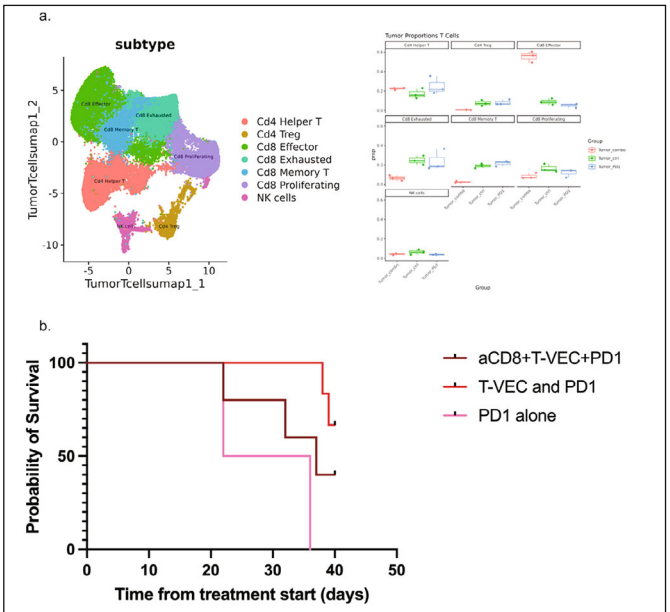
Figure 1. Gross surgical specimen (A) and intraoperative specimen radiograph confirming successful retrieval of two intra-tumoral radar-guided localization reflectors (B).

P151. T-VEC Shifts CD8 Phenotype to Reverse Anti-PD1 Resistance

Aparna Vancheswaran, MD[1]; Joe Frost, DPhil[2]; Fatima Salman, BS[3]; Cristian Mantilla-Rosa [4]; Emma Andretta, BS[5]; Jared Theriot, MD[6]; Jian Hu, PhD[7]; Danielle Vaithilingan, MS Biostatistics[8]; Xinjun Wang, PhD[9]; Alexander Rudensky, PhD[10]; Charlotte Ariyan, MD, PhD[11]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Metropolitan Hospital Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US; [11]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Though immune checkpoint inhibitor (ICI) therapy has revolutionized melanoma treatment, a significant percentage of patients continue to experience disease progression on ICI. We have shown previously that T-VEC, an oncolytic virus, synergizes with anti-PD1 to significantly enhance tumor control and confer survival advantage compared to anti-PD1 monotherapy in a murine melanoma model of anti-PD1 resistance. This study investigates the mechanisms reversing resistance to PD-1 blockade. **METHODS:** Mice were grafted subcutaneously with B16-OVA. After tumors grew out for 7 days, mice were treated with anti-PD1 for 14 days. Tumors grown out on anti-PD1 therapy were deemed resistant and then treated with continued anti-PD1, or T-VEC and anti-PD1 combination therapy, and tumor growth was followed. Singe cell RNA sequencing (ScRNAseq) and flow cytometry were used to phenotype the elicited anti-tumour immune response in the tumor and tumor draining lymph node(tdLN). **RESULTS:** By scRNAseq we observed that combination therapy shifted the phenotype of CD8 T cells from an exhausted profile to a cytotoxic, interferon signaling responsive effector phenotype (Figure 1a). We corroborated this by flow cytometry, where T-VEC expanded cytotoxic granzyme B expressing CD4 and CD8 T cells in both the tumors and tdLNs. Antibody depletion of CD8 T cells suppressed therapeutic benefit of T-VEC treatment demonstrated in reduction of median survival that was not reached in the T-VEC+anti PD1 group to 38 days with CD8 depletion (Figure 1b), confirming the essential role of CD8 T cells in this setting of anti-tumor immunity. Flow cytometry and scRNAseq also provided candidate cell populations which may further modulate tumor immunity in the setting of T-VEC treatment. Combination therapy significantly depleted immunosuppressive T regulatory (Treg) cells in the tumor, while stimulating a robust humoral response delineated by a greater proportion of germinal center B cells and plasma cells in the tdLN. **CONCLUSIONS:** We demonstrate that T-VEC can break the immunological stalemate in anti-PD-1 resistant melanoma, driving a functional anti-tumor cytotoxic effector CD8 T cell response. Concurrently, combination therapy induces a shift in CD4+ cells, a robust humoral immune cell response and intratumoral Treg depletion. Further functional studies are ongoing to elucidate the roles of these populations in the antitumor response, with the aim to identify pathways which would enhance efficacy of T-VEC in the context of anti-PD-1 treatment failure.



a) **Tumor T Cell Subclusters:** Combination PD1 and T-VEC (red bar) is associated with an increase in CD8 effector and loss of CD8 exhausted phenotype, as well as CD4 Tregs. b) **Kaplan-Meier curves:** Treatment with PD-1 was started at Day 0, while T-VEC treatment and anti-CD8 was started at Day 14. Survival endpoints included death or sacrifice for tumors greater than 100mm^2. Median survival was 37 days, 29 days, and not reached for CD8 depletion, anti-PD1, and T-VEC+anti PD1 groups respectively.

P152. 900 patients later: outcomes of cytoreduction and heated intraperitoneal chemotherapy for appendiceal neoplasms

Heidy Cos, MD[1]; Sydney Smith [2]; Perry Shen, MD[3]; Edward Levine, MD[4]; Konstantinos I. Votanopoulos, MD, PhD[5]

[1]Atrium Health Wake Forest Baptist Medical Center, Winston Salem, NC, US; [2]Atrium Health Wake Forest Baptist, Winston Salem, NC, US; [3]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [4]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [5]Wake Forest Institute for Regenerative Medicine, Winston-Salem, NC, US

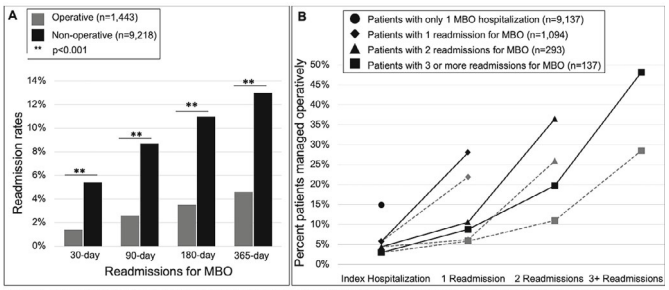
INTRODUCTION: Low PCI and completeness of cytoreduction have been shown to correlate with improved survival in patients undergoing CRS/HIPEC for appendiceal neoplasms. However, more data is needed regarding elements associated with greater completeness of cytoreduction and overall survival after CRS/HIPEC. **METHODS:** A prospectively maintained database of 1900 CRS/HIPEC procedures was reviewed and outcomes of 949 patients with appendiceal neoplasms were explored. Student's t-test, Fisher's Exact Test, and Chi-square estimates of the Log-Rank tests were used for applicable variables. Kaplan-Meier estimates were used to estimate overall survival (OS). P-values <0.05 were considered statistically significant. **RESULTS:** 949 patients underwent CRS/HIPEC for non-neuroendocrine appendiceal neoplasms at our institution from 1993 to 2023 and had appropriate follow-up. Most patients were female (55.9%) with a mean age of 55 years old. The average PCI was 16.4 (SD 9.8). When stratified by tumor grade, patients with low grade tumors and a PCI <15 were more likely to attain R0/R1 resection compared to those with low grade tumors and PCI >15 (85% vs 14%, p<0.001). In patients with high grade tumors, those with PCI <15 were also more likely to have an R0/R1 resection compared to PCI >15 (81.4% vs 18.6%, p<0.001). When stratifying by tumor pathology, 54% of patients with adenocarcinoma underwent R0/R1 resection, compared to 45% of patients with LAMN and 0.5% of patients with HAMN (p=0.044). In univariate analysis, performance status, hemoglobin and albumin were associated with higher likelihood of R0/R1 resection, p<0.001. In univariate analysis, higher PCI was correlated with incomplete resection (R2c), OR 1.3, CI 1.16-1.5, p<0.001 in patients with low grade disease. In patients with high grade disease, increasing PCI and EBL were associated with incomplete resection. PCI (OR 1.2, CI 1.1-1.4, p <0.001) and EBL (OR 1.0, CI 1.000 – 1. 001, p-0.030). Median OS after R0/R1 resection for patients with low grade disease was 226 months compared to 43 months in high grade disease, p<0.001. Median OS after R2c resection was 27 months for patients

with low grade disease compared to 12 months in high grade disease, p=0.018. **CONCLUSIONS:** Patients with appendiceal neoplasms and PCI <15 are more likely to attain an R0/R1 resection regardless of tumor grade. Higher albumin, hemoglobin and performance status are significantly associated with R0/R1 resection. Increasing PCI is correlated with incomplete resection (R2c). Meaningful survival is observed in low grade primary appendiceal neoplasms even with incomplete cytoreduction.

P153. A multi-state cohort study of hospital utilization and treatment modality for malignant small bowel obstruction

Rachael C Acker, MD[1]; Jasmine Hwang, MD[2]; Shane Williams, BSE[3]; James E Sharpe, MS[4]; Giorgos Karakousis, MD[5]; Heather Wachtel, MD, MSTR[6]; Rachel r Kelz, MD, MSCE, MBA[7]
[1]University of Pennsylvania, Philadelphia, PA, US; [2]University of Pennsylvania, Philadelphia, PA, US; [3]University of Pennsylvania, Philadelphia, PA, US; [4]University of Pennsylvania, Philadelphia, PA, US; [5]University of Pennsylvania, Philadelphia, PA, US; [6]University of Pennsylvania, Philadelphia, PA, US; [7]University of Pennsylvania, Philadelphia, PA, US

INTRODUCTION: Malignant bowel obstruction (MBO) is associated with significant morbidity, mortality, and impaired quality of life. Many patients develop recurrent obstruction requiring hospitalization and substantial practice variation in the management of MBO exists. We aimed to characterize the incidence, treatment modality, and outcomes of patients who present with MBO in a large, multi-state cohort. **METHODS:** We performed a retrospective cohort study of patients with a principal diagnosis of malignant small bowel obstruction hospitalized in 12 states using the Healthcare Cost & Utilization Project State Inpatient Database, 2016-2020. Study enrollment began at the time of the first hospitalization for MBO. A one year look back was used to exclude patients with a prior MBO hospitalization. All patients were enrolled for at least one year. Primary outcome was operative management. Secondary outcomes included discharge status, readmission, and interval operation. Categorical variables were analyzed with $\chi 2$ and Fisher's exact tests. **RESULTS:** Of 10,661 patients, 25.6% had a peritoneal malignancy, 21% gynecologic, 20.5% genitourinary, and 25.4% hepatobiliary cancer. Mean age was 67.5 years, 59.5% of patients were female with a mean of 3.4 comorbid conditions. A total of 1,443 received an operation at the index hospitalization (13.5%). Among the operative patients, 3.8% had an operation on their appendix, 38.5% on the small bowel, 54.2% lysis of adhesions, and 25.2% underwent gastrostomy tube placement. A higher proportion of operative patients compared to non-operative patients died during their index hospitalization (4.8% vs. 2.7%, p<0.001) and were discharged home with hospice (30.8% vs 17%, p<0.001). Operative patients had significantly lower 30-, 90-, 180-, and 365-day readmission rates compared to non-operative patients (Figure 1A). The use of operative treatment increases with the number of MBO readmissions (Figure 1B). The median time between hospitalizations shortens as patients are readmitted repeatedly (e.g. median 53 days [IQI 13, 170.5] between index hospitalization and 1st readmission compared to median 34 days [IQI 15, 112] between the 2nd and 3rd readmissions). **CONCLUSIONS:** There is variation in the number of hospitalizations patients experience before operative management with a trend toward deferring operation until multiple readmissions. These data will be helpful when counseling patients with MBO.



Panel A. Readmissions rates for recurrent malignant bowel obstruction by treatment assignment at the index hospitalization (e.g., operative vs. non-operative) over time excluding patients who died. P-values compare operative and non-operative groups within each readmission timeframe.
Panel B. Percent of patients managed operatively during each hospitalization for MBO. Dashed lines depict proportion of operative treatment during a specific admission and solid lines depict cumulative proportion of operative treatment over the course of multiple admissions. Pairs of lines reflect groups of patients by the total number of hospitalizations for MBO.

P154. A Novel Pre-clinical Model for Peritoneal Metastasis Utilizing Cross-Polarization Imaging for Independent Scoring

Vashti Bandy[1]; Jose Trevino[2]; Adam Khader[3]; Vignesh Vudatha[4]; Savannah Gregg[5]; Bhaumik Patel[6]; Leopoldo Fernandez[7]; Arunima Punjala, MD[8]
[1]Virginia Commonwealth University, Richmond, VA, US; [2]VCU Health, Richmond, VA, US; [3]Central Virginia VA Healthcare System, Massey Comprehensive Cancer Center, VCU School of Medicine, Richmond, VA, US; [4]VCU Health, Richmond, VA, US; [5]Richmond VA Medical Center, Richmond, VA, US; [6]Central Virginia VA Healthcare System, Massey Comprehensive Cancer Center, VCU School of Medicine, Richmond, VA, US; [7]VCU Health, Richmond, VA, US; [8]VCU Health, Richmod, VA, US

INTRODUCTION: Colorectal cancer (CRC) is treatable when localized, but survival drops sharply with metastasis, especially to the peritoneum (PM), which has the worst prognosis. The *Prodige 7* trial highlighted the lack of benefit from intraperitoneal chemotherapy, emphasizing the need for models replicating CRC PM biology for drug discovery. This study establishes reproducible CRC PM patient-derived xenografts (PDX) from a racially diverse population. **METHODS:** A racially & ethnically diverse patient population with CRC PM, including five (5) African-American patients, were recruited for a tissue collection study at a single tertiary center. Tumor samples were collected under sterile conditions and prepared for subcutaneous propagation into NOD.Cg-Prkdcscid/J mice (NSG). Peritoneal metastasis was induced via 1) intraperitoneal injection or 2) direct intraperitoneal implantation via laparotomy. Post-necropsy, PM index was calculated and pictures were obtained using a cross-polarization technique. **RESULTS:** We achieved >90% success in subcutaneous propagation of tumor samples *in vivo*, with tumors reaching 1000–1500 mm³. We report on four successful CRC PM PDX models. PDX1 was derived from a 62-year-old non-Hispanic White female (H22) with left-sided colon adenocarcinoma (KRAS G12V, APC E1408, SMAD4 A118V, MSS). A 3x3 mm subcutaneous tumor was minced and implanted intraperitoneally (IP). The mouse was euthanized after three weeks with a PM index of 20, indicating diffuse peritoneal involvement (Figure). PDX2, also from H22, involved injecting 90 µL of 5x10^6 cells in 50% Matrigel via laparotomy with micro-abrasions. At ten weeks, the PM index was 2, with tumors limited to the subhepatic and back regions. PDX3, from H22, involved direct IP injection of 135 µL of 15x10^6 cells in 10% Matrigel, resulting in a PM index of 10 at ten weeks (Figure), with tumors in the left diaphragm, subhepatic, subgastric, pelvic, and back regions. PDX4 was derived from a 60-year-old non-Hispanic White female (H32) with sigmoid adenocarcinoma (KRAS wild-type, MSS). Propogation was performed by suturing a 3x3 mm tumor fragment to the parietal peritoneum, yielding a PM index of 8 at ten weeks with development of parenchymal liver metastases. PM involved the right & left-sided diaphragm, and subgastric regions. Following initial PM index scoring, tumors from all four PDX models were captured with cross-polarization imaging to improve tumor visualization, allowing independent scoring by another investigator (Figure). **CONCLUSIONS:** Early findings show that CRC PM PDX models can be successfully established from a racially diverse population. Cross-polarization imaging improved tumor visualization and allowed independent PM index scoring by another investigator. We aim to expand our PDX library to better represent CRC PM heterogeneity and support drug development.

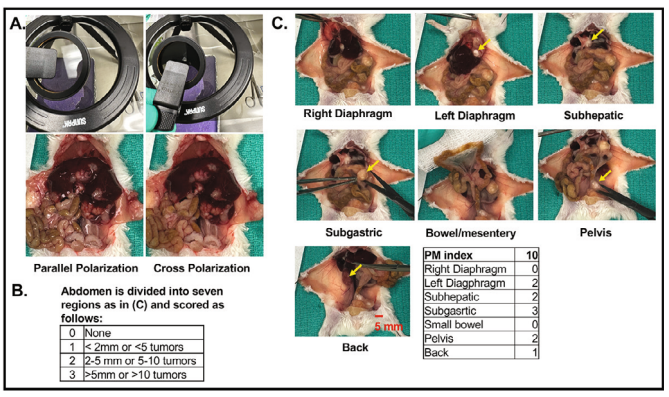
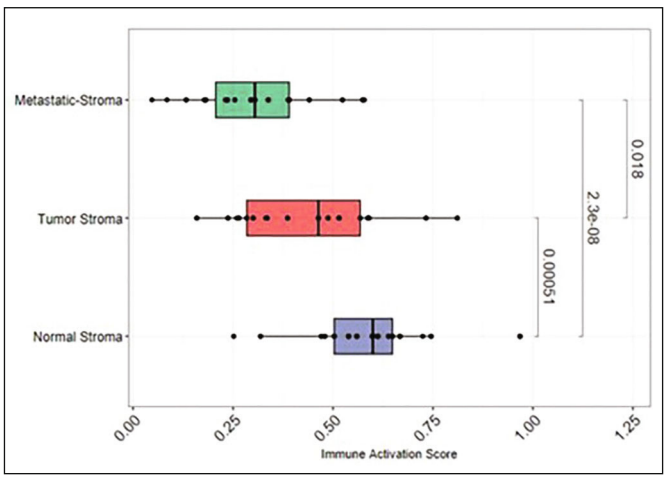


Figure. Establishing Colorectal Cancer (CRC) Peritoneal Metastasis (PM) Patient-derived Xenograft (PDX). A. Cross polarization technique conducted by the placement of polarizing film on the light source and a perpendicular polarizing film on the camera lens significantly improves glare. B. Scoring of PM index. C. Representative images of CRC PM PDX #3.

P155. Appendiceal cancers display immunosuppressed microenvironment and mucin infiltration on multiplex immunofluorescence analysis

Solomon O Alhassan, PhD[1]; Carlos I Ayala-Navarro, MD, PhD[2]; Margaret A Park, PhD[3]; Maria C Genilo Delgado[4]; Alexandra Tassielli[5]; John Mullinax, MD[6]; Michael Wach[7]; Iman Imanirad[8]; Jennifer B. Permuth[9]; Sean P Dineen[10]
[1]H Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]H Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [4]H Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [5]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [6]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [7]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [8]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [9]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [10]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Appendiceal cancers are rare malignancies of the gastrointestinal tract with unique histological features and clinical behaviors. The tumor mutational burden of appendiceal tumors is low, however, specific details of the immune microenvironment of appendiceal cancers remain poorly understood. In turn, this has negatively impacted the development of immunotherapy for these patients.
METHODS: A tissue microarray was created consisting of matched normal appendix, primary appendiceal tumor and peritoneal metastases from 14 patients. We used multiplex immunofluorescence (mIF) to characterize the immune microenvironment in the stroma of the matched tissues. A total of 17 immune and stromal/tumor cell markers were quantified. The percentage of cells positive for each marker were analyzed to characterize differences between sites. We also computed an immune activation score, derived from abundance of CD8+ T-cells and CD68+/CD163+ M2 macrophages, to characterize the overall immunologic activity of a compartment.
RESULTS: A total of 14 patients including 10 females constituted the cohort. The age range was 38-67 years. Multiplex immunofluorescence identified a number of significant differences in the composition of the tumor immune microenvironment. CD163+ and CD68+CD163+ cells were significantly elevated in the metastatic stroma compared to normal appendix (19.8 ± 2.33% vs 12.7 ± 2.87% $p < 0.015$ and 9.27 ± 1.25% vs 4.13 ± 0.68%, $p < 0.0014$ respectively). CD8+ T Cells less abundant in metastatic tumors compared to normal appendix (4.98 + 1.1% vs. 7.35 + 1.2%; $p < 0.05$). Immune checkpoint expression was significantly reduced in metastatic tumor microenvironment compared to normal appendix (PD-1: 0.04 ±0.02% vs 1.1 ±0.36%, $p < 0.01$) (TIGIT: 19.3 ±3.6% vs. 35.3 ±5.9%, $p < 0.05$). A composite immune activation score was significantly higher in the normal appendix compared to either primary tumor or the metastatic sites (0.60 ± 0.02; 0.48±0.04; 0.47±0.06; $p < 0.0001$ for both comparisons).
CONCLUSIONS: The study underscores the critical role of the immune microenvironment in appendiceal cancers. Our data support an interpretation of metastatic sites as containing a present but inactive immune infiltrate. This data can assist in determining appropriate investigational approaches for immune oncology in appendiceal tumors. Additionally, the differential expression of immune markers and the immune activation score could serve as valuable biomarkers to stratify patients for conventional immunotherapy approaches (i.e. checkpoint inhibition).



P156. Characteristics and Outcomes of External Referral Patients Undergoing Cytoreductive Surgery at an International Peritoneal Surface Malignancy Program

Edward A Joseph, MBBS[1]; Muhammad Muntazir Mehdi Khan, MBBS[2]; Gordon Hua[3]; Catherine Lewis[4]; Patrick Wagner[5]; David Bartlett[6]; Casey J. Allen, MD[7]
[1]Allegheny Health Network, Pittsburgh, PA, US; [2]Allegheny Health Network, Pittsburgh, PA, US; [3]Drexel University, Philadelphia, PA, US; [4]Allegheny Health Network, Pittsburgh, PA, US; [5]Allegheny Health Network, Pittsburgh, PA, US; [6]Allegheny Health Network, Pittsburgh, PA, US; [7]Allegheny Health Network, Pittsburgh, PA, US

INTRODUCTION: Given the limited number of high-volume centers offering cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC), patients often seek care outside their health systems. To understand the implications of care for external referral patients, we conducted a comprehensive assessment of an international peritoneal surface malignancy (PSM) referral program. **METHODS:** We analyzed patients with PSM treated at Allegheny Health Network from January 2022 to March 2024. Patients were categorized into two groups: in-system (IS), consisting of those referred from within our integrated network, and out-of-system (OOS), representing patients referred from outside our health system. Patient and disease characteristics, surgical outcomes, and institutional costs were compared between the two groups. **RESULTS:** We identified 171 patients who underwent CRS±HIPEC at our institution. The mean age was 56 ± 12 years, 57% were female, and 92% were White. The most common histological diagnoses included non-invasive appendiceal neoplasms (21%), adenocarcinoma of the appendix (32%), adenocarcinoma of the colon (21%), and ovarian carcinoma (8%). Overall, 59% (n=101) of patients were OOS. Compared to IS patients, OOS patients had a higher proportion of poorly differentiated adenocarcinoma of the appendix/colon (33% vs 17%, $p=0.005$), higher peritoneal cancer index scores, required longer operative times, and hospital stays (all $p<0.050$). There was no difference in completeness of cytoreduction (CC) scores, readmission rates, Clavien-Dindo complications, or 90-day mortality rates between IS and OOS patients (all $p>0.050$). OOS patients incurred higher direct institutional costs ($p<0.001$). Of all OOS patients, 72 (71%) were originally unable to achieve a complete cytoreduction at an outside institution (54 not offered surgery, 12 were aborted intraoperatively, 6 underwent incomplete cytoreduction). Of these, the majority subsequently achieved complete cytoreduction (85%, n=61) or surgical palliation (10%, n=7) at our facility. **CONCLUSIONS:** Compared to IS patients, OOS patients present with a higher disease burden, higher rate of high-grade tumor histology, require more extensive surgery, and incur longer hospital stays with higher costs of care. The majority of OOS patients previously deemed unresectable at outside institutions were able to achieve complete cytoreduction at a high-volume PSM referral program.

Table. Demographic and clinical characteristics of patients undergoing cytoreductive surgery at an international peritoneal surface malignancy program.

	In-System (n=70)	Out-of-System (n=101)	p-value
Age[a]	58.9±12.2	53.8±12.0	0.003
Sex			
Male	24 (34.3%)	50 (49.5%)	0.048
Female	46 (65.7%)	51 (50.5%)	
Race			
White	64 (91.4%)	93 (92.1%)	0.859
Black	2 (2.9%)	1 (1.0%)	
Asian	2 (2.9%)	3 (3.0%)	
Hispanic	1 (1.4%)	1 (1.0%)	
Other	1 (1.4%)	3 (3.0%)	
Histology			
LAMN/HAMN	11 (15.7%)	25 (24.8%)	0.005
Appendiceal adenocarcinoma			
Well to moderately differentiated	7 (10.0%)	19 (18.8%)	
Poorly differentiated	6 (8.6%)	23 (22.8%)	
Colon adenocarcinoma			
Well to moderately differentiated	8 (11.4%)	12 (11.9%)	
Poorly differentiated	6 (8.6%)	10 (9.9%)	
Ovarian carcinoma			
Low grade serous	3 (4.3%)	0 (0.0%)	
High grade serous	9 (12.9%)	1 (1.0%)	
Borderline mucinous	3 (4.3%)	1 (1.0%)	
Small Bowel Adenocarcinoma	1 (1.4%)	1 (1.4%)	
Mesothelioma	4 (5.7%)	2 (2.0%)	
Sarcoma	3 (4.3%)	1 (1.0%)	
High grade mullerian carcinoma	2 (2.9%)	0 (0.0%)	
Other	7 (10.0%)	6 (5.9%)	
Prior cytoreduction at outside facilities			
CRS not offered	n/a	54 (53.5%)	
Aborted intraoperatively	n/a	12 (11.9%)	
CC0/1	n/a	29 (28.7%)	
CC2/3	n/a	6 (5.9%)	
Cytoreduction at our facility			
Total PCI[b]	13.0 (6.0-18.0)	18.5 (12.0-29.0)	<0.001
CC score at our facility			
CC0/1	57 (87.7%)	85 (85.0%)	0.626
CC2/3	8 (12.3%)	15 (15.0%)	
Length of stay (days)[b]	9.0 (6.0-15.0)	14.0 (9.0-21.0)	<0.001
Operative Time (minutes)[b]	321 (214-490)	518 (381-630)	<0.001
Estimated blood loss (mL)[b]	400 (250-800)	600 (300-1100)	0.048
Readmissions	11 (15.7%)	21 (20.8%)	0.403
Clavien-Dindo complication grade			
CD0-2	50 (71.4%)	64 (63.4%)	0.271
CD≥3	20 (28.6%)	37 (36.6%)	
90-day Mortality	0 (0.0%)	4 (4.0%)	0.092
90-day Direct institutional cost (USD)[b]	58,375 (35,363-82,635)	76,620 (56,527-99,072)	<0.001
90-day Indirect institutional cost (USD)[b]	20,743 (12,690-35,887)	30,788 (20,581-40,037)	<0.001

CD: Clavien–Dindo; LAMN: Low grade appendiceal mucinous neoplasm; HAMN: High grade appendiceal mucinous neoplasm; CRS: Cytoreductive surgery; CC: Completeness of cytoreduction score; PCI: Peritoneal Carcinomatosis Index; USD: United States Dollars; p<0.050 is statistically significant; [a] Reported as mean ± standard deviation; [b] Reported as median (inter-quartile range)

P157. Clinical outcomes of high-grade appendiceal mucinous neoplasms

Ashlee Seldomridge, MD[1]; Yi-Ju Chiang[2]; Paul Mansfield, MD[3]; Yun SongMD[4]; Melissa Taggart, MD[5]; Wai Chin Foo[6]; Jean P Shen[7]; Keith Fournier, MD[8]; Beth Helmink, MD, PhD[9]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [4]University of Texas MD Anderson Cancer Center, Houston, TX, US; [5]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [6]University of Texas MD Anderson Cancer Center, Houston, TX, US; [7]University of Texas MD Anderson Cancer Center, Houston, TX, US; [8]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [9]MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Appendiceal mucinous neoplasms (AMNs) are rare tumors with dysplastic epithelium exhibiting "pushing," non-infiltrative invasion of the appendiceal wall and abundant mucin production. Rupture can cause mucinous ascites and/or peritoneal implants. Most AMNs have low-grade morphologic and low-grade cytologic features (low-grade appendiceal mucinous neoplasm, LAMN). High grade cytologic atypia occurs occasionally and is now classified (as of 2016) as high-grade appendiceal mucinous neoplasms (HAMNs). Clinical behaviors of HAMNs is not well-understood. **METHODS:** A retrospective review of patients diagnosed with HAMNs (2016-2024) at a single quaternary care center was conducted. Data was extracted from chart review, and disease features were summarized with descriptive statistics. Kaplan-Meier analysis was used for survival. **RESULTS:** A total of 144 patients with HAMN were identified. Of these, 97 (67.3%) represented HAMN only, while 47 (32.6%) had invasive adenocarcinoma arising from HAMN (70.2% moderately/poorly-differentiated vs 27.7% well-differentiated). Peritoneal dissemination occurred in 84 (86%) patients with pure HAMN. Peritoneal disease histology was acellular mucin (36%), cellular mucin (3.1%), well-differentiated adenocarcinoma (15%) and moderately/poorly-differentiated adenocarcinoma (32.1%). Recurrence-free (RFS) was influenced by peritoneal metastasis histology. Acellular mucin resulted in 100% RFS and OS after definitive surgery, with median follow-up of 3.9 years; 40.9% underwent CRS and HIPEC. By contrast, RFS for cellular mucin/well-differentiated adenocarcinoma and moderately/poorly differentiated adenocarcinoma was 59.0% and 22.8% at 5 years, respectively (HR 2.5 [95% CI 1.0-6.2], p=0.05). **CONCLUSIONS:** This cohort represents the largest described for HAMNs, which is a new diagnostic category as of 2016. Outcomes are largely dependent on peritoneal metastasis histology. A significant portion of HAMN patients develop high-grade peritoneal metastases, though those with acellular mucin exhibit excellent RFS and OS, similar to LAMNs. Invasive adenocarcinoma arising from HAMN warrants further investigation as a potential precursor to adenocarcinoma.

P158. Collagenolysis by Enterococcus faecalis induces DDR1 signaling, proliferation and immune evasion in colorectal cancer

Richard A. Jacobson[1]; Sean P Dineen[2]; John Mullinax, MD[3]; Michelle McGee[4]; Rachel Wolansky[5]; Timothy Nywening[6]; Timothy Yeatman[7]; Jason Fleming[8]

[1]University of South Florida, Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [4]University of South Florida, Tampa, FL, US; [5]University of South Florida, Tampa, FL, US; [6]University of South Florida, Tampa, FL, US; [7]University of South Florida, Tampa, FL, US; [8]UT Southwestern, Dallas, TX, US

INTRODUCTION: The gut pathogen *Enterococcus faecalis* is implicated in progression of colorectal cancer (CRC), yet the mechanism is unclear. The discoidin domain receptor-1 (DDR1) pathway is activated by cleaved collagen and leads to immune evasion by CRC. Since the principal virulence factors of *E. faecalis* are collagenolytic, we measured the effect of *E. faecalis* on immune evasion by CRC peritoneal metastases and probed underlying pathways. **METHODS:** Collagenolysis and DDR1 activation were measured using kinetic fluorogenic assays and immunoblotting, respectively. We employed a mouse model of metastatic CRC with syngeneic CT26 cells seeded into the peritoneum of balb/c mice (4mice/group) under three experimental conditions: 1) sterile CT26 cells (Sterile); 2) CT26 cells cultured with *E. faecalis* strain V583 (EF), or 3) CT26 cells cultured with an EF mutant strain deficient in the collagenolytic factors GelE and SprE (**ΔΔ**). **RESULTS:** Kinetic assays revealed increased collagenolysis when CT26 cells were incubated with EF but not ΔΔ (Fig 1A). Western blot of CT26 cells incubated with bacterial supernatant demonstrated increased DDR1 phosphorylation at 24 hours and increased cleaved C terminal domain at 72 hours with EF but not Δ (Fig 1B). Cell proliferation is a downstream effect of DDR1 signaling. MTT assays showed increased CT26 proliferation after incubation with EF supernatant compared to sterile media (Fig 1C). DDR1 signaling induced endocytosis of cleaved collagen in pancreatic cancer. To measure this downstream effect in CRC we used fluorescence cytometry and observed increased cytoplasmic staining of cleaved collagen when CT26 cells were incubated with EF supernatant vs. controls (Fig 1D). Sterile, EF and Δ-seeded tumors were harvested from the peritoneal cavity 20 days after surgery. Tumor bulk was similar across treatment groups (Fig 1E). Immunofluorescence illustrated the distribution of immune cells in the tumor microenvironment (Fig 1F). EF tumors had increased total CD4+ and CD4+FoxP3+ (Treg) cells/mm2, and approached significance in F/480+ macrophages compared to sterile tumors (Fig 1G). **CONCLUSIONS:** Our data demonstrate bacterial-mediated collagenolysis induces DDR1 activation and is associated with impaired antitumor immunity in CRC peritoneal metastases. Presence of EF and DDR1 signaling were implicated in immune evasion and progression of CRC, but the mechanistic link to bacterial collagenolysis is novel. This study supports the conclusion that intratumoral collagenolytic bacteria directly contribute to tumor progression through targetable pathways

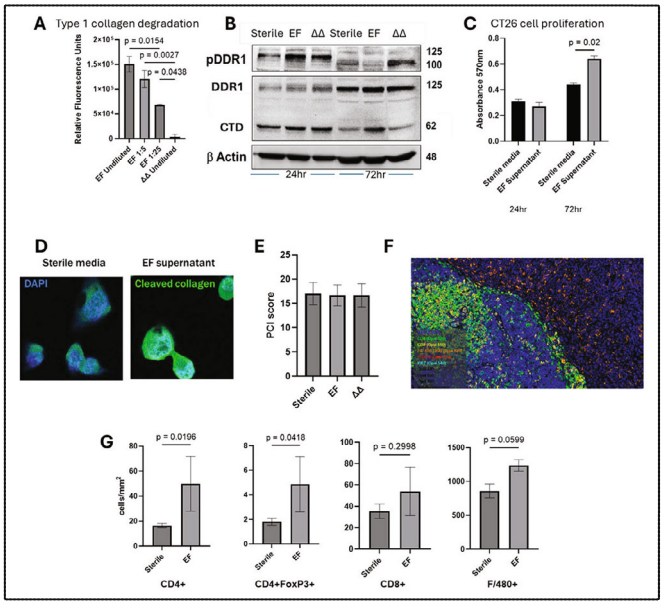


Figure 1. A) Collagen degradation assay of CT26 cells incubated with serial dilutions of EF or ΔΔ supernatant demonstrating increased collagenolysis in a fashion dependent on the presence of bacterial SprE and GelE B) Western blot of CT26 cells incubated with EF or ΔΔ supernatant, with EF exposure leading to increased phosphorylation of DDR1 at 24 hours, and cleavage of DDR1 by 72 hours indicated by increased staining of the 62kDA C terminal domain (CTD). C) MTT assay demonstrating increased proliferation of CT26 cells 72 hours after exposure to EF supernatant. D) Fluorescence cytometry of CT26 cells exposed to either EF supernatant or sterile media showing increased uptake of fluorescent cleaved type I collagen. E) Measured peritoneal carcinomatosis index at day 20 endpoint of mice given tumors that were either sterile, seeded with EF or ΔΔ. F) Example immunofluorescence panel of harvested tumor, stained for CD4 (green), CD8 (yellow), FoxP3 (red) and F/480 (orange) with a DAPI (blue) counterstain. G) Counts of CD4+, CD4+FoxP3+ (Treg), CD8+ and F/480+ (macrophage) taken from images generated in (F).

P159. Decision Regret and Quality of Life in Caregivers of Patients with Appendiceal Cancer Undergoing Hyperthermic Intraperitoneal Chemotherapy

Lauren Marek, MD[1]; Alexander Graves[2]; Mikaela Kosich[3]; Shane Pankratz[4]; Shiraz Mishra[5]; Yazmin Irazoqui-Ruiz[6]; Matthew C Hernandez[7]; Erin P. Ward, MD[8]; Sarah Popek[9]; Vinay K Rai[10]; Lara McKean Baste[11]; Bridget Fahy[12]; Alissa Greenbaum, MD[13]

[1]UNM Department of Surgery, US; [2]Sunrise Hospital, Las Vegas, NV, US; [3]University of New Mexico Comprehensive Cancer Center, Albuquerque, NM, US; [4]University of New Mexico Comprehensive Cancer Center, Albuquerque, NM, US; [5]University of New Mexico Comprehensive Cancer Center, Albuquerque, NM, US; [6]University of New Mexico Comprehensive Cancer Center, Albuquerque, NM, US; [7]University of New Mexico Comprehensive Cancer Center, Albuquerque, NM, US; [8]University of Utah- Huntsman Cancer Institute, Salt Lake City, UT, US; [9]University of New Mexico Comprehensive Cancer Center, Albuquerque, NM, US; [10]University of New Mexico Comprehensive Cancer Center, Albuquerque, NM, US; [11]University of New Mexico Comprehensive Cancer Center, Albuquerque, NM, US; [12]University of New Mexico Comprehensive Cancer Center, Albuquerque, NM, US; [13]University of New Mexico Comprehensive Cancer Center, Albuquerque, NM, US

INTRODUCTION: A recent study demonstrated that patients with appendiceal cancer (AC) undergoing hyperthermic intraperitoneal chemotherapy (HIPEC) had low overall levels of regret regarding their procedure. However, those who expressed regret had worse quality of life (QOL) and higher rates of surgical complications. The aim of this study was to assess the correlation between decision regret and QOL in caregivers of patients with AC who underwent HIPEC. **METHODS:** An anonymous, IRB-exempt survey was administered to caregivers through a collaboration with the Appendix Cancer and Pseudomyxoma Peritonei Research Foundation. Caregivers with completed demographic information and the Zarit-Burden Interview (ZBI-12) were included in the analysis. The Decision Regret Scale (DRS) was employed to measure levels of regret, PROMIS-29 v 2.0 for QOL, and the FACT-COST to assess financial toxicity. **RESULTS:** Forty caregivers met inclusion criteria. As overall DRS scores were very low (mean [SD] 6.0 [5.6], regret was analyzed as a continuous variable. Most respondents were spouses (n=22, 55.0%), followed by children (n=9, 22.5%), 97.5% were non-Hispanic White, with 52.5% being male and 77.5% being married. Regarding income, 35% of caregivers reported < $74,062 annually, and 60% traveled more than 50 miles for the patient to undergo HIPEC. No patient demographic, tumor or surgical outcomes were related to caregiver regret, other than if the patient did not receive a complete cytoreduction (DRS 10 vs. 4 for complete; p=0.002). Financial toxicity did not correlate with regret (mean [SD] FACT-COST 25.9 [11.4]; p=0.221). Regret was significantly associated with worse QOL in all categories (Spearman correlation coefficients all greater than 0.49 in absolute value, maximum of 0.76, all p<0.01), as well as increased caregiver burden (mean ZBI-12 16.3 ± 8.8; p=0.042, qualifying as moderate burden). Caregivers reported being frequently stressed (55.0%), with some reporting losing control of their life because of their relative's illness (30%). **CONCLUSIONS:** Caregivers of patients with AC had overall very low levels of decision regret regarding their loved one's HIPEC procedure. Higher caregiver burden and worse QOL were strongly correlated with regret. Future studies will explore opportunities to improve support and resources for caregivers of patients undergoing HIPEC, both perioperatively and in the long-term.

P160. Experiences and Decisional Outcomes After Cytoreductive Surgery for Peritoneal Surface Malignancy: A Survey from the DECISIVE Study

Elizabeth L. Godfrey[1]; Safraz A. Hamid[2]; Meghan Lindsay[3]; Ardaman Shergill[4]; Rachel A. Greenup[5]; Kiran Turaga[6]

[1]Yale New Haven Health/Yale School of Medicine, New Haven, CT, US; [2]Yale School of Medicine, New Haven, CT, US; [3]Yale School of Medicine, New Haven, CT, US; [4]University of Chicago Medical Center, Chicago, IL, US; [5]Yale School of Medicine, New Haven, CT, US; [6]Yale School of Medicine, New Haven, CT, US

INTRODUCTION: Individuals with peritoneal surface malignancies considering cytoreductive surgery (CRS) face substantial barriers to informed, value-concordant decision-making. We sought to characterize decisional needs and priorities for this population. **METHODS:** In 2024, the DECISIVE Study (Decisions and Expectations in Cytoreduction: Informed Surgery Incorporating Value Exploration) was launched in partnership with patient advocates and key stakeholders. We developed a comprehensive survey including validated instruments addressing care and decisional outcomes, and study-specific items exploring decisional and treatment experiences, priorities, and needs. Individuals with gastrointestinal cancer + peritoneal involvement who considered cytoreductive surgery as a treatment and/or their caregivers were eligible to participate. The survey was distributed to a convenience sample of two patient organizations for individuals with appendiceal tumors. **RESULTS:** To date, 52 complete and 91 partial responses have been recorded. Overall, 82% of respondents reported satisfaction with their decision. Among caregivers (n=10), decisional satisfaction was much lower for those related to deceased individuals (n=4), with 50% reporting decisional uncertainty or regret. Although most respondents (>75%) reported adequate counseling about preparation for surgery and recovery, half reported inadequate counseling about treatment outcomes. Study participants most highly prioritized cancer control (e.g. removing tumor, slowing progression) and survival when making surgical decisions, followed by quality of life and symptom control. Concerns around affordability and burden of care were polarized; half of participants highly prioritized concerns related to financial and time toxicity of treatment, while others prioritized them minimally. Participants highlighted emotional symptoms of their cancer (53.5%) and time pressure (35.7%) as the most significant barriers to high quality decision making. Qualitative review of free-responses identified a desire for decision support tools addressing the following key themes: (i) support for self-efficacy (support group contacts, reliable references, and clear treatment guidelines), (ii) evidence-based prognostic data based on disease characteristics; and (iii) discussion guides. Notably, participants reported desire for decision support to counteract contradictory information received from non-specialists that led to distress and delayed care. **CONCLUSIONS:** The DECISIVE survey identified a critical need for development of high-quality decision support tools for patients and caregivers considering CRS, as well as preliminary constructs to inform this work.

P161. External Validation of Basingstoke Prognostic Nomogram in Patients with Mucinous Appendix Cancer Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy

Sergei Iugai, MD[1]; Armando Sardi, MD FACS[2]; Mary Caitlin King, BS[3]; Vladislav Kovalik, MD MSPH[4]; Vladimir Milovanov, MD[5]; Luis Felipe Falla-Zuniga, MD[6]; Kseniia Uzhegova, MD[7]; Carol Nieroda, MD[8]; Vadim Gushchin, MD FACS[9]

[1]Mercy Medical Center, Baltimore, MD, US; [2]Mercy Medical Center, Baltimore, MD, US; [3]Mercy Medical Center, Baltimore, MD, US; [4]Mercy Medical Center, Baltimore, MD, US; [5]Basingstoke and North Hampshire Hospital, Basingstoke, GB; [6]Mercy Medical Center, Baltimore, MD, US; [7]Mercy Medical Center, Baltimore, MD, US; [8]Mercy Medical Center, Baltimore, MD, US; [9]Mercy Medical Center, Baltimore, MD, US

INTRODUCTION: Despite an existing consensus on cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) in mucinous appendix cancer (MAC), patient prognosis after the procedure remains variable. To address this, the Peritoneal Malignancy Institute Basingstoke (PMIB) developed a nomogram to predict survival based on perioperative factors. We aimed to externally validate PMIB's model and assess its performance in a United States patient population. **METHODS:** We performed an external validation of PMIB's model using a single-center prospective database (1999-2023). The validation cohort (VC) included MAC patients who underwent complete (CC-0/1) CRS/HIPEC. Perioperative characteristics were described. The Kaplan Meier method and Cox regression were used for survival analysis. Model discrimination was assessed by calculating C-index. Model calibration was performed for progression-free (PFS) and overall (OS) survival at 3 and 5 years with sensitivity analysis for low-grade vs high-grade MAC. **RESULTS:** VC included 311 patients. Median age was 55 years (interquartile range [IQR]: 46-55). Low-grade mucinous carcinoma peritonei (LGMCP) (n=127, 40.8%) was the most common histology. Median peritoneal cancer index (PCI) was 28 (IQR: 13-35), while 201 (64.6%) patients had PCI≥22. Most patients had normal tumor markers (TM: CA19.9, CA125, CEA) (n=181, 58.2%), and 52 (16.7%), 46 (14.8%), and 32 (10.3%) had an elevation of 1, 2 or 3 TM, respectively. Partial gastrectomy was performed in 62 (19.9%) patients. After a median follow-up of 91 months, 3- and 5-year PFS was 66% and 60%, respectively. The 3- and 5-year OS was 81% and 74%, respectively. Among factors included in the model, PCI and tumor grade were significantly associated with both OS and PFS, while age was associated with OS only and elevation of 2 or more TM with PFS only. C-index for 3/5-year PFS was 0.780 and 0.785, while for 3/5-year OS, it was 0.742 and 0.753, respectively. Calibration plots showing the correlation between predicted vs observed survival probabilities (SP) were presented. Sensitivity analysis identified substantial differences in SP for low vs high-grade MAC with no overlap between OS calibration curves at 3 or 5 years (Figure 1). **CONCLUSIONS:** Despite a tendency to overestimate survival, PMIB's model shows good predictive accuracy for both PFS and OS. Given the high prognostic significance of tumor histology, we discourage conducting further studies that analyze biology of appendix neoplasms as a single disease entity.

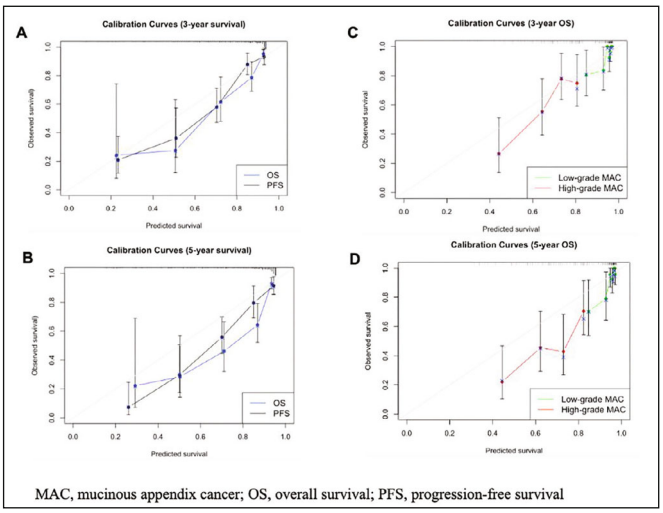


Figure 1. Calibration curves for observed vs predicted survival probability at 3-and 5-years (A,B) and sensitivity analysis for overall survival in subgroups of low-grade vs high-grade MAC (C,D).

P162. Feasibility and Accuracy of Sentinel Lymph Node Biopsy (SLNB) in Primary Epithelial Ovarian Cancer (PEOC) (FIGO Stage I-III) - A Prospective Pilot Study

Ashutosh Mishra, MCh, FACS[1]; Pranjal Banthia, MS[2]; Babul Bansal[3]; M D Ray, MS, FACS, FRCS[4]

[1]All India Institute of Medical Sciences, New Delhi, New Delhi, Delhi, IN; [2]AIIMS, New Delhi, New Delhi, Delhi, IN; [3]AIIMS, New Delhi, New Delhi, Delhi, IN; [4]AIIMS, New Delhi, New Delhi, Delhi, IN

INTRODUCTION: Sentinel Lymph Node Biopsy (SLNB) offers a minimally invasive approach for nodal staging in primary epithelial ovarian cancer (PEOC). This study aims to assess the feasibility, safety, and accuracy of SLNB using a dual dye technique (Indocyanine Green and Methylene Blue) in PEOC (FIGO Stage I-III). Establishing the diagnostic accuracy of SLNB could refine surgical management, minimizing the need for extensive lymphadenectomy. **METHODS:** This prospective study enrolled 30 patients with suspected PEOC (FIGO Stage I-III) undergoing surgery at Dr. BRAIRCH AIIMS. SLNB was performed using dual dyes injected at the ovarian pedicle, followed by systematic lymphadenectomy. All detected sentinel lymph nodes (SLNs) underwent ultra staging with multiple histological sections and immunohistochemical staining. Key outcomes included detection rate, sensitivity, specificity, and negative predictive value (NPV). **RESULTS:** The SLNB detection rate was 80%, with a sensitivity of 89% and specificity of 90.48%. The NPV reached 95%, indicating the technique's accuracy in identifying node-negative patients. SLNB identified micrometastases in 14% of cases not detected by routine imaging, leading to upstaging in these patients. The combined procedure allowed for effective internal validation without additional morbidity compared to systematic lymphadenectomy alone. There were no significant differences in complications between the two groups. **CONCLUSIONS:** SLNB using dual dye in PEOC is feasible and provides high sensitivity and specificity for nodal staging, allowing for accurate identification of node-negative patients. While this study did not directly demonstrate reduced operative time or blood loss, SLNB shows promise as an alternative to systematic lymphadenectomy in selected patients, reducing surgical morbidity. Further studies are needed to validate these findings in larger cohorts.

P163. Five Year Experience with Perioperative and Oncological Outcomes of Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) in Israel

Dan Assaf[1]; Haggai Benvenisti[2]; Eyal Mor[3]; Douglas Zippel[4]; Aviram Nissan[5]; Mohammad Adileh[6]; Almog Ben-Yaacov[7]

[1]Sheba Medical Center, Ramat Gan, IL; [2]Sheba Medical Center, Ramat Gan, IL; [3]Sheba Medical Center, Ramat Gan, IL; [4]Sheba Medical Center, Ramat Gan, IL; [5]Chaim Sheba Medical Ceter, Ramat-Gan, IL; [6]Hadassah Medical Center Mount Scopus, Jerusalem, IL; [7]Chaim Sheba Medical Center, Ramat Gan, IL

INTRODUCTION: Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) is increasingly utilized in the treatment of peritoneal metastases. It has been demonstrated to be safe and well-tolerated. In this study we report our 5-year experience in patients with peritoneal carcinomatosis undergoing PIPAC at our institution. **METHODS:** A retrospective analysis of a prospectively maintained peritoneal surface malignancies database between 2019 and 2024 was performed. Patient demographics, primary tumor, perioperative and oncological outcomes were analyzed. **RESULTS:** Between 2019-2024, 120 patients had 284 PIPAC procedures, with a median of 2 procedures per patient (range 1-14). The median age was 62.6 years (range 28-85), 58.3% were females with median PCI of 20 (range 1-39). During a median follow up of 8 months (range 2-58) 23 patients (19.2%) had tumor regression enabling a cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC), of whom 14 patients (60.9%) have completed successfully. There was one intraoperative complication (0.35%) and one severe postoperative complication (0.35%). The estimated median overall survival was 10 months (95% CI 7.8-12.2), the estimated median progression free survival was 5 months (95% CI 3.5-6.5). Multivariate analysis showed that the number of PIPAC procedures performed (p=0.006), PCI (p<0.001) and primary tumor pathology (p<0.001) were independently significantly associated with OS. The number of PIPAC procedures performed (p=0.021), and primary tumor pathology (p=0.009) were independently significantly associated with PFS. **CONCLUSIONS:** Our five-year experience describes the perioperative and oncologic outcomes of PIPAC in the management of peritoneal metastases. PIPAC procedures were performed with low rates of intraoperative and postoperative complications. Nineteen percent of the cohort was referred to CRS/HIPEC following PIPAC surgery. These results demonstrate the safety and efficacy of PIPAC in the treatment strategy of peritoneal metastases.

P164. Genomic alterations in the skeletal muscle of patients with appendiceal peritoneal carcinomatosis

Vignesh Vudatha[1]; Devon Freudenberger[2]; Jeremy Ducharme[3]; Arunima Punjala, MD[4]; Vashti Bandy[5]; Andrew Judge[6]; Jose Trevino[7]
[1]VCU Health, Richmond, VA, US; [2]VCU Health, Richmond, VA, US; [3]UF Health, Gainesville, FL, US; [4]VCU Health, Richmod, VA, US; [5]virginia Commonwealth University, Richmond, VA, US; [6]UF Health, Gainesville, FL, US; [7]VCU Health, Richmond, VA, US

INTRODUCTION: Patients with peritoneal carcinomatosis (PC) can experience significant morbidity and mortality secondary to cancer associated cachexia. This is further exacerbated by decreased gastrointestinal motility, systemic chemotherapy, and ascites. The objective of this study was to characterize the genomic events involved in cachexia in the setting of appendiceal peritoneal disease. **METHODS:** Patients with peritoneal carcinomatosis of appendiceal origin undergoing surgery (either diagnostic laparoscopy or cytoreductive surgery) at a single institution were identified. Measures of cachexia including skeletal muscle index (SMI), muscle radiation attenuation (MRA), and 6-month weight loss were obtained at time of diagnosis. Rectus muscle samples were obtained at the time of surgery and RNA-seq was performed to explore pathways related to cachexia and weight loss. **RESULTS:** Samples were collected from 18 patients with appendiceal PC and 18 patients with appendiceal PC. In the appendiceal patients, comparison between low and high MRA patients revealed 171 differentially expressed genes (DEGs). Many of these, including *ANPEP*, *EFNA5*, *CSF3R* and *PRG4*, are involved in skeletal muscle remodeling, repair, and regeneration and others, such as *C1R*, *C1QTNF*, and *GDF15*, are involved in inflammatory pathways. Similarly, between patient with low versus high SMI, there was decreased expression of tumor suppressing genes including *MT1A* and *NPTX2*. In comparing Black vs White patients, there were a few DEGs; notably the tumor suppressor *ADARB2* was not expressed in Black patients, whereas *MAOA*, which is known to promote tumor growth, had increased expression in the same cohort. **CONCLUSIONS:** Patients with appendiceal carcinomatosis demonstrate changes in the genomic landscape of their skeletal muscle based on SMI, MRA, and race. The DEGs identified in this study could serve as potential markers or targets for cancer associated cachexia and tumor progression. Further analysis will need to be performed correlating the expression of these genes with clinical morbidity and mortality.

P165. Histology of Recurrent Mucinous Appendiceal Cancer after CRS-HIPEC for Low Grade Peritoneal Metastases

Sohini Khan, MD[1]; Jula Veerapong, MD[2]; Andrew M. Lowy, MD[3]; Joel M. Baumgartner, MD, MAS[4]
[1]University of California San Diego, La Jolla, CA, US; [2]University of California San Diego, La Jolla, CA, US; [3]University of California San Diego, La Jolla, CA, US; [4]University of California San Diego, San Diego, CA, US

INTRODUCTION: Low-grade mucinous carcinoma peritonei (LGMCP) that arises from low grade appendiceal neoplasms (LAMN) often presents with a large burden of peritoneal metastases and is typically treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC). Although there is some evidence that approximately half of patients with LGMCP may recur after CRS-HIPEC, the rate of recurrence with higher grade histology is not well known. **METHODS:** A retrospective study of all CRS-HIPEC procedures performed from 2007-2024 at our institution was performed using a prospectively maintained database. Patients with low grade (LG) peritoneal histology, defined as LGMCP, acellular mucin, or benign histology (peritoneal nodules without mucin or neoplastic cells on final pathology) with LG primary tumors, were included. Recurrence histology was defined as LG or high grade (HG), with HG histology defined as high-grade mucinous carcinoma peritonei (HGMCP) or adenocarcinoma (AC). Electronic medical records of patients with appendiceal cancers were reviewed to identify patients with recurrence. Kaplan-Meier survival analysis was performed to estimate overall and progression-free survival (PFS). **RESULTS:** We identified 315 CRS-HIPEC procedures with LG peritoneal histology during the study period: 225 (71.4%) had LGMCP, 80 (25.4%) had acellular mucin, and 10 (3.2%) had benign histology. One-hundred and eight patients (34.3%) had recurrence after a median follow-up of 77.3 months (range: 0.2-199.2 months). Demographic and operative details for those with and without recurrence are shown in Table 1. The histology at recurrence was known for 80 cases: 50 (62.5%) had LG histology and 30 (37.5%) had HG histology (3 with HGMCP and 27 with adenocarcinoma, including four patients who initially recurred with LG histology but later had HG histology). Median PFS for the study group was 137.7 months (95% CI 107.1-168.2). Median PFS for those with LG recurrence was 19.2 months (95% CI 11.2-27.3) vs. 21.9 months (95% CI 15.3-28.4) for those with HG recurrence (p=0.47, by log rank test). Median overall survival was not reached, but the 10-year OS rate was 36.0% in the LG group vs. 13.3% in the HG group (p=0.028). **CONCLUSIONS:** Approximately one-third of patients undergoing CRS-HIPEC for LG appendiceal cancer developed recurrence, and approximately one-third of these recurred with higher grade histology. Those with LG recurrence had improved survival than those with HG recurrence. These findings have important implications for patient counselling and management, and warrant further investigation.

Patient variables	No recurrent disease (n = 207)	Recurrent disease (n = 108)	p value
	n (%) or median (range)		
Age	57 (26-86)	56 (27-82)	0.80[1]
Gender (female)	115 (55.5)	59 (54.6)	0.88[2]
CEA	3.3 (1-192)	8.4 (1.1-313)	**< 0.001**[1]
PCI	13 (0-36)	20 (1-39)	**< 0.001**[1]
OR time (min)	401 (194-951)	483 (200-935)	**< 0.001**[1]
EBL (mL)	150 (5-1500)	300 (15-3000)	
CC-score			**< 0.001**[2]
CC-0	167 (80.7)	64 (59.2)	
CC-1	40 (19.3)	38 (35.2)	
CC-2	0	4 (3.7)	
CC-3	0	4 (3.7)	
No. anastomoses	0 (0-3)	1 (0-6)	**< 0.001**[1]
No. visceral resections	1 (0-5)	2 (0-10)	**< 0.001**[1]
Intra-op blood transfusion	23 (11.1)	20 (18.5)	0.06[2]
Post-op blood transfusion	24 (11.6)	27 (25)	**0.02**[2]

CEA carcinoembryonic antigen (pre-operative); *PCI* peritoneal carcinomatosis index; *EBL* estimated blood loss; *CC* completeness of cytoreduction
[1] = Student's t-test
[2] = Chi-square test

P166. Impact of Peritoneal Carcinomatosis and Malignant Ascites on the Outcome of Malignant Bowel Obstruction: Secondary Analysis of SWOG S1316

Kristen E Dougherty, MD[1]; Jaewon Lee[2]; Robert Krouse, MD, MS[3]; Virginia Sun, PhD, RN[4]; Gary B Deutsch[5]; Angeles Alvarez Secord[6]; Garnet L Anderson[7]; Kathryn B Arnold[8]; Elizabeth Gleeson, MD, MPH[9]; Jeremiah L Deneve[10]
[1]University of North Carolina - Chapel Hill, Chapel Hill, NC, US; [2]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [3]University of Pennsylvania, Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, PA, US; [4]City of Hope National Medical Center, Duarte, CA, US; [5]Northwell Health Cancer Institute, New Hyde Park, NY, US; [6]Duke Cancer Institute, Durham, NC, US; [7]Fred Hutchinson Cancer Center, Seattle, WA, US; [8]Fred Hutchinson Cancer Research Center, Seattle, WA, US; [9]University of North Carolina Chapel Hill, Chapel Hill, NC, US; [10]University of North Carolina at Chapel Hill, Chapel Hill, NC, US

INTRODUCTION: The presence of peritoneal carcinomatosis (PC) and malignant ascites (MA) in the setting of malignant bowel obstruction (MBO) is associated with a poor prognosis and has significant implications on the quality of life and end of life care for MBO patients. SWOG S1316 was a pragmatic comparative effectiveness trial that examined surgical and non-surgical treatment of MBO and demonstrated no differences in survival or "good days" between treatment. We further examine the impact of PC and MA on outcome in the setting of MBO. **METHODS:** Data from S1316 trial were secondarily analyzed between "as treated" groups with continuous variables are reported as mean with standard deviation or median with range. Categorical variables are reported as count and percent. Mann-Whitney U test was performed for continuous variables and Fisher's exact test was used for categorical variables. Overall survival (OS) was analyzed using log-rank test and hazard ratios (HR) were calculated using cox proportional hazards model. Grant funding was received by NCORP. **RESULTS:** There were 199 patients (pts) evaluated in the study: 49 randomized and 150 not randomized. Of 150

available CT scan reports, 31 pts had PC-only, 13 MA-only and 86 had both. Of pts who underwent surgery (58 available operative reports), 23 pts (40%) had PC and MA and no pt had MA without having the presence of PC. The presence of PC and MA had no impact on total number of any hospitalizations (p=0.527), MBO-related hospitalizations (p-0.918), days with a nasogastric tube (p=0.55) or hospital length of stay (p=0.551). For non-operative pts, total parenteral nutrition (TPN) was administered to 100% of MA-only pts and 53% of pts with PC and MA (p=0.0004), while there was no difference in duration of TPN (p=0.299). Furthermore, 67% of PC-only pts received subsequent chemotherapy while zero pts with MA-only disease received chemotherapy (p=0.012). Of the 82 pts who had surgery (as-treated), the presence of MA was associated with worse survival (HR 4.38 p=0.007). **CONCLUSIONS:** The presence of PC and MA are frequent findings in the setting of MBO, are often identified at the time of surgery, irrespective of pre-operative CT findings, and associated with a worse outcome. For pts undergoing surgery for MBO, the presence of MA, in particular, is associated with a profoundly worse outcome and surgery should approached with caution.

P167. Impact of Systematic Discontinuation of Mitomycin C HIPEC for Colorectal Peritoneal Metastasis on Oncologic Outcomes at an NCI Cancer Center

Muhammad Talha Waheed, MD[1]; Isaac B Paz, MD[2]; Thinzar Lwin, MD[3]; Alessio Pigazzi, MD[4]; Laleh Melstrom, MD[5]; Yuman Fong, MD[6]; Gagandeep Brar, MD[7]; Dani Castillo, MD[8]; Pashtoon M Kasi, MD[9]; Marwan Fakih, MD[10]; Mustafa Raoof, MD[11]

[1]City of Hope National Medical Center, Duarte, CA, US; [2]City of Hope National Medical Center, Duarte, CA, US; [3]City of Hope National Medical Center, Duarte, CA, US; [4]City of Hope National Medical Center, Duarte, CA, US; [5]City of Hope National Medical Center, Duarte, CA, US; [6]City of Hope National Medical Center, Duarte, CA, US; [7]City of Hope National Medical Center, Duarte, CA, US; [8]City of Hope National Medical Center, Duarte, CO, US; [9]City of Hope National Medical Center, Duarte, CA, US; [10]City of Hope National Medical Center, Duarte, CA, US; [11]City of Hope National Medical Center, Duarte, CA, US

INTRODUCTION: PRODIGE7 demonstrated a lack of effectiveness of Oxaliplatin HIPEC after cytoreductive surgery (CRS) for colorectal peritoneal metastasis (CRCPM). Many centers switched to Mitomycin C (MMC) HIPEC. However, the oncologic benefit of MMC-HIPEC remains unclear.
METHODS: In 2021 our center systematically discontinued use of any HIPEC for CRCPM. This is a retrospective analysis of consecutive patients undergoing MMC-HIPEC after complete CRS (2009-2021) to those undergoing complete CRS alone (2021-2024). HIPEC was performed at 42oC with MMC (25 mg/m2) for 90 minutes. Survival outcomes (Recurrence free survival – RFS, Peritoneal RFS, and overall survival – OS) were compared between the two groups without and with propensity score matching (1:2 nearest neighbor) on known prognostic factors (age, sex, performance status, location of primary, extraperitoneal disease, completeness of cytoreduction score, peritoneal carcinomatosis index -PCI, and perioperative chemotherapy). **RESULTS:** A total of 107 patients (median age: 56 years; median PCI: 8; 48% male; 45% left-side primary) were included, of which 68 (64%) underwent CRS-HIPEC with MMC. Median follow-up for the entire cohort was 25.2 months (15.5 months CRS alone; 49.2 months CRS-HIPEC). Most patients (75-77%) in each cohort experienced a recurrence by the end of follow up. After matching, we had a well-balanced cohort of 72 patients (24 CRS alone; 48 CRS-HIPEC). Patients undergoing CRS alone vs. CRS-HIPEC had comparable RFS (median 8.7 [95%CI 5.6-13.1] vs. 8.7 [95%CI 4.3-16.4] months; p =0.407; Figure 1a) and Peritoneal-RFS (median 12.7 [95%CI 8.4-NR] vs. 18.2 [95%CI 6.2-19.8] months; p =0.864). Patients undergoing CRS-HIPEC had a median OS of 37.5 months (95%CI 30.6-NR). Although CRS alone cohort did not reach median survival due to limited follow-up, it was associated with a higher OS at 1-year (100% vs. 87.5%; p = 0.017; Figure 1b). Furthermore, sub-group analysis did not reveal an oncologic benefit of MMC-HIPEC by any of the known prognostic factors. **CONCLUSIONS:** For CRCPM, systematic omission of MMC-HIPEC did not lead to a detriment in oncologic outcomes after complete CRS. The study supports CRS alone (without HIPEC) as the established standard-of-care for CRCPM.

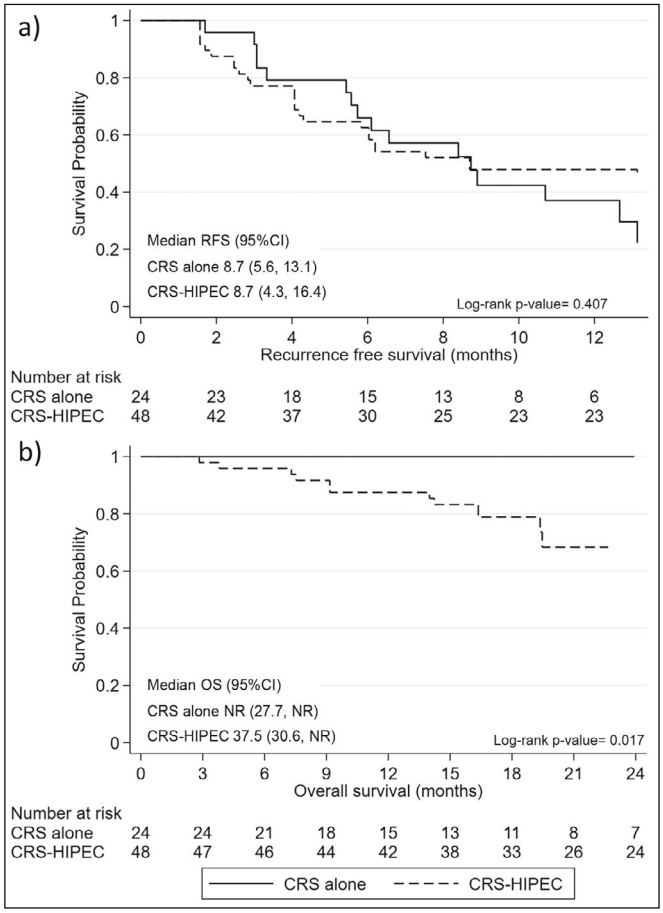


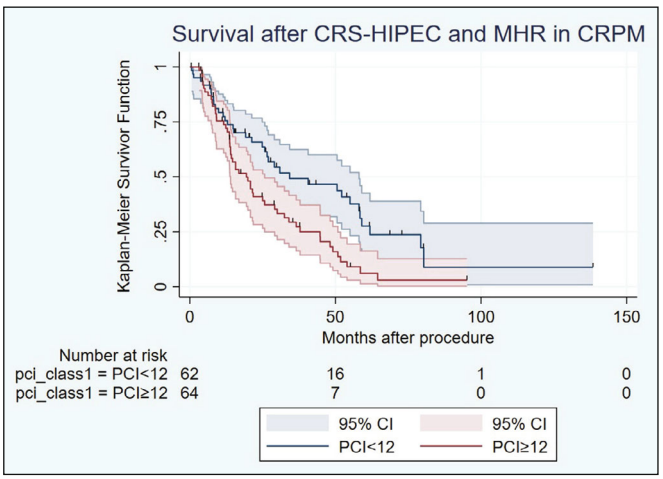
Figure.1 Kaplan Meier plots demonstrating a) RFS; and b) OS of matched cohort

P168. Inclusion of Minor Hepatic Resections during Cytoreductive Surgery-Hyperthemic Intraperitoneal Chemotherapy for Metastatic Colorectal Cancer with low peritoneal tumor burden does not worsen post-operative outcomes and survival

Ahmed Hamed, MD, MS[1]; Joshua Derby[2]; Matthew Holtzman[3]; Melanie Ongchin, MD[4]; David Bartlett[5]; James Pingpank[6]; M. Haroon A Choudry, MD[7]
[1]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [2]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [3]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [4]University of Pittsburgh, Pittsburgh, PA, US; [5]Allegheny Health Network, Pittsburgh, PA, US; [6]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [7]University of Pittsburgh Medical Center, Pittsburgh, PA, US

INTRODUCTION: Metastatic colorectal cancer (mCRC) presents with peritoneal metastases (CRPM) and hepatic involvement in a subset of patients. Cytoreductive surgery-hyperthemic intraperitoneal chemotherapy has been utilized in well-selected patients with CRPM, but it is unclear if including minor hepatic resections (MHR) worsens postoperative recovery and survival. We studied patient factors associated with these outcomes after CRS-HIPEC and MHR. **METHODS:** A retrospective cohort study investigated clinico-oncologic and perioperative factors from all patients undergoing both CRS-HIPEC and MHR for mCRC, with complete cytoreduction achieved (CC score 0), at a high-volume center in 2001-2022. MHR was defined as ≤2 liver segments removed. Multivariable Cox regression identified associations with overall survival (OS). Chi-squared tests showed associations with major postoperative complications (Clavien-Dindo III or higher). **RESULTS:** Of 126 patients (mean age 56 yrs, 57% female), median age-adjusted Charlson comorbidity index (AACCI) was 9, and all had ECOG performance score 0-1. Pre-CRS-HIPEC chemotherapy was given in 85 cases (67%), and median peritoneal carcinomatosis index (PCI) at time of CRS-HIPEC was 12. Median postoperative follow-up was 62 months and median OS was 26 months. On multivariable Cox analysis, PCI≥12 (HR 1.7, p=0.02) and AACCI (HR 1.2 for each point, p=0.03) were associated with OS. Fig 1 illustrates divergent survival according to PCI range.

Median postoperative survival was 34 months if PCI<12, vs 19 months if PCI≥12. The major complication rate was significantly lower in the PCI<12 group (39%) vs. PCI≥12 (61%) p=0.046. Furthermore, gastrointestinal (30% vs 70%, p=0.02) and pulmonary (31% vs 69%, p=0.04) major complication rates were significantly lower in the PCI<12 group. **CONCLUSIONS:** Our study shows that patients with limited CRPM (PCI<12) who undergo CRS-HIPEC combined with MHR have similar post-operative complication rates and long-term survival as is known for those undergoing CRS-HIPEC alone. We suggest that the need for minor hepatic resections to achieve CC-score 0 should not exclude patients from CRS-HIPEC if PCI<12.



P169. Inhibiting coagulation factor XIIIa in colorectal cancer peritoneal metastasis

Savannah Gregg[1]; Rio Boothello[2]; Sareh Bayatpour[3]; Shoja M Haneefa Hajira[4]; Adam Hawkridge[5]; Umesh Desai[6]; Jose Trevino[7]; Leopoldo Fernandez[8]; Bhaumik Patel[9]; Adam Khader[10]

[1]Central Virginia VA Healthcare System, Richmond Institute for Veterans Research, Richmond, VA, US; [2]VCU School of Medicine, Richmond, VA, US; [3]Richmond Institute for Veterans Research, Richmond, VA, US; [4]VCU Medical Center, Richmond, VA, US; [5]Massey Comprehensive Cancer Center, Richmond, VA, US; [6]VCU School of Pharmacy, Richmond, VA, US; [7]VCU Health, Richmond, VA, US; [8]VCU Health, Richmond, VA, US; [9]Central Virginia VA Healthcare System, Massey Comprehensive Cancer Center, VCU School of Medicine, Richmond, VA, US; [10]Central Virginia VA Healthcare System, Massey Comprehensive Cancer Center, VCU School of Medicine, Richmond, VA, US

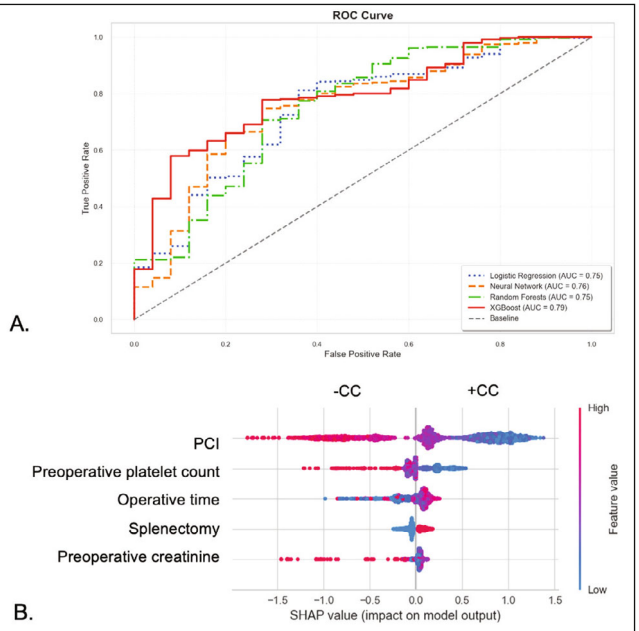
INTRODUCTION: Colorectal cancer (CRC) is highly treatable in its early stages and considered curable when localized; however, metastasis to the peritoneum (PM) significantly worsens the prognosis. Tumors are often described as wounds that do not heal, with fibrin clot deposition observed in many tumors. Factor XIII, a transglutaminase in the coagulation cascade, and its expression correlates with survival in CRC PM. This study aims to demonstrate activated FXIII (FXIIIa) as a promoter of the CSC phenotype in CRC, investigate the inhibition of FXIIIa as a therapeutic strategy, and evaluate novel anti-FXIIIa NSGMs as promising therapeutic agents. **METHODS:** Using a fibrin matrix model (7-day culture with thrombin and fibrinogen, in the presence or absence of FXIIIa 10 ug/mL), we assessed the impact of FXIIIa on CSC phenotype by measuring primary, secondary, and tertiary spheroid regeneration, chemoresistance, and CSC marker expression. We also employed a subcutaneous xenograft model with HT-29 CRC cells embedded in a fibrin matrix, with and without FXIIIa, to verify FXIIIa's effects on mouse tumor volumes. FXIIIa was targeted using the pan transglutaminase inhibitor T101. Additionally, we screened the novel NSGM G4.2 for its ability to inhibit FXIIIa using a dansyl-cadaverine assay and evaluated its effect on spheroid formation in the presence or absence of FXIIIa. **RESULTS:** FXIIIA1 RNA expression increased in CRC PM compared to CRC primary and is associated with worse overall survival. In vitro, FXIIIa supplementation increased primary spheroid formation, secondary and tertiary spheroid regeneration, and oxaliplatin chemoresistance, with a 2.7-fold increase in oxaliplatin IC_{50}. An increase in CSC marker protein expression CD133 (2.2-fold), CXCR4 (1.7-fold), and NANOG (1.5-fold), was observed in CRC spheroids cultured in a fibrin matrix compared to no added FXIIIa. T101 completely neutralized FXIIIa's effects on primary spheroid formation ($p < 0.05$). In vivo, FXIIIa-treated tumors exhibited a significantly faster growth rate, with an additional 17.2 mm³ increase in tumor volume per day ($t = 4.376$, $p < 0.001$) compared to the no-FXIIIa group. The novel NSGM G4.2 inhibited FXIIIa with an IC_{50} of 9.91 μM and selectively reduced spheroid formation in the presence of FXIIIa, with a lower IC_{50} for G4.2 in FXIIIa-supplemented conditions compared to FXIIIa-free conditions. **CONCLUSIONS:** FXIIIa promotes the CSC phenotype in CRC. Inhibiting FXIIIa, either through T101 or novel NSGMs like G4.2, may abrogate its CSC-promoting effects, highlighting the therapeutic potential of targeting FXIIIa in CRC and CRC PM.

P170. Leveraging Machine Learning to Predict Completeness of Cytoreduction after CRS-HIPEC

Amir Ashraf Ganjouei[1]; Jane Wang[2]; Ahmed Hamed[3]; Laleh Foroutani[4]; Fernanda Romero Hernandez[5]; Bahaa Aburayya[6]; Yusuf Althawadi[7]; Adnan Alseidi[8]; M. Haroon A Choudry, MD[9]; Mohamed A. Adam, MD[10]

[1]University of California San Francisco, San Francisco, CA, US; [2]University of California San Francisco, San Francisco, CA, US; [3]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [4]University of California San Francisco, San Francisco, CA, US; [5]University of California San Francisco, San Francisco, CA, US; [6]UCSF, San Francisco, CA, US; [7]UCSF, San Francisco, CA, US; [8]University of California San Francisco, San Francisco, CA, US; [9]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [10]University of California, San Francisco, San Francisco, CA, US

INTRODUCTION: Existing models predicting the completeness of cytoreduction following cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) are limited by small sample sizes and predictive accuracy. This study aimed to develop and validate a machine algorithm that accurately predict the likelihood of achieving complete cytoreduction, utilizing a large cohort of CRS-HIPEC cases. **METHODS:** Patients who underwent CRS-HIPEC at the University of Pittsburgh Medical Center were selected from a prospectively maintained database (2001-2022). The primary endpoint was completeness of cytoreduction, defined as a completeness of cytoreduction score of 0 (no residual peritoneal disease) or 1 (minimal residual disease, <2.5 mm). The dataset was randomly divided into training and testing sets with an 80:20 ratio. We developed and tested the predictive accuracy of three machine learning algorithms (neural network, random forest, and XGBoost), alongside a conventional logistic regression model. The selection of predictive variables was refined using recursive feature elimination, and the importance of each variable was quantified using Shapley Additive exPlanations (SHAP) values. Finally, a web-based calculator was developed to predict personalized probabilities of achieving completeness of cytoreduction. **RESULTS:** A total of 2,083 cases were included 53% were female and 92% White. The median age was 56 years (IQR: 47–64). The median peritoneal carcinomatosis index (PCI) was 14 (IQR 9-21). The most frequent pathological primary diagnosis was appendiceal tumor (46%), followed by colorectal cancer (26%). Completeness of cytoreduction with a score of 0 was achieved in 69% of patients, while 24% achieved a score of 1. We optimized predictive performance by identifying 10 key variables using recursive feature elimination. After training the models on 80% of the dataset, the XGBoost algorithm demonstrated the highest predictive performance on the unseen test dataset (AUC 0.79). This was followed by the neural network (AUC 0.76), random forest (AUC 0.75), and logistic regression models (AUC 0.75) (Figure 1A). Analysis of SHAP values revealed that the most important predictors of complete cytoreduction were a lower PCI score, a normal platelet count, longer operative time, undergoing splenectomy, and a normal preoperative creatinine (Figure 1B). **CONCLUSIONS:** Using machine learning models, we were able to predict the completeness of cytoreduction after CRS-HIPEC with good accuracy. The developed web-based calculator can aid in clinical decision-making and enhance surgeon-patient discussions about treatment outcomes.



(A); SHAP values of the XGBoost model for predicting completeness of cytoreduction (B).

AUC, area under the curve; CC, completeness of cytoreduction; PCI, peritoneal carcinomatosis index; ROC, receiver operating characteristic; SHAP, shapley|additive explanations.

Figure 1. Receiver operating characteristic curves for logistic regression, neural network, random forest, and XGBoost models

P171. Multidisciplinary management of locally advanced adenocarcinoma of the appendix

Ian W Folkert, MD, PhD[1]; Jessica J Lie, MD[2]; Neal Bhutiani, MD, PhD[3]; Prajnan Das, MD[4]; Yun Song, MD[5]; Paul Mansfield, MD[6]; Richard E Royal, MD[7]; Christopher P Scally, MD[8]; Sean P Dineen, [9]; Keith F Fournier, MD[10]; Beth Helmink, MD, PhD[11]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [4]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [5]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [6]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [7]Maine Health, Portland, ME, US; [8]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [9]Moffitt Cancer Center, Tampa, FL, US; [10]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [11]The University of Texas MD Anderson Cancer Center, Houston, TX, US

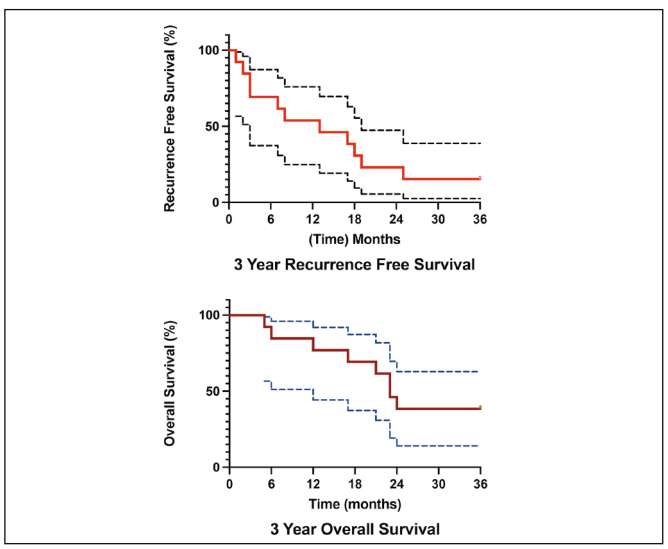
INTRODUCTION: Adenocarcinoma of the appendix is a rare gastrointestinal tumor with a well-recognized potential for peritoneal dissemination. A less common presentation is that of the locally advanced appendiceal adenocarcinoma that directly invades the retroperitoneum, abdominal wall or adjacent organs in the absence of peritoneal disease. While cytoreductive surgery with heated intraperitoneal chemotherapy (CRS/HIPEC) remains the standard of care for patients with peritoneal dissemination, the optimal treatment strategies for patients with locally advanced tumors are not known. **METHODS:** We performed a single-institution retrospective review of all patients with appendiceal neoplasms who underwent surgical management. All patients who underwent surgery for locally advanced tumors with direct invasion into the retroperitoneum, abdominal wall or surrounding viscera without widespread peritoneal dissemination of disease from 1997 - 2024 were included. **RESULTS:** We identified 37 patients who underwent surgery for locally advanced appendix tumors. Median age at diagnosis was 57.85. Thirty percent of patients were female. All patients underwent surgery with the goal of margin-negative resection. Intraoperative radiotherapy was utilized in 17/37 cases (45.9%). Twenty-six patients were treated with neoadjuvant systemic therapy (70.3%) and seven patients were treated with external beam radiation (18.9%). No patients underwent HIPEC at their primary operation. At the time of diagnosis, 34/37 patients (91.9%) had moderately differentiated histology. Five patients (13.5%) had lymph node metastasis at the index operation. At a median follow up time of 4.53 years (IQR 2.47-7.29 years), 14 patients developed recurrence (37.8%), with 5-year recurrence free survival of 55.4% (95% CI 40.0-76.7%). Of those who recurred, six developed distant recurrence (42.9%), six developed local recurrence (42.9%), and two (14.3%) developed distant and local recurrence. Of the 14 patients who recurred, 11 underwent re-resection and seven of those (63.6%) had no evidence of disease at the time of last follow-up. Four patients who recurred (28.6%) underwent CRS/HIPEC at the time of reoperation for peritoneal recurrence. 5-year overall survival was 92.7% (95% CI 83.5-100.0%). **CONCLUSIONS:** We describe here the largest series of patients with locally advanced appendiceal adenocarcinoma. Multimodality therapy centered around margin-negative radical resection leads to favorable outcomes. Our experience supports the omission of HIPEC in patients with locally advanced disease in the absence of peritoneal dissemination.

P172. Multimodality Management of Desmoplastic Small Round Cell Tumor Offers the Potential for Improved Outcome

Mohammad Mahmoud Noubani[1]; Dhruv J Patel[2]; Elizabeth Gleeson, MD, MPH[3]; Jeremiah L Deneve[4]

[1]UNC at Chapel Hill, Chapel Hill, NC, US; [2]University of North Carolina, Chapel Hill, NC, US; [3]University of North Carolina Chapel Hill, Chapel Hill, NC, US; [4]University of North Carolina at Chapel Hill, Chapel Hill, NC, US

INTRODUCTION: Desmoplastic small round cell tumor (DSRCT) is a rare intra-abdominal sarcoma affecting adolescents and young adults. Neoadjuvant chemotherapy followed by cytoreduction and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) and adjuvant radiotherapy may offer improved local control. We review our experience with patients (pts) who undergo multimodality management for DSRCT. **METHODS:** A retrospective review of DSRCT patients who underwent CRS/HIPEC between 2017-2024 was performed. Clinical, operative, pathologic and outcome data were reviewed. **RESULTS:** Fifteen DSRCT patients who received multimodality treatment (2 pts excluded- did not undergo an operation) were identified. The median age at diagnoses was 24 years (7-38) of which 60% were Caucasian and 70% were male. All patients received neoadjuvant chemotherapy. The median length of CRS/HIPEC was 763 minutes (375-1041 min) and median blood loss was 520 mL (250-2000 mL). Cisplatin was the primary agent for HIPEC. The median peritoneal cancer index score was 19 (range, 6-34) and complete cytoreduction (CCR 0/1) was performed in 77% of patients. The median ICU length of stay (LOS) was 3 days (range, 2-19) and median hospital LOS was 15 days (range, 10-33). The median time to recurrence was 11 months (range, 1-25) and the 3-year recurrence free survival was 15%, while the median overall survival (OS) was 22 months (range, 5-42) and 3-year OS was 38%. **CONCLUSIONS:** DSRCT is a rare sarcoma with an aggressive presentation and prone to development of recurrence. Multimodality therapy consisting of neoadjuvant chemotherapy, CRS/HIPEC and adjuvant radiation offers the potential for long-term disease control with associated acceptable potential morbidity but significant resource utilization. Recurrence is common and long-term survival is possible in select patients, highlighting the need for additional research.



P173. Neutrophil Infiltration in the Peritoneal Tissue Microenvironment in Carcinomatosis

Christopher Sherry, DO[1]; Neda Dadgar[2]; Hyun Park[3]; Chelsea Knotts, MD[4]; Rosie Blodgett[5]; Erin Grayhack[6]; Ali Zaidi[7]; Kunhong Xiao[8]; Ashten Omstead[9]; Vera Donnenberg[10]; Albert Donnenberg[11]; David Bartlett, MD[12]; Patrick Wagner, MD[13]
[1]Allegheny Health Network, Pittsburgh, PA, US; [2]Cleveland Clinic Foundation, Cleveland, OH, US; [3]Allegheny Health Network, Pittsburgh, PA, US; [4]Allegheny Health Network, Pittsburgh, PA, US; [5]Allegheny Health Network, Pittsburgh, PA, US; [6]Allegheny Health Network, Pittsburgh, PA, US; [7]Allegheny Health Network, Pittsburgh, PA, US; [8]Allegheny Health Network, Pittsburgh, PA, US; [9]Allegheny Health Network, Pittsburgh, PA, US; [10]Allegheny Health Network, Pittsburgh, PA, US; [11]Allegheny Health Network, Pittsburgh, PA, US; [12]Allegheny Health Network, Pittsburgh, PA, US; [13]Allegheny Health Network, Pittsburgh, PA, US

INTRODUCTION: The 'background' immune microenvironment in peritoneal carcinomatosis (PC) remains poorly defined relative to the extensive literature on metastatic tumor tissue itself. Previous studies have found high levels of IL-8—a key cytokine in neutrophil activation—in the peritoneal fluid of patients with PC, suggesting that the well-documented tumor-promoting effects of neutrophils across a range of primary tumor types could be relevant to peritoneal tumor biology. As a first step toward investigating this possibility, we tested the hypothesis that tissue neutrophil infiltration might be increased in PC. **METHODS:** Non-neoplastic 'background' peritoneal tissue and fluid were obtained from 29 patients with and 31 without PC. Using immunohistochemistry and automated image analysis software (Bond Aperio), we analyzed MPO+ (neutrophil), CD3+ and CD8+ lymphocyte, M1-like (CD86+/CD68+) and M2-like macrophage (CD206+/CD68+) cell densities in the peritoneal and immediate submesothelial tissues. Cell densities were tested for association with carcinomatosis, as well as key peritoneal fluid soluble analytes (using a 60-plex Luminex assay) and peritoneal tissue proteomic analytes (using liquid chromatography/tandem mass-spectrometry) with non-parametric measures of association (Wilcoxon rank sum for categorical and Spearman's rank correlation tests for continuous variables). **RESULTS:** We found a mean 100-fold increase in neutrophil density in mesothelial tissue from patients with PC relative to those without (p<0.0001). By contrast, no differences in CD3+/CD8+ lymphocytes or M1/M2-type macrophages were seen. Neutrophil infiltration in PC patients was associated with decreased levels of several key cytokines in the peritoneal fluid, including fractalkine (r=-0.7, p=0.004), IL1-b (r=-0.7, p=0.005) and GM-CSF (r-0.7, p=0.005). Interestingly, tissue neutrophil infiltration was not associated with peritoneal fluid IL-8 concentration. Among ~1000 quantifiable tissue proteins, we identified a subset of four proteins negatively correlated with neutrophil density, including S1001A16—a known suppressor of gastrointestinal tumor progression—as well as NCCRP1, IGHa2 and cystatin B. **CONCLUSIONS:** Neutrophil infiltration is a distinguishing hallmark of the peritoneal tissue microenvironment in carcinomatosis and is associated with a distinct milieu of peritoneal fluid cytokines and peritoneal tissue proteins. The significance of these findings and implications for peritoneal tumor progression and potential therapeutic intervention await further validation and functional studies.

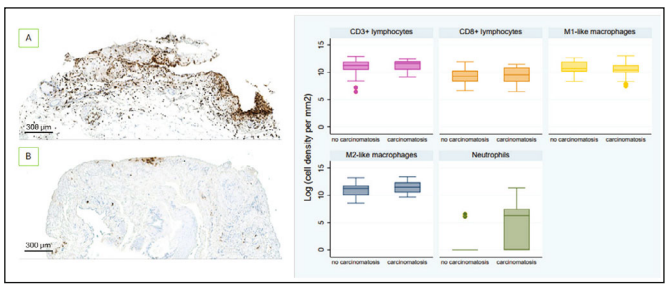


Figure. Left panel: IHC staining for myeloperoxidase showing high- (panel A) and low- (panel B) density neutrophil infiltration in peritoneal tissue samples. Right panel: lymphocyte, macrophage and neutrophil densities compared in the presence or absence of carcinomatosis (p<0.0001 for neutrophils; NS for all other cell types).

P174. Next generation sequencing identifies key targetable mutations in the treatment of appendiceal neoplasms

Rui Zheng-Pywell[1]; Salvatore J. Lumia[2]; Daniel J. Gironda[3]; Lance D. Miller[4]; Edward Levine[5]
[1]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [2]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [3]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [4]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [5]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US

INTRODUCTION: Appendiceal neoplasms are a group of rare, heterogeneous tumors that exhibit varying malignant potential. Systemic treatment options for disseminated appendiceal cancer are limited. We sought to review rates of mutations that may indicate potential roles for routine next-generation sequencing to evaluate for targetable therapies. **METHODS:** An analysis of 976 appendiceal tumor samples (appendiceal adenocarcinoma, goblet cell adenocarcinoma, mucinous adenocarcinoma, signet ring cell adenocarcinoma, and low-grade appendiceal mucinous neoplasm) submitted to AACR GENIE consortium was performed to compare patient demographics and the rates of mutations that may confer drug susceptibility. **RESULTS:** Low-grade appendiceal neoplasms (LAMNs) exhibited fewer mutation counts than other appendiceal tumors (4.5 ± 4.6, p = 0.01), a high percentage of KRAS mutations (88.9%, p < 0.01), and associated with a significantly higher number of living patients (85.2%, p < 0.01). Of the LAMNs with KRAS mutations, 92% occur at codon G12, with 52.0% being G12V and 36% involving G12D. In contrast, 5.7%, 29.7%, 53.0%, and 71.8% of goblet cell adenocarcinoma, signet ring cell adenocarcinoma, appendiceal adenocarcinoma, and mucinous adenocarcinoma respectively had KRAS mutations. Of these, only 5.8% of samples, collectively, had a drug targetable mutation at KRAS G12C. The second most prevalent therapeutic target was PIK3CA at 6.9% followed by 33 cases (3.4%) with mutations in the DNA mismatch repair genes (MLH1, MSH2, MSH6, and PMS2). The prevalence of other therapeutically targetable mutations remained low (<3%): BRAF (2.6%), ALK (2.2%), ERBB2 (2.0%), AKT1 (2.0%), MET (1.5%), NTRK1 (1.5%), FGFR2 (1.2%), PDGFRA (1.2%), and EGFR (1.1%) and showed minimal overlap. Collectively, 21.5% of appendiceal cancer cases were associated with at least one gene mutation with drug targeting potential, and 4.3% of cases had multiple gene mutations with drug targeting potential. **CONCLUSIONS:** While mutations suggesting available drug targeting occur at low frequency in appendiceal tumors, minimal overlap of these mutations results in a sizeable subpopulation of patients that may benefit from targeted therapies. Next-generation sequencing may enable tailored therapeutic approaches for a minority of patients with disseminated appendiceal cancer.

	ERBB2 (N = 18)	BRAF (N = 24)	AKT1 (N = 18)	ALK (N = 20)	EGFR (N = 10)	FGFR2 (N = 11)	PDGFRA (N = 11)	MET (N = 14)	NTRK1 (N = 14)	MLH1 (N = 5)	MSH2 (N = 7)	MSH6 (N = 12)	PMS2 (N = 11)	PIK3CA (N = 40)
Wild Type (N = 432)	1.6%	4.4%	0.9%	2.5%	1.6%	1.4%	1.4%	1.6%	1.2%	0.9%	0.9%	1.2%	0.9%	5.3%
KRAS Mut (N = 484)	2.3%	1.0%	2.9%	1.9%	0.6%	1.0%	1.0%	1.4%	1.9%	0.2%	0.6%	1.4%	1.4%	8.3%
	p = 0.78	p < 0.01	p = 0.06	p = 0.77	p = 0.22	p = 0.57	p = 0.55	p = 0.41	p = 0.02	p = 0.14	p = 0.03	p = 0.02	p = 0.01	p = 0.81
G12 (N = 401)	2.0%	0.5%	2.5%	1.0%	0.5%	1.2%	1.2%	1.5%	2.0%	0.2%	0.7%	1.7%	1.7%	8.2%
G13 (N = 46)	4.3%	0.0%	6.5%	6.5%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	8.7%
Q61 (N = 16)	0.0%	6.3%	0.0%	6.3%	0.0%	0.0%	0.0%	6.3%	6.3%	0.0%	0.0%	0.0%	0.0%	0.0%
A146 (N =10)	10.0%	20.0%	0.0%	0.0%	10.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	20.0%
Other (N = 11)	0.0%	0.0%	9.1%	9.1%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	9.1%

Figure 1. Simultaneous Mutation Rates of KRAS with other Targetable Genes

P175. NF2 and Downstream Genes are Potential Targets for Treatment in Peritoneal Mesothelioma

Salvatore J. Lumia[1]; Rui Zheng-Pywell[2]; Lance D. Miller[3]; Edward Levine[4]
[1]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [2]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [3]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [4]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US

INTRODUCTION: Mesothelioma is a group of rare neoplasms arising from serosal tissue. Those of peritoneal origin account for only 30% of cases. Historically, even with next-generation sequencing (NGS), targetable therapy is limited. Recently, NF2 and downstream targets of the Hippo-YAP and PI3K-AKT-mTOR pathways have been implicated as treatment targets in malignant pleural mesothelioma. We sought to evaluate whether peritoneal disease had a similar genetic profiles, thus making this a viable target. **METHODS:**

An analysis of 180 tumor samples submitted to the GENIE consortium was performed to compare patient demographics and mutation status for oncogenes amendable to targeted therapy: KRAS, ERBB2, BRAF, AKT1, AKT2, AKT3, DNA mismatch repair genes (MLH1, MSH2, MSH6, PMS), ALK, EGFR, FGFR2, FGFR3, PDGFRA, PDGFRB, MET, PIK3CA, KIT, RET, NTRK1, NTRK2, NF2, LATS1, and LATS2. **RESULTS:** Across 180 samples, the average mutation count was 3.9 (± 4.3) mutations/specimen and 63 samples (35%) had at least 1 mutation in a targetable oncogene. Of those with mutations, 35 samples (19.4%) had mutations in NF2. Within NF2, the most common mutations was homozygous deletion (20%) followed by Q362*, R341*, and X_39 splice mutations (8.6% each). A greater percentage of NF2 mutation patients were deceased as compared to those with Wild Type mutations (48.6% vs 40.1%, p =0.04). The next two most prevalent oncogene mutations were LATS2 at 3.3% followed by LATS1 at 2.8%. The rate of mutational overlap between NF2, LATS1, and LATS2 is low, with the greatest overlap seen between NF2 and LATS2 at 2.9%. Additionally, mutations in other prevalent oncogenes (AKT1, AKT2, AKT3, MET, and PIK3Ca) did not overlap with NF2 mutation (p<0.01). The rest of the oncogenes from the screening panel demonstrated minimal yield in the samples surveyed. **CONCLUSIONS:** The rate of actionable mutations is low overall. However, the mutation rate of NF2 in this data set of peritoneal mesothelioma seems comparable to the prevalence published for pleural mesothelioma. Mutations in the downstream genes of the Hippo-YAP and PI3K-AKT-mTOR pathways are similarly better represented than other oncogenes from the screening panel, making therapies targeting these two pathways promising.

Percentage of Individual NF2 group

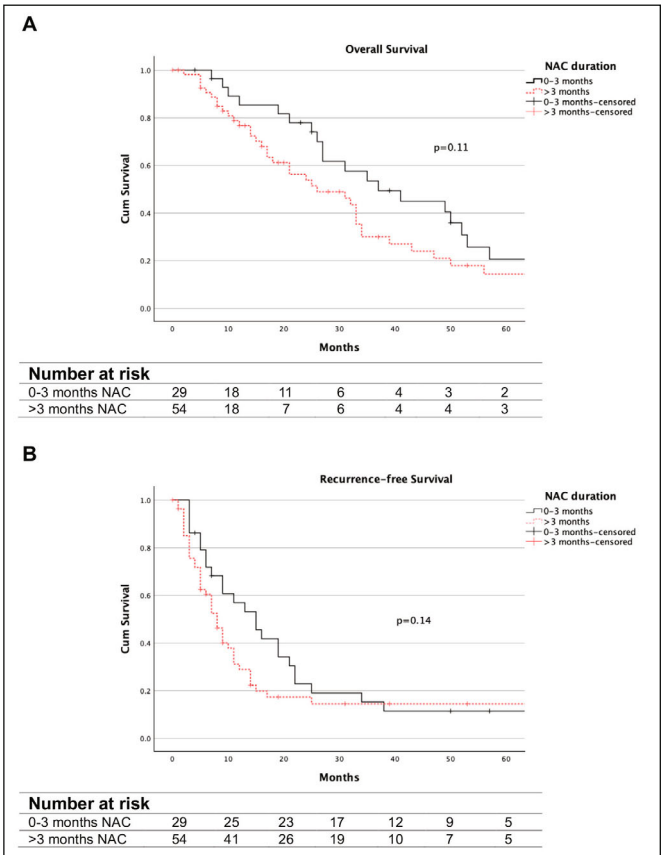
	LATS1 (N = 5)	LATS2 (N = 6)	AKT1 (N = 1)	AKT2 (N = 1)	AKT3 (N = 1)	MET (N = 1)	PIK3CA (N = 3)
Wild Type (N = 137)	3.6%	3.6%	0.7%	0.7%	0.7%	0.7%	2.2%
Mutant (N = 35)	0.0%	2.9%	0.0%	0.0%	0.0%	0.0%	0.0%
	p < 0.01	p < 0.01	p = 1.00	p < 0.01	p < 0.01	p < 0.01	p = 1.00

P176. Optimal duration of neoadjuvant chemotherapy prior to CRS±HIPEC for colorectal cancer: An assessment of survival and postoperative outcomes

Frances J. Bennett, MD[1]; Kailey M. Oppat, MD[2]; Mohammad Y. Zaidi, MD[3]; Joshua WIner, MD[4]; Maria C. Russell, MD[5]; Charles Staley, MD[6]; Shishir K. Maithel, MD, FACS, FSSO[7]; Seth J. Concors, MD[8]

[1]Emory University, Atlanta, GA, US; [2]Emory University, Atlanta, GA, US; [3]Emory University, Atlanta, GA, US; [4]Emory University, Atlanta, GA, US; [5]Emory University, Atlanta, GA, US; [6]Emory University, Atlanta, GA, US; [7]Winship Cancer Institute, Atlanta, GA, US; [8]Emory University, Atlanta, GA, US

INTRODUCTION: Cytoreductive surgery (CRS) with or without heated intraperitoneal chemotherapy (HIPEC) represents a viable therapy for select patients with colorectal cancer peritoneal metastases. Given high recurrence rates after surgery, neoadjuvant chemotherapy (NAC) is common. The optimal duration when considering oncologic value and postoperative outcomes is not known. We sought to determine if clinical outcomes differ based on duration of neoadjuvant chemotherapy in patients with colorectal cancer undergoing CRS±HIPEC. **METHODS:** A single institution database (2009-2024) of colorectal cancer (CRC) patients that underwent CRS±HIPEC was reviewed. CRC patients undergoing CRS±HIPEC for curative intent (completeness of cytoreduction 0 or 1) with known NAC duration were included. Analysis was stratified by NAC duration of 0-3 months (mos) or greater than 3 mos. Co-primary outcomes were recurrence free survival (RFS) and overall survival (OS). Secondary outcomes included clinically significant complications, defined as Grade 3-5 adverse events based on Common Terminology Criteria for Adverse Events Version 5.0. **RESULTS:** From 2009-2024, 108 patients with CRC underwent CRS±HIPEC. Final analysis included 84 patients that underwent curative intent surgery and had a known duration of NAC (>3 mos NAC: 55 patients, 0-3 mos NAC: 29 patients). Median peritoneal cancer index (PCI) score was similar between the two cohorts (>3 mos: median PCI 11 versus (vs) 0-3 mos: median PCI 12; p=0.42). RFS was 9 mos for the entire cohort and not significantly different based on duration of NAC (>3 mos: 8 mos vs 0-3 mos: 15 mos, p=0.14). OS was also similar between both cohorts (>3 mos: 26 mos vs 0-3 mos: 37 mos; p=0.11). On univariate analysis, >3 mos of NAC was associated with an increased rate of complications of any severity (>3 mos: 83.6% vs 0-3 mos: 55.2%; p=0.01), clinically significant complications (>3 mos: 54.5% vs 0-3 mos: 31.0%; p=0.07), and increased median length of stay (>3 mos: 10 days vs 0-3 mos: 8 days; p=0.01). When controlling for other perioperative variables on multivariable analysis, >3 mos of NAC trended towards an increased risk of clinically significant complications (HR 1.76, 95% CI 0.59-5.30; p=0.32). **CONCLUSIONS:** Even with a similar disease burden, as measured by PCI, an extended duration of NAC prior to CRS±HIPEC does not appear to be associated with improved RFS or OS. Conversely, postoperative outcomes are worse with higher complication rates and increased length of stay. Thus, despite high recurrence rates after CRS/HIPEC for this disease, it still appears that in well selected patients, an extended duration of neoadjuvant chemotherapy may not be the best treatment strategy.



(A) overall survival and (B) recurrence-free survival in patients with colorectal cancer undergoing CRS±HIPEC, stratified by duration of neoadjuvant chemotherapy of either 0-3 months or greater than 3 months.

Figure 1. Overall survival and recurrence-free survival curves comparing duration of neoadjuvant chemotherapy prior to CRS±HIPEC in patients with colorectal cancer. Kaplan Meier analysis evaluating

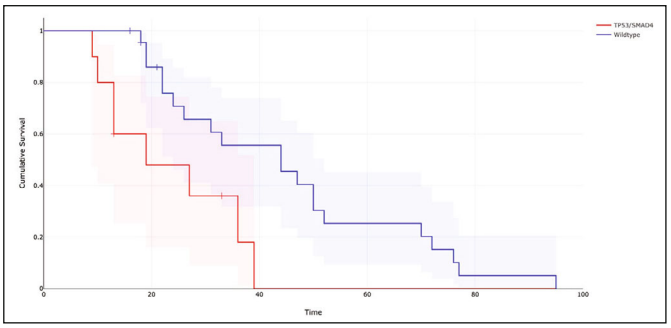
P177. P53 and/or SMAD4 mutations are associated with poorest survival in high-grade appendiceal peritoneal metastasis and may be a potential preoperative marker for CRS/HIPEC selection

Chunmeng M Zhang[1]; Valerie K Shostrom[2]; Allison Cushman-Vokoun[3]; Jason M Foster[4]

[1]University of Nebraska Medical Center, Omaha, NE, US; [2]University of Nebraska Medical Center, Omaha, NE, US; [3]University of Nebraska Medical Center, Omaha, NE, US; [4]University of Nebraska Medical Center, Omaha, NE, US

INTRODUCTION: Expanded mutation profiling has been utilized to guide clinical decision making in multiple cancer types but has not yet been adopted in the treatment of high-grade appendiceal peritoneal metastasis (HG-APM). There is currently a paucity of data for mutation profile impact on outcomes and also rates of actionable mutations in HG-APM. **METHODS:** A single-institution retrospective study was performed on 45 HG-APM patients referred for surgical intervention between 2008-2023. A fifty-gene NGS mutation panel analysis was performed in CLIA approved lab. All patients underwent CRS/

HIPEC with mitomycin C. Outcome data including PCI, optimal CRS, overall and progression free survival (OS & PFS) were collected. Survival analyses were performed on all HG-APM stratified by mutation profile. **RESULTS:** Forty percent were male with a median age of 57. Median PCI was 26, and 80% achieved optimal CRS (R0-R2a). Actionable mutations were detected in 66%. Most common mutations were KRAS (39%), followed by P53 (26%), GNAS (11%), and SMAD4 (8%). While KRAS/GNAS mutations were associated with a trend of more indolent disease course (OS 44 vs. 27 months, $p > 0.05$), TP53 and/or SMAD4 mutations were associated with significantly decreased OS (19 vs. 45 months, $p = 0.012$, Fig. 1) as well as PFS (5 vs.9 months, $p = 0.030$). **CONCLUSIONS:** While 70% of patients experience a prolonged survival following CRS/HIPEC, patients with P53 and/or SMAD4 mutations experience a poor outcome where CRS/HIPEC did not benefit this subset. While these results identify a critical area for development of targeted therapies, they also identify a subset of patients where the surgical benefit of CRS/HIPEC in the current treatment model needs to be further explored. In summary p53 and SMAD4 mutations represent an important preoperative surrogate marker of surgical outcomes and the next step is to collaborate with other high-volume centers to further validate results.



P178. Partial Hepatectomy is Safe and Effective for Patients Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy

Alexander Didier[1]; Rupak Mukherjee, PhD[2]; Andrea Abbott, MD[3]; Jeffrey M. Sutton, MD FACS FSSO[4]

[1]University of Toledo College of Medicine and Life Sciences, Toledo, OH, US; [2]Medical University of South Carolina, Charleston, SC, US; [3]Medical University of South Carolina, Charleston, SC, US; [4]Medical University of South Carolina, Charleston, SC, US

INTRODUCTION: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) is utilized in the treatment of primary and secondary peritoneal surface malignancies, with solid organ involvement traditionally considered a contraindication. In select cases, CRS-HIPEC may be combined with partial hepatectomy to achieve optimal cytoreduction. However, the impact of adding hepatectomy to HIPEC on patient outcomes and survival remains unclear. This study aims to evaluate overall survival and major morbidity in patients who underwent CRS-HIPEC with or without concurrent hepatectomy. **METHODS:** We queried the TriNetX database, a real-world database consisting of over 100 million patient records in the United States, for cases of patients who underwent CRS-HIPEC with or without partial hepatectomy for metastatic appendiceal, colorectal, or ovarian malignancies a well as primary peritoneal surface malignancies. Descriptive analysis using Chi-squared and t-test was performed to compare baseline characteristics between cohorts. Major morbidity (defined as a composite outcome of acute heart failure, acute myocardial infarction, stroke, acute renal failure, and acute respiratory failure requiring mechanical ventilation) at 30 and 90 days post-CRS-HIPEC was evaluated using the log-rank test. Overall survival (OS) was evaluated using Kaplan-Meier and the log-rank test at time intervals between 30 days and 5 years. **RESULTS:** A total of 2,209 patients were included in the non-hepatectomy cohort and 206 patients were included in the hepatectomy cohort. The mean age of the hepatectomy cohort was 53.4 vs 56.7 in the non-hepatectomy cohort. More patients who underwent hepatectomy had a diagnosis of appendiceal cancer (48% vs 31%, $p<0.001$) and colon cancer (47% vs 25%, $p<0.001$), while more patients who did not undergo hepatectomy had a diagnosis of ovarian cancer (46% vs 16%, $p<0.001$). Major morbidity was similar at all time points (1 month: 7.3% in the hepatectomy cohort vs 3.8% in the non-hepatectomy cohort, $p=0.3193$; 3 months: 7.3% in the hepatectomy cohort vs 5.9% in the non-hepatectomy cohort, $p=0.2604$). Both cohorts had comparable OS at all time points (1 year OS: 90.4% in hepatectomy cohort vs 90.2% in non-hepatectomy cohort, $p=0.9681$; 5-year OS: 54.1% in hepatectomy cohort vs 56.7% in non-hepatectomy cohort, $p=0.9476$). **CONCLUSIONS:** The results of this study suggest that major perioperative morbidity as well as overall survival following CRS-HIPEC were comparable between patients undergoing CRS-HIPEC with or without hepatectomy as a component of their cytoreduction. These findings indicate that partial hepatectomy can be performed safely during CRS-HIPEC without negatively impacting short- or long-term outcomes, providing support for its use in carefully selected patients in whom an optimal cytoreduction can be achieved.

P179. Perioperative Chemotherapy in Stage IVA-B Appendiceal Cancer Undergoing Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy

Ekaterina Baron, MD[1]; Alessandro Paro, MD[2]; Jessica A. Wernberg, MD, FACS[3]; Rohit Sharma, MD, FACS[4]

[1]Marshfield Medical Center, Marshfield, WI, US; [2]Marshfield Medical Center, Marshfield, WI, US; [3]Marshfield Medical Center, Marshfield, WI, US; [4]Marshfield Medical Center, Marshfield, WI, US

INTRODUCTION: Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is commonly accompanied by perioperative systemic chemotherapy (pSCT) to treat appendiceal cancer (AC) with peritoneal spread. However, the impact of pSCT on survival remains unclear with some small studies reporting worse outcomes with neoadjuvant SCT for high-grade AC. We evaluated the impact of CRS/HIPEC with pSCT on survival across various AC subtypes. **METHODS:** A retrospective cohort study was conducted using the National Cancer Database (2004-2022). Patients with stage IVA-B AC treated with CRS/HIPEC were included. Overall survival (OS) was analyzed with multivariable Cox regression and the Kaplan-Meyer method in patients who received pSCT and those who did not, stratified by tumor subtypes: low-grade mucinous (LG-MAC), low-grade non-mucinous (LG-NMAC), high-grade mucinous (HG-MAC), high-grade non-mucinous AC (HG-NMAC), and signet ring cell carcinoma (SRC). **RESULTS:** Of 53,255 patients, 1,061 were included: 337 received CRS/HIPEC+pSCT and 724 had CRS/HIPEC alone. The median age was lower in the pSCT group (55 vs 57 years, $p<0.01$). pSCT patients were more likely to have private insurance (75.1% vs 63.3%, $p<0.01$). Mucinous AC was more common in the CRS/HIPEC-only group (91.6% vs 67.4%), while non-mucinous AC (19.3% vs 5.0%) and SRC (13.4% vs 3.5%) were predominant in the pSCT group ($p<0.01$). High-grade histology was more frequent in the pSCT group (29.4% vs 6.2%), whereas low-grade histology was more common in the CRS/HIPEC-only group (60.2% vs 35%, $p<0.01$). Administration of pSCT was independently associated with high-grade histology (odds ratio 7.93, 95%CI: 4.11-15.30) in multivariable logistic regression analysis. The median follow-up was 77.9 months. For LG-MAC, pSCT patients had significantly worse median OS compared to CRS/HIPEC alone (100.4 vs 165.8 months, $p<0.01$), with a hazard ratio (HR) of 1.91 (95%CI: 1.37-2.66) after adjusting for confounders (Figure 1). No significant differences in OS were observed between the pSCT and CRS/HIPEC-only groups within LG-NMAC (HR 2.65, 95%CI: 0.74-9.51), HG-MAC (HR 0.67, 95%CI: 0.30-1.51), HG-NMAC (HR 0.54, 95%CI: 0.20-1.44), and SRC (HR 1.33, 95%CI: 0.75-2.34). **CONCLUSIONS:** Adding pSCT to CRS/HIPEC provided no survival benefit across all AC subtypes and was associated with worse outcomes in LG-MAC. This may be attributed to a higher tumor burden in patients receiving pSCT or delay of CRS/HIPEC. Further research is needed to identify optimal candidates for pSCT within AC patients undergoing CRS/HIPEC.

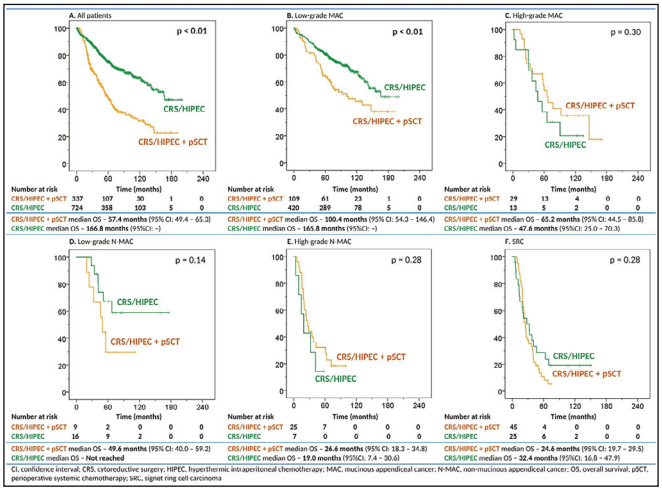


Figure 1. Overall Survival

P180. Real-Time, AI-Guided Photodynamic Laparoscopy Enhances Detection in a Rabbit Model of Peritoneal Cancer Metastasis

Hyoungil Kim[1]
[1]*Yonsei University College of Medicine, Seoul, KR*

INTRODUCTION: Accurate diagnosis is essential for effective cancer treatment, particularly in peritoneal surface malignancies, where failure to detect metastatic lesions can mislead the treatment plan. This study assessed the diagnostic accuracy of staging laparoscopy using the integration of artificial intelligence (AI)-guided photodynamic diagnosis (PDD) with the photosensitizer Phonozen, activated at 405 nm in a rabbit model. **METHODS:** To create peritoneal carcinomatosis, VX2 cells were inoculated laparoscopically into the peritoneum of female New Zealand white rabbits. Conventional and PDD-guided laparoscopy utilized a customized light source that emitted broad-spectrum white light or 405-nm blue light, respectively. The surgical procedure comprised a tripartite approach: exploration and labeling of suspected nodules under white-light visualization, identification of additional metastatic tumors under blue-excitation fluorescent light, and confirmatory open laparotomy to locate overlooked nodules by palpation. **RESULTS:** The initial experimental data from 398 nodules in 16 rabbits, comparing conventional diagnostic laparoscopy and PDD, showed increased detection sensitivity from 84.2% ± 3.7% (conventional) to 93.9% ± 2.4% (PDD). In the second experimental data set from 270 nodules in 10 rabbits, the addition of a real-time AI algorithm further increased the sensitivity to 100% ± 0.0%. **CONCLUSIONS:** Combining PDD with AI enhances the detection of peritoneal cancer metastasis in staging laparoscopy.

P181. Shaping surgical success: A qualitative analysis of attitudes towards prehabilitation for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy

Caroline Rieser, MD[1]*; Aaron Richardon*[2]*; Neha Dole*[3]*; Thien Le*[4]*; Shannon Altpeter*[5]*; AJ Rio-Glick*[6]*; Kimberly Rak, PhD*[7]*; Melanie Ongchin, MD*[8]
[1]*University of Chicago Medical Center, Chicago, IL, US;* [2]*University of Pittsburgh, Pittsburgh, PA, US;* [3]*University of Pittsburgh, Pittsburgh, PA, US;* [4]*UPMC, Pittsburgh, PA, US;* [5]*UPMC, Pittsburgh, PA, US;* [6]*University of Pittsburgh, Pittsburgh, PA, US;* [7]*University of Pittsburgh, Pittsburgh, PA, US;* [8]*University of Pittsburgh, Pittsburgh, PA, US*

INTRODUCTION: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS HIPEC) can significantly extend survival for patients with peritoneal metastases. High rates of preoperative frailty, malnutrition, and depression impact surgical outcomes, ultimately resulting in longer length of stays, high rates of complications, and readmissions. Multimodal preoperative initiatives targeting nutritional and physical optimization, termed prehabilitation, have shown to be effective in reducing postoperative complications and hastening recovery. However, those with advanced cancers have largely been excluded from existing work, and the potential impact and ideal program for patients undergoing CRS HIPEC is unknown. This study aimed to understand values and outcomes important to CRS HIPEC patients, care givers, and healthcare providers and determine optimal implementation of prehabilitation in this unique patient population. **METHODS:** We conducted in-depth interviews among patients who had undergone CRS HIPEC (PT; n=13), care givers (CGs; n=13), and health care providers (HCPs; n=10) with experience in caring for CRS HIPEC patients. Data were analyzed through thematic coding using a modified theoretical domains framework. **RESULTS:** A majority of participants found prehabilitation both acceptable and feasible (PT, CG, HCP). Social support, an adaptable intervention, and championing among the medical team were identified as facilitators of participation (PT, CG). Emotional burden of the diagnosis, physical symptoms related to the cancer, and time were identified as major barriers among all groups. Despite this, prehabilitation was also seen as an avenue for patient empowerment when dealing with an uncertain future and as a tool to strengthen mental and physical resiliency (PT, CG). Participants expressed a desire for expanded mental health support, preoperative education, and opportunities for peer support as part of a proposed prehabilitation program (PT, CG). An option for virtual or hybrid engagement was seen as essential (PT, HCP). Primary outcomes of interest were quality of life, particularly return to normal physical function and mental health (PT, HCP). **CONCLUSIONS:** In this qualitative analysis of essential stakeholders, participants expressed strong support for engagement in prehabilitation prior to CRS HIPEC. Prehabilitation programs should ideally be tailored to patient abilities and limitations, target emotional as well as physical health, and offer virtual options for participation.

P182. Single-cell spatial transcriptomic analysis of malignant peritoneal mesothelioma: novel insights into inter-patient and intra-patient tumor heterogeneity

Shruthi R Perati, MD[1]*; Jing Bian*[2]*; Evsen A Arikan, MD*[3]*; Jatinder Singh*[4]*; Michael Kelly, PhD*[5]*; Jennifer Matta*[6]*; Darryl Nousome*[7]*; Andrew Warner*[8]*; Jiyeun Kim*[9]*; Noemi Kedei, MD*[10]*; Amber F Gallanis, MD*[11]*; Leila Sarvestani, MD*[12]*; Jonathan M Hernandez, MD*[13]*; Sun A Kim, MD*[14]*; Maggie Cam, PhD*[15]*; Jeremy L. Davis, MD*[16]*; Raffit Hassan, MD*[17]*; Andrew M Blakely, MD*[18]
[1]*National Institutes of Health/National Cancer Institute, Bethesda, MD, US;* [2]*National Institutes of Health, Bethesda, MD, US;* [3]*National Institutes of Health, Bethesda, MD, US;* [4]*National Institutes of Health, Bethesda, MD, US;* [5]*National Institutes of Health, Bethesda, MD, US;* [6]*National Institutes of Health, Molecular Histopathology Lab, Frederick, MD, US;* [7]*National Institutes of Health, Bethesda, MD, US;* [8]*National Institutes of Health, Molecular Histopathology Lab, Frederick, MD, US;* [9]*National Institutes of Health, Molecular Histopathology Lab, Frederick, MD, US;* [10]*National Institutes of Health, Bethesda, MD, US;* [11]*National Institutes of Health/National Cancer Institute, Bethesda, MD, US;* [12]*National Institutes of Health/National Cancer Institute, Bethesda, MD, US;* [13]*National Institutes of Health, Bethesda, MD, US;* [14]*National Institutes of Health, Bethesda, MD, US;* [15]*National Institutes of Health, Bethesda, MD, US;* [16]*National Cancer Institute, Bethesda, MD, US;* [17]*National Institutes of Health, Bethesda, MD, US;* [18]*National Institutes of Health, Bethesda, MD, US*

INTRODUCTION: Malignant peritoneal mesothelioma (MPM) is exceedingly rare, with only 500 new cases per year nationally. Most existing RNA sequencing for mesothelioma describes pleural primary tumors. We aim to characterize MPM heterogeneity across various disease sites and germline mutations (BAP1, MUTYH). **METHODS:** We evaluated parietal and visceral peritoneal samples from patients with epithelioid MPM enrolled on clinical trial NCT04847063 who underwent cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy from 2021 to 2024. Representative formalin-fixed/paraffin-embedded tissue sections were selected for tumor-enriched bulk RNA sequencing and single-cell spatial transcriptomic (scST) sequencing using a custom panel of genes commonly mutated in MPM. As MPM is often of a flat morphology with low tumor cellularity, scST has particular utility. Robust Cell Type Deconvolution (RCTD) was used to annotate tissue spots using a pleural mesothelioma reference dataset. Seurat unsupervised clustering was performed under a range of resolutions to assess cell heterogeneity. **RESULTS:** In all, 26 unique MPM samples (15 parietal and 11 visceral) were sequenced. Samples were derived from 7 patients (median age of 48, IQR 38-72), of whom 4 (57.1%) were male, 4 (57.1%) had germline mutations (n=3 BAP1, n=1 MUTYH), and 5 (71.4%) received neoadjuvant chemotherapy or immunotherapy. Median PCI at time of CRS was 24 (IQR 18-27). Bulk RNA sequencing of tumor-enriched regions demonstrated tumor heterogeneity of cellular processes across various sites within a single patient. For scST analysis, RCTD annotations were overlaid on each tissue to confirm spatial correlation. Unsupervised clustering (Figure) showed distinct sub-populations of MPM cells derived from multiple samples, which held true across clustering resolutions 0.2-0.6; this suggests that multiple cell states may exist within a given tissue sample. Germline-mutant and wild type samples both showed sub-clustering of MPM cells derived from

certain visceral samples, distinct from parietal peritoneum-derived MPM cells. **CONCLUSIONS:** This novel, deep transcriptomic assessment demonstrated MPM heterogeneity both within individual sites of disease and across locations of disease, regardless of germline mutation status. Future work will aim to evaluate whether there is an association between number of MPM sub-clusters (i.e. cell states) and differential expression of genes associated with stemness/de-differentiation.

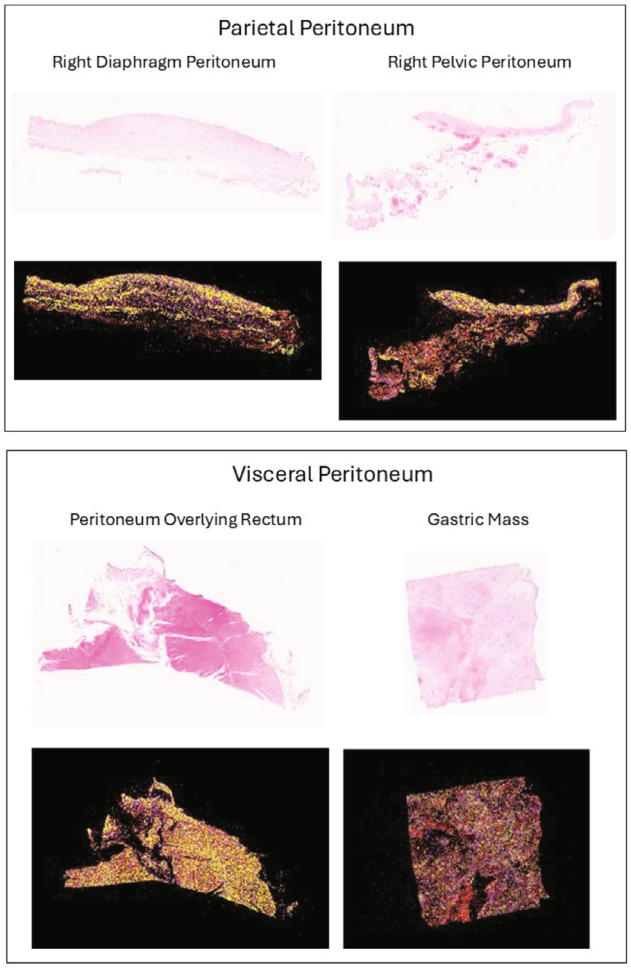


Figure. Images from hematoxylin and eosin staining (top row) and single-cell spatial transcriptomic sequencing (bottom row) of MPM tissue sections (2 parietal and 2 visceral). These images represent 4 of 26 total MPM tissue sections included in this study.

P183. Successful Pregnancy Following Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy in Patients with Peritoneal Malignancy

Haggai Benvenisti[1]; Dan Assaf[2]; Eyal Mor[3]; Danielle Mor-Hadar[4]; Vahan Kapenekian[5]; Nicolas Flamey[6]; Rui Yang[7]; Douglas Zippel[8]; Almog Ben-Yaacov[9]; Yan Li[10]; Brendan Moran[11]; Olivier Glehen[12]; Aviram Nissan[13]
[1]Sheba Medical Center, Ramat Gan, IL; [2]Sheba Medical Center, Ramat Gan, IL; [3]Sheba Medical Centerq, Ramat Gan, IL; [4]Sheba Medical Center, Ramat Gan, IL; [5]CHU Lyon Sud, Oncologic Surgery Department; Equipe Accueil 37-38, CICLY - Université Claude Bernard, Lyon, FR; [6]Basingstoke Hospital, Peritoneal Malignancy Institute, North Hampshire Hospital Foundation Trust, Basingstoke, GB; [7]Tsinghua University Affiliated Beijing Tsinghua Changgung Hospital, Department of Surgical Oncology, Beijing, CN; [8]Sheba Medical Center, Ramat Gan, IL; [9]Sheba Medical Center, Ramat Gan, IL; [10]Tsinghua University Affiliated Beijing Tsinghua Changgung Hospital, Department of Surgical Oncology, Beijing, CN; [11]Basingstoke Hospital, Peritoneal Malignancy Institute, North Hampshire Hospital Foundation Trust, Basingstoke, GB; [12]CHU Lyon Sud, Oncologic Surgery Department; Equipe Accueil 37-38, CICLY - Université Claude Bernard, Lyon, FR; [13]Sheba Medical Center at Tel Hashomer, General and Oncological surgery; Ziv Medical Center, Departmen, Ramat Gan, IL

INTRODUCTION: Cytoreductive surgery (CRS) with Hyperthermic Intraperitoneal Chemotherapy (HIPEC) has become a successful, potentially curative, treatment option for peritoneal surface malignancies (PSM). CRS and HIPEC are performed with curative intent for several intra-peritoneal pathologies. An increasing number of patients with PSM are diagnosed at a relatively young age. Given the long-term survival in some patients following CRS/HIPEC, the reproductive health of patients in this age group requires consideration. **METHODS:** Surgical oncology teams participating in the Peritoneal Surface Oncology Group International (PSOGI) were offered the opportunity to share their experience and data regarding the obstetric outcomes of female patients who had undergone CRS/HIPEC. **RESULTS:** Nineteen (19) patients were reported to have had a baby following CRS/HIPEC. The median interval between CRS/HIPEC and pregnancy was 37 months, and 16 patients had a normal vaginal delivery. All of the newborns were healthy, without medical issues attributed to CRS or HIPEC chemotherapy. Overall 89% of mothers had no evidence of disease at their last follow up. **CONCLUSIONS:** Successful pregnancies following CRS/HIPEC are seldom reported in the literature and fertility preservation is not uniformly discussed. Data from this international collaboration highlights the reproductive potential in patients with PSM following CRS/HIPEC and the value of preoperative obstetric, and fertility advice, management to achieve that end.

P184. Surgical intervention for Malignant Bowel Obstruction May Offer Improved Survival: Secondary Analysis of SWOG S1316

Jaewon Lee[1]; Kristen Dougherty[2]; Robert S Krouse, MD, MS[3]; Virginia Sun, PhD, RN[4]; Gary B Deutsch[5]; Angeles Alvarez Secord[6]; Garnet L Anderson[7]; Kathryn B Arnold[8]; Elizabeth Gleeson, MD, MPH[9]; Jeremiah L Deneve[10]
[1]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [2]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [3]University of Pennsylvania, Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, PA, US; [4]City of Hope National Medical Center, Duarte, CA, US; [5]Northwell Health Cancer Institute, New Hyde Park, NY, US; [6]Duke Cancer Institute, Durham, NC, US; [7]Fred Hutchinson Cancer Center, Seattle, WA, US; [8]Fred Hutchinson Cancer Research Center, Seattle, WA, US; [9]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [10]University of North Carolina at Chapel Hill, Chapel Hill, NC, US

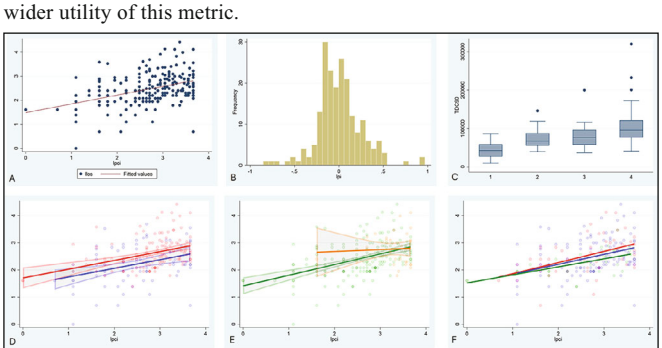
INTRODUCTION: Malignant bowel obstruction (MBO) contributes to significant morbidity and mortality in patients with intra-abdominal malignancies and optimal treatment (non-surgical or surgical) remains unclear. SWOG S1316 was a pragmatic comparative effectiveness trial that demonstrated no significant differences in survival or "good days" between surgical and non-surgical treatment. **METHODS:** Data from S1316 trial were secondarily analyzed between "as-treated" groups. Continuous variables are reported as mean with standard deviation or median with range. Categorical variables are reported as count and percent. Mann-Whitney U test was performed for continuous variables and Fisher's exact test was used for categorical variables. Overall survival (OS) was analyzed using log-rank test and hazard ratios (HR) were calculated using Cox proportional hazards model. Grant funding was received from the NCI Community Oncology Research Program (NCORP). **RESULTS:** A total of 199 patients were included in the secondary analysis, of which 94 underwent surgery during initial hospitalization with 2 patients undergoing additional surgery during subsequent hospitalizations. 16 of 105 patients (15%) who did not undergo surgery initially had MBO surgery during subsequent encounters. Lysis of adhesions (69%), small bowel resection (41%), loop ileostomy (22%), gastrostomy placement (22%), and intestinal bypass (19%) were the most common surgeries performed. Surgery was associated with overall reported iatrogenic injury rate of 26%. Patients who underwent surgery during the study period had improved OS (median 114 days surgery group, HR 0.6, vs 71 days non-surgical group, $P = 0.002$). Patients who underwent surgery during their initial hospitalization had lower rates of recurrent hospitalizations for MBO (28 hospitalizations non-surgical vs. 9 hospitalization surgery group, $P = 0.012$), but there was no significant difference in all-cause hospitalizations ($P = 0.662$). Surgical intervention during initial hospitalization was associated with longer combined length of stay (LOS) after study registration (median 14 days vs. 6 for non-surgical group, $P < 0.001$) and more days on total parenteral nutrition (TPN; median 3.5 days vs. 0 for non-surgical group, $P < 0.001$). There was no significant difference in length of days with nasogastric tube (NGT) between the two groups (median 4 days for surgery vs. 3 days for non-surgical group, $P = 0.062$). Surgery group trended on having lower health quality score at 4 weeks and 12 weeks after registration ($P = 0.081$ and

0.074, respectively). **CONCLUSIONS:** Evaluation of "as-treated" analysis of S1316 data revealed longer median survival for upfront surgery, which was also associated with lower rate of rehospitalizations for MBO. However, surgery was associated with longer LOS, more days on TPN, and lower health score within 3 months but not associated with days with NGT. In this highly selected, aggressive disease-biology MBO population, these results should be interpreted with caution but suggest a potential benefit of surgical intervention for MBO.

P185. The LOS-PCI Index: An exploratory benchmark metric for quality of care in cytoreductive surgery

Kara Bowers[1]; Mathangi Chandramouli[2]; Edward A Joseph[3]; Muhammad MM Khan[4]; David Bartlett[5]; Casey J Allen[6]; Patrick Wagner[7]
[1]Allegheny Health Network, Pittsburgh, PA, US; [2]Allegheny Health Network, Pittsburgh, PA, US; [3]Allegheny General Hospital, Pittsburgh, PA, US; [4]Allegheny General Hospital, Pittsburgh, PA, US; [5]Allegheny Health Network, Pittsburgh, PA, US; [6]Allegheny Health Network, Pittsburgh, PA, US; [7]Allegheny Health Network, Pittsburgh, PA, US

INTRODUCTION: Cytoreductive surgery (CRS) is an important component of comprehensive management for selected patients with peritoneal surface malignancies (PSM), however, in spite of efforts at standardization and improvement in perioperative care pathways, the risk and cost associated with CRS remain high. Evaluation of quality in CRS across centers or within individual centers over time is limited by the complexity and heterogeneity of patients and the lack of granular metrics. In this study, we explored the use of a novel metric comprising a ratio of the hospital length of stay (LOS) to peritoneal carcinomatosis index (PCI) to evaluate perioperative outcomes in a large single-institution series of surgical management for PSM. **METHODS:** 274 consecutive patients undergoing CRS for PSM at a single high-volume quaternary referral center between 2022-2024 were included. Patient demographic variables, PCI, LOS, utilization of heated intra-peritoneal chemotherapy (HIPEC), completeness of cytoreduction (CC) score, morbidity, mortality, and 90-day-total direct cost (TDC) were tabulated from a prospectively maintained internal database. For each case, the ratio of log-transformed LOS to log-transformed PCI was calculated. The distribution of this metric, which we termed the "PCI-LOS index" (LPI) was then characterized and tested for association with clinical and outcome variables using linear or logistic regression for continuous or binary outcomes, respectively. **RESULTS:** A linear relationship between log(LoS) and log(PCI) was confirmed. LPI was strongly associated with 30-day morbidity (number of complications per case, p<0.001; and proportion of cases with grade>3 complications, odds ratio 24.2 [5.7, 102.8], p<0.001), 90- and 365- day mortality OR 38.2 [1.3,1164.2], p=0.04 and OR 11.5 [2.0, 67.0], p=0.007, respectively, and total 90-day direct cost (cost differential $83,071 [65,513; 100,629], p< panel C). LPI varied by addition of HIPEC (p=0.001, Panel D); but not by completeness of cytoreduction (Panel E, p=0.9). Within our cohort, we observed a trend toward stepwise improvement over the three years of the study (p=0.06, Panel F). **CONCLUSIONS:** We describe an exploratory metric, the LOS-PCI index/LPI, which may simplify global assessment of quality of care of patients with PSM. This metric was easily calculated, was closely associated with morbidity, mortality and cost of care, and is likely to be modifiable over time with attention to care pathways and standardization. Further studies will need to incorporate validation cohorts from other centers and to include patient-reported outcomes to assess the wider utility of this metric.

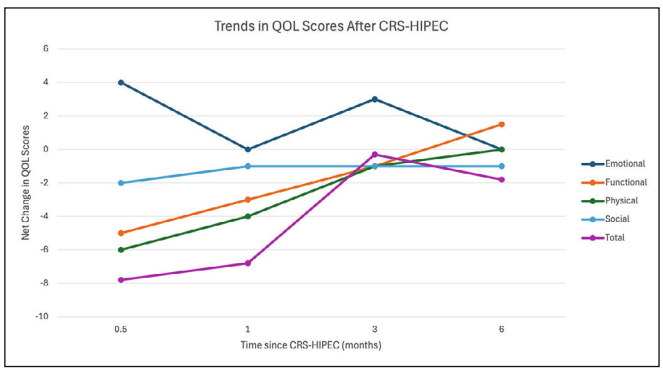


A. Scatterplot of ln(LOS) vs. ln(PCI) showing a linear correlation of the transformed values (p<0.001). B. Histogram of LPI values across cases. C. Total 90-day direct cost is associated with LPI (p <0.001). D. Variation in LPI by HIPEC (red) vs. without HIPEC (blue); p=0.001). E. Overlapping lines indicate no difference by completeness of cytoreduction (complete, green; incomplete, orange; p=0.9). F. LPI by year, indicating sequential reduction over time from year 1 (read) to year 2 (blue) to year 3(green); p=0.08, year 1 vs. year 3.

P186. Understanding the Quality of Life and Recovery of Patients Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy

Beatrice J Sun, MD[1]; Tiffany M Yue, BS[2]; Byrne Lee, MD[3]
[1]Stanford University School of Medicine, Stanford, CA, US; [2]Stanford University School of Medicine, Stanford, CA, US; [3]Stanford University School of Medicine, Stanford, CA, US

INTRODUCTION: Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) are complex, heterogeneous operations that can be difficult for patients to understand and prepare for. We aim to characterize patient experiences and quality of life (QOL) after CRS-HIPEC. **METHODS:** A prospective, longitudinal study of patients undergoing CRS-HIPEC by a single experienced surgeon at a tertiary academic center (Jan 2023-June 2024). Functional Assessment of Cancer Therapy (FACT-G) QOL surveys were completed preoperatively, then at 2 weeks, 1 month, 3 months, and 6 months postoperatively. Surveys also evaluated post-HIPEC perspectives and recovery. Semi-structured interviews were conducted with a subset of patients. **RESULTS:** 27 patients underwent CRS-HIPEC: 70% were female, median age was 49 years (range 35-74), and length of stay was 7 days (range 4-29). Primary cancers were low-grade appendiceal mucinous neoplasm (30%), appendiceal adenocarcinoma (7%), colon adenocarcinoma (26%), goblet cell adenocarcinoma (11%), uterine sarcoma (19%) and peritoneal mesothelioma (7%). Median peritoneal cancer index (PCI) was 9 and 100% achieved complete cytoreduction (CC 0-1). Mitomycin was the most commonly used perfusate (70%). Overall QOL scores were stable at 6 months compared to preoperatively (Figure). Functional and physical components dropped immediately postoperatively but increased steadily to baseline or better by 6 months. Emotional QOL improved slightly after surgery while social QOL remained stable throughout recovery. In addition to counseling by their surgeon, patients used the internet (85%), Youtube (37%), and other patients (11%) as resources to learn about HIPEC. While most felt "almost completely" recovered by 6 months, the emotional, physical, and functional aspects of recovery were all "harder than expected." Many wished they had known the challenges with long-term nausea and diarrhea, extent of surgery and organs resected, and longer-than-expected recovery time. Despite this, at both 1 and 6 months after surgery, all patients felt that CRS-HIPEC was "worth it." **CONCLUSIONS:** In our study, recovery after CRS-HIPEC was longer and more challenging than patients expected, yet all believed it was worth it and would repeat their decision on surgery. By 6 months, QOL scores had recovered and patients felt almost completely back to normal. Improving preoperative education and incorporating adjunct resources may aid patients in setting expectations and managing their postoperative recovery.



P187. Upfront Colectomy vs. Initial Appendectomy followed by Completion Colectomy for Appendiceal Cancer: Comparison of Outcomes

Muhammad Talha Waheed, MD[1]; Ibrahim Malik, BS[2]; Philip HG Ituarte, PhD[3]; Andrew M Blakely, MD[4]; Christopher J. LaRocca, MD[5]; Oliver S Eng, MD[6]; Byrne Lee, MD[7]; Isaac B Paz, MD[8]; Thinzar Lwin, MD[9]; Mustafa Raoof, MD[10]
[1]City of Hope National Medical Center, Duarte, CA, US; [2]Wayne State University, Detroit, MI, US; [3]City of Hope National Medical Center, Duarte, CA, US; [4]National Institutes of Health, Bethesda, MD, US; [5]University of Minnesota, Minneapolis, MN, US; [6]University of California Irvine Medical Center, Orange, CA, US; [7]Stanford University School of Medicine, Stanford, CA, US; [8]City of Hope National Medical Center, Duarte, CA, US; [9]City of Hope National Medical Center, Duarte, CA, US; [10]City of Hope National Medical Center, Duarte, CA, US

INTRODUCTION: The decision to perform right hemicolectomy for appendiceal tumors depends on histologic features of the primary tumor. A staged approach (initial appendectomy followed by completion colectomy - IA+CC) allows for histologic assessment of primary tumor and may avoid unnecessary right colectomy. Whether staged approach vs. Upfront right colectomy (UC) is detrimental to oncologic outcomes is unknown. **METHODS:** We identified patients with stage I-III appendiceal cancers undergoing resection from 2000-2019 using California Cancer Registry. Tumor histologies (mucinous [MAA] and non-mucinous adenocarcinoma [NMAA]; mixed adenoneuroendocrine carcinoma (MANEC); signet ring cell) for which consensus guidelines recommend right hemicolectomy were included. Factors associated with type of resection were evaluated using logistic regression. We propensity matched non-emergent cases undergoing UC vs. IA+CC using coarsened exact matching (CEM) and compared overall survival (OS) and survival hazard using Kaplan-Meier method and Cox proportional hazards model, respectively. **RESULTS:** A total of 669 patients met the inclusion criteria (median age 58 years, 46% female, 34% MAA, 33% NMAA, 29% MANEC, and 4% signet). Of these, 349 (52%) patients underwent UC, whereas 320 (48%) underwent IA+CC. UC (vs. IA+CC) was more likely to be performed for larger tumors (size > 5cm; 17% vs. 10%), high grade disease (13% vs. 9%), and higher stage (Stage III; 10% vs. 5%) (all p <0.001). Expectedly, patients undergoing UC (vs. IA+CC) had worse OS (ref: IA+CC; Hazard Ratio [HR] 2.15; p <0.001). We then performed a subset analysis of elective cases (N=245) without and with propensity matching which demonstrated that patients undergoing IA+CC had comparable predicted survival to patients undergoing UC (ref: IA+CC; HR: 1.25; p=0.589; Figure 1). **CONCLUSIONS:** After adjusting for covariates, compared to UC, a staged approach does not cause a detriment in oncologic outcomes. Therefore, a staged approach should be prioritized as it may prevent unnecessary right colectomy in many patients.

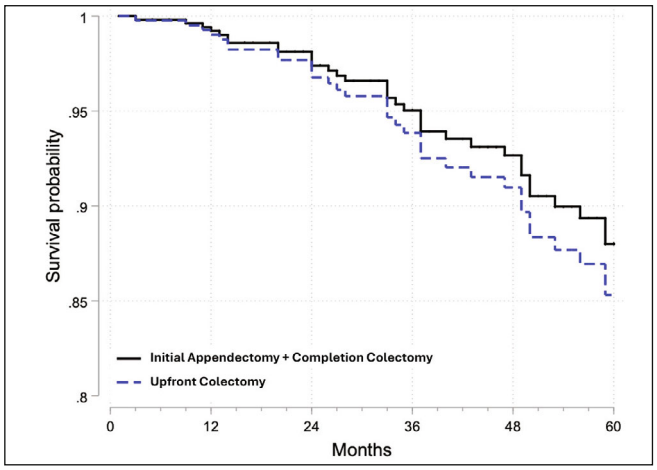
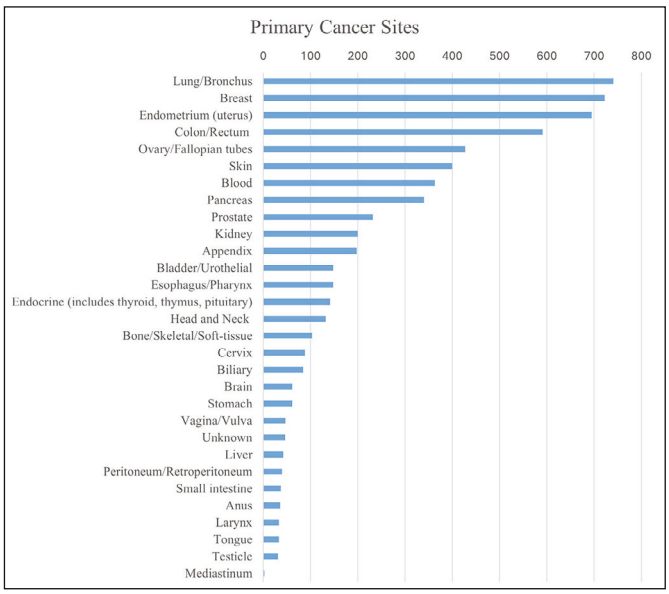


Figure 1. Predicted adjusted overall survival (OS) curve using Cox proportional hazard model for the matched cohort.

P188. A System-Wide Clinical Data and Biobank Repository Initiative Across an Integrated Health Network: Insights from the "Moonshot" Program

Ruchita Dunung[1]; David Bartlett[2]; Patrick Wagner[3]; William Laframboise[4]; Casey J. Allen, MD[5]; Philip Schumacher[6]
[1]Allegheny Health Network, Pittsburgh, PA, US; [2]Allegheny Health Network, Pittsburgh, PA, US; [3]Allegheny Health Network, Pittsburgh, PA, US; [4]Allegheny Health Network, Pittsburgh, PA, US; [5]Allegheny Health Network, Pittsburgh, PA, US; [6]Allegheny General Hospital, Pittsburgh, PA, US

INTRODUCTION: Advances in cancer treatment depend on the rapid translation of new scientific discoveries into patient care. To facilitate this, Allegheny Health Network launched the "Moonshot" program in 2021, aimed at prospectively collecting patient clinical data and integrating it with cancer genomics from blood and tissue samples across an integrated health network. Here, we present an overview and insights into the progress of the program to date. **METHODS:** Eligible cancer patients within our network who consented to enroll provided sequential blood samples during routine lab tests, and patients undergoing surgical resection contributed portions of their tumor specimens. The program is built on the standardized mCODE (minimal Common Oncology Data Elements) clinical data framework. It integrates data from electronic health records, genomics labs, and the network oncology registry, which includes detailed surgical and treatment information. Genomic variants in both tumor and corresponding blood samples were analyzed to assess concordance between matched samples. **RESULTS:** To date, 5,899 participants from multiple centers within our network have provided blood and/or tissue specimens. The cohort was predominantly female (60%) and Caucasian (92%), with a mean age of 64 ± 13 years. The most common primary cancer sites were the lung/bronchus (12%), breast (12%), endometrium/uterus (11%), and colon/rectum (11%) (Figure 1). The stage distribution was 34% stage I, 25% stage II, 26% stage III, and 15% stage IV. The most common histological types were adenocarcinoma (60%), squamous cell carcinoma (10%), and melanoma (6%). Analysis of matched blood and tumor samples showed a high level of concordance (97.0% ± 0.9%) in detecting genomic variants. Additionally, circulating tumor DNA (ctDNA) assays identified specific mutations that were undetectable in tumor specimens. **CONCLUSIONS:** The development of the "Moonshot" program demonstrates proof of concept for the effective capture of clinical and genomic data from a large population of cancer patients within an integrated health network. There is a high level of agreement in detecting genomic variants in matched tumor and blood samples. Ongoing refinement of the initiative will further advance cancer research and personalized care.

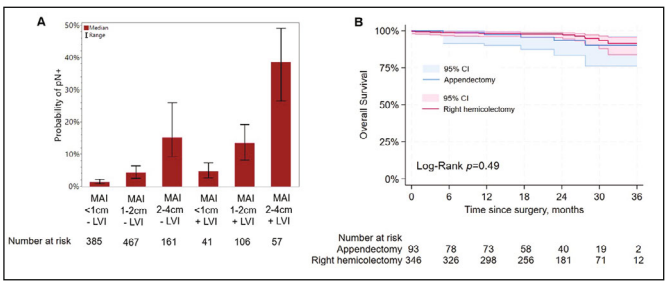


P189. Appendiceal Neuroendocrine Tumors: Prognostic Role of Mesoappendiceal Invasion and Implications for Recommending Right Hemicolectomy Versus Simple Appendectomy

Diamantis I. Tsilimigras, MD, PhD[1]; Pamela Lu, MD[2]; Susan Tsai, MD[3]; Tim Pawlik[4]; Bhavana Konda[5]; Vineeth Sukrithan[6]; Jordan M Cloyd, MD[7]
[1]The Ohio State University, Columbus, OH, US; [2]The Ohio State University, Columbus, OH, US; [3]The Ohio State University, Columbus, OH, US; [4]The Ohio State University, Columbus, OH, US; [5]The Ohio State University, Columbus, OH, US; [6]The Ohio State University, Columbus, OH, US; [7]The Ohio State University, Columbus, OH, US

INTRODUCTION: Mesoappendiceal invasion (MAI) is considered a poor prognostic factor among patients with appendiceal neuroendocrine tumors (aNET). Current ENETS and NCCN guidelines are conflicting as to whether MAI alone warrants right hemicolectomy (RHC) especially in the absence of other concomitant high-risk features. We sought to examine the prognostic role of MAI in patients with resected aNET focusing on the probability of nodal disease and long-term outcomes following RHC versus simple appendectomy. **METHODS:** Patients who underwent resection of aNET between 2018-2019 were identified in the National Cancer Database. aNET with a pathologic pT3 stage according to the 8th AJCC staging system (i.e. size >4cm or MAI+) were identified and further sub-stratified as pT3a (size ≤4cm, +MAI) or pT3b (size >4cm, +/-MAI). The association of MAI with nodal metastasis (pN+) relative to the presence/absence of other risk factors was examined. The prognostic impact of extent of resection (i.e. RHC versus appendectomy) among patients with MAI was assessed. **RESULTS:** Among 4,819 patients who underwent resection for aNET, 1,662 had pT3 tumors of which 1,309 (78.7%) were pT3a

and 353 (21.2%) were pT3b. The overall incidence of pN+ disease among all patients who underwent resection of aNET was 7.5% and varied by AJCC pT stage (pT1: 0.9%, pT2: 9.2%, pT3: 8.5%, pT4: 29.8%, p<0.001). pT3a stage was less frequently associated with pN+ disease compared with pT3b disease (6.8% vs 14.7%, p=0.02). In contrast, increasing tumor size (p<0.001), and lymphovascular invasion (LVI) (p<0.001) were the strongest predictors of pN+ among patients with pT3 aNET. In the absence of other established risk factors, the presence of MAI alone was associated with a low probability of pN+ (Figure 1a). Although RHC yielded a higher number of LNs than simple appendectomy (median: 18 LNs vs median: 0, p<0.001), the median number of metastatic LNs among individuals with pT3 disease was similar (median: 0 vs median: 0, p=0.10). The 3-year OS among patients with pT3 aNET was comparable following RHC versus simple appendectomy (91.6% vs 90.5%, p=0.49) (Figure 1b). On multivariable analysis, the presence of MAI was not independently associated with worse OS following aNET resection (HR=0.67, 95%CI 0.42-1.09, p=0.11). **CONCLUSIONS:** Among patients with resected aNETs, mesoappendiceal invasion alone, in the absence of other established risk factors, was associated with a low likelihood of nodal metastasis and equivalent long-term outcomes, with no differences observed based on extent of surgical resection. The presence of MAI alone should not be an indication for RHC and current guidelines should be revisited.



P190. Assessing Opioid Exposure in Pain Management After Cytoreductive Surgery: A Comparison of Epidural Analgesia and Continuous Wound Infiltration

Panagiota Chrysovalanto Koukoutsidi, MD, MSc[1]; Konstantin Balonov, MD[2]; Martin D. Goodman, MD[3]
[1]Tufts Medical Center, Boston, MA, US; [2]Tufts Medical Center, Boston, MA, US; [3]Tufts Medical Center, Boston, MA, US

INTRODUCTION: Epidural analgesia (EA) and ON-Q infiltrating catheters are common methods for postoperative pain management following cytoreductive surgery (CRS) with or without hyperthermic intraperitoneal chemotherapy (HIPEC). We aim to compare immediate postoperative outcomes after CRS ± HIPEC with EA versus CWI analgesia. **METHODS:** We retrospectively reviewed a prospectively maintained database of patients who underwent CRS ± HIPEC. The epidural group received opioid with local anesthetic (LA). ON-Q catheters were infiltrated with LA. All patients received acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDS) postoperatively. Patients with history of opioid use were excluded. Wilcoxon rank-sum test was used for comparative statistics and significance threshold was set at p<0.05. **RESULTS:** During our institution's transition from epidural use to CWI catheters between 2018 and 2023, ninety-two (92) patients underwent CRS ± HIPEC. Fifty-one (51) received EA and forty-one (41) patients received ON-Q catheters. Detailed results are presented in Table 1. No statistically significant differences were observed in pain scores on postoperative day 1 and 5 (p=0.15), duration of analgesia (p=0.12), return of bowel function (p=0.19) or hospital length of stay (p=0.16). Regarding in-hospital opioid exposure, there was no significant difference in the median IV (p=0.15) and per os (p=0.9) use of opioids. **CONCLUSIONS:** We observed no significant differences in immediate postoperative outcomes or IV/per os opioid exposure after CRS ± HIPEC between patients receiving EA or ON-Q catheters. Notably, patients receiving EA which contains opioids, may experience increased total opioid exposure compared to ON-Q patients. This highlights the potential advantage of ON-Q catheters in minimizing opioid exposure postoperatively after CRS ± HIPEC.

	Epidural (n=51)	ONQ Catheters (n=41)	*p* value
	Median (IQR)		
Postoperative outcomes			
Pain score POD 1	3.5 (1.5-4.5)	4.75 (3.75-5.75)	0.15
Pain score POD 5	2.5 (0.5-4.5)	3.75 (1.5-6)	0.11
Duration of analgesia	4.5 (3.4-5.6)	5 (3.5-6.5)	0.12
Return of bowel function	4.5 (3-6)	5 (4-6)	0.19
Length of stay	9 (7-11)	8 (5.5-10.5)	0.16
IV Opioids (MME)	44.4 (0-90.1)	20.4 (0-54.75)	0.15
Per os Opioids (MME)	30 (0-60)	30 (0-58.13)	0.9
Total Opioids IV/per os (MME)	30 (0-100)	40.25 (0-81.35)	0.41

P191. Automating the Identification of Postoperative Complications in Cancer Surgery Using Large Language Models

Meghan Conroy[1]; Adhitya Ramamurthi, MD, MS[2]; Nathan Wolfrath[3]; Bhabishya Neupane[4]; Yun Xing, PhD[5]; Kathleen Christians[6]; Callisia Clarke, MD, MS, FSSO[7]; Ugwuji N Maduekwe, MD, MMSc, MPH, FACS, FSSO[8]; Priya Deshpande[9]; Anai N Kothari, MD, MS[10]
[1]Medical College of Wisconsin, Milwaukee, WI, US; [2]Medical College of Wisconsin, Milwaukee, WI, US; [3]Medical College of Wisconsin, Milwaukee, WI, US; [4]Medical College of Wisconsin, Milwaukee, WI, US; [5]Medical College of Wisconsin, Milwaukee, WI, US; [6]Medical College of Wisconsin, Milwaukee, WI, US; [7]Medical College of Wisconsin, Milwaukee, WI, US; [8]Medical College of Wisconsin, Milwaukee, WI, US; [9]Medical College of Wisconsin, Milwaukee, WI, US; [10]Division of Surgical Oncology, Department of Surgery, Medical College of Wisconsin, Milwaukee, WI, US

INTRODUCTION: Postoperative complications in oncology patients can delay adjuvant treatment, negatively impact quality of life, and increase early mortality. Efficient and accurate reporting of complications is essential. Manual extraction from electronic health records (EHRs) is time-consuming and error-prone. This study evaluated the performance of large language models (LLMs) in identifying postoperative complications from clinical notes and other EHR data. **METHODS:** Patients undergoing gastrointestinal oncologic resections from 2016-2023 were identified from an institutional quality improvement database. Clinical notes, lab results, and imaging reports from postoperative days 0-90 were analyzed. Four LLMs—GPT-4o, GPT-4o-mini, Mistral-large, and Mistral-NeMo—were deployed in a HIPAA-compliant Azure cloud environment. Each model was tasked with identifying eight complications: surgical site infection (SSI), sepsis, pulmonary embolism (PE), clostridium difficile colitis (C. Diff), urinary tract infection (UTI), pneumonia (PNA), readmission within 30 days, and unplanned return to the operating room (ROR). Model outputs were compared to manually abstracted data, and metrics including accuracy, sensitivity, specificity, and F1 scores were calculated. **RESULTS:** A total of 1,620 cases were included. Model accuracy ranged from 88.2% to 94.4%, with GPT-4o performing best (94.4%, 90.4-99.3%), followed by Mistral-large (94.0%, 91.0-98.8%) and GPT-4o-mini (92.5%, 90.4-93.9%). GPT-4o's sensitivity/specificity ranged from 0.58/0.95 for SSI to 1.00/0.99 for PE, excelling in PE and ROR identification. Mistral-NeMo performed best for C. Diff (0.71/0.98), PNA (0.80/0.89), and readmission (0.93/0.54), while GPT-4o-mini had the highest performance for sepsis (0.41/0.94), and Mistral-large for SSI (0.65/0.93) and UTI (0.63/0.94). **CONCLUSIONS:** LLMs can identify postoperative complications in oncology patients from EHR data, demonstrating high sensitivity, specificity, and accuracy. However, no single LLM performs optimally across all complications, emphasizing the need for task-specific models. LLMs offer the opportunity to automate manual abstraction processes, requiring computations in privacy-secure environments, task-specific LLM development, and human-in-the-loop verification for correctness.

P192. Characteristics of older patients undergoing major oncological surgery: Insights from the Geriatric Surgery Verification Program

Omid Salehi[1]; Irving Zhao[2]; Joanna Abi Chebl[3]; Ponnandai Somasundar[4]; Abdul Saied Calvino[5]; N Joseph Espat[6]; Lidia Vognar[7]; Mohammad Ali[8]; Sasha L Lightfoot, DO[9]; Sung Kwon, MD MPH[10]
[1]Roger Williams Medical Center, Providence, RI, US; [2]Boston University School of Medicine, Boston, MA, US; [3]Roger Williams Medical Center, Providence, RI, US; [4]Roger Williams Medical Center, Providence, RI, US; [5]Roger Williams Medical Center, Providence, RI, US; [6]Roger Williams Medical Center,

Providence, RI, US; [7]Roger Williams Medical Center, Providence, RI, US; [8]Roger Williams Medical Center, Providence, RI, US; [9]Roger Williams Medical Center, Providence, RI, US; [10]Roger Williams Medical Center, Providence, RI, US

INTRODUCTION: Geriatric oncology patients represent a distinctive population with unique vulnerabilities that impact perioperative considerations and management. Studies outlining the burden of geriatric medical conditions and syndromes among those undergoing major oncological surgery are lacking, along with understanding of the goals of care for this population. **METHODS:** We performed a single-institutional review of the initial 50 patients who enrolled in the American College of Surgeons' Geriatric Surgery Verification Program (GSV) program implemented for those ≥65 years undergoing major oncological surgery during the year 2023. Patient variables were categorized into four domains - somatic, functional, psychological, and social. Patients' primary goal of care was classified as extending life, maintaining independence, reducing pain, and reducing other symptoms. **RESULTS:** The mean age of participants was 75.4 years (± 7.5). They were mostly White (72%), English-speaking (78%), with similar distribution of sex (54% female). In the somatic category, nearly 40% were at moderate to high nutrition risk and 61.5% had a Geriatric 8 score of ≤14. In the functional category, 34.7% used a cane or walker, 6.4% had history of falls, and 22.4% had some degree of frailty. In the psychological category, >70% reported some degree of depression. Delirium risk factors were identified in 43% of the patients. In the social category, more than half (54.3%) of patients were never married, widowed, or divorced. Financial distress screening was positive in 23.3%. In regard to goals of care, majority (79.3%) reported wanting to maintain independence while only 37.9% reported extending life as primary concern. **CONCLUSIONS:** We found high proportions of patients with low G8 score, frailty, perioperative risk of falls and delirium, lack of social support, and financial distress. To meet the care goals of this population, a comprehensive geriatric surgery program is essential to preoperatively capture and mitigate risk factors.

P193. Characterizing an Acute Care General Surgery Service and Patients Receiving Care at a Stand-Alone Cancer Center after One Year of New Service Initiation

Erin A Strong, MD, MBA, MPH[1]; Kelcie M Jagodzinski, PA[2]; Jessica N Collera, NP[3]; Sean P Dineen[4]; Ji Fan, MD, MBA[5]
[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4]Moffitt Cancer Center, Tampa, FL, US; [5]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Patients with cancer diagnoses often require acute care general surgery (ACS) consultation, whether for complications from their cancer, their cancer treatment, or unrelated to their cancer but while undergoing cancer-directed therapy. This unique population that may benefit from a carefully designed care service to meet their needs. The purpose of this study was to describe the organization of a new ACS service at a stand-alone cancer center and characterize the patients receiving ACS care. **METHODS:** We performed a retrospective review of patients receiving care with the ACS service via inpatient or Urgent Care consultation or referral to clinic at a stand-alone cancer center from July 2023 to September 2024. Demographic, clinical, and operative details were obtained. Descriptive statistics were utilized. **RESULTS:** During workdays, the ACS team included a dedicated ACS surgeon, two advanced practice providers, and rotating residents and/or fellows. 602 patients were seen as urgent care or inpatient consults during the study period. Of those, 276 (46%) were women, and median age 63 years (IQR 54-72). Consults resulted in surgery during the same admission in 88 (15.3%) of cases. A total of 184 operations were performed by the primary surgeon for the service. Of those operations, 51 (27.7%) were categorized as emergent. The most common primary cancer diagnoses were hematologic in 39 (21.2%), colorectal in 32 (17.4%), and genitourinary in 28 (15.2%). The most common indications for surgery were related to bowel etiologies in 48 (26.1%), hernias in 32 (17.4%), gallbladder in 31 (16.8%), and gastric or jejunostomy tube placement in 23 (12.5%). While 88 (47.8%) operative approaches were open, 47 (25.5%) were robotic and 30 (16.3% laparoscopic). In the outpatient setting, the ACS surgeon had 330 clinic visits. Most patients (48.5%) were already established with other services at the institution, while 19.4% were established patients with the ACS service, and 31.5% were postop visits. **CONCLUSIONS:** An ACS service with a dedicated surgeon and clinical team at a standalone cancer center provides timely care for a unique patient population, while also increasing operative and scheduling capacity to allow subspecialty surgeons to focus on new and established patients in their practice niches. Careful attention should be paid to optimizing utilization and flow of the service, including dedicated resources such as clinic time and space and operative block time. It also provides a valuable educational experience for trainees and potential for outcomes research.

P194. Clinical utility of preoperative Ga-68 DOTATATE-PET imaging in GEP-NETs

Teodora C Dumitra[1]; Monica R Justo, MD[2]; Marco Ventin[3]; Nicholas Nissen, MD[4]; Andrew Hendifar[5]; Cristina R. Ferrone, MD, MS, FSSO[6]; Alexandra Gangi, MD, FSSO[7]
[1]Cedars Sinai Medical Center, Los Angeles, CA, US; [2]Cedars Sinai Medical Center, Los Angeles, CA, US; [3]Cedars-Sinai Medical Center, Los Angeles, CA, US; [4]Cedars-Sinai Medical Center, Los Angeles, CA, US; [5]Cedars Sinai Medical Center, Los Angeles, CA, US; [6]Cedars-Sinai Medical Center, Los Angeles, CA, US; [7]Cedars-Sinai Medical Center, Los Angeles, CA, US

INTRODUCTION: Although imaging technologies are continually evolving, accurate preoperative staging of gastroenteropancreatic neuroendocrine tumors (GEP-NETs) remains inadequate. The goal of this study was to determine the rate of nodal upstaging and its determinant factors in patients undergoing resection for GEP-NETs. **METHODS:** A single institution retrospective cohort study was performed from 2013-2024. Patients with well differentiated non-functional GEP-NETs who underwent surgical resection and had preoperative Ga-68 DOTATATE-PET imaging were identified. Clinicopathologic features and imaging reports were reviewed. Nodal upstaging was defined as higher pathologic nodal burden than seen and described on imaging. Usual descriptive statistics were applied. Chi2 exact test and univariate logistic regression were used to assess the association between imaging and pathologic nodal status. **RESULTS:** A total of 318 patients were identified, of which 115 were formally resected and had preoperative Ga-68 DOTATATE-PET imaging (54% pancreatic primary, 46% small bowel (SB)). The majority of patients were male (59%) and mean age at diagnosis was 62 years old (SD 13). Pathology confirmed Ki67<3 in 56% of patients, mitosis <2 in 77%. A mean of 18 lymph nodes (LN) (SD 12) were examined and LN metastasis were found in 59% of patients. Preoperative imaging identified the primary lesion in 86% of cases (80% SB, 94% pancreas) and LN metastasis in 47% of patients. Nodal upstaging was identified in 26% of this cohort, with a significantly higher proportion of nodal upstaging in tumors with lymphovascular invasion (p=0.001), perineural invasion (p=0.039), and in higher T stages (p=0.02). On univariate logistic regression, positive LN on Ga-68 DOTATATE-PET was significantly associated with findings of pathologically confirmed postive LN (OR 45, 95%CI 12.5-167.3; p<0.001). **CONCLUSIONS:** Despite the utility of Ga-68 DOTATATE-PET imaging, there is still a significant rate of nodal upstaging, which may impact preoperative planning and prediction of disease progression. Future work integrating artificial intelligence could enhance risk stratification and lead to more precise staging and treatment planning for these patients.

P195. Defining the Surgical Oncology Experience During General Surgery Residency: A Multi-Institutional Study from the US ROPE Consortium

Anna Reagan, MD[1]; Kelsey Montgomery, MD MSPH[2]; Matthew Woeste, MD PhD[3]; Jeffrey Sutton, MD[4]; Jitesh Patel, MD[5]; Joseph Kim, MD[6]; Alex Cortez, MD[7]; Leah Winer, MD[8]
[1]University of Kentucky, Lexington, KY, US; [2]University of Alabama-Birmingham, Birmingham, AL, US; [3]University of Louisville, Louisville, KY, US; [4]Medical University of South Carolina, Charleston, SC, US; [5]University of Kentucky, Lexington, KY, US; [6]University of Kentucky, Lexington, KY, US; [7]Mayo Clinic, Rochester, MN, US; [8]University of Kentucky, Lexington, KY, US

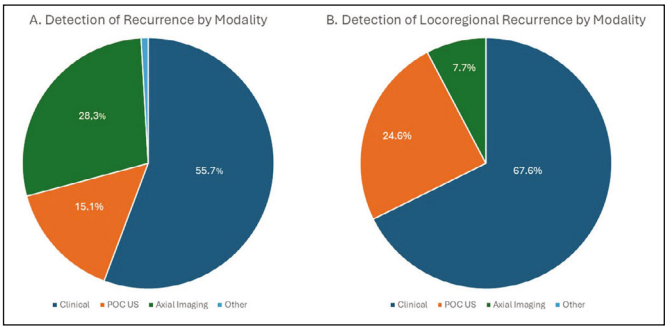
INTRODUCTION: Complex general surgical oncology (CGSO) remains a competitive fellowship match, but clinical exposure to surgical oncology during general surgery residency is not well characterized. In this study, we examined the training environment and experience of general surgery residents pursuing CGSO fellowship. **METHODS:** Demographics, program characteristics, and ACGME case logs were collected for graduates from 20 general surgery residency programs in the US Resident OPerative Experience (ROPE) Consortium from 2010-2020. CGSO fellowship matriculants (CGSO Group) were compared to graduates entering other surgical fellowships/practice (Non-CGSO Group). Surgical oncology relevant (SOR) cases included liver, pancreas, breast, endocrine, laparoscopic colorectal, and abdominoperineal resection. **RESULTS:** Among 1343 graduates, 80 (6%) matriculated into CGSO fellowship. Of the CGSO Group, 99% (N=79) graduated from university programs, 65% (N=52) were male, 66% (N=53)

were white, and 10% (N=8) were underrepresented minorities, similar to Non-CGSO demographics (all p>0.05). CGSO residents were more likely to graduate from programs with CGSO-trained faculty (95% v 86%), a dedicated surgical oncology division (81% v 66%), and an NCI-designated cancer center (85% v 68%, all p<0.05). Median total cases were similar between CGSO and Non-CGSO Groups (1172 v 1163, p>0.05). However, CGSO-bound graduates logged greater median SOR procedures (162 v 141), including liver (+4), pancreas (+10), endocrine (+7), and laparoscopic colorectal cases (+5, all p<0.05). CGSO residents from programs with an affiliate CGSO fellowship participated in more SOR cases (181 v 155); this association was most pronounced at the surgeon junior level (133 v 93, both p<0.05) and did not impede chief SOR volume. In adjusted analysis, CGSO matriculation was associated with residency training at an NIH-funded department (OR 4.8, CI 1.2-19.8), dedicated research time (OR 5.6, CI 3.0-10.4), and increased SOR cases (OR 5.6, CI 1.3-24.7, all p<0.05). **CONCLUSIONS:** Graduates matriculating into CGSO fellowship have a unique general surgery training experience and finish with more surgical oncology cases. This could reflect concerted efforts to prepare for fellowship and/or the influence of surgical oncology immersion on career interest. By characterizing the surgical oncology pipeline and clinical exposure during general surgery residency, these data highlight opportunities for educators to bolster CGSO recruitment and strengthen fellowship training.

P196. Detection of Recurrence in Stage II and III Melanoma Patients Using Point of Care Ultrasound

Julia Geaghan-Breiner[1]; Conor H. O'Neill[2]; Jessica A. Cintolo-Gonzalez, MD[3]
[1]Larner College of Medicine, University of Vermont, Burlington, VT, US; [2]Division of Surgical Oncology, University of Vermont Medical Center, Burlington, VT, US; [3]Division of Surgical Oncology, University of Vermont Medical Center, Burlington, VT, US

INTRODUCTION: National Comprehensive Cancer Network (NCCN) provides clear guidelines for nodal surveillance with clinical evaluation and ultrasound (US) for patients with a positive sentinel lymph node biopsy (SLNB). However, the role of US is not clarified for Stage II patients nor for Stage III patients with in-transit or clinically positive melanoma. Given our surgical oncology group employs point of care (POC) ultrasound for nodal surveillance for all Stage II and III patients, we aimed to determine the contribution of US in detection of recurrence to assess value of POC US in this patient population. **METHODS:** A single-institution retrospective review was conducted of patients presenting with Stage II and III melanoma using the American Joint Commission on Cancer (AJCC) 7th and 8th edition, based on year of diagnosis. Patients who experienced any recurrence of disease were identified. Type of recurrence, classified as local, lymph node, in transit, or distant, was recorded as was the method for recurrence detection: clinical assessment, US, and axial imaging (PET or PET/CT, CT, or MRI). We defined detection by clinical assessment as either a finding on physical exam or a finding on imaging that was ordered based on an elicited patient symptom. Given that US detected only locoregional recurrences (local, and in-transit recurrences), we also assessed the rate of detection for each modality specifically for locoregional recurrences. **RESULTS:** There were a total of 207 patients identified with Stage II melanoma of whom 39 recurred (18.8%) and 202 patients with Stage III melanoma of whom 67 (33.1%) experienced recurrences. In the overall cohort, 55.7% of recurrences were detected with clinical assessment (61.5% in Stage II and 52.2% in Stage III). Ultrasound detected 15.1% of recurrences (15.4% in Stage II and 13.4% in Stage III) with axial imaging identifying 28.3% of recurrences (20.5% Stage II and 32.8% Stage III) (Figure 1A). Locoregional recurrence made up 65 (61.3%) of recurrences (64% Stage II and 60% Stage III). For locoregional recurrences, 44 [67.6 %] were identified clinically, 16 (24.6%) by US as compared with 5 [7.7 %] by axial imaging (Figure 1B). **CONCLUSIONS:** Clinical evaluation detected the majority of recurrences highlighting the importance of clinical surveillance. POC US identified about 1/4th of locoregional recurrences, with axial imaging detecting fewer locoregional recurrences than clinical exam or US. Additional cost-benefit analysis may further inform value of incorporating routine POC US with clinical evaluation in melanoma surveillance.



P197. Diagnostic time intervals and patterns of referral in pelvic soft tissue sarcomas

Catherine Sarre Lazcano[1]; Harini Suraweera[2]; Wendy Johnston[3]; Rebecca Gladdy[4]; Savtaj Brar[5]; Carol J Swallow[6]
[1]University of Toronto, Toronto, ON, CA; [2]University of Toronto, Toronto, ON, CA; [3]Mount Sinai Hospital, Toronto, ON, CA; [4]Mount Sinai Hospital, Toronto, ON, CA; [5]University of Toronto, Toronto, ON, CA; [6]Mount Sinai Hospital, Toronto, ON, CA

INTRODUCTION: Given the rarity of soft tissue sarcoma (STS) relative to epithelial cancers as a source of pelvic malignancy, patients often experience significant delays in diagnosis, referral and appropriate management. We aimed to capture the patient experience by measuring pre-treatment time intervals in patients with Pelvic (P-) STS. **METHODS:** Consecutive patients with an eventual diagnosis of P-STS (arising between the pubis/inguinal ligaments, sacrum, parietal peritoneum and pelvic floor), assessed at a single high volume referral center between 01/2000 and 07/2024 were identified from a prospectively maintained database. Retrospective chart review was conducted to ascertain 5 time intervals that describe the patient journey from first symptom/finding to start of treatment at the sarcoma center (Fig. 1). Comparisons between groups were made using Mann-Whitney U test. **RESULTS:** 177 patients with P-STS were included (M/F = 91/86, median age 56). 151 patients (85%) presented with symptoms. Median tumor size was 8.2 cm (range 1.8-37). The top 3 histologies were leiomyosarcoma, dedifferentiated liposarcoma and solitary fibrous tumor (n= 38, 31 and 19, respectively). Pre-treatment biopsy was done in 146 patients (82%), with 41 (23%) needing ≥2 biopsies to reach a diagnosis. In 71 cases (40%), histologic diagnosis was changed after pathology review at the sarcoma center. Prior to being referred, 64 (36%) patients underwent surgery, 10 (6%) systemic treatment and 4 (2.3%) radiation. The median interval from symptoms to first seeing a physician was 2 wks (IQR 0.7-7.4), and from the latter to being seen at the sarcoma center was 16.3 wks (IQR 8-33.1). 137 patients (77%) saw ≥2 physicians prior to initial consultation at the sarcoma center. The median interval from that initial consultation to start of treatment was 6 wks (IQR 3-9.4). The median diagnostic interval (time from 1st seeing a physician to receiving a diagnosis of P-STS) was 11.1 wks (IQR 5.3-25.5). The total pre-treatment interval (from 1st seeing a physician to starting treatment) was a median of 21.4 weeks (IQR 13.9-40.7)**.** There were no differences in any of the time intervals based on patient sex, age, or histologic subtype. **CONCLUSIONS:** In patients with P-STS managed at a sarcoma referral center, the most significant source of delay prior to starting treatment related to making a diagnosis and referring appropriately, i.e. system-level factors. Patient and tumor factors did not appreciably contribute to delays. Greater awareness and referral prior to diagnosis could address these challenges to optimize P-STS patient care.

P198. Evaluating the relationship between anemia, transfusion, and thromboembolic events in surgical geriatric cancer patients: a national study

Leah Hendrick[1]; Erin A Strong, MD, MBA, MPH[2]; Cindy Yeoh[3]; Seth Felder, MD[4]; Sophie Dessureault[5]; Julian Sanchez, MD[6]; Sean P Dineen[7]; Michael Wach[8]; Daniel A Anaya, MD[9]; Amalia Stefanou[10]
[1]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [4]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [5]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [6]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [7]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [8]H. Lee

Moffitt Cancer Center and Research Institute, Tampa, FL, US; [9]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US; [10]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, US

INTRODUCTION: Anemia and blood transfusion are associated with poor outcomes in cancer patients. Although geriatric cancer patients often have more baseline anemia than younger patients, the relationship between anemia, transfusion, and surgical outcomes in geriatric cancer patients has not been well described. We sought to evaluate the impact of anemia and transfusion on development of postoperative deep vein thrombosis (DVT) and pulmonary embolism (PE) for geriatric patients undergoing abdominal cancer operations. **METHODS:** Adult patients undergoing abdominal cancer operations between 2005 and 2020 were identified in the ACS-NSQIP database. Patients were stratified by age, degree of anemia and transfusion requirements, and primary disease site. Anemia was classified by the World Health Organization (WHO) system. DVT was defined as any deep venous thrombosis requiring anticoagulation. Factors associated with development of DVT and PE were evaluated by logistic regression. **RESULTS:** 411,710 patients underwent abdominal cancer operations. 226,240 were >65yo, and 105,280 were >75yo. Primary sites were lower GI (46.3%), genitourinary (GU) (25.7%), hepatobiliary (16.4%), upper GI (7.2%), and gynecologic (GYN) (4.4%). 16,383 had postoperative anemia requiring transfusion (PART). With increasing age, patients were more likely to be underweight (p<0.001), partially or totally dependent (p<0.001), anemic (p<0.001), require transfusion (p<0.001), and to have a surgical complication (p<0.001). After adjusting for covariates, male sex (p=0.005), age >65 years (p=0.036), higher ASA classification (p<0.001), BMI over 24.9 (p<0.001), upper GI operations (p<0.001),disseminated cancer (p <0.001), discharge to a location other than home (p<0.001), and PART (p<0.001) were all associated with increased incidence of DVT or PE. By subgroup analysis of patients with severe anemia, increasing age (OR 1.105, 95% CI 1.042-1.171, p<0.001) and PART remained associated with DVT or PE compared to those not transfused, with PART demonstrating an almost two-fold increased risk (OR 1.99, 95% CI 1.88-2.10, p<0.001). **CONCLUSIONS:** Geriatric surgical patients with PART have increased risk of postoperative DVT and PE, regardless of anemia severity. Preoperative optimization is imperative in this population. Further prospective data is needed to delineate which geriatric cancer patients are at highest risk of PART.

P199. Factors Influencing Independent Medical Review Decisions in Oncology Care: A Mixed Methods Analysis of 2583 Cases

Anna Schoenbrunner, MD[1]; Adrian Diaz[2]
[1]Rush Medical Center, Chicago, IL, US; [2]University of Chicago, Chicago, IL, US

INTRODUCTION: Independent medical reviews (IMRs) play a critical role in determining patient access to oncological treatments, particularly when coverage is denied by health plans. Understanding the factors that influence these decisions can inform clinical practice, policy development, and patient advocacy. **METHODS:** A comprehensive thematic and quantitative analysis was conducted on 2583 anonymized IMR cases involving patients who requested authorization and coverage for various solid tumor diagnosis and treatments after initial denial by health plans. The dataset included patient demographics, cancer subtypes, treatment categories, and IMR outcomes (upheld or overturned). Data were coded and analyzed to identify recurring themes and assess the influence of specific factors on IMR outcomes. **RESULTS:** Overall, 1153 cases were overturned (44.6%) while 1,430 decision were upheld (55.4%). Most reviews were of patients aged 41 to 64 years (n= 2,044, 80.2%) and 56.1% of patients were female. The most common cancer subtype was breast (n=752, 29.1%), followed by urologic (n=596, 23.1%), gastrointestinal (n=383, 14.8%), and skin and soft tissue (n=320, 12.4%). The most common claim reviewed was for additional diagnostic test (n=1,103, 42.7%), followed by cancer treatment, not including chemotherapy (n=959, 37.1%) and for pharmaceuticals including chemotherapy (n= 291, 11.3%). On risk-adjusted logistic regression, breast cancer was the only cancer subtype associated with a statistically significant odds of having an overturned decision (OR: 1.41, 95% CI 1.05 to 1.89). Additional diagnostic tests were the only claim with statistically significant odds of being overturned (OR: 2.14, 95% CI 1.15 to 3.98). Qualitative analysis of IMR findings identified 5 major themes: 1. Adherence to Clinical Guidelines and Evidence-Based Practice, 2. Evaluation of Medical Necessity, Clinical Benefit, and Patient Safety, 3. Emerging Treatments and Experimental Therapies, 4. Personalized Medicine and Genomic Testing, and 5. Access to Care, Cost-Effectiveness, and Resource Utilization. Subthemes and exemplary quotes are reported in table 1. **CONCLUSIONS:** IMR decisions in oncology are multifaceted, balancing evidence-based practice, patient-specific factors, safety considerations, and resource utilization. Adherence to clinical guidelines and robust evidence are paramount in approvals. Understanding these factors can help clinicians navigate coverage determinations and advocate for patient access to necessary treatments, enhancing authorization requests and improving patient outcomes.

Table 1. Thematic Analysis of Independent Medical Review Summary

Theme	Subthemes	Exemplary quote
Adherence to Clinical Guidelines and Evidence-Based Practice	Alignment with National Guidelines	...represents the standard approach for the management of metastatic breast cancer and is recommended by the NCCN.
	Reliance on Peer-Reviewed Clinical Evidence	…there is a lack of clinical data published in the peer-reviewed medical literature to support …
Evaluation of Medical Necessity, Clinical Benefit, and Patient Safety	Evaluation of Medical Necessity and Clinical Benefit	…this added level of precision does not provide significant clinical benefits."
	Safety and Risk Management	… has an acceptable safety profile and demonstrated single-agent activity with confirmed partial …
Emerging Treatments and Experimental Therapies	Experimental and Investigational Treatments	The Health Plan considers IMRT experimental/ investigational in the treatment of pancreatic cancer and has denied coverage
	Technological Advancements and Emerging Treatments	"Emerging evidence suggests that low metastatic tumor burden may have an improved response to contemporary treatments ...
	Need for Further Clinical Investigation	…HIFU warrants further investigation as an emerging local therapy, but noted that data are lacking to establish its role in the treatment…
Personalized Medicine and Genomic Testing	Use of Targeted Therapies Based on Genetic Profiles	…all patients with recurrent disease should undergo biomarker testing to evaluate for targeted therapies.
	Appropriateness of Genetic Testing	the requested Tempus Gene Panel genetic testing is likely to be more beneficial for evaluation of the patient's medical condition than any available standard therapy.
Access to Care, Cost-Effectiveness, and Resource Utilization	Access to Care and Provider Networks	…enrollee has requested reimbursement and out of network surveillance studies for her pancreatic cancer.
	Cost-Effectiveness and Resource Utilization	The scan is a recognized, cost-effective, independent predictor of future disease …

P200. Impact of Declining Curative Resection on Patient-centered Outcomes in Older Adults with Gastrointestinal Cancer

Alexa D Melucci, MD, MS[1]; Bailey Hilty Chu, MD[2]; Totadri Dhimal[3]; Anthony Loria, MD[4]; Christopher T Aquina, MD[5]; Erika Ramsdale, MD[6]; Paula Cupertino, PhD[7]; Larissa K Temple, MD[8]; Fergal J Fleming, MD[9]
[1]University of Rochester Medical Center, Department of Surgery, Rochester, NY, US; [2]University of Rochester Medical Center, Rochester, NY, US; [3]University of Rochester Medical Center, Rochester, NY, US; [4]University of Rochester Medical Center, Department of Surgery, Rochester, NY, US; [5]AdventHealth Orlando, Department of Surgery, Orlando, FL, US; [6]University of Rochester Medical Center, Department of Oncology, Rochester, NY, US; [7]University of Rochester Medical Center, Department of Surgery, Rochester, NY, US; [8]University of Rochester Medical Center, Department of Surgery, Rochester, NY, US; [9]University of Rochester Medical Center, Department of Surgery, Rochester, NY, US

INTRODUCTION: The treatment paradigm of older adults with GI cancer is evolving with increased focus on multidisciplinary geriatric oncologic and surgical care. Despite advances in chemoradiotherapy older patients are offered oncologic resection. The extent to which older adults with GI cancers decline resection remains unclear, and we aimed to assess trends, factors, and outcomes associated with declining recommended oncologic resection. **METHODS:** Patients aged >65 diagnosed with stage I-III esophageal, gastric, pancreatic, or colorectal cancer between 2004-2017 were identified in the New York State Cancer Registry and Statewide Planning and Research Cooperative System. The exposure was whether a patient declined oncologic resection. Patients not recommended to undergo resection or lost to follow-up were excluded. Outcomes included trends and factors associated with declining resection, number of unplanned admissions and surgical procedures, 1-year days alive and out of hospital, and 1-year mortality. **RESULTS:** Of the 17,848 eligible patients, 506 (2.8%) declined oncologic resection and the rate of declining resection decreased from 3.8% in 2004 to 2.4% in 2017. Patients who declined resection were significantly older (median age 84 vs. 75), female (61.9% vs. 46.9%), more likely to have a geriatric syndrome at diagnosis (46.6% vs. 23.9%), did not receive chemoradiotherapy (99.6% vs. 62.2%), and had upper GI cancer (81.6% vs. 75.3%). After risk adjustment, age, neighborhood poverty, congestive heart failure, geriatric syndrome at diagnosis, cancer type, and stage III cancer were associated with increased odds of declining resection while marriage, chemoradiotherapy, stage II cancer, and diagnosis year were associated with decreased odds (Figure 1). Among patients who declined resection, 253 (50%) had an unplanned admission (range 1-10) within one year of diagnosis and 8 (1.6%) had an unplanned surgical procedure. Declining resection was associated with a 2.2 times greater risk of 1–year mortality (HR, 2.22; 95% CI 1.94-2.53). The median (IQR) 1-year survival from diagnosis was 239 (65-598) days, and the 1-year days alive and out of hospital was 220 (59-

361) days. **CONCLUSIONS:** Older adults are undergoing oncologic resection, but understanding outcomes associated with declining resection is important in counseling older adults who are considering forgoing resection. These data suggest patients who decline resection are at increased risk of unplanned hospital admissions and only 60% of time alive and out of the hospital in the year after diagnosis. These patient-centered outcomes should be considered when managing patient expectations should they decide to decline surgical resection.

P201. Implementation of standardized venous thromboembolism prophylaxis for surgical oncology patients: a multidisciplinary quality improvement initiative

Jakob A Durden, MD[1]; Peter J Klauck, MD[2]; Vivian Leite Abud, MD[3]; Lindsey Knott, PA-C[4]; Benedetto Mungo[5]; Marco Del Chiaro, MD PhD[6]; Jason Brainard, MD[7]; Sarah Tevis, MD[8]

[1]University of Colorado School of Medicine, Aurora, CO, US; [2]University of Colorado School of Medicine, Aurora, CO, US; [3]University of Colorado School of Medicine, Aurora, CO, US; [4]University of Colorado School of Medicine, Aurora, CO, US; [5]University of Colorado School of Medicine, Aurora, CO, US; [6]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [7]University of Colorado School of Medicine, Aurora, CO, US; [8]University of Colorado School of Medicine, Aurora, CO, US

INTRODUCTION: Venous thromboembolism (VTE) is a significant and preventable postoperative complication leading to increased morbidity, mortality, and cost burden. Surgical oncology patients face particularly elevated risks of postoperative VTE due to confluence of myriad risk factors including longer operative times, advanced age, and chemotherapy. Prior studies have indicated that effective pharmacologic prophylaxis—including agent selection, dosage, timing, and adherence to treatment protocols—is crucial in mitigating post-operative VTE incidence. We addressed this critical issue through a quality improvement (QI) initiative aimed at enhancing VTE prophylaxis in the surgical oncology population. **METHODS:** We assembled a dedicated multidisciplinary QI team which conducted a chart review of surgical oncology patients diagnosed with perioperative VTE during fiscal years (FY) 22-23. We identified key areas for improvement, particularly in the standardization and implementation of pharmacologic VTE prophylaxis. Drawing from current literature and national guidelines, we developed a comprehensive "gold-standard" VTE prophylaxis protocol specifically tailored for surgical oncology (figure 1). This guideline detailed the selection of pharmacologic agents, appropriate dosing, and timing across pre-operative, intraoperative, and post-operative phases, while also addressing considerations for epidural management. The new protocol was presented to surgical oncology leadership for approval, followed by extensive education for perioperative teams to ensure adherence and minimize missed doses. Implementation began in July 2023, and post-implementation data were subsequently analyzed. **RESULTS:** The documented incidence of perioperative VTE in surgical oncology patients was 14 cases in FY22 and 12 cases in FY23. Retrospective compliance review of FY22 VTE cases revealed that 93% of patients received appropriate preoperative VTE prophylaxis; however, 0% of patients received appropriately timed initial postoperative medications, and 0% of patients had low molecular weight heparin as their first line agent. Following the introduction of the "gold-standard" VTE prophylaxis guidelines in July 2023, the incidence decreased to a total of 2 cases in FY24. This represents an 83% reduction in perioperative VTE rates. There was no change in postoperative hemorrhage rates between FY23 and FY24. **CONCLUSIONS:** The implementation of an evidence-based, department-wide VTE prophylaxis guideline achieved a substantial reduction in perioperative VTE rates among surgical oncology patients from FY23 to FY24 without an increase in postoperative hemorrhage rates.

P202. Improving Patient Care and Optimizing Resource Utilization through the Establishment of a Diagnostic Oncology Clinic

Richard Hoehn, MD[1]; Lauren Brister[2]; Peter Pronovost[3]; Brett Glotzbecker[4]; Ted Teknos[5]; Marcus Paschall[6]; Matt Kemmann[7]; Jordan Winter[8]

[1]University Hospitals Cleveland Medical Center, Cleveland, OH, US; [2]University Hospitals, Cleveland, OH, US; [3]University Hospitals, Cleveland, OH, US; [4]University Hospitals, Cleveland, OH, US; [5]University Hospitals, Cleveland, OH, US; [6]University Hospitals, Cleveland, OH, US; [7]University Hospitals, Cleveland, OH, US; [8]University Hospitals Cleveland Medical Center, Cleveland, OH, US

INTRODUCTION: Patients with symptoms or radiologic findings concerning for cancer are often admitted to the hospital for workup, diagnosis, and treatment planning. In the absence of a cancer diagnosis, there are no trained resources in conventional health care to efficiently manage this heterogeneous group of patients. Our health system established a Diagnostic Oncology Clinic (DOC) to 1) work up these findings in a timely and cost-effective manner, and 2) to prevent any new cancers from going undiagnosed. **METHODS:** Starting in April 2023, two advanced practice providers (APPs) already employed in our cancer center started seeing patients referred to the DOC, initially via email list serve and subsequently referred through an electronic order. With a goal of eliminating unnecessary inpatient care, we presented the new program at group meetings of our Emergency Department, Internal Medicine Department, and Trauma Division. After a 12-month pilot phase, we presented the DOC to the system-wide Primary Care Institute in April 2024. As referrals to the DOC increased, we received hospital support to hire a full-time nurse navigator in February 2024 and a full-time APP in August 2024. **RESULTS:** The DOC has seen 562 patients (average 43 per month, 54% female, 14% minority race/ethnicity), from 12 referrals in June 2023 to 81 in May 2024. Overall, 15% of patients are seen in person, 5% are seen virtually, and 80% are navigated directly to the appropriate specialty provider. The majority of referrals (27%) are from the Emergency Department, 46% of which do not have a regular primary care provider. The most common diagnoses for referral are lymphadenopathy (21%), masses within the GI tract (18%), and new lung mass (12%). Referrals are confirmed within 24hrs and patients contacted within 48hrs. On average, it took 20 days from date of referral to diagnostic resolution. Qualitative feedback from our referring providers has been universally positive and Emergency physicians report that many patients are now being discharged (with DOC referral) when they previously would have been admitted for workups. Ongoing analyses will quantify the number of unnecessary hospital admissions that have been avoided and potential dollars saved. **CONCLUSIONS:** Establishing a Diagnostic Oncology Clinic has improved patient and provider experience by creating a reliable, streamlined process for diagnosing and treating patients with new findings concerning for cancer. This program has also improved cost-effectiveness and highlighted "pain points" in our system for quality improvement.

P203. Introducing Checkbox Format for Remote Symptom Monitoring in Surgical Oncology Patients

Norma E Farrow, MD MHS[1]; Andrew Vickers[2]; Rebecca Yu[3]; Sigrid Carlsson[4]; Melissa Assel[5]; Jennifer Cracchiolo[6]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US

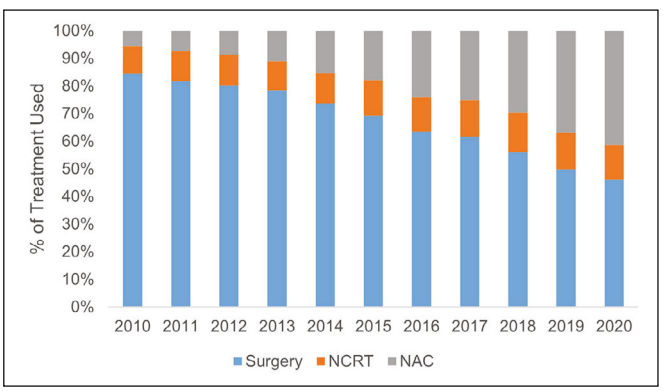
INTRODUCTION: There is great optimism with respect to use of ePROs in routine surgical oncology care given benefits seen in clinical trials including improved communication, reduced acute hospital encounters, and improved overall survival. However, "real world" clinical application will require novel approaches to survey delivery and visualization to ensure the tool is clinically useful, assesses symptoms accurately, and engages patients effectively. The objective of this study was to determine if presenting ePROs items for remote symptom monitoring in a checkbox format that uses hide and show logic to only present patients with the full assessment item if they check that they are experiencing the symptom, changed patient engagement or the psychometric properties of the legacy tool. **METHODS:** We used an interrupted before-after time-series design to test the new checkbox format to our historic experience using our well-established remote symptom monitoring platform, Recovery Tracker. All patients undergoing one of five most common procedures (prostatectomy, nephrectomy, mastectomy, hysterectomy and thyroidectomy) at the ambulatory surgery center of an NCI-designated Comprehensive Cancer Center- were assigned remote symptom monitoring questionnaires either with checkboxes (after period) or without checkboxes (before period). Patient engagement of the two formats was evaluated by comparing response rates using a Chi-square test. Mixed effects models were used to test the association between questionnaire type and each symptom adjusting for patient and operative factors, as well as questionnaire completion time. **RESULTS:** Among 31,702 patients undergoing surgery, the survey response rate (completing at least one survey) was higher in the checkbox group (89%; 95% CI 89%, 90%) compared to the group without checkboxes (75%; 95% CI 74%, 75%) by 15% (95% CI 14%, 16%; $p<0.001$). It took patients longer to complete the questionnaire without checkboxes than with checkboxes (1.98 vs 1.27 minutes, 95% CI 36.6, 40.8;0.001). Symptom scores were lower when using checkboxes in comparison to questionnaires without checkboxes, with the largest differences seen in fatigue interference (mean difference 0.9; 95% CI 0.9, 0.9). The checkbox

format demonstrated robust psychometric properties, measured by no change in variance, and correlation with known predictors of post-operative outcomes. **CONCLUSIONS:** The checkbox format for remote symptom monitoring in surgical oncology is completed at a higher rate and faster, highlighting ease of use and low patient burden, and had better psychometric properties because of stronger correlations known predictors. Use of a checkbox format is one strategy to improve patient engagement while accurately capturing clinically actionable symptoms postoperatively.

P204. Machine Learning Guided Neoadjuvant Chemoradiation in Pancreatic Ductal Adenocarcinoma

Lauren M Janczewski, MD, MS[1]; Joseph H Cotler, PhD[2]; Kelley Chan, MD, MS[3]; Bryan E Palis, MA[4]; Judy C. Boughey, MD[5]; John Abad, MD[6]; David Bentrem, MD, MS[7]; Akhil Chawla, MD[8]
[1]Northwestern Medicine, Chicago, IL, US; [2]American College of Surgeons, Chicago, IL, US; [3]Loyola University Medical Center, Maywood, IL, US; [4]American College of Surgeons, Chicago, IL, US; [5]Mayo Clinic, Rochester, MN, US; [6]Northwestern Medicine, Chicago, IL, US; [7]Northwestern Medicine, Chicago, IL, US; [8]Northwestern University, Chicago, IL, US

INTRODUCTION: While neoadjuvant chemotherapy (NAC) has shown improved outcomes for patients with pancreatic ductal adenocarcinoma (PDAC), the role of neoadjuvant chemoradiation (NCRT) remains controversial. We sought to (1) characterize trends in neoadjuvant treatment (2) identify characteristics of patients treated with NCRT and (3) evaluate the predictive ability of a machine learning model to identify patients who benefit from NCRT with resected PDAC. **METHODS:** This retrospective cohort study using the National Cancer Database identified patients with stage I-III PDAC (2010-2020) who underwent surgical resection, stratified by use of NCRT, NAC, or upfront surgery. Trends in treatment modalities were evaluated across the study period. Multivariable logistic regression assessed characteristics associated with NCRT use. Unadjusted rates of achieving negative margins and 1 year survival were compared between NCRT, and upfront surgery cohorts using chi-squared tests. A neural network machine learning model was constructed to predict which patients benefit from NCRT in terms of achieving negative margins and 1 year survival. **RESULTS:** Of 49,460 patients, 6,053 (12.3%) received NCRT, 10,893 (22.0%) NAC, and 32,514 (65.7%) upfront surgery. The proportion of patients treated with NCRT only ranged from 10.1-14.4% across all years whereas those treated with NAC increased from 5.5% in 2010 to 41.4% in 2020 (Figure). On multivariable analysis, patients treated with NCRT were more likely to have increasing clinical T category disease (vs T1, all $p>0.05$) yet were less likely older (>61 years old, all $p<0.05$) and treated at community hospitals (vs academic, OR 0.46, 95% CI 0.35-0.60). Patients treated with NCRT more frequently had negative margins (84.0% vs 76.8% for upfront resection vs 79.7% for NAC, $p<0.001$) and survival at 1 year (89.9% vs 74.5% for upfront resection vs 89.6% for NAC, $p<0.001$). Internal validation of a neural network model revealed good predictive abilities in estimating 1 year survival for patients treated with NCRT (accuracy: 0.9001, AUC-ROC: 0.6723), whereas a model predicting margin status (accuracy: 0.9298, AUC-ROC: 0.5571) was unsatisfactory. **CONCLUSIONS:** Although the use of NCRT remains less common for patients with PDAC, identifying which patients may benefit from NCRT in terms of 1 year survival is feasible through a neural network machine learning model. These results demonstrate the possible utility of machine learning in selection of NCRT for patients with PDAC; however, alternative models, datasets and/or biomarkers may be needed to accurately predict additional outcomes.



P205. Maximizing Quality Improvement Impact: Insights from Surgeons to Overcome Challenges in Patient Care

Doris Goubran, BHSc[1]; Iresha Ratnayake[2]; Pamela Hebbard[3]; Caroline Park[4]; Maziar Fazel Darbandi[5]; Kathleen Decker[6]; Megan Delisle[7]
[1]University of Manitoba, Winnipeg, MB, CA; [2]CancerCare Manitoba, Winnipeg, MB, CA; [3]Department of Surgery, University of Manitoba, Winnipeg, MB, CA; [4]Athabasca University, Athabasca, AB, CA; [5]Department of Surgery, University of Manitoba, Winnipeg, MB, CA; [6]CancerCare Manitoba, Winnipeg, MB, CA; [7]Department of Surgery, University of Manitoba, Winnipeg, MB, CA

INTRODUCTION: For quality improvement (QI) initiatives to yield meaningful improvements in patient care, they must lead to changes in clinical practices. To effectively change clinical practices, QI initiatives need to influence the behaviors of those directly involved in patient care. The objective of this study is to understand surgeon's vision of excellence and the factors that influence surgeons' behaviors when striving for excellence in patient care. **METHODS:** We created an interview guide based on the Theoretical Domains Framework. We recruited surgeons who performed breast cancer surgery in Manitoba, Canada between 2021-2024 using convenience sampling. Sixty-minute, virtual, semi-structured interviews were conducted by a trained qualitative interviewer. Inductive and deductive thematic analyses were conducted in duplicate by two independent coders. **RESULTS:** Twelve surgeons participated in the interviews. Their vision of excellence was to provide patient-centered, up-to-date, evidence-informed breast cancer care. Patient-centered care was described as providing timely care close to home with good oncological outcomes. Up-to-date and evidence-informed care included having expertise in multidisciplinary breast cancer care, access to the latest technology, and incorporating new oncoplastic techniques. Initially, surgeons perceived resource constraints within the healthcare system as insurmountable barriers to QI. Upon further probing, they identified strategies to help address these obstacles. These strategies included tracking their own quality metrics (e.g., wait time to surgery, using photographs to monitor and enhance the aesthetic outcomes of surgery), obtaining regular feedback from their patients, formalizing supportive groups for immediate expert insight, engaging in peer-to-peer learning, and uniting surgeons in advocacy. **CONCLUSIONS:** Surgeons who perform breast cancer surgery in Manitoba are strongly motivated to deliver patient-centered, up-to-date, evidence-informed care. By understanding barriers to QI and identifying practical strategies to help address them, we can better support surgeons to provide the best care possible. This approach may enhance surgeon engagement in QI initiatives, leading to better patient care and outcomes.

P206. Minimally Invasive Approaches to Gastric Cancer – Does Hospital Type Matter?

Julia Nowik, Medical Student[1]
[1]Medical College of Wisconsin, Milwaukee, WI, US

INTRODUCTION: Curative surgery for gastric adenocarcinoma has expanded to include minimally invasive (MIS) approaches to gastrectomy which are purported to increase the odds of achieving high quality post-operative and oncologic outcomes. Despite rapid uptake, it is unclear if these benefits are uniformly distributed. We hypothesized that hospital type influences the benefit of MIS approaches to gastric adenocarcinoma. **METHODS:** We used the National Cancer Database to perform a retrospective analysis of patients aged 40 years or older who underwent gastrectomy for gastric adenocarcinoma between 2010-2021. A composite exposure variable integrating surgical approach (MIS, open, or MIS converted to open) and hospital type (academic or non-academic) was created. High-quality surgical outcome was defined as $\geq$ 15 lymph nodes examined, negative margin status, no readmission within 30 days, and no 30-day mortality. Multivariable logistic and Cox regression analyses were performed to assess the relationship between the exposure and a high-quality surgical outcome and overall survival respectively. **RESULTS:** 19,597 patients were identified. 10,540 (53.7%) underwent curative gastrectomy at academic centers; 7,198 (36.7%) were performed via MIS approaches. When compared to open gastrectomy at an academic center, the likelihood of achieving high-quality surgical outcome with an MIS approach differed by center type: academic OR 1.19 (95%CI: 1.10-1.29) compared to non-academic OR 0.78 (95%CI: 0.71-0.85), after adjusting for age, sex, race, Hispanic ethnicity, Charlson-Deyo score, insurance payor and gastrectomy type. When MIS approach was converted to open, there was decreased likelihood of a high-quality outcome: academic OR 0.82 (95%CI: 0.68 – 0.99), non-academic OR: 0.68 (95%CI: 0.55 – 0.84). There was also a trend towards decreased survival at non-academic facilities (open approach HR 1.20 (95%CI: 1.14-1.26), MIS approach HR 1.02 (95%CI: 0.95 – 1.09) compared to an open approach at academic center after adjusting

previously listed factors and including stage, poor differentiation, margin status, receipt of chemotherapy, and radiation. **CONCLUSIONS:** The benefits of MIS approach accrued differently by hospital type. At academic centers, the MIS approach was associated with increased odds of a high-quality surgical outcome and improved overall survival compared to an open approach, a benefit not observed at non-academic institutions. The dissemination of new technologies for the management of gastric cancer warrants further study/planning to determine how best to ensure uniform benefits across treatment sites.

Table 1. Likelihood of Achieving High Quality Surgical Outcome

Variable	Odds Ratio	95% Confidence Interval		P-value
		Lower	Upper	
Age categorized, years				
40 - 54	0.94	0.85	1.04	0.231
55 - 64	0.95	0.87	1.03	0.215
65 - 79	Reference			
80+	0.79	0.70	0.88	0.000
Race				
White	Reference			
American Indian/Indigenous	0.87	0.55	1.37	0.547
Asian/Pacific Islander	1.36	1.19	1.56	0.000
Black	1.16	1.04	1.31	0.010
Other/Unknown	1.18	0.97	1.43	0.107
Hispanic ethnicity	1.13	1.01	1.27	0.032
Female sex	1.05	0.98	1.12	0.157
Charlson-Deyo Score				
0	Reference			
1	0.94	0.88	1.01	0.081
2	0.92	0.82	1.03	0.166
3	0.88	0.76	1.02	0.096
Composite exposure variable				
Open/academic	Reference			
Open/non-academic	0.57	0.53	0.61	0.000
MIS/academic	1.19	1.10	1.29	0.000
MIS/non-academic	0.78	0.71	0.85	0.000
MIS converted to open /academic	0.82	0.68	0.99	0.041
MIS converted to open /non-academic	0.68	0.55	0.84	0.000

*High quality surgical outcome defined as negative margin, ≥ 15 lymph nodes examined, no readmission within 30 days, and no mortality within 30 days.
*Model also adjusted for insurance payor status and gastrectomy type, not shown"

P207. Optimal Timing of Nasogastric Tube Removal and its Outcomes in Esophageal Surgery

Sumaya Ghaffar, MD[1]; Andrii Khomiak, MD[2]; Caitlin M Blades, Medical Student[3]; Haley C Perkins, Medical Student[4]; Keiko Fox, Medical Student[5]; Mark C Beatty, Medical Student[6]; Aline Hikari Ishida, MD[7]; Alison Mungo, MD[8]; Elizabeth David, MD[9]; Simran Randhawa, MBBS[10]; Akshay Chauhan, MD[11]; Robert Meguid, MD MPH[12]; John D Mitchell, MD[13]; Martin D McCarter, MD[14]; Benedetto Mungo, MD[15]

[1]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [2]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [3]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [4]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [5]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [6]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [7]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [8]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [9]University of Colorado School of Medicine, Aurora, CO, US; [10]University of Colorado School of Medicine, Aurora, CO, US; [11]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [12]University of Colorado School of Medicine, Aurora, CO, US; [13]University of Colorado School of Medicine, Aurora, CO, US; [14]University of Colorado School of Medicine, Aurora, CO, US; [15]University of Colorado School of Medicine, Aurora, CO, US

INTRODUCTION: The Enhanced Recovery After Surgery (ERAS) guidelines for esophageal surgery recommend early removal of the nasogastric tube (NGT). However, evidence supporting this recommendation is limited, and practices vary widely among surgeons. This study evaluates the patterns of use of NGT in elective esophagectomies at a single institution. **METHODS:** We retrospectively reviewed our surgical oncology database for patients who underwent esophagectomy between January 2012 and February 2024 with NGT placement. Exclusion included patients with missing data, emergency surgeries, or multiple complications requiring repeated interventions. Categorical variables were analyzed using the Chi-Square Test, and continuous variables with the Mann-Whitney U Test. **RESULTS:** A total of 320 patients met the inclusion criteria. The median NGT removal time was 5 days. In 109 (34.0%) the NGT was removed early (≤ 3 days, ER group), while 211 (66.0%) had late removal (> 3 days, LR group). The cohort had a median age of 65 years, predominantly male (82.2%) and white (93.4%). The LR group had higher overall pre-operative comorbidity rates (74.4% vs 63.3%, p = 0.038), but no significant differences in other baseline characteristics. Most surgeries were cancer-related, with no technical differences. The LR group more frequently underwent open abdominal (19.1% vs 9.2%, p = 0.024) and thoracic approaches (11.8% vs 0, p = 0.0025), and less often a robotic approach (25.5% vs 46.8%, p < 0.001). Median NGT use was 2 days for ER, and 6 days for LR, with no significant differences in accidental removal, postoperative vomiting, reinsertion, or hospital length of stay. Both groups had a median of 6 days for bowel function return. The LR group was discharged on more advanced diets, such as full liquids and post-esophagectomy (16.1% vs 9.2%; 54.4% vs 46.8%, p = 0.044). No significant differences were found in the rates of anastomotic leak, pneumonia, aspiration, or reintubation. Long-term complications like diaphragmatic hernia, tracheoesophageal fistula, and anastomotic stricture were not significantly different. **CONCLUSIONS:** No significant differences in complications were observed between early and late NGT removal groups. Given that NGTs often cause subjective discomfort, early removal should be considered. Further prospective studies are needed to clarify this matter.

Table 1. Comparison of Early vs Late NGT Removal in Esophagectomy.

Optimal Timing of Nasogastric Tube Removal and its Outcomes in Esophageal Surgery.

Variable	ER (n=109)	LR (n=211)	P value
Age	65 years (32-84)	64 years (17-88)	0.376
Comorbidities	69 (63.3%)	157 (74.4%)	**0.038**
Diagnosis			
Adenocarcinoma	100 (91.7%)	187 (88.6%)	
SCC	7 (6.4%)	14 (6.6%)	
NET	0 (0)	1 (0.5%)	
Achalasia	1 (0.9%)	8 (3.8%)	
Barret's	1 (0.9%)	1 (0.5%)	0.490
Type of Surgery			
Ivory-Lewis	89 (81.6%)	176 (83.4%)	
Transhiatal	10 (9.2%)	15 (7.1%)	0.807
3-field Esophagectomy	10 (9.2%)	20 (9.5%)	
Type of Conduit			
Stomach	108 (99.1%)	207 (98.1%)	0.503
Colon	1 (0.9%)	4 (1.9%)	
Initial Approach – Abdomen			
Laparoscopic	48 (44.0%)	117 (55.4%)	
Robotic	51 (46.8%)	54 (25.5%)	**0.0003**
Open	10 (9.2%)	40 (19.1%)	
Initial Approach – Thorax			
VAMIE	80 (73.4%)	144 (68.2%)	
RAMIE	19 (17.4%)	27 (12.7%)	
Open	0 (0)	25 (11.8%)	**0.0025**
Type of Anastomosis			
OrVil EEA Transoral stapler	76 (69.8%)	163 (77.3%)	
EndoGIA ± Hand Sewn	32 (29.3%)	45 (21.3%)	0.270
Hand Sewn	1 (0.9%)	3 (1.4%)	
LOS	10 days (7-90)	11 days (3-71)	0.495
Discharge Nutrition			
Clear Liquids Diet	24 (22.0%)	23 (10.9%)	
Full Liquids Diet	10 (9.2%)	34 (16.1%)	
Tube Feeds	59 (54.1%)	105 (49.7%)	
Post-Esophagectomy Diet	51 (46.8%)	115 (54.5%)	
Total Parenteral Nutrition	4 (3.6%)	6 (2.8%)	**0.044**
Surgical Complications	61 (56.0%)	129 (61.1%)	0.372
Chyle Leak	5 (4.6%)	5 (2.3%)	0.280
Recurrent Nerve Injury	2 (1.9%)	6 (2.9%)	0.584
Anastomotic Leak	26 (23.9%)	41 (19.4%)	0.357
Pneumonia	10 (9.2%)	23 (10.9%)	0.630
Atrial Fibrillation	26 (23.9%)	42 (19.9%)	0.413
Reintubation	11 (10.1%)	23 (10.9%)	0.824
Need for Tracheostomy	4 (3.6%)	7 (3.3%)	0.870
Aspiration	7 (6.4%)	12 (5.6%)	0.792
Long-term Complications			
Diaphragmatic Hernia	10 (9.2%)	11 (5.2%)	0.175
Tracheoesophageal Fistula	6 (5.5%)	6 (2.8%)	0.235
Anastomotic Stricture	15 (13.8%)	29 (13.7%)	0.741
Days until removal of NGT	2 days (1-3)	6 days (4-37)	
Accidental removal	9 (8.3%)	26 (12.3%)	0.269
Post-operative vomiting	15 (13.8%)	25 (11.8%)	0.624
Reinsertion of NGT	4 (3.7%)	10 (4.7%)	0.658
POD of reinsertion	8 days (6-21)	7 days (4-35)	0.710
POD of return of bowel function	6 days (3-14)	6 days (2-24)	0.266

P208. Palliative Gastrojejunostomy: Determining Efficacy through Palliative Outcomes and Identifying Predictors of Delayed Gastric Emptying

Jaewook Shin, MD, MACS[1]; Shriya Perati, BA[2]; Joshua T Cohen, MD[3]; Timothy D Murtha, MD, MHS[4]; Rachel E Beard, MD, FACS[5]; Thomas J Miner, MD, FACS[6]

[1]Rhode Island Hospital/Alpert Medical School of Brown University, Providence, RI, US; [2]Alpert Medical School of Brown University, Providence, RI, US; [3]Memorial Sloan Kettering Cancer Center, New York City, NY, US; [4]Rhode Island Hospital/Alpert Medical School of Brown University, Providence, RI, US; [5]Rhode Island Hospital/Alpert Medical School of Brown University, Providence, RI, US; [6]Rhode Island Hospital/Alpert Medical School of Brown University, Providence, RI, US

INTRODUCTION: Palliative gastrojejunostomy (PG) is performed for symptom relief but robust data for efficacy are lacking. Delayed gastric emptying (DGE) is a common complication of PG that affects quality of life and is challenging to manage. Our objective was to investigate the effectiveness of PG in symptom relief and explore potential predictors of DGE after PG. **METHODS:** A retrospective examination of a prospective database with patients who underwent gastrojejunostomy (2005-2022) at an academic tertiary care center was performed. Demographics, palliative intent, palliative outcomes such as symptom improvement and diet resumption were collected. Logistic regression was used to identify patient factors predicting DGE. **RESULTS:** Of the 569 patients, 93 (16.3%) underwent PG and had a mean age of 66 ± 14.3 years, 35.5% female, average BMI of 24.4, 25.8% with diabetes, and 89.2% with malignancy. Pancreatic (38.7%) and gastric cancers (22.6%) were the most common indications of PG and 37.6% of all cancers were metastatic. PG group had median overall survival of 297 days (IQR: 74-1519), 30-day mortality of 8.6%, 1-year survival of 41.9%, median length of stay of 11 days (IQR: 7-18), and median days with NGT of 5 days (IQR: 3-8). Compared to non-PG group, PG group showed high symptom improvement (89.2%vs91.8%, p=0.55) and full or low-residue diet resumption rates (90% vs 93.8%, p=0.08), low reoperation (6.5% vs 9.9%, p=0.4) and SBO (2.1% vs 0.6%, p=0.41) rates, significantly lower anastomotic leak (3.2% vs 10.5%, $p < 0.05$) rate, and comparable NGT reinsertion (18.3% vs 14.3%, p=0.41), ileus (9.7% vs 8.4%, p=0.84), and infection (18.3% vs 20.8%, p=0.68) rates. Of note, PG group had a significantly higher rate of DGE than non-PG group (20.4% vs 9.2%, $p < 0.05$). From a multivariate analysis of patient factors (Table 1), maximum stomach surface area (MSA) on preoperative CT scan showed statistically significant association with DGE occurrence (OR 1.03; 95% CI 1.01-1.05; p = 0.003), indicating every 1 cm2 increase in MSA was associated with 3% higher chance of DGE. PG patients who developed DGE had a higher mean MSA compared to those who did not (141 cm2 vs 89 cm2; $p < 0.01$). **CONCLUSIONS:** PG is effective in symptom improvement and diet resumption with low procedure-related complication rates. PG patients also suffer a high rate of postoperative DGE for which higher MSA on preoperative CT was independently associated with DGE. Measurement of preoperative MSA is a simple, practical, and clinically relevant tool to predict DGE and facilitate patient counseling and postoperative risk stratification.

Table 1. Multivariate analysis of patient factors predicting delayed gastric emptying after palliative gastrojejunostomy.

	Odds Ratio	95% Confidence Interval	p value
Age > 65	0.63	0.13-3.10	0.56
Female	3.58	0.60-21.3	0.16
BMI	0.97	0.77-1.22	0.81
Metastatic	1.24	0.24-6.28	0.80
Obesity	2.19	0.11-44.1	0.61
Diabetes	0.47	0.07-3.27	0.43
Weight loss	1.60	0.31-8.28	0.59
PO intake	1.14	0.59-2.19	0.70
Chemotherapy	2.44	0.33-18.0	0.39
Radiation	3.79	0.23-61.9	0.39
NGT prior to OR	0.35	0.05-2.53	0.27
MSA on CT	1.03	1.01-1.05	0.003*

P209. Peripheral blood cell-free DNA concentration is a pan-cancer, stage-independent prognostic biomarker in solid tumors

Wasay Nizam, M.D[1]; Patrick Wagner[2]; Patricia Petrosko[3]; Phillip Gallo[4]; Louis Gil Acevedo[5]; Harmeet Kharoud, MD[6]; Robin Barr[7]; Tong Lam[8]; Thomas Rachman[9]; Russell Schwartz[10]; Oana Karja[11]; Ali Zaidi[12]; William Laframboise[13]; David Bartlett[14]

[1]Allegheny Health Network Cancer Institute, Pittsburgh, PA, US; [2]Allegheny Health Network, Pittsburgh, PA, US; [3]Allegheny Health Network, Pittsburgh, PA, US; [4]Allegheny Health Network, Pittsburgh, PA, US; [5]Allegheny Health Network, Pittsburgh, PA, US; [6]Allegheny Health Network, Pittsburgh, PA, US; [7]Allegheny Health Network, Pittsburgh, PA, US; [8]Allegheny Health Network, Pittsburgh, PA, US; [9]Carnegie Mellon University, Pittsburgh, PA, US; [10]Carnegie Mellon University, Pittsburgh, PA, US; [11]Carnegie Mellon University, Pittsburgh, PA, US; [12]Allegheny Health Network, Pittsburgh, PA, US; [13]Allegheny Health Network, Pittsburgh, PA, US; [14]Allegheny Health Network, Pittsburgh, PA, US

INTRODUCTION: Commercial circulating tumor DNA assays utilize peripheral blood cell-free DNA (cfDNA) to detect biomarkers of tumor activity or treatment response. However, the characteristics and prognostic applicability of baseline cfDNA concentration is poorly defined. We assessed the distribution and prognostic significance of cfDNA concentration in a pan-cancer cohort of patients. **METHODS:** 878 unique patients at a single integrated oncology institution were enrolled in a registry/repository study with peripheral blood drawn during or prior to the initiation of cancer therapy. Patient demographics, disease-related variables (site of primary tumor, AJCC Stage, number of tumors, size of largest tumor and presence of diffuse metastatic disease), intent of treatment, response to treatment and oncologic outcome were tested for association with baseline cfDNA concentration. Non-parametric (Spearman or Kruskal-Wallis tests) and parametric (linear regression) techniques were utilized to study association of cfDNA concentration with clinical variables, and survival outcomes were assessed using Cox regression. **RESULTS:** The distribution of cfDNA concentration was right-skewed (median 6.3, IQR 3.8, 12.3; mean 13.8), and concentration was associated with advanced age and AJCC stage. cfDNA concentration varied by site of primary tumor (p=0.0001), with pronounced effects in stages III (p=0.0002) and IV (p=0.0001). The size of the largest discrete measurable tumor was a dominant predictor of cfDNA level regardless of the overall number of tumors ($p<0.0001$), even in the presence of diffuse metastatic disease (p=0.006). Patients undergoing palliative treatment had greater cfDNA concentration than those undergoing adjuvant or curative therapy ($p<0.0002$. cfDNA concentration was strongly associated with poor prognosis in patients undergoing palliative ($p<0.001$) or curative therapy ($p<0.001$) for both overall (OS) and progression-free survival (PFS), effects which were independent of age, primary tumor site, AJCC stage, and treatment intent for both OS and PFS ($p<0.001$). **CONCLUSIONS:** Baseline circulating cfDNA concentration was a powerful prognostic determinant in a pan-cancer cohort, independent of the outcome of downstream biomarker assays for which it is used. Future research is warranted to define how peripheral blood cfDNA concentration can be integrated into oncologic risk stratification and treatment decision-making.

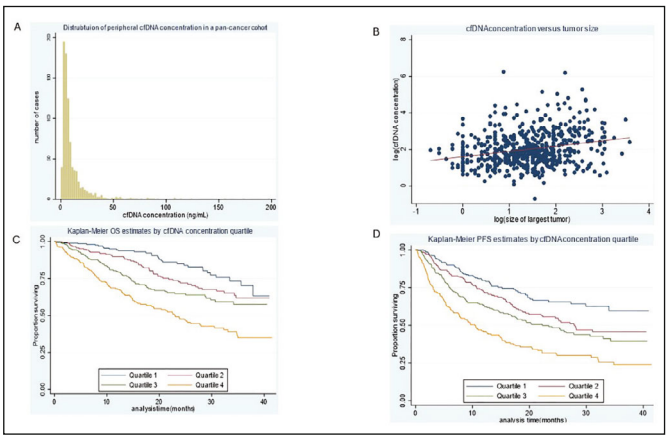
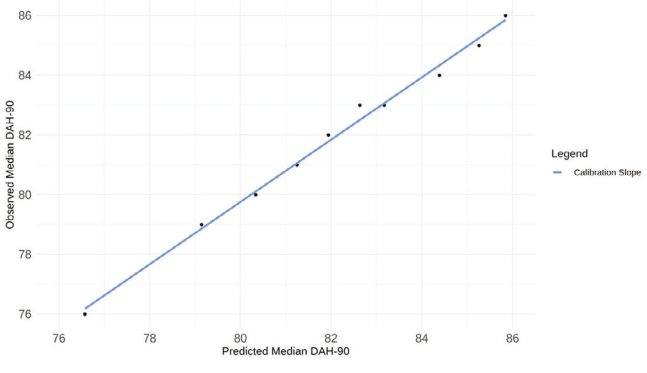


Figure 1. A: Distribution of peripheral cell-free DNA (cfDNA) concentrations in the study population. B: Scatter plot showing correlation between peripheral cfDNA concentration and increasing tumor size. C, D: Kaplan-Meier curve estimating overall survival and progression-free survival stratified by cfDNA concentration quartiles, demonstrating the prognostic utility of this variable.

P210. Predicting days at home after gastrointestinal cancer surgery: Model development and internal validation

Tiago Ribeiro, MD, MSc[1]; Adom Bondzi-Simpson, MD MSc[2]; Wing C Chan, MSc[3]; Alyson Mahar, PhD[4]; Angela Jerath, MD MSc[5]; Natalie G Coburn, MD, MPH[6]; Julie Hallet, MD, MSc[7]
[1]University of Toronto, Toronto, ON, CA; [2]University of Toronto, Toronto, ON, CA; [3]ICES, Toronto, ON, CA; [4]Queens University, Kingston, ON, CA; [5]Sunnybrook Health Sciences Centre, Toronto, ON, CA; [6]University of Toronto, Toronto, ON, CA; [7]Sunnybrook Health Sciences Centre, Toronto, ON, CA

INTRODUCTION: Prediction tools have the potential to derive personalized patient-centered estimates to improve the cancer care experience. Days at home (DAH) is an optimal measure of life impact capturing days spent in health care institutions after surgery. We developed and internally validated a prediction model, DAYSHOME, for DAH 90 days (DAH-90) after gastro-intestinal (GI) cancer surgery. **METHODS:** We conducted a population-based retrospective cohort study of adults undergoing elective GI cancer surgery between 2003-2021. DAH-90 was calculated as institution days minus days in healthcare institutions (acute care hospital, rehabilitation, nursing home, and emergency department visits). Candidate predictors were identified a priori relying on clinical rationale and literature review. Median quantile regression was used. Final predictor selection and model specification incorporated tests of collinearity, linearity, and additivity guided by mean absolute error (MAE), g-index, calibration slope and intercept. Internal validation was performed using bootstrap methods with 500 repetitions to derive optimism corrected metrics. **RESULTS:** Among 91,290 patients included, the distribution of DAH-90 was left skewed with a spike at zero and median at 82 days (IQR 77–85). DAH-90 varied across patient, cancer, and treatment related factors. The final model included 23 predictors covering patient, and treatment factors with 3 interaction terms. The strongest independent predictors of DAH-90 were operative approach, age, and procedure type ($p<0.0001$). Index model performance metrics were MAE=8.67, g-index=3.27, intercept=0, calibration slope=1.0 (Figure). These results indicate the model is well calibrated with strong accuracy when compared to related models. Using bootstrap methods, the internal validity of this prediction model was supported suggesting a stable model with low bias (optimism corrected performance metrics: MAE=8.68, g-index=3.26, intercept=0.29, calibration slope=1.0). Model performance was stable across multiple sensitivity analyses. **CONCLUSIONS:** This tool makes use of information available pre-operatively to predict DAH-90 after GI cancer surgery. It presents good discrimination and is well calibrated. An online calculator is being built to provide individualized risk estimates from this tool, which can be used for counselling, shared decision-making, preparation, and setting expectations prior to GI cancer surgery. External validation and clinical usability testing are underway.



(DAH-90) after gastro-intestinal cancer surgery for full cohort. Schematic summary of final model: DAH-90 = sex + age (RCS, 3 knots) + rurality + histology + procedure + metastatic + operative approach + neoadjuvant chemotherapy + neoadjuvant radiotherapy + myocardial infarction + arrythmia + cerebrovascular disease + heart failure + chronic obstructive pulmonary disease + diabetes mellitus + neurologic disease + hypertension + liver disease + kidney disease + operative approach*procedure + operative approach*age + procedure*age

Figure. Decile calibration plot for final prediction model for median Days at home 90 days

P211. RNA Sequencing as a viable option to reclassify Variants of Uncertain Significance at splice sites in genomic testing for malignancy

Haley A Zlomke, MD[1]; Sarayu Parise[2]; Kiersten Meeder[3]; Clare McTighe[4]; Raegan Roy[5]; Kevin Hughes[6]; Andrea Abbott, MD[7]
[1]Medical University of South Carolina, Charleston, SC, US; [2]Medical University of South Carolina, Charleston, SC, US; [3]Medical University of South Carolina, Charleston, SC, US; [4]Medical University of South Carolina, Charleston, SC, US; [5]Medical University of South Carolina, Charleston, SC, US; [6]Medical University of South Carolina, Charleston, SC, US; [7]Medical University of South Carolina, Charleston, SC, US

INTRODUCTION: With expanding access to genetic testing, the population of patients who are found to have a Variant of Uncertain Significance (VUS) is growing. RNA sequencing (RNA-seq) has emerged as a pivotal tool in resolving these uncertainties by elucidating their impact on gene expression, alternative splicing patterns, and transcript stability particularly at the splice-site. The aim of this study is to determine if RNA-seq can distinguish between benign or pathogenic variants, thereby enhancing diagnostic accuracy, informing clinical management decisions, avoiding over-treatment, and lessening patient anxiety when clinical uncertainty is encountered. **METHODS:** This single institution study evaluated all patients who underwent genetic testing after a cancer diagnosis who had a splice site variant denoted by a "+" or "-" in the variant name (e.g., c.2880+5G>A). After identification of the patient cohort, the medical record was reviewed and their genomics analyzed to determine if RNA-seq would be beneficial in clarifying the VUS. Patients were then contacted to submit an RNA sample for sequencing utilizing Invitae Laboratories. RNA was sequenced from a cDNA library and the data was used to detect splice site variations +/- 20 base pairs with a 95% sensitivity and specificity. These results, paired with the genomic data, determined the pathogenic likelihood of the variant. **RESULTS:** 145 patients were identified with intronic, splice-site VUS and 14/145 (9.6%) were eligible for RNA-Seq, 23/145 (15.8%) had already been reclassified by RNA-seq or other methods, and 6/145 (4.1%) remained a VUS. The remaining 102/145 (70%) of patients had variants in which RNA would not be useful due to a mosaic mutation, a promoter region variant, a single variant in a recessive gene, copy number variant or RNA analysis not being offered. Thus far, 6/14 eligible patients have successfully completed RNA testing resulting in 3 variants that were downgraded to likely benign and the other 3 remained a VUS. **CONCLUSIONS:** A VUS result can be challenging and anxiety provoking for both patients and their providers. RNA-seq can reclassify many splice site variants, however our study demonstrates that this may be an underutilized resource. Our study highlights that patients can be easily identified from an existing database and the sequencing performed with a simple blood test. This approach could allow selected use of RNA-seq in patients who still have a VUS to clarify the pathogenicity of the variant. The use of this technology will help address a growing population of patients with a VUS who live with uncertainty and the medical community that must remain vigilant for changes in classification of genetic variants.

P212. Supporting the PACT Act: Top Cancers Diagnosed in Young Veterans who Deployed to Iraq and Afghanistan

Robert Young[1]; James Duncan, Chairman of Surgery, Washington DC Veterans Affairs Medical Center[2]; Vance Sohn[3]
[1]George Washington University Hospital, Washington, DC, US; [2]Washington DC Veterans Affairs Medical Center, Washington, DC, US; [3]Washington DC Veterans Affairs Medical Center, Washington, DC, US

INTRODUCTION: The Promise to Address Comprehensive Toxins (PACT) Act is a law signed by Congress in 2022 that widely broadened medical coverage for Veterans of foreign deployments. The PACT Act expands Veterans Affairs (VA) medical care and benefits to all Veterans with documented toxic exposures, including exposures to Agent Orange, ionizing radiation, and burn pits, as well as to Veterans deployed during the Vietnam, Gulf War, and post-9/11 eras. The Act defines a list of presumptive medical conditions that are assumed to be related to toxic military exposures encountered during the Veteran's time in-service. This list includes a wide variety of cancers. However, to date, the associations between specific toxic military exposures and the development of cancer are not yet well-defined. In this study, we seek to define the top cancers afflicting young Veterans who deployed in the conflicts in Iraq and Afghanistan. The National Institutes of Health (NIH)'s Surveillance, Epidemiology, and End Results (SEER) program classifies cancers of "adolescents and young adults" (AYAs) as patients between the ages of 15 and 39. We used the VA Informatics and Computing Infrastructure (VINCI) database to identify all cases of cancer in Veterans who served in Iraq and Afghanistan and were diagnosed below the age

of 40. **METHODS:** Approval was obtained from the Washington DC Veterans Affairs Medical Center Institutional Review Board. The VA's VINCI database was mined to build a retrospective cohort of all Veterans who served in Iraq and Afghanistan who were diagnosed with various cancers. The cohort was limited to Veterans below the age of 40, who were diagnosed with cancer between the years of 2017-2022. This time frame was selected to compare with the 2024 SEER report, defining cancer incidence in young adults (Surveillance Research Program, National Cancer Institute; 2024 Apr 17). Data analysis and graphing were performed in SAS Enterprise Guide and Microsoft Excel. **RESULTS:** Among young male (<40 years old) Veterans who previously deployed to Iraq and Afghanistan, the five most diagnosed cancers were testicular cancer (20.7%), melanoma (13.2%), lymphoma (8.9%), leukemia (6.4%) and kidney cancer (6.3%). Among young females, the five most common were breast (25.3%), cervical (18.8%), thyroid (15.8%), melanoma (10.5%), and leukemia (4.3%). This largely parallels trends in the SEER database for young adults, ages 15-39, except that male veterans have double the rate of melanoma; 13.2% in male Veterans, as compared to 6.6% (SEER 5-Year Age-Adjusted Incidence Rates, 2017-2021). **CONCLUSIONS:** This retrospective review identifies the most frequently diagnosed cancers in young Veterans who served in Iraq and/or Afghanistan in the post-9/11 period. This is particularly relevant in light of the recently passed PACT Act, which ties significant VA healthcare benefits to a variety of cancers that are presumed to be related to wartime exposures. While further analysis remains to be done in different Veteran populations, this preliminary study identifies that melanoma is diagnosed in young male Veterans at twice the rate seen in the NIH's SEER database. This suggests that, for young Veterans who deployed to Iraq and Afghanistan, one of their most toxic exposures in wartime was, in fact, the Middle Eastern sun.

P213. The Role of Nutritional Prehabilitation in Improving Surgical Outcomes for Patients with Pancreatic Cancer

Molly Greenblat, MS3[1]; Conor H. O'Neill[2]
[1]University of Vermont Larner College of Medicine, Burlington, VT, US; [2]Division of Surgical Oncology, University of Vermont Medical Center, Burlington, VT, US

INTRODUCTION: The objective of the study was to increase treatment completion rates and improve surgical outcomes in patients undergoing pancreatic cancer resection. By providing nutritional prehabilitation, this study looked at the relationship between nutritional status and incidence of perioperative complications including deconditioning, weight loss, and dehydration. **METHODS:** We reviewed ten years of patients with tumors of the pancreas per the Vermont Cancer Registry to identify a retrospective cohort. A prospective cohort was enrolled in nutritional prehabilitation beginning at time of surgical consultation. We captured patients of both cohorts' chemotherapy prescriptions, dose-reductions, cycle interruptions, and treatment-related adverse events. We also noted hospital re-admissions related to treatment. Furthermore, we reported surgical morbidity through measures such as length of admission and perioperative complications. These data were analyzed to assess perioperative fitness of patients with and without prehabilitation. **RESULTS:** Overall, this review included 33 patients in the retrospective group, and 18 patients in the prospective cohort. When comparing the retrospective and prospective cohorts, there were no significant differences in numbers of perioperative complications such as leak or hemodynamic instability. Within the prospective cohort, 83% of patients required dietician intervention prior to surgery, and 50% of these patients had severe symptom derangements from malnutrition at initial assessment. In this cohort, nutrition recommendations and tube feeds, if necessary, were initiated prior to surgery. The average perioperative length of stay (LOS) in this group was 7.5 days, while in the retrospective cohort, the average LOS was 12.4 days ($p=0.026$). Additionally, interval results show that preoperative chemotherapy prescription completion, measured as relative dose intensity (RDI), increased from 50.4% to 85.9% ($p<0.001$) from the retrospective to prospective cohort. There was also a fivefold increase in total pancreatic resection volumes in the prehabilitated cohort compared to the retrospective cohort, controlled for population and perioperative complications. **CONCLUSIONS:** Many patients in the prospective group were candidates for nutritional prehabilitation as they received chemotherapy ahead of surgical resection. Completion of chemotherapy was improved in this group, and length of time admitted to the hospital was decreased. Further research is warranted to explore how to implement the most effective, generalizable perioperative prehabilitation for patients with pancreatic cancer.

P214. The Role of Synoptic Operative Reporting in Accurate and Efficient Data Capture for Patients Undergoing Pancreatectomy

Brittany C. Fields, MD, MPH[1]; Laura R. Prakash, MD[2]; Cong Pan, PhD[3]; Elsa M Arvide, PA-C[4]; Whitney L. Dewhurst, MS, APRN, NP-C[5]; Morgan L. Bruno, MS, ACNP-BC[6]; Virgina Doherty, MPAS, PA-C[7]; Jessica E. Maxwell, MD, MBA[8]; Rebecca A. Snyder, MD, MPH[9]; Naruhiko Ikoma, MD, MS[10]; Michael P. Kim, MD[11]; Ching-Wei D. Tzeng, MD[12]; Jeffrey E. Lee, MD[13]; Matthew H.G. Katz, MD[14]; Heather G. Lyu, MD, MBI[15]
[1]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [4]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [5]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [6]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [7]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [8]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [9]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [10]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [11]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [12]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [13]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [14]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [15]The University of Texas MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Standardized reporting mechanisms aimed to capture essential operative details such as surgical technique and intraoperative findings have been advocated by the Cancer Surgery Standards Program of the American College of Surgeons in the form of synoptic operative reports (SOR). Compared to narrative operative reports, SOR have demonstrated increased accuracy, efficiency, and quality of operative reports and subsequent data collection. This study aims to describe and evaluate the development and implementation of a pancreas-specific SOR on the quality of data collection at a high-volume pancreas center. **METHODS:** A multidisciplinary team comprised of surgeons, clinicians, a clinical informatician, and a team of electronic health record (EHR) analysts developed a custom, EHR-based synoptic operative note template containing pancreas-specific structured data elements. This template was implemented into the operative note workflow in February 2024. All subsequent pancreas operative reports were audited and matched 1:1 by surgeon and procedure with narrative operative reports from 2022-2023, to compare captured data. Manual review of narrative reports for the pancreas-specific data elements was performed by a surgical resident and timed for each report. **RESULTS:** The SOR template consisted of 83 structured data elements (Table 1) and was used to automatically capture data in an EHR database from 125 patients between February-September 2024. A total of 3,946 variables were automatically captured with a mean of 31 (range 15-44) variables per patient. Conversely, the rate of data capture with manual review of narrative reports was 87% (3,444 variables). Total time to review all narrative operative reports for pancreas-specific variables was 352 minutes, with a mean time of 2.8 minutes per patient. The most frequently omitted variables in narrative operative reports for completed pancreatectomy (n=93) were the intraoperative assessment of R status (84% absence rate), gland texture (63%), pancreatic duct size (59%), descriptions of tumor-vessel interfaces and/or management of resected vasculature (30%), and nodal stations (20%). **CONCLUSIONS:** Implementation of a synoptic operative report template increases the efficiency and completeness of data collection for pancreas-specific intraoperative details. This improvement in surgical documentation supports the integration of structured data entry into other clinical settings for improved data collection and time-cost savings.

Table 1. Pancreas-Specific Variables Included in Synoptic Operative Note Template

Patient/Identifying Information	***Preoperative Mangement***	***Vascular Management***
Medical Record Number	Preoperative Treatment (Yes, No)	Tumor-Vessel Interface, SMV/PV (e.g., separable)
Patient Name	Preoperative Treatment Type (e.g., chemotherapy, CXRT)	Tumor-Vessel Interface, SMA
Date of Birth	Preoperative Treatment Type, Other	Tumor-Vessel Interface, Common Hepatic Artery
Date of Surgery	Preoperative Treatment Chemotherapy Type	Tumor-Vessel Interface, Celiac Trunk
Case Details	Preoperative Treatment Chemotherapy Type, Other	Tumor-Vessel Interface, Inferior Vena Cava
Primary Surgeon	Preoperative Treatment Radiation Dose	Management of SMV-PV
Procedures	Preoperative Treatment Radiosensitizing Agent	SMV-PV Prosthesis
Clinical Diagnosis	Preoperative Treatment on Protocol	Management of Hepatic Artery
Clinical Diagnosis Other	***Surgical Approach***	Hepatic Artery Prosthesis
Primary Procedure Planned	Initial Surgical Approach	Management of Celiac Trunk
Primary Procedure Planned, Other	Minimally Invasive Procedure Type (Laparoscopic, Robotic)	Celiac Trunk Prosthesis
Procedure Performed	Minimally Invasive Robotic Platform	SMA Reconstruction Method
Procedure Performed, Other	Minimally Invasive Hand-Assisted Laparoscopy	SMA Prosthesis
Operation Status (e.g., elective, urgent, emergent)	Minimally Invasive Conversion to Open (Yes, No)	***Pathologic Data***
Primary Intent of Operation (e.g., curative, staging)	Minimally Invasive Conversion Type (e.g., emergent)	Local Tumor Extent
Redo Operation (Yes/No)	Minimally Invasive Conversion Reason	Tumor Involvement of Additional Organs
Procedure Terminated or Altered	Minimally Invasive Conversion Reason, Other	Additional Organs Resected En Bloc
Added Case Complexity	***Anatomic & Technical Details***	Additional Organs Resected Not En Bloc
Case Complexity Type	Anatomic Variations	Additional Organ Name
Associated with Patient Obesity	Vascular Anatomic Variations	Discontiguous Metastatic Disease
Associated with Comorbidities	Pancreatic Duct Size (mm)	Sites of Metastases
Associated with Excess Blood Loss	Pancreas Gland Texture (e.g, soft, intermediate, firm)	Sites of Metastases, Other
Associated with Difficult Surgical Approach	Severity of Fibrosis and/or Pancreatitis	Final Intraoperative Assessment of R Status
Associated with Redo Operation	Nodal Dissection or Sampling	***Intraoperative Findings & Complications***
Associated with Other Procedure Interferences	Nodal Station(s) Dissected	General Findings
Associated with Pathology	Nodal Station(s) Dissected, Other	Intraoperative Complication
Associated with Extensive Trauma	Nodal Station(s) Sampled	Intraoperative Complication Type
Associated with Extended Anesthesia	Nodal Station(s) Sampled, Other	Intraoperative Complication, Other
Due to Pancreatic Fibrosis and/or Pancreatitis	SMA Dissection Plane (e.g., periadventitial)	***Other***
	SMA Dissection Plane, Other (e.g., plexus-preserving)	Prospective Risk-Stratified Pathway
		Final Risk-Stratified Pathway

CXRT: chemoradiation; mm: millimeters; SMV: superior mesenteric vein; PV: portal vein; SMA: superior mesenteric artery

P215. Variation of peripheral blood cell-free DNA concentration and prognostic utility by site of metastasis in a pan-cancer cohort

Patrick Wagner[1]; Samuel A Yellin[2]; Patricia Petrosko[3]; Phillip Gallo[4]; Louis Gil Acevedo[5]; Harmeet Kharoud, MD[6]; Robin Barr[7]; Tong Lam[8]; Ali Zaidi[9]; William Laframboise[10]; David Bartlett[11]

[1]Allegheny Health Network, Pittsburgh, PA, US; [2]Allegheny Health Network, Pittsburgh, PA, US; [3]Allegheny Health Network, Pittsburgh, PA, US; [4]Allegheny Health Network, Pittsburgh, PA, US; [5]Allegheny Health Network, Pittsburgh, PA, US; [6]Allegheny Health Network, Pittsburgh, PA, US; [7]Allegheny Health Network, Pittsburgh, PA, US; [8]Allegheny Health Network, Pittsburgh, PA, US; [9]Allegheny Health Network, Pittsburgh, PA, US; [10]Allegheny Health Network, Pittsburgh, PA, US; [11]Allegheny Health Network, Pittsburgh, PA, US

INTRODUCTION: Circulating biomarkers are gaining increasing utility in the real-time management of solid tumors in clinical oncology, but their sensitivity and specificity may be biased by differences in yield of cell-free DNA (cfDNA) among patients. Although primary tumor characteristics are well studied in their influence on peripheral blood cfDNA yield, the impact of metastatic disease site are not. In this study we used a large, single-institution, pan-cancer cohort to assess whether measurable differences in peripheral cfDNA concentration exist based on site of metastatic disease. **METHODS:** Among a pan-cancer series of 878 patients enrolled in a registry/repository study at Allegheny Health Network, 354 had metastatic malignancy. The raw, log-transformed concentration of an in-house, cfDNA purification process from peripheral blood was tested for association with ten common sites of metastatic disease: regional lymph nodes, non-regional lymph nodes, lung, liver, pleural effusion, peritoneal carcinomatosis, malignant ascites, brain, bone, and adrenal. Comparisons were made for each site against patients with metastatic disease not involving that site using Student's t test and association with survival was assessed using Cox regression. **RESULTS:** Among stage 4 patients, those with regional lymph nodes (p=0.003), non-regional lymph nodes (p=0.0009), pleural (p=0.0009), liver (p=0.0001) and adrenal (p=0.04) metastases had increased peripheral blood cfDNA concentration relative to metastatic disease to different sites; whereas ascites (p=0.7), peritoneal carcinomatosis (p=0.5), lung (p=0.2), brain (p=0.6) and bone (p=0.2) did not. cfDNA concentration was predictive of poor prognosis (overall survival) in patients with regional and non-regional lymph node metastases (p<0.001), peritoneal carcinomatosis (p=0.003), liver (p<0.001), lung (p<0.001), brain (p=0.04), bone (p=0.002), and possibly pleural (p=0.09) metastases, by not malignant ascites (p=0.1) or adrenal metastases (p=0.1). **CONCLUSIONS:** Site of metastatic disease is strongly associated with the yield of peripheral blood cfDNA. Whether the implications of this finding may introduce bias into the interpretation of downstream biomarkers utilizing cfDNA remains to be determined. In spite of differences in cfDNA yield by site of metastatic disease, cfDNA concentration proved to be strongly associated with overall survival for most sites of metastatic disease.

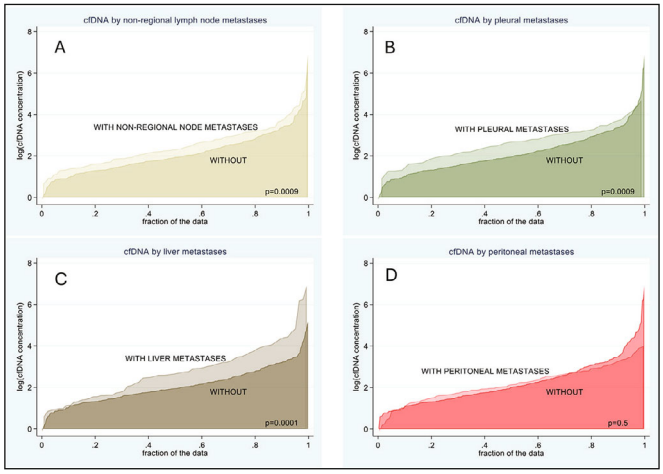


Figure. Influence of metastatic site on peripheral cfDNA yield. Distribution of cfDNA concentration by non-regional lymph node (panel A), pleural (panel B) and liver(panel C) metastases. Regional lymph node and adrenal metastases were also significantly associated with increased cfDNA concentration (not shown). By contrast, peritoneal metastases (panel D), malignant ascites, lung, brain, and bone (not shown) metastases were not associated with elevated cfDNA relative to other metastatic sites.

P216. Defining the Role of Systemic Immunotherapy for Clear Cell Sarcoma

Aparna Vancheswaran, MD[1]; Cristian Mantilla-Rosa[2]; Shanie Shemla, MD[3]; Aimee Crago, MD[4]; Danielle Bello[5]; Edmund K. Bartlett, MD[6]; Samuel Singer, MD[7]; Sandra P. D'Angelo, MD[8]; Charlotte Ariyan, MD, PhD[9]

[1]Memorial Sloan Kettering Cancer Center, New York City, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Slaon Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Clear cell sarcoma (CCS) is a rare soft tissue sarcoma with a poor prognosis. CCS has often been confused with melanoma, as it has melanocytic pathologic features and spreads to lymph nodes, until a specific translocation (t(12;22) (q13;q12)/EWSR1 fusion defined the disease. There are rare reports of response to immunotherapy and tyrosine kinase inhibitors in CCS. This single-institution retrospective cohort study aims to better characterize this rare tumor in patients with a known EWSR1 fusion, and clarify the role of systemic treatment. **METHODS:** After IRB approval, patients were identified through a retrospective review of melanoma and sarcoma databases. The population was limited to age >- 16 diagnosed with CCS with molecular testing, with follow-up of at least 6 months. **RESULTS:** 45 patients diagnosed with CCS from 1988 to 2023 met the inclusion criteria, with ages from 16 to 80 (median=34). Most were male (66.7%; 30), White (77.7%; 35), presenting with disease localized to the extremities (84.4%). 46.7% (21) patients presented with local disease while 17.8% (8) presented with local disease and 35.5%(16) presented with metastatic disease. Median tumor size was 4.8 cm (range 0.4-16 cm). The majority of the cohort had the classic EWSR1/ATF fusion (88%), while alternative fusions were identified EWSR1-CREM(6%), EWSR1-CREB(3%), and an unknown fusion partner(3%). Additional targeted exome sequencing was performed for 15 patients. All tumors had the EWSR fusion and were microsatellite stable, without any significant associated mutation, other than TERT which was identified in 4 patients. Patients received multiple treatment modalities: surgery (84.4%), chemotherapy (71.1%), RT (60%), and systemic IO (28.9%). Median overall survival (OS) was 54 months, with a 5-year disease specific survival rate of 47.5%. As seen in Table 1, 13 patients received IO; 10 IO alone and 3 with tyrosine kinase inhibitor(TKI). 10 patients received tyrosine kinase inhibitors (TKI) alone. Response to checkpoint inhibition was poor with only combination anti CTLA4/anti PD1 resulting in stable disease for up to 6 months. Patients receiving TKI therapy fared better with one patient's disease course stabilizing for 82 months. **CONCLUSIONS:** This study highlights the poor response of clear cell sarcoma to existing treatments, including checkpoint

blockade. Sequencing confirmed an immunologically quiet tumor. Together this data solidifies that CCS should not be treated like melanoma. Future studies should focus on developing treatments that target the fusion in a pharmacologic, or fusion-specific T-cell therapy.

Table 1. Systemic IO/ TKI therapies and outcomes

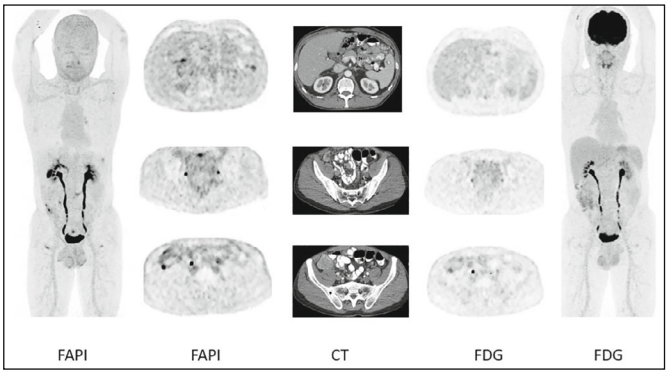
Treatment	N	Prior Rx?	Treatment Stage (LR or Metastatic)	Response	Progression free survival	Relapse free survival
TKI alone (n=10)[1]						
pazopanib (adjuvant)	1	yes	metastatic	NA		6 months
sunitinib (adjuvant)	1	no	LR (n=1) metastatic (n=2)	NA		1 month
cabozatinib	3	yes	metastatic	33% POD 66% PR	2 months 4 months; 4 months	
Pazopanib	5	yes	metastatic	40% POD 20% PR 40% SD	2 months; <1month 3 months 82 months; 3 months	
Systemic IO alone (n=10)[2]						
IFN (adjuvant)	2	yes	metastatic(n=1) LR (n=1)	NA		74 months 2 months
IFN	2	yes	metastatic	POD	<1 month;<1 month	
anti PD1	2	yes	LR(n=1) metastatic(n=1)	POD	1 months; 2 months	
anti PD1/ anti CTLA4	4	No(n=1) Yes(n=3)	LR(n=1) Metastatic (n=3)	SD	3 months; 4 months; 5 months; 6 months	
TKI and Systemic IO together (n=3)						
levatinib + anti PD1	2	Yes(n=1) No(n=1)	metastatic	POD	2 months 2 months	
cabozatinib + anti-PD1	1	Yes	LR	POD	2 months	
cabozatinib + anti-PD1 /anti CTLA4	1	Yes	metastatic	POD	2 months	

1 – includes 3 patients who also got IO separately from TKI at different time of treatment
2 – includes 3 patients who also got TKI separately from IO at different times of treatment

P217. Evaluation of Tumor Burden in Sarcoma Patients Using 18F-FAPI-Based PET-CT: A Proof-of-Concept Study

Meni N Brakha[1]; Aviad Zick[2]; Omer Or[3]; Noam Olshinkaa[4]; Jonathan A Demma[5]; Alon Pikarsky[6]; Gideon Zamir[7]; Judith Diment[8]; Aron Popovtzer[9]; Simona Ben Haim[10]; Yuri Fishman, MD[11]
[1]Hadassah Ein-Karem Medical Center, Jerusalem, IL; [2]Hadassah Ein-Karem Medical Center, Jerusalem, IL; [3]Hadassah Ein-Karem Medical Center, Jerusalem, IL; [4]Hadassah Ein-Karem Medical Center, Jerusalem, IL; [5]Hadassah Ein-Karem Medical Center, Jerusalem, IL; [6]Hadassah Ein-Karem Medical Center, Jerusalem, IL; [7]Hadassah Ein-Karem Medical Center, Jerusalem, IL; [8]Hadassah Ein-Karem Medical Center, Jerusalem, IL; [9]Hadassah Ein-Karem Medical Center, Jerusalem, IL; [10]Hadassah Ein-Karem Medical Center, Jerusalem, IL; [11], US

INTRODUCTION: Soft tissue sarcomas are rare, diverse tumors with over 100 subtypes. Surgery is the primary treatment, with or without adjuvant/ neoadjuvant therapy. Imaging with CT/MRI guides decisions, but FDG-PET-CT has limited sensitivity/specificity. FAPI PET-CT has shown promise for tumors with fibrosis, like sarcomas. This proof-of-concept study evaluates 18F-FAPI PET-CT for assessing tumor burden in sarcoma patients. **METHODS:** Patients with various soft tissue sarcomas treated in our center were prospectively recruited. 18F-FAPI PET CT was acquired 60 minutes post-injection. Adverse events were monitored. A senior nuclear medicine specialist interpreted all scans. FAPI was compared to FDG and other imaging modalities that were performed within 60 days, upon availability. **RESULTS:** Ten patients were recruited: Leiomyosarcoma (n=2), Fibromyxoid Sarcoma (n=2), Small Round Cell Sarcoma (n=2), Spindle Cell Sarcoma (n=1), Rhabdomyosarcoma (n=1), Ewing Sarcoma (n=1), and GIST (n=1). No adverse events occurred with F18-FAPI administration. Background SUVmax values were consistent across liver (mean 1.7), blood pool (2.8), spine (2.1), and soft tissue (1.3). In 5 cases, FDG PET-CT was available, CT was available for all cases. No metastatic site detected by FDG was missed by FAPI, while FAPI showed higher SUVmax, wider disease distribution and other metastatic sites in 4 out of 5 patients who had FDG for comparison. Findings by subtype: **Ewing's Sarcoma (n=1)**: No metastases on either scan; high uptake in the primary tumor in both FDG and FAPI (SUVmax 9.2, 10.4). **Fibromyxoid Sarcoma (n=2)**: FAPI identified skeletal, peritoneal, and retroperitoneal metastases. **Leiomyosarcoma (n=2)**: FAPI showed more diffuse uptake and higher SUVmax in metastatic sites than FDG. **Small Round Cell Sarcoma (n=2)**: One patient had widespread metastases, and the other had benign lung nodules on FAPI. **GIST (n=1)**: FAPI detected an intra-splenic lesion missed by FDG, with a corresponding lesion on CT. **Spindle Cell Sarcoma (n=1)**: FAPI identified a pelvic mass and lung metastases. **Rhabdomyosarcoma (n=1)**: FAPI detected an intra-prostate avidity that was not apparent on FDG. **CONCLUSIONS:** In this proof-of-concept study, F18-FAPI PET-CT has demonstrated its potential to evaluate tumor burden in patients with various sarcoma subtypes, showing non-inferiority and at times superiority to FDG PET-CT. This underscores the urgent need for larger studies to confirm and further explore the role of FAPI PET-CT in sarcoma management.



P218. New insights into the role of retroperitoneal soft-tissue sarcoma derived extracellular vesicles in angiogenesis

Sapir Milshtain[1]; Shelly Loewenstein[2]; Emily Rothenberg[3]; Talya Bornstein[4]; Daniela Neuman[5]; Guy Lahat[6]
[1]Tel Aviv Sourasky Medical Center, Tel Aviv, IL; [2]Tel Aviv Sourasky Medical Center, Tel Aviv, IL; [3]Tel Aviv Medical Center, Tel Aviv, IL; [4]Tel Aviv Medical Center, Tel Aviv, IL; [5]Tel Aviv Medical Center, Tel Aviv, IL; [6]Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel, IL

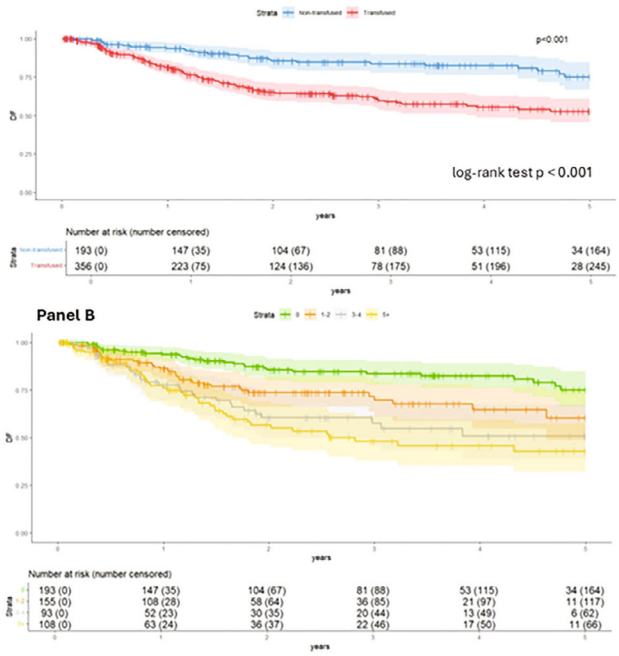
INTRODUCTION: Retroperitoneal soft-tissue sarcoma (RSTS) comprises a rare and heterogeneous group of solid tumors. Angiogenesis, a key hallmark of cancer, is essential for tumor growth and metastasis. Extracellular vesicles (EVs) are membranous structures that facilitate intercellular communication, influencing processes such as angiogenesis through the transfer of molecular cargo, particularly microRNAs (miRNAs). Recent research highlights the role of specific miRNAs, termed angio-miRs, in angiogenesis. This study investigates the role of EVs derived from RSTS cells and their angio-miRs in promoting angiogenesis. **METHODS:** EVs were isolated from human liposarcoma, fibrosarcoma, and leiomyosarcoma cell cultures and used to stimulate human endothelial cells (EC). Proliferation, migration, and invasion assays were used to evaluate the phenotypic behavior of treated EC. Matrigel tube- and plug-formation assays were used to demonstrate angiogenesis in vitro and in vivo. The expression levels of key angoi-miRNAs (miR-34a, miR-21 and miR-126) in stimulated EC were evaluated using qRT-PCR. Finally, anti-miR-34a was used to downregulate miR-34a expression in EC, and its effect on specific targets and signaling pathways was determine using western blotting and qRT-PCR. **RESULTS:** Our findings demonstrate that all three human RSTS cell lines derived EVs enhance EC proliferation as measured by mitochondrial activity. Similarly, all tested RSTS derived EVs increased migration and invasion of EC compared to non-treated cells. We also demonstrate that RSTS derived EVs significantly augment the number of tube like structures in EC and induce angiogenesis in immunocompromised mice. CD31 immunohistochemical staining of sections from the in vivo plugs demonstrated a significant increment in the number of blood vessels in the EVs treated mice. In addition, miR-34a, miR-21, and miR-126 levels were upregulated in EC following stimulation with RSTS derived EVs. Notably, downregulation of miR-34a in EC resulted in reduced angiogenesis and decreased expression of its targets, the pro-angiogenic factors VEGF and ANG2. **CONCLUSIONS:** This study is the first to demonstrate that EVs derived from RSTS cells are taken up by EC and actively induce angiogenesis. We also demonstrate that the transfer of specific angi-miRS by the EVs into EC may mediate these effects, highlighting their potential role as key regulators of angiogenesis. These findings suggest that RSTS derived EVs may contribute significantly to the progression of RSTS by promoting angiogenesis.

P219. Prognostic Impact of Perioperative Blood Transfusions and Percentage of Massive Transfusions in Patients Operated for Retroperitoneal Sarcoma

Gabriele Zuanetti[1]; Giuditta Fallabrino[2]; Marco Fiore[3]; Paolo Luca Proto[4]; Stefano Radaelli[5]; Dario Callegaro, MD[6]; Chiara Colombo[7]; Marco Baia[8]; Luca Fumagalli[9]; Franco Valenza[10]; Alessandro Gronchi[11]

[1]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [2]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [3]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [4]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [5]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [6]Fondazione IRCCS Istituto Nazionale dei Tumori, Milano, IT; [7]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [8]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [9]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [10]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [11]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT

INTRODUCTION: Surgery for retroperitoneal soft tissue sarcoma (RPS) requires major abdominal procedures with high postoperative morbidity. Hemorrhage is common, often requiring perioperative red blood cell transfusions (PBT). Emerging evidence suggests PBT may affect tumor recurrence, but data on RPS is limited. We aimed to study the link between PBT and RPS outcome, with a focus on massive blood transfusions (MBT) in a large recent monoinstitutional cohort. **METHODS:** Patients operated for primary localized RPS between 2017 and 2024 were reviewed. PBT was defined as any transfusion from one day before surgery to one day after; MBT as >10 packed red blood cells (pRBC) in 24hours. The association between PBT and disease-free survival (DFS) was assessed using Kaplan-Meier curves and Cox proportional hazard models, adjusting for patient factors (age, gender, BMI, pertinent blood tests, and ASA score), tumor factors (grade, histology, and tumor rupture), surgical factors (resected organ score [ROS] and duration of surgery), chemotherapy and radiotherapy. MBT rate and reasons for massive hemorrhage were reported. **RESULTS:** 549 patients were included, with median age of 62 years and 52.8% were males. PBT was required in 356 (64.8%) cases. In this group, the median number of pRBC was 3 with 52 patients receiving 1 pRBC, while 11 (3.1%) required MBT. After a median follow-up of 2.5 years, 140 patients (25.6%) experienced disease recurrence. The 5-yr DFS was 61% (95%CI:55.4-67.3) overall, 52.7% (95%CI:45.5-60.1) in the PBT group and 75.1% (95%CI:84.8-66.7) in the non-transfused group (Fig.1). Multivariable analysis confirmed PBT as independently associated with higher recurrence risk (HR 2.57, p = 0.005). Risk increased along with number of pRBC (HR 2.36, 2.92, and 3.17 for 1-2, 3-4, and ≥5 pRBC, respectively). MBT patients had higher ASA scores (p=0.04), lower preoperative hemoglobin (p=0.02) and albumin levels (p=0.03), and larger tumors (p=0.01), requiring longer surgical procedures (p<0.001), higher ROS (p=0.046) and more vascular resections (p<0.001). In this subgroup, 30 and 90-day mortality rate were 0% and 18%, respectively. **CONCLUSIONS:** PBT was significantly associated with increased recurrence in RPS. Although PBT was frequent, MBT were extremely low. These findings suggest that minimizing transfusion may be feasible in a proportion of RPS procedure. Actionable domains include prehabilitation, intraoperative measures, and identification of patients at risk for MBT. Whether this will improve also DFS is left to be proven.



Solid lines represent estimated survival probabilities, and shaded areas 95% confidence intervals. Number of patients at risk are reported, with censored in brackets. Panel A: KM curves for the transfused group (red) and non-transfused group (blue). Panel B: KM curves according to number of transfused units: non-transfused (green), 1-2 pRBC units (orange). 3-4 pRBC units (grey), and ≥5 pRBC units (yellow).

Figure 1. Kaplan-Meier for DFS.

P220. Single cell RNA-seq analysis of murine gastrointestinal stromal tumor reveals distinct transcriptional metaprograms and their response to imatinib

Juan Esteban Perez, MD[1]; Jonathan Sussman[2]; Ronald DeMatteo, MD[3]

[1]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [2]University of Pennsylvania, Philadelphia, PA, US; [3]Hospital of the University of Pennsylvania, Philadelphia, PA, US

INTRODUCTION: Gastrointestinal stromal tumor (GIST) is the most common sarcoma, arising from Interstitial cells of Cajal (ICC). In the majority of cases, it is secondary to a single mutation in the tyrosine kinase receptor *Kit*. The tyrosine kinase inhibitor imatinib leads to a significant yet incomplete response. We hypothesize that the transcriptional identity of tumor cells can be used to identify novel treatment targets. **METHODS:** We obtained droplet based single-cell RNA sequencing of six KitV558Δ/+ mice, who spontaneously develop an intestinal GIST. Three of the mice received treatment with imatinib, three did not receive any treatment. The consensus non-matrix factorization (cNMF) method was applied to the tumor raw count matrix on a per-specimen basis. Conserved gene programs among all tumor samples were identified, and the top 100 genes were used for signature gene scoring and compared based on treatment response. **RESULTS:** Tumor cells were identified by the GIST signature of *Kit, Dog1,* and *Etv1* positivity. Consensus NMF revealed three major gene programs that could coexist within tumor cells. Oncogenic (*Kit, Dog1, Etv1*), Metabolic (*Cox6a, Ndufa4*) and Interferon-related (*Stat1, Irf7*). Tyrosine kinase inhibition with imatinib resulted in a decrease in the oncogenic and interferon modules. Additionally, there was an increase in the metabolic module score. Traditional cluster-based analysis revealed 4 distinct clusters characterized by opposing metabolic and oncogenic activity. Cluster 1 showed the highest metabolic signature score followed by 2, 3, and 4, while cluster 4 had the highest oncogenic signature score, followed by clusters 3,2 and 1 respectively. **CONCLUSIONS:** Imatinib treatment of murine GIST results in a suppressed oncogenic program as expected, given the predominance of Kit and related genes. Reduced interferon program scores reveal that imatinib creates an immunosuppressive pro-tumoral state. The metabolic gene program is induced, raising the question of possible compensatory mechanisms driving

tumor-cell survival, as well as a binary paradigm of competing oncogenic and metabolic transcriptomic states with imatinib treatment.

P221. Effectiveness of Enhanced Recovery after Surgery after Laparoscopic or Robotic Distal Gastrectomy for Gastric Cancer: A Randomized Clinical Trial

Do Joong Park[1]
[1]*Seoul National University Hospital, Seoul, KR*

INTRODUCTION: The objectives of the study was to assess the impact of a recent evidence-based multimodal enhanced recovery after surgery program on the quality of early recovery after gastric cancer surgery. **METHODS:** In a single-center, open-label, randomized controlled trial, patients undergoing elective laparoscopic or robotic distal gastrectomy for gastric cancer were assigned to either ERAS or Conventional group. The primary outcome was the total Quality of Recovery-15 score assessed 24, 48, and 72 h postoperatively. Differences between both groups were evaluated using a linear mixed-effects model. We hypothesized that an increase of at least 8 points in the Korean version of the Quality of Recovery-15 scores 24, and 72 h postoperatively would indicate a clinically significant improvement, consistent with the minimal clinically important difference (≥8) for Quality of Recovery-15. Secondary outcomes included pain scores at rest and during coughing, cumulative fentanyl consumption through intravenous patient-controlled analgesia, incidence of postoperative nausea/vomiting, and gastrointestinal dysfunction as measured using the I-FEED score, all assessed 24, and 72 h postoperatively. **RESULTS:** Among the 92 patients analyzed (enhanced recovery after surgery, n=45; Conventional, n=47), the estimated difference in the postoperative Korean version of the Quality of Recovery-15 total scores between the two groups during the first days was significantly larger than the minimal clinically important difference of the Quality of Recovery-15 (mean difference: 16.0, 95% confidence interval: 8.9–23.0, P < 0.001). Therefore, excluding the incidence of postoperative nausea/vomiting, the enhanced recovery after surgery group demonstrated statistically significant improvements in other secondary outcomes. **CONCLUSIONS:** Our evidence-based multimodal enhanced recovery after surgery program significantly improved the quality of early postoperative recovery after minimally invasive distal gastrectomy.

P222. Impact of Extended Pharmacologic Prophylaxis For Venous Thromboembolism On Short- And Long-Term Outcomes After Surgery For Esophagogastric Cancer: A 10-Year Bi-Institutional Analysis

Mark A Eckardt, MD[1]*; Patrick V Heindel, MD, MPH*[2]*; Brittany Powell, MD, MPP, MBA*[3]*; Albofazl Salari, MD*[4]*; Liang Zong, MD, PhD*[5]*; Jiping Wang, MD, PhD*[6]*; John T Mullen, MD*[7]
[1]*Mass General Brigham / Dana-Farber Cancer Institute, Boston, MA, US;* [2]*Brigham and Women's Hospital, Boston, MA, US;* [3]*Brigham and Women's Hospital, Boston, MA, US;* [4]*Brigham and Women's Hospital, Boston, MA, US;* [5]*Brigham and Women's Hospital, Boston, MA, US;* [6]*Brigham and Women's Hospital, Boston, MA, US;* [7]*Massachusetts General Hospital, Boston, MA, US*

INTRODUCTION: Guidelines recommend extended venous thromboembolism prophylaxis (eVTEP) for high-risk populations undergoing major cancer operations. Furthermore, some studies suggest long-term survival benefits from eVTEP due to the purported anti-neoplastic properties of heparin derivatives. We sought to evaluate the impact of eVTEP on short- and long-term outcomes after curative-intent surgery for esophagogastric cancer. **METHODS:** A prospective database of patients undergoing potentially curative surgery for esophagogastric cancer at two academic medical centers was analyzed from 2014 – 2024. Three patient cohorts were defined based on receipt of eVTEP and/or antiplatelet medications post-discharge. Patients with <3 months follow-up were excluded. The primary outcomes were VTE rates within 90 days of discharge and 3-year disease-specific (DSS) and overall survival (OS) rates. **RESULTS:** A total of 524 patients were identified; 23 had a preoperative VTE and 117 were on an antiplatelet/anticoagulant (AC) prior to surgery. Thirty (5.7%) patients developed a postoperative VTE, 12 (2.3%) as an inpatient and 13 (2.5%) within 90 days of discharge. A total of 104 patients were discharged on their prior maintenance or prior/new anticoagulation (cohort 1), 234 patients were discharged on eVTEP alone (cohort 2), and 186 patients on no eVTEP or AC (cohort 3). There were no differences in 90-day post-discharge VTE rates (1.0% vs 3.8% vs 1.6%; $P = 0.19$) amongst the three cohorts. At a median follow up of 31 months, there were no differences in 3-year DSS or OS rates amongst the 3 cohorts (DSS, $P = 0.83$, OS, $P = 0.41$). **CONCLUSIONS:** Extended VTE prophylaxis after curative-intent surgery for esophagogastric cancer is not associated with either a reduced rate of post-discharge VTE nor improved survival. Further research is needed to identify those patients at highest risk of VTE who might benefit from eVTEP.

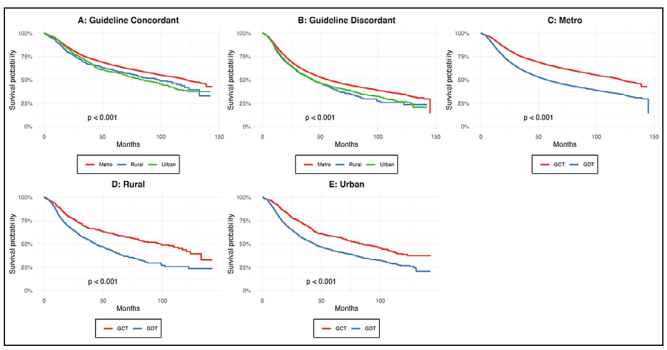
Discharge Regimen	90-day Post-Discharge VTE Rate	3-Year DSS Rate	3-Year OS Rate
Prior/New Maintenance/Therapeutic AC (n=104)	1.0% (1/104)	82%	74%
eVTEP Alone (n=234)	3.8% (9/234)	82%	78%
No eVTEP or AC (n=186)	1.7% (3/186)	83%	79%

AC = antiplatelet or anticoagulant medication; eVTEP = extended venous thromboembolism prophylaxis; VTE = venous thromboembolism; DSS = disease-specific survival; OS = overall survival

P223. Influence of Rurality on the association between guideline concordant treatment and survival in Gastric Cancer

Jason M. Lizalek, MD[1]*; Collin E. Dougherty, BS*[2]*; Michelle Zhang, MD*[3]*; Bradley N. Reames, MD, MS*[4]
[1]*University of Nebraska Medical Center, Omaha, NE, US;* [2]*University of Nebraska, Omaha, NE, US;* [3]*, US;* [4]*University of Nebraska Medical Center, Omaha, NE, US*

INTRODUCTION: Multimodal treatment of nonmetastatic gastric cancer has evolved in the last decade. Multidisciplinary management is essential for the delivery of guideline-concordant treatment (GCT). Rurality has been reported as prognostic indicator for overall survival and receipt of multimodal treatment. There is a paucity of data regarding the influence of the metropolitan to rural continuum on the receipt of GCT in gastric cancer. This study aims to investigate the influence of the metropolitan to rural continuum on the receipt of GCT in gastric cancer as well as its effect on overall survival. **METHODS:** The National Cancer Database Participant User File for gastric cancer was queried from 2011-2021 for patients with gastric adenocarcinoma (AJCC 7th or 8th ed. Stages IB-IVA). GCT was defined as the following: perioperative (neoadjuvant and adjuvant) systemic therapy and surgery or upfront surgery followed by chemoradiation for patients diagnosed 2011-2017, and neoadjuvant (+/- adjuvant) systemic therapy plus surgery for patients diagnosed 2018-2021, consistent with National Comprehensive Cancer Network guidelines. Chi-square test was used to determine differences in receipt of GCT. 5-year overall survival (OS) was calculated and tested for significance using log-rank testing. **RESULTS:** A total of 36,351 patients composed the final study cohort, of which 30,138 (82.5%) were metropolitan, 3,091 (8.5%) were urban, and 1,664 (4.6%) were residing in rural counties. Overall receipt of GCT was 35.0%. Metropolitan county residence was associated with increased likelihood of GCT (36.0%) compared to urban (30.9%) and rural (31.6%) counties (p<0.0001). Receipt of GCT was associated with a significant increase in 5-year OS (64.6%; 95% CI [63.8%-65.6%]) compared to guideline-discordant treatment (GDT) (47.9%; 95% CI [47.1%-48.7%]) (p<0.0001). Metropolitan county residence was associated with an increased 5-yr OS (55.6%) compared to urban (47.7%) or rural residence (47.5%) (p<0.0001). **CONCLUSIONS:** Despite an improvement in overall survival, less than half of patients with nonmetastatic gastric cancer receive GCT. Metropolitan patients are more likely to receive GCT compared to those residing in urban or rural areas and in turn, have improved survival. The factors associated with the overall rate of GCT and its disparate delivery to nonmetropolitan patients should be further investigated.



P224. Mediastinalization of the Gastric Conduit by Pleural Closure in Robotic Ivor Lewis Esophagectomy: Short-Term Quality of Life Assessment

Faisal S Jehan, MD, FICS[1]; Todd Demmy, MD[2]; Zachary Stiles, DO[3]; Maureen Brady, PA-C.[4]; Megan Diegelman, MS[5]; Nikki Suchak, BS[6]; Moshim Kukar, MD, FACS.[7]

[1]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [2]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [3]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [4]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [5]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [6]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [7]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US

INTRODUCTION: Gastric conduit dysfunction is becoming more common as the number of Ivor Lewis (IL) esophagectomies continue to increase. The conduit location in the right chest as compared to mediastinum can lead to angulation and narrowing at hiatus with poor emptying. We hypothesized that closing the pleural flap over the conduit may lead to better mediastinal location of conduit and potentially better emptying and lower reflux symptoms. We aim to assess the impact of this approach on clinical outcomes and short-term quality of life. **METHODS:** Utilizing our prospectively maintained dataset, we conducted a retrospective analysis of consecutive patients undergoing robotic assisted IL esophagectomy for esophageal and gastroesophageal junction cancers, in which the gastric conduit was mediastinalized by pleural closure over the conduit in the chest. The primary outcome was the assessment of short-term quality of life using the validated Esophagus-Specific Quality of Life Questionnaire (QLQ-OES18). This questionnaire assessed domains of dysphagia, deglutition (pharyngeal swallowing), eating, reflux, pain and anxiety as well as single items like dry mouth, taste, trouble talking, trouble coughing. All questions were assessed on a 1–4-point Likert scale with a low score mean less dysfunction and better quality of life. Scores reported in as mean with a standard deviation. **RESULTS:** A total of 26 patients were included in the study, with a mean age of 64 ± 8 years; 73% were male. All patients underwent a CT esophagogram on postoperative day 4 (POD4), which demonstrated a well-positioned gastric conduit in the mediastinum with rapid emptying into the abdomen. The anastomotic leak rate was 0%, and only one patient required reoperation for takedown of the pleural flap. All patients were started on a clear liquid diet on POD4. The median hospital length of stay was 6 days. There were no 30-day readmissions or 30-day mortality. The median time to quality-of-life assessment was 55 days. On the QLQ-OES18 questionnaire, patients reported excellent quality of life, particularly in the domains of dysphagia (1.4 ± 0.5), deglutition (1.08 ± 0.3), trouble talking (1.02 ± 0.1), taste (1.1 ± 0.3), and trouble coughing (1.1 ± 0.4). In the eating domain, patients had no difficulty with liquids (1.3 ± 0.4), soft foods (1.4 ± 0.5), or solid foods (1.9 ± 0.6). Scores were moderate in the domains of pain (2.5 ± 0.7), anxiety (2.2 ± 0.8), and reflux (2.6 ± 0.6). **CONCLUSIONS:** Mediastinalization of the gastric conduit by pleural closure in robotic IL esophagectomy is associated with excellent short-term clinical outcomes. Patients demonstrated excellent scores in quality-of-life metrics, particularly in dysphagia and eating-related domains. With continued modification of our technique over the last decade, we believe that this modification has the most potential to improve QOL while adding minimal time in the operating room and no additional morbidity.

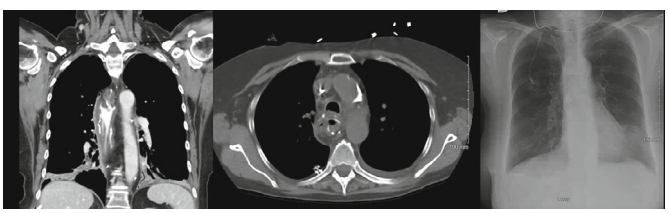


Figure 1. Post operative CT esophagogram and Chest X-ray demonstrating gastric conduit in the mediastinum.

P225. Neoadjuvant chemotherapy for locally advanced gastric cancer is not associated with post-operative complications or poor surgical outcomes.

Mahtab Vasigh[1]; Monica T Minassian[2]; Celeena R Jefferson[3]; Ashley K Savoy[4]; Eric S Watson[5]; Aung Oakkar[6]; Taleaa Masroor[7]; Fassika Molla Abreha[8]; Fabian M. Johnston, MD, MHS, FSSO[9]; Joyce X Wong[10]; Norman G Nicolson[11]

[1]Johns Hopkins, Baltimore, MD, US; [2]2. Kaiser Permanente Mid-Atlanletic Permanente Medical Group, Mid-Atlantic Permanente Research Insti, Rockville, MD, US; [3]2. Kaiser Permanente Mid-Atlantic Permanente Medical Group, Mid-Atlantic Permanente Research Institu, Rockville, MD, US; [4]2. Kaiser Permanente Mid-Atlantic Permanente Medical Group, Mid-Atlantic Permanente Research Institu, Rockville, MD, US; [5]Kaiser Permanente Mid-Atlantic Permanente Medical Group, Mid-Atlantic Permanente Research Institute, Rockville, MD, US; [6]Kaiser Permanente Mid-Atlantic Permanente Medical Group, Mid-Atlantic Permanente Research Institute, Rockville, MD, US; [7]Johns Hopkins Medical Institute, Baltimore, MD, US; [8]Johns Hopkins Medical Institute, Baltimore, MD, US; [9]Johns Hopkins University, Baltimore, MD, US; [10]2. Kaiser Permanente Mid-Atlantic Permanente Medical Group, Mid-Atlantic Permanente Research Institu, Rockville, MD, US; [11]Johns Hopkins Medical Institute, Baltimore, MD, US

INTRODUCTION: Standard treatment of advanced gastric cancer (GC) includes neoadjuvant chemotherapy (NAC) and surgical resection. The oncologic benefits of perioperative chemotherapy in this disease are well-documented, but concerns about the effect of NAC on surgical outcomes have not been well-studied. **METHODS:** This retrospective cohort evaluated patients (age ≥18) with non-metastatic GC who underwent surgery at Kaiser Permanente Mid-Atlantic States and Johns Hopkins Hospitals between 2015 and 2021. Early post-operative (post-op) complications and surgical outcomes, including length of hospital stay (LOS), readmission, and mortality within the first thirty days after GC surgery, were evaluated and compared between those who did and did not receive NAC. **RESULTS:** A total of 226 GC surgeries were evaluated. NAC was administered in 145 patients (64.6%). Older patients (p=0.03), higher Charlson comorbidity index (CCI) (p=0.04), Higher Neighborhood Deprivation Index (NDI) (p=0.04), and a positive history of another malignancy (p<0.001) were less likely to receive NAC. Post-op complications were observed in 69 cases (30.5%): anastomotic leak in 5.3%, gastrointestinal bleeding in 2.2%, intra-abdominal abscess in 7.4%, pneumonia in 6.5%, surgical site infection in 2.3%, and other infections in 11.9%. The median LOS was seven days. LOS above 14 days was more common in pT3-4 patients compared to pT0-2 patients (p= 0.003) and total gastrectomy patients compared to partial gastrectomy (p=0.01). The patients with better Eastern Cooperative Oncology Group (ECOG) performance status (ECOG≤1) had lower LOS than ECOG>1 (p=0.004), and laparoscopy-treated patients had a lower LOS than the open surgery group (p<0.001). The readmission rate was 12.6%, higher among patients who underwent laparoscopic surgery (p<0.001) than open surgery and current or former smokers (p<0.001) than never smokers. Early post-op mortality was observed in 4 (1.8%) patients. Patients with a higher CCI (p=0.03) and higher pT (p<0.001) had higher post-op mortality rates. NAC administration did not increase the rate of post-op complications (OR: 1.3, 95%CI: 0.9- 2.0; p=0.2), LOS (p=0.5), or early post-op mortality (p=0.7). Readmission was less common in NAC-treated patients (9.0% vs 20.0%, p= 0.03). **CONCLUSIONS:** The administration of NAC for gastric cancer is safe and does not negatively impact early surgical outcomes. However, higher CCI, higher pT, smoking history, and total gastrectomy are associated with worse early surgical outcomes.

Table. Patients' characteristics stratified by the presence of post-op complications

	Without complication N (%) 157 (69.5%)	With complication N (%) 69 (30.5)	Total N (%) 226	p
Age				0.81
65 or above	81 (51.9)	37 (53.6)	118 (52.4)	
below 65	75 (48.1)	32 (46.4)	107 (47.6)	
RACE				0.28
African American	42 (26.8)	17 (24.6)	59 (26.1)	
Asian	31 (19.7)	6 (8.7)	37 (16.4)	
White	62 (39.5)	36 (48.0)	96 (42.5)	
Other	15 (9.6)	8 (11.6)	23 (10.2)	
Unknown	7 (4.5)	4 (5.8)	11 (4.9)	
Ethnicity				0.92
Hispanic	18 (11.5)	9 (13)	27 (11.9)	
Non-Hispanic	102 (65.0)	45 (65.2)	147 (65)	
Unknown	37 (23.6)	15 (21.7)	52 (23)	
Insurance				0.73
ACA	8 (5.1)	2 (2.9)	10 (4.4)	
Commercial	46 (29.3)	17 (24.6)	63 (27.9)	
Government	1 (0.6)	2 (2.9)	3 (1.3)	
Medicaid	13 (8.3)	6 (8.7)	19 (8.4)	
Medicare	76 (48.4)	35 (50.7)	111 (49.1)	
None	1 (0.6)	0	1 (0.4)	
Unknown	12 (7.6)	7 (10.1)	19 (8.4)	
NDI_FINAL				0.17
Mean (SD)	-0.58±1.10	-0.42± 1.20	-0.53±1.13	
ECOG performance status				0.90
0	70 (44.6)	29 (42)	99 (43.8)	
1	54 (34.4)	24 (34.8)	78 (34.5)	
2	7 (4.5)	5 (7.2)	12 (5.3)	
3	3 (1.9)	2 (2.9)	5 (2.2)	
Unknown	23 (14.6)	9 (13)	32 (14.2)	
Charlson Comorbidity Index				0.42
1 – 2	90 (68.7)	38 (59.4)	128 (65.6)	
3 – 4	32 (24.4)	21 (32.8)	53 (27.2)	
≥5	9 (6.9)	5 (7.8)	14 (7.2)	

P226. Operative outcomes and learning curve of robotic gastrectomy for gastric adenocarcinoma

Morgan F Pettigrew, MD[1]; Amr I. Al Abbas, MD[2]; Skylar L. Nahi, MD[3]; Sai Govindu, BS[4]; Patricio M. Polanco, MD[5]; Adam C. Yopp, MD[6]; Cecilia G Ethun, MD[7]; Herbert J Zeh, MD[8]; Sam C. Wang, MD[9]; Matthew R. Porembka, MD[10]
[1]UT Southwestern Medical Center, Dallas, TX, US; [2]UT Southwestern Medical Center, Dallas, TX, US; [3]UT Southwestern Medical Center, Dallas, TX, US; [4]UT Southwestern Medical Center, Dallas, TX, US; [5]UT Southwestern Medical Center, Dallas, TX, US; [6]UT Southwestern Medical Center, Dallas, TX, US; [7]UT Southwestern Medical Center, Dallas, TX, US; [8]UT Southwestern Medical Center, Dallas, TX, US; [9]UT Southwestern Medical Center, Dallas, TX, US; [10]UT Southwestern Medical Center, Dallas, TX, US

INTRODUCTION: Robotic gastrectomy (RG) is a safe alternative to open gastrectomy (OG) for treating gastric cancer (GC). Our institution, a high-volume center for robotic pancreas surgery, implemented an RG program in 2018. We compared outcomes of OG and RG and determined the learning curve for RG at a high-volume robotic center. **METHODS:** We retrospectively reviewed patients with GC who underwent gastrectomy at our institution from 2017 to 2024. We compared clinicopathologic and operative outcomes of patients who underwent RG to those who underwent OG. Multivariable cumulative analysis (CUSUM) was used to construct a learning curve for RG using operative time (ORT), estimated blood loss (EBL), lymph node harvest, and major complications (Clavien-Dindo ≥3). **RESULTS:** Of 103 total patients, 33 (32%) underwent OG, and 70 (68%) underwent RG. In the RG group, there were 28 subtotal and 42 total gastrectomies. 91% of RG patients had locally advanced disease, and 82% received neoadjuvant chemotherapy. Patients in the RG group were older than in the OG group (median: 64 vs 51 years, P = 0.02). Sex, Body Mass Index, and American Society of Anesthesiology scores were similar between the OG and RG groups. ORT was higher in the RG group (median: 243 vs 222 minutes, P = 0.006). There was no significant difference in EBL, R0 resection rates, and lymph nodes harvested. There was also no difference in post-operative length of stay (LOS) or rates of 30-day complications, emergency room (ER) visits, or readmissions. OG patients were more likely to develop abdominal wall hernias (19% vs 3%, P = 0.01). Only 1 RG was converted to open. Based on CUSUM analysis, an initial learning phase of 15 cases, an intermediate improvement phase of 25 cases, and a proficiency or plateau phase of 30 cases were identified. While there was no significant difference in operative time during each phase, there was significant improvement in EBL (P = 0.02) and lymph node harvest (P < 0.001). There was also improvement in post-operative LOS (P = 0.04) and 30-day ER visits (P = 0.004), but no significant improvement in complication (P = 0.06) or readmission rates (P = 0.13). Once the proficiency phase was achieved, there was no difference in ORT, post-operative LOS, 30-day ER visits, complications, or readmissions between OG and RG, but RG was associated with lower EBL (P = 0.007). **CONCLUSIONS:** In the setting of an experienced robotic surgery program, RG has a short learning curve and outcomes similar to OG. This was true even though a majority of patients had locally advanced GC.

Table 1. Operative characteristics and outcomes of open gastrectomy compared to robotic gastrectomy, and robotic gastrectomy stratified by learning stage.

	Open Gastrectomy	Robotic Gastrectomy	P value
Total	33 (32)	70 (68)	
Age	51 (47-65)	64.0 (50-70)	**0.02**
Sex			0.41
Male	20 (61)	36 (51)	
Female	13 (39)	34 (49)	
Body Mass Index (kg/m^2)	26.1 (22.7-29.5)	26.0 (23.0-29.4)	0.76
American Society of Anesthesiology Score			0.87
II	3 (9)	6 (9)	
III	29 (88)	63 (90)	
IV	1 (3)	1 (1)	
Operative Time (minutes)	222 (180-252)	243 (220-286)	**0.006**
Estimated Blood Loss (milliliters)	100 (50-225)	75 (50-150)	0.10
R0 Resection			0.26
No	4 (12)	4 (6)	
Yes	28 (88)	66 (94)	
Lymph Nodes Harvested	28 (19-48)	23 (18-33)	0.18
Post-operative Length of Stay (days)	6 (5-7)	6 (6-8)	0.86
30-day Emergency Room Visits			0.07
No	30 (91)	52 (74)	
Yes	3 (9)	18 (26)	
30-day Complications			0.22
No	31 (94)	58 (83)	
Yes	2 (6)	12 (17)	
30-day Readmissions			0.14
No	31 (94)	57 (81)	
Yes	2 (6)	13 (19)	
	Robotic Gastrectomy Learning Phases		
	Initial Phase	Improvement Phase	Proficiency Phase	P value[a]
Total	15 (21)	25 (36)	30 (43)	
Operative Time (minutes)	255 (220-301)	251 (223-288)	232 (218-257)	0.42
Estimated Blood Loss (milliliters)	100 (75-150)	100 (50-150)	50 (30-80)	**0.02**
R0 Resection				0.92
No	0 (0)	3 (12)	1 (3)	
Yes	15 (100)	22 (88)	29 (97)	
Lymph Nodes Harvested	17 (14-25)	22 (18-27)	30 (22-43)	**<0.001**
Post-operative Length of Stay (days)	7 (5-26)	6 (4-8)	5 (4-6)	**0.04**
30-day Emergency Room Visits				**0.04**
No	8 (53)	19 (76)	25 (83)	
Yes	7 (47)	6 (24)	5 (17)	
30-day Complications				0.06
No	9 (60)	23 (92)	26 (87)	
Yes	6 (40)	2 (8)	4 (13)	
30-day Readmissions				0.13
No	9 (60)	23 (92)	25 (83)	
Yes	6 (40)	2 (8)	5 (17)	

Categorical data are *n* (%), and continuous data are median (interquartile range). Complication grades are according to the Clavien-Dindo classification.

P227. Presentation, Treatment Patterns, and Outcomes in Patients Receiving Care for Esophageal Carcinoma in a Low-Resource Setting: An Observational Cohort Study at Queen Elizabeth Central Hospital and Malamulo Adventist Hospital in Southern Malawi

Joseph N Mkandawire[1]; Sharon Bonya[2]; Emmanuel Kyobe[3]; Brent Sherwin[4]; Chifundo Chuka[5]; Irene Chidothe[6]; Laurel Gurhrie[7]; Leo Masamba[8]; Kasumba M Kaggya[9]; Mark E. Reeves, MD, PhD[10]
[1], US; [2], US; [3], US; [4], US; [5], US; [6], US; [7], US; [8], US; [9]Loma Linda University, Pan-African Academy of Christian Surgeons, VANCOUVER, BC, CA; [10]Loma Linda University Health, Loma Linda, CA, US

INTRODUCTION: Esophageal cancer presents a significant health burden, especially in resource-limited settings like Malawi. This study aimed to assess clinical presentation, treatment patterns, and outcome among patients with esophageal cancer at two major hospitals in Southern Malawi. **METHODS:** A prospective cohort of 172 patients diagnosed with esophageal cancer were enrolled from July 2022 to July 2024. Demographics, clinical presentation, treatment modalities, and outcomes data were collected. Survival was assessed using Kaplan-Meier methods, and factors associated with mortality were evaluated using multivariate Cox regression. **RESULTS:** The median age of 56 years, predominantly primary-educated (95 55.88%), and one-third HIV-positive (59, 34.71%). The median time to endoscopy was 4.85 months, with a median survival of 8.52 months (95% CI: 6.55-10.53 months). The majority of participants had squamous cell carcinoma (SCC) histology (93.6%), while a small proportion (2.33%) had adenocarcinoma Most patients received

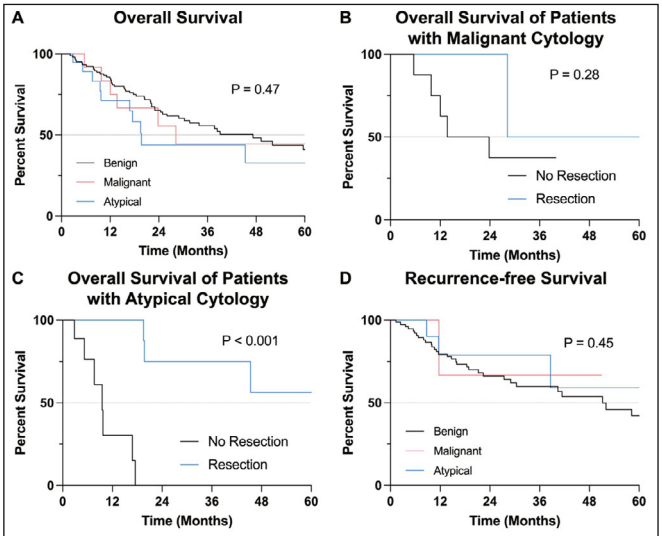
chemotherapy (78, 45.3%), while a smaller portion underwent stenting or received a feeding tube. Seven (4%) patients had esophagectomy, and, overall, only six (3.4%) survived by the study's end. Cox proportional-hazard models revealed that alcohol consumption (HR: 1.70, 95% CI: 1.13-2.57), smoking (HR: 1.81, 95% CI: 1.15-2.84), and feeding tube placement (HR: 2.56, 95% CI: 1.63-4.01) were associated with worse survival, while chemotherapy improved survival (HR: 0.52, 95% CI: 0.34-0.78). Inability to swallow saliva was linked to worse survival initially (HR: 8.12, 95% CI: 2.65-24.90), but this effect decreased over time. Additionally, taking hot drinks, and higher BMI were associated with worse outcomes at different time points. In a multivariable model controlling for confounders, feeding tube (HR: 2.57, 95% CI: 1.03-6.37), higher BMI at later stages, and hot drinks at early stages were significant predictors of lower survival. Missing data reduced the sample size, limiting power. **CONCLUSIONS:** Late-stage presentation and limited treatment options resulted in poor survival outcomes for esophageal cancer patients in Southern Malawi. A very small percentage accessed surgery. Expanding access to early detection and comprehensive treatment, comprising chemoradiotherapy and surgery, could improve outcomes in similar resource-limited settings. Infrastructure development, for instance radiotherapy, surgical services and resource allocation are critical to enhancing care for esophageal cancer.

P228. Prognostic impact of "atypical cells" on staging laparoscopy for gastric cancer

Morgan F Pettigrew, MD[1]; Ryan T Heslin, MD[2]; Ricarcdo E. Nunez-Rocha, MD[3]; Nafeesah Fatimah, MD[4]; Scott I. Reznik[5]; Matthew R. Porembka, MD[6]; Sam Wang, MD[7]; Suntrea T.G. Hammer, MD[8]

[1]UT Southwestern Medical Center, Dallas, TX, US; [2]UT Southwestern Medical Center, Dallas, TX, US; [3]UT Southwestern Medical Center, Dallas, TX, US; [4]UT Southwestern Medical Center, Dallas, TX, US; [5]UT Southwestern Medical Center, Dallas, TX, US; [6]UT Southwestern Medical Center, Dallas, TX, US; [7]UT Southwestern Medical Center, Dallas, TX, US; [8]UT Southwestern Medical Center, Dallas, TX, US

INTRODUCTION: Laparoscopic staging for gastric cancer is recommended as cytology positive abdominal washings are considered metastatic disease. However, cytologic diagnosis of adenocarcinoma is difficult as cells are often limited in number and lack spatial context. As a result, cells with atypical features that lack diagnostic criteria for adenocarcinoma may result in a diagnosis of "atypical cells". The prognostic value of these atypical cells is not well-defined. We sought to determine outcomes of gastric cancer patients with atypical cells in abdominal washings. **METHODS:** We retrospectively reviewed final cytology reports of gastric cancer patients who underwent pre-treatment staging laparoscopy with washings at UT Southwestern Medical Center or Parkland Memorial Hospital from 2014 to 2023. Patients with visible metastatic disease on imaging or laparoscopy were excluded. Primary outcome was overall survival (OS). Secondary outcome was recurrence-free survival (RFS) after curative-intent resection. **RESULTS:** Of 139 patients included, 107 (78%) had benign cytology, 20 (14%) had atypical cells, 12 (8%) had malignant cells. There were no differences in age, sex, race, tumor location, or Lauren histology among groups. 78 patients (73%) with benign cytology, 10 (50%) with atypical cytology and 4 (33%) with malignant cytology underwent curative-intent resection (P = 0.007). Median OS was 47 months in patients with benign cytology, 19 months with atypical washings, and 28 months with metastatic washings (P = 0.47). In patients with malignant cytology, median OS was 19 months without resection and 45 months in those who underwent resection (P = 0.28). In patients with atypical cytology, those who did not undergo resection had median OS of 10 months, and median OS was not reached in those who received resection (P < 0.0001). Of the 96 patients who underwent resection, 34 (44%) with benign cytology, 2 (20%) with atypical cytology, and 1 (25%) with malignant cytology recurred. Median RFS was 51 months in patients with benign cytology and was not reached in those with atypical or malignant cytology (P = 0.45). 3 patients (4%) with benign cytology recurred in the peritoneum, while all patients with atypical or malignant cytology who recurred, recurred in the peritoneum. **CONCLUSIONS:** In gastric cancer patients found to have atypical cells on pre-treatment abdominal washings, gastrectomy was associated with improved OS compared to those who did not undergo resection. Gastrectomy should be considered in patients with atypical cytology who have a favorable response to systemic therapy and can result in prolonged survival.



A. Overall survival stratified by cytology. B. Overall survival in patients with malignant cytology stratified by receipt of curative-intent resection. C. Overall survival in patients with atypical cytology stratified by receipt of curative-intent resection. D. Recurrence-free survival in patients who underwent curative-intent resection stratified by cytology.

Figure 1. Kaplan-Meier curves of patients with gastric cancer who underwent staging laparoscopy with washings.

P229. Prognostic Significance of Epithelioid Cell Type in Patients with Gastrointestinal Stromal Tumor

Steve Huy D Phan[1]; Angelina Wang[2]; Oliver S Eng[3]; Thuy B. Tran[4]

[1]UCI School of Medicine, Irvine, CA, US; [2]University of California Irvine Department of Surgical Oncology, Irvine, CA, US; [3]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [4]University of California Irvine Department of Surgical Oncology, Irvine, CA, US

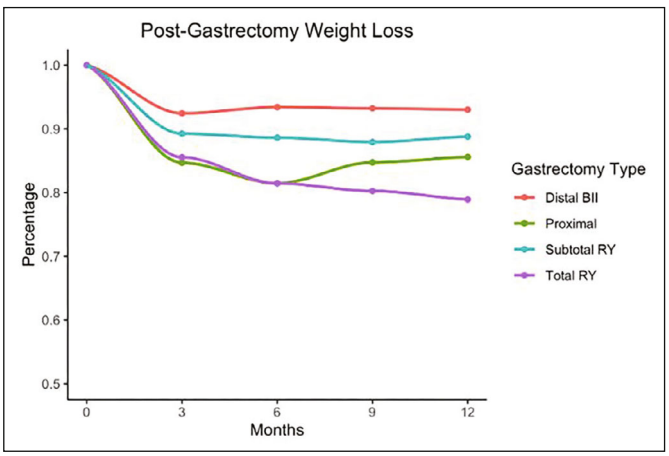
INTRODUCTION: Gastrointestinal stromal tumors (GIST) are the most common mesenchymal malignancy of the gastrointestinal tract. While most GISTs are spindle cell type, a smaller subset presents with epithelioid cell type. Implementation of surgery and targeted therapy strategies with tyrosine kinase inhibitors (TKIs) have largely been studied for spindled type GIST, but literature is scarce for associations between GIST histologic type and mutational profile and treatment outcomes. This study aims to compare pathologic and mutational characteristics between epithelioid and spindle GIST subtypes and assess long-term oncologic outcomes. **METHODS:** Patients diagnosed and treated for GIST at an academic tertiary hospital from 2004 to 2022 were retrospectively reviewed. Patient demographics, tumor characteristics, treatment, and oncologic outcomes were evaluated. Descriptive statistics compared the two groups. Kaplan Meier analysis estimated overall survival (OS). Multivariable Cox regression was performed to identify predictors of OS. **RESULTS:** Among 131 patients diagnosed with GIST, the median age was 64 years. Spindle cell type was identified in 93 (71.0%) patients and epithelioid cell type was identified in 38 patients (29.0%) patients. Spindle cell GIST was more common in Asian patients (39.8 vs. 15.8%), while epithelioid subtype was more frequently observed in Hispanic (13.2 vs. 9.7%) and Black patients (13.2 vs. 4.3%) (P=0.038). Those with epithelioid GIST tended to be associated with symptoms such as weight loss and pain (36.8% vs. 14%, P=0.005). Epithelioid GIST were significantly larger tumors (8.2 vs. 5.9cm, P<0.001). Those with spindle cell GIST tended to have wider pathologic margins compared to those with epithelioid GIST (46.5 vs. 25.8%, P=0.038). CD117 KIT mutation was identified in 122 (93.1%) patients. DOG-1 over-expression was similar between the two groups while there was a higher rate of CD56, S-100, and desmin expression with epithelioid subtype. The use of TKIs was similar between the two groups. The 5-year OS was higher for spindle cell compared to epithelioid (79.6 vs 65%). On multivariate analysis, margin status was the strongest predictor of survival, but histologic subtype was not. **CONCLUSIONS:** Although margin status was the most significant predictor of poor outcomes, epithelioid subtype, although rarer than spindle subtype, had worse survival rates, despite similar

treatment interventions. This highlights a need for future studies to better understand and improve treatment strategies for rare GIST histologic subtype.

P230. Proximal Gastrectomy for Locally Advanced Gastric Cancer

Emily L Siegler[1]; EeeLN Buckarma, MD[2]; Hallbera Gudmundsdottir[3]; Travis E. Grotz, MD, FSSO[4]
[1]Mayo Clinic, Rochester, MN, US; [2]Mayo Clinic, Rochester, MN, US; [3]Mayo Clinic, Rochester, MN, US; [4]Mayo Clinic, Rochester, MN, US

INTRODUCTION: Proximal gastrectomy (PG) is used to treat early gastric cancer (GC) involving the upper third of the stomach preserving the distal stomach and its function. The oncologic practicality in locally advanced GC remains uncertain. **METHODS:** Retrospective analysis of patients with locally advanced (≥T2 or N+) GC treated with robotic PG or total gastrectomy (TG) from December 2022 to January 2024 at a single institution. **RESULTS:** Eleven patients underwent PG and 35 patients underwent TG. The median hospital length of stay was 5 (IQR 4-5), the 90-day major morbidity was 36%, the 30-day readmission rate was 18% and the 90-day mortality was 0% and did not differ significantly from those undergoing TG (p> 0.05). All PG cases had an R0 resection, and the median number of lymph nodes removed was 25 (IQR 18-38), only one (9%) patient had <15 lymph nodes examined. The mean % actual body weight loss at 6 months following PG was similar to TG (19% vs 19%) however, at 12 months the PG weight loss rebounds while TG continues to lose weight (14% vs 21%, p =0.25). At a median follow up of 18 months there were no locoregional recurrences and the 18-month OS was 91% for those undergoing PG. **CONCLUSIONS:** PG with modified D2 lymphadenectomy may result in less weight loss than TG while providing promising early oncologic outcomes in locally advanced GC involving the upper third of the stomach. Further prospective and long-term evaluation of the functional and oncologic outcomes is necessary.



P231. Treatment Patterns of Anal Melanoma in the Era of Immunotherapy

Hannah E Sofield, MD[1]; Rachel Nation, MD[2]; T Hess, MD[3]; Gena Topper, MD[4]; Matthew Moccia, MD[5]; Michael E Kwiatt, MD[6]; Steven McClane, [7]; Danica Giugliano, MD[8]; Francis Spitz, MD[9]; Young K Hong, MD[10]; Madeline B. Torres, MD[11]
[1]Cooper University Hospital, Camden, NJ, US; [2]Cooper University Hospital, Camden, NJ, US; [3]Cooper University Hospital, Camden, NJ, US; [4]Cooper University Hospital, Camden, NJ, US; [5]Cooper University Hospital, Camden, NJ, US; [6]Cooper University Hospital, Camden, NJ, US; [7]Cooper University Hospital, Camden, NJ, US; [8]Cooper University Hospital, Camden, NJ, US; [9]Cooperhealth.edu, Camden, NJ, US; [10]Cooper University Hospital, Camden, NJ, US; [11]Cooper University Hospital, Camden, NJ, US

INTRODUCTION: Anal melanoma (AM) is a rare and aggressive type of melanoma associated with poor survival. There are no standardized guidelines to guide treatment. The purpose of this study is to determine stage specific treatment patterns and survival before and after the introduction of immunotherapy (IT). **METHODS:** The National Cancer Database for Anal Cancer (2004-2021) was queried to identify patients with AM. We assigned three staging groups, local (I-II), regional (III), and metastatic (IV) to patients with data entries that contained criteria for TNM staging. The year (2011) IT received FDA approval for melanoma was used as the cutoff year for group comparisons. Patient characteristics, treatments and outcomes were then compared. Statistical analyses were performed using Kaplan-Meier and Fischer exact tests. **RESULTS:** A total of 1,474 patients were identified. The median age was 68 years (range 24-90), 873 (59%) were female, and 1,314 identified as White (89%). There were 459 patients in the pre-IT period (2004-2010) and 1,015 in the post-IT period (2011-2021). Stage classification was assigned to 762 (51.6%) patients in whom appropriate criteria were available. All stage I-II received surgery during both time periods, while the surgical rate in stage IV patients decreased by 8% post-IT (57% vs. 49%). Most in stage I-II were treated with surgery alone (62%), while stages III and IV received multimodal treatment (61% and 66% respectively). Use of IT increased to 37% in 2015 (previously <21%) and continued to rise through 2021 across all stages, with the most utilization in stage IV in the post-IT period (14% vs. 58%). Less abdominoperineal resections (APR) occurred during the post-IT period (17.1% vs. 28.7%, $p < 0.0001$) in both community (16.8% vs. 34.6%, $p < 0.001$) and academic (17% vs. 26%, $p = 0.0019$) settings. There was no statistically significant difference in APR rate between community and academic facilities pre-IT (34.6% vs. 26%, $p = 0.06$) or post-IT (16.8% vs. 17%, $p > 0.99$). Median overall survival (OS) in the post-IT and pre-IT periods was 62.5 vs 20.4 months ($p < 0.0001$). Patients with stage I-II, III, and IV disease had median OS of 39.6, 23.7, and 8.6 months respectively ($p < 0.0001$). Patients with stage III disease were more likely to receive IT in addition to surgery compared to stage I-II (OR 3.22, 95% CI: 1.96-5.35, $p < 0.0001$) and stage IV (OR 1.89, 95% CI: 1.31-2.74, $p = 0.0006$). Patients with stage IV disease received more IT overall than Stage I-II (OR 5.26, 95% CI: 3.38-8.17, $p < 0.0001$) and Stage III (OR 1.53, 95% CI: 1.10-2.11, $p = 0.0105$). **CONCLUSIONS:** IT use is increasing for the treatment of AM with an associated decrease in APRs and increased median OS in patients with stage III and IV disease.

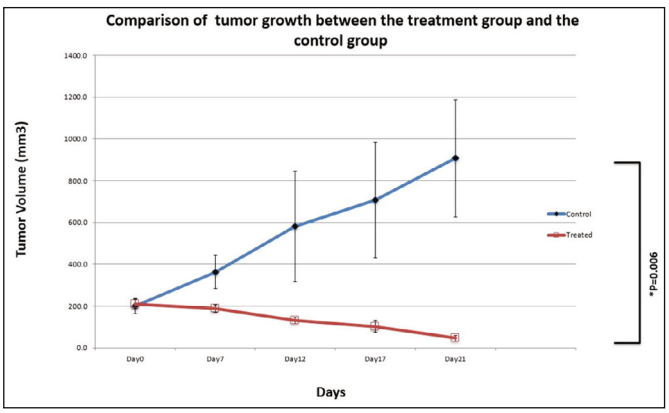


Figure 1. Tumor growth comparison between treatment group and control group

P232. A Single Institution Experience with CDH1 Mutations and Cancer Penetrance

Caitlyn Balsay-Patel, MD[1]; Adrienne B Shannon, MD[2]; Weihong Sun, MD[3]; Marie C Lee, MD[4]; Jose M Pimiento, MD[5]; Seth Felder, MD[6]; Andrew J Sinnamon, MD[7]; Melissa Mallory, MD[8]; Christine Laronga[9]
[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4]Moffitt Cancer Center, Tampa, FL, US; [5]Moffitt Cancer Center, Tampa, FL, US; [6]Moffitt Cancer Center, Tampa, FL, US; [7]Moffitt Cancer Center, Tampa, FL, US; [8]Moffitt Cancer Center, Tampa, FL, US; [9]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Germline mutations in high penetrance gene CDH1 have a significantly increased risk of breast cancer (BC)(absolute risk 30-55%), specifically invasive lobular carcinoma (ILC), and hereditary diffuse gastric carcinoma (HDGC)(14-33% in females, 20-42% in males). High risk surveillance and discussion of risk reducing surgery is recommended starting at age 30 for BC and age 20-40 for HDGC. We report our institutional experience with CDH1. **METHODS:** This is a single-institution, IRB-approved retrospective review of a prospective database of patients (pts) identified from a combination of sources (genetics clinic, breast department, GI department) who underwent next generation sequencing between 2012-2024 and had a hereditary cancer pathogenic mutation (PM) or variant of unknown significance (VUS) in CDH1. Patients with PM or VUS in CDH1 were selected for evaluation. Clinical and treatment characteristics were analyzed. **RESULTS:** 37 pts [9

male (24.3%), 28 female (75.7%)] with PM or VUS in CDH1 were identified. Median age at genetic testing was 43.8 years (yrs) [range: 21-70 yrs]. 27 pts (73.0%) had a family history of BC and/or HDGC in >1 family member. 6/37 pts (16.2%) had a VUS, all female, of whom 2 had cancer (1 ILC, 1 pancreas). Of 22 female pts with a PM, 11 had BC (50%); 10 were ILC (91%) and 1 was invasive ductal carcinoma (9%). Median age at BC diagnosis was 51.3 yrs [range: 28-69 yrs]. BC pts underwent bilateral mastectomy (55%), unilateral mastectomy (27%) or lumpectomy (18%). 3 of 11 PM pts (27%) without BC elected bilateral prophylactic mastectomy. In total, 59% of PM (with and without BC) elected active surveillance over risk reducing surgery. 16 pts had HDGC (5 males, 11 females); median age at diagnosis was 43.8 yrs [range: 27-79 yrs]. 10 pts with PM underwent prophylactic gastrectomy, 6 with occult HDGC on final pathology (5 TIa and 1 Tis). 6 pts had both ILC and HDGC; all were female and were diagnosed with BC before HDGC (median time from BC to HDGC diagnosis: 11.5 yrs [range 0-20 yrs]). HDGC was treated with total gastrectomy in 14/16 pts (87.5%); 2 pts were advanced at diagnosis (12.5%). **CONCLUSIONS:** Risks of BC and/or HDGC with CDH1 PM are high yet rates of bilateral risk reducing mastectomy and prophylactic gastrectomy are relatively low. Increased provider and patient awareness/education is needed to target better prevention strategies.

	VUS N = 6		PM N = 31	
	Male	Female	Male	Female
Total	0	6	9	22
Breast Cancer (n, %)	0	1 (17%)	0	11 (50%)
Gastric Cancer (n, %)	0	0	5 (56%)	11 (50%)
Breast + Gastric Cancer (n, %)	0	0	0	6 (27%)

P233. A systematic review of occult malignancy and sentinel lymph node metastasis at the time of contralateral prophylactic mastectomy

Jenna L. Sturz-Ellis, DO[1]; Christopher D Vetter, MD, MSc[2]; Courtney N. Day, MS[3]; Judy C. Boughey, MD[4]
[1]Mayo Clinic, Rochester, MN, US; [2]Mayo Clinic, Rochester, MN, US; [3]Mayo Clinic, Rochester, MN, US; [4]Mayo Clinic, Rochester, MN, US

INTRODUCTION: Occult malignancy (OM) identified on contralateral prophylactic mastectomy (CPM) presents a challenge for axillary management. Herein we compile all published instances of invasive OM in CPM specimens and characterize the OM pathology and rate of sentinel lymph node (SLN) metastasis. **METHODS:** A total of 45 retrospective studies were identified using PubMed, Embase, and Cochrane Reviews with the keywords OM and CPM. Full text was reviewed in all 45 papers. For the purposes of this study, OM was defined as invasive disease only. 19 studies were excluded due to overlapping data (n=9), failure to separate invasive disease/DCIS and/or CPM from BPM (n=4), and failure to report on outcome of interest (n=6). Number of CPMs, number of OMs, and nodal pathology in each study were recorded along with details of the index cancer and OM in those with OM. MedCalc software was used to determine the proportion of OM and node positivity rates. Fischer's exact test was used to compare factors contributing to omission of axillary staging. **RESULTS:** Across the 26 included studies, 5702 patients underwent CPM with a total of 87 OM identified. Pooled incidence of OM was 1.53%. The OM weighted summary proportion was 1.555 (95% CI: 1.251, 1.910). 27 patients had omission of axillary staging (31%) and 19 patients had no axillary staging data reported. 41 patients with OM underwent surgical axillary staging (47.1%). Axillary staging appeared more likely with T2 disease (1 vs 0, p=0.527), grade 3 disease (2 vs 0, p=0.318), and lobular histology (4 vs 2, p=0.465) but there was not a statistically significant association. 8 patients had a positive SLN [19.5% (8.8, 34.9)]. 4/8 had subsequent ALND with no additional positive lymph nodes identified. 1 additional patient had N0(i+) disease. T category was available for 64/86 patients with OM of which 62 (97%) were pT1 and 2 (3%) were pT2. Histologic subtype was available for 52 OMs with 39 (75%) ductal, 8 (15.4%) lobular and 5 (9.6%) other. Biomarkers were available for 33 OMs of which 21 (64%) were luminal A, 3 (9%) luminal B, 3 (9%) luminal Her2 and 6 (18%) were triple negative. **CONCLUSIONS:** OM in CPM is uncommon (1.55%) and when it occurs is predominantly pT1, luminal A, invasive ductal carcinoma. Nodal positivity rate of patients selected for axillary staging for OM was 19.5% and was limited to the SLNs in cases where ALND was performed, reflecting low nodal burden. Understanding the characteristics of OM identified at CPM and rate of nodal metastasis can help inform decisions and guide management regarding axillary staging.

Table 1. Characteristics of the 29 studies included in the systematic review

Study	Years	Country	Design	Patients	Occult Invasive Cancers	Rate
Evans, Ingham, Baildam, et al.	1985-2010	UK	Retrospective	105	4	3.81%
Goldflam, Hunt, Gershenwald, et al.	1987-1999	USA	Retrospective	239	4	1.67%
Khurana, Loosmann, Numann, et al.	1989-1996	USA	Retrospective	26	1	3.85%
Laronga, Lee, McGuire, et al.	1995-2006	USA	Retrospective	420	6	1.43%
Chung, Huynh, Lawrence, et al.	1995-2008	USA	Retrospective	177	4	2.26%
King, Gurevich, Sakr, et al.	1997-2005	USA	Retrospective	407	5	1.23%
Lee, Orel, Woo, et al.	1999-2001	USA	Retrospective	6	0	0.00%
Soran, Falk, Bonaventura, et al.	1999-2004	USA	Retrospective	155	2	1.29%
Yi, Meric-Bernstam, Middleton, et al.	2000-2007	USA	Retrospective	542	8	1.48%
Czyszczon, Roland, Sahoo, et al.	2004-2010	USA	Retrospective	169	2	1.18%
Frietas, Crystal, Kulkarni, et al.	2004-2010	Canada	Retrospective	116	1	0.86%
Mattos, Gfrerer, Ling, et al.	2004-2011	USA	Retrospective	384	7	1.80%
Chung, Huynh, Lawrence, et al.	2004-2018	Spain	Retrospective	46	3	6.52%
Burger, Thurtle, Owen, et al.	2005-2010	UK	Retrospective	60	0	0.00%
Wong, Ferroum, Apostolova, et al.	2005-2021	Canada	Retrospective	115	1	0.87%
Kuwajerwala, Dekhne, Pentiak, et al.	2007-2009	USA	Retrospective	170	2	1.18%
Nomikos, Husain, Graham et al.	2007-2016	UK	Retrospective	218	1	0.46%
Mangiardi-Veltin, Chamming's, Jaffre, et al.	2007-2017	France	Retrospective	79	2	2.53%
Erdahl, Boughey, Hoskin, et al.	2008-2013	USA	Retrospective	740	17	2.30%
Murthy, Chamberlain	2009-2015	Portugal	Retrospective	258	0	0.00%
Xia, Schroeder, et al.	2010-2013	USA	Retrospective	134	0	0.00%
Yamauchi, Okawa, Yokoyama, et al.	2013-2016	Japan	Retrospective	53	1	1.89%
Kapur, Warburton, Pao, et al.	2013-2017	Canada	Retrospective	355	2	0.56%
Madan, Mamounas	2013-2019	USA	Retrospective	120	0	0.00%
Yochimura, Okumura, Sawaki, et al.	2014-2016	Japan	Retrospective	10	0	0.00%
Thompson, Sinco, McCaffrey, et al.	2016-2021	USA	Retrospective	598	14	2.34%
			Total	5702	87	1.55%

P234. Academic productivity among breast surgical oncology fellows

Caterina Aiello, DO[1]; Joyce L. Eum, DO[2]; Sydney H. Smilen, DO[3]; Susan K. Boolbol, MD, FACS[4]; Carinne W. Anderson, MD, FACS[5]
[1]Nuvance Health, Danbury, CT, US; [2]Nuvance Health, Danbury, CT, US; [3]Nuvance Health, Danbury, CT, US; [4]Nuvance Health, Danbury, NY, US; [5]Nuvance Health, Danbury, CT, US

INTRODUCTION: Participation in research is a requirement for a breast surgical oncology training program. Engagement in research is essential to the education of fellows and may be obtained through manuscript preparation, writing, and submission. This study aims to describe contributions to the literature among breast surgical oncology fellows, and predictors of academic productivity during fellowship. No previous study has compiled and analyzed this data. **METHODS:** Fellowship programs and their characteristics were obtained from the SSO directory and institutional websites. Program specific features including number of fellowship positions, geographic location, associated general surgery residency program, Alliance membership, NCCN member institution status, and NCI designation were abstracted. Fellowship director specific features including age, sex, additional degrees, number of publications, number of citations, and h-index were abstracted from a previously complied database. A list of graduating breast fellows from 2021-2023 was obtained. The number of peer-reviewed publications for each fellow was compiled through searches from Scopus, PubMed, Google Scholar, and ResearchGate. Current online profiles were referenced to confirm current and past institution associations. Multivariable linear regression was used to identify statistically significant factors associated with increased academic productivity during fellowship. **RESULTS:** We investigated academic productivity for three consecutive fellowship classes, a total of 233 fellows. The average number of peer-reviewed publications during fellowship was 1.2 (SD 2.5); the average number during fellowship and the subsequent 12 months was 2.8 (SD 4.7). There was no statistically significant difference in publication rate across the three classes. The number of pre-fellowship publications was the greatest predictor of publication rate during fellowship ($p < .0001$). Several fellowship director features including number of publications ($p=.04$) and number of citations ($p=.01$) were also statistically significantly associated with fellow publication rate. **CONCLUSIONS:** Academic productivity is difficult to predict. Through an extensive search and statistical analysis, we conclude that number of pre-fellowship publications is the most significant predictor of fellowship publications. This data can serve as a benchmark for institutional self-assessment. Our analysis can also aid institutions who wish to increase their academic productivity with targeted initiatives.

Table 1. Summary Data

Number of fellows	233
Total Publications Pre-Fellowship	1213
Average Publications Pre-Fellowship	5.2 (SD 7.1)
Median Publications Pre-Fellowship	2 (IQR 1-7)
Total Publications During Fellowship	271
Average Publications During Fellowship	1.2 (SD 2.5)
Median Publications During Fellowship	0 (IQR 0-1)
Total Publications During Fellowship and Subsequent Year	610
Average Publications During Fellowship and Subsequent Year	2.8 (SD 4.7)
Median Publications During Fellowship and Subsequent Year	1 (IQR 0-3)

P235. Age as a Predictor for Lymphovenous Anastomosis Receipt in Breast Cancer Patients Requiring Axillary Nodal Dissection: A Single-institution Analysis

Alexis Graham-Stephenson, MD[1]; Lauren M Perry, MD, MAS[2]; Paige Myers, MD, MPH[3]; Melissa Pilewskie, MD[4]

[1]University of Michigan, Ann Arbor, MI, US; [2]University of Michigan, Ann Arbor, MI, US; [3]University of Michigan, Ann Arbor, MI, US; [4]University of Michigan, Ann Arbor, MI, US

INTRODUCTION: Lymphedema can be a debilitating source of postoperative morbidity following axillary lymph node dissection (ALND). Recent efforts toward risk reduction with prophylactic lymphovenous anastomosis (LVA) have emerged to decrease postoperative lymphatic dysfunction and the development of lymphedema. The purpose of this study is to identify factors associated with receipt of LVA and its impact on time to surgery (TTS) for breast cancer patients undergoing ALND at an academic medical center. **METHODS:** A retrospective review of patients with a diagnosis of breast cancer who underwent ALND from 2022 to 2024 was performed. Patients were divided into cohorts based on receipt of prophylactic LVA at the time of axillary nodal dissection. The primary outcome was TTS; secondary outcomes were factors associated with LVA receipt. Univariate and multivariable logistic regression models assessed for characteristics associated with each outcome. **RESULTS:** Of 43 patients who underwent ALND, most presented with cT2 (60%, n=24) and cN2-3 disease (47%, n=20) with ductal histology (67%, n=28) at a median age of 53 years (IQR 43, 65). Few patients presented with cN0 disease (14%, n=6). Most tumors were ER positive (91%, n=39), while HER-2 (7%, n=3) and triple-negative disease (9%, n=4) were less common. Nearly half of the cohort (44%, n=19) received neoadjuvant chemotherapy (NAC). LVA was performed in 30% (n=13) of cases and frequency of LVA receipt increased over the study period; 92% (n=12) of LVAs resulted in successful anastomosis. Most LVAs were performed after NAC (62%, n=8). LVA receipt was not associated with increased TTS (p=0.51). Increasing age was a predictor of decreased odds of LVA receipt (median age LVA vs no LVA: 44 vs 62 years; OR 0.90, 95% CI 0.84-0.96, p=0.005). Patients older than the cohort median age (53 years) were less likely to undergo LVA (p<0.0001) and had increased TTS after initial surgical visit compared to younger patients (p=0.004). Tumor histology, grade, receptor status, or NAC were not associated with differential LVA receipt. **CONCLUSIONS:** Among breast cancer patients requiring ALND at an academic medical center, 30% received LVA at the time of nodal dissection over the past 2 years. As stronger evidence regarding this technique emerges, appropriate patient selection and strategies to ensure equal access to LVA for breast cancer-related lymphedema risk reduction are paramount.

P236. Ancestry-Specific Differences in Pathogenic Germline Variants among BRCA1 Breast Cancer Patients

Diana Kantarovich, MD[1]; Divya Rao[2]; Shrutika Yeola, MMSc, CGC[3]; Angel Lee, MBChB[4]; Katelynn Cai[5]; Kam Yau Li[6]; Lisa Baron, MD[7]; Steven Cai, MD[8]; Paul Baron, MD, FACS[9]

[1]Lenox Hill Hospital/Northwell Health, New York, NY, US; [2]New York Medical College, New York, NY, US; [3]Myriad Genetics, Salt Lake City, UT, US; [4]Lenox Hill Hospital/ Northwell Health, New Yok, NY, US; [5]Manhasset High School, Manhasset, NY, US; [6]Lenox Hill Hospital/Northwell Health, New York, NY, US; [7]Lenox Hill Hospital/Northwell Health, New York, NY, US; [8]Lenox Hill Hospital/Northwell Health, New York, NY, US; [9]Lenox Hill Hospital/Northwell Health, New York, NY, US

INTRODUCTION: Research exploring germline variants and *BRCA1* gene mutations across different ethnicities is still expanding, but existing evidence points to variability among populations. The heterogeneity in North America is crucial for building a more representative database of pathogenic germline variants among different ancestry groups. The goal of our study was to compare germline variants across ancestries. **METHODS:** We used the Myriad Collaborative Research Registry to access de-identified information on specific *BRCA1* germline variants in breast cancer patients. We compared the most common pathogenic/likely pathogenic germline variants among patients with self-identified ancestry as White (including Central/Eastern and Western/Northern European but excluding Ashkenazi Jewish), Black, Asian, and Hispanic. We excluded patients with variants of unknown significance. **RESULTS:** A total of 11,552 White, 1,988 Black, 584 Asian, and 2,112 Hispanic breast cancer patients were identified with *BRCA1* pathogenic variants. In the White patient group, the most common variants were c.5266dupC (9.7%), c.68_69del (6.4%), and c.181T>G (5.2%). This is consistent with prior reports showing both c.5266dupC and c.68_69del as founder mutations in patients of Jewish and Eastern European descent. Among Black patients, the predominant variants were c.815_824dup (13.5%), 5324T>G (9.3%), and c.5177_5180del (8.8%). Reports show that the founder mutation c.815_824dup of *BRCA1* is likely of West African origin. We found that the most common pathogenic mutations in Asian patients were c.5251C>T (5.8%), c.188T>A (4.4%), and c.68_69del (4.2%). Finally, in Hispanic patients, the leading pathogenic mutations were del exons 9-12 (7.9%), c.68_69del (7.6%), and c.2433del (5.5%). In those of Mexican decent, del exons 9-12 has been previously identified as a founder mutation. Of note, in this database variant c.68_69del was present as a predominant mutation in most ancestry groups reported here except for the Black group of patients. **CONCLUSIONS:** Our data demonstrates the presence of unique ancestry-specific pathogenic variants of *BRCA1* genes in a large heterogeneous population, some of which have been previously described as founder mutations in specific racial groups. Interestingly, there is limited information about the pathogenic variants identified in our Asian population. This data can help improve genetic screening, risk assessment, and personalized healthcare strategies for diverse populations.

Table 1. Three Predominant Pathogenic Germline Variants by Ancestry among BRCA1 Breast Cancer Patients.

	White (n = 11,552)	Black (n = 1,988)	Asian (n = 584)	Hispanic (n = 2,112)
Number of Distinct *BRCA1* Variants	11,818	2,010	595	2,165
1	c.5266dupC (9.72%)	c.815_824dup (13.53%)	c.5251C>T (5.8%)	del exons 9-12 (7.85%)
2	c.68_69del (6.47%)	c.5324T>G (9.25%)	c.188T>A (4.4%)	c.68_69del (7.6%)
3	c.181T>G (4.21%)	c.5177_5180del (8.81%)	c.68_69del (4.2%)	c.2433del (5.50%)

P237. Assessing the differential response to immunotherapy in BRCA1/2 mutation carriers with triple-negative breast cancer

Minna K. Lee[1]; Natalia Polidorio[2]; Varadan Sevilimedu[3]; Lauren Perry[4]; Giacomo Montagna[5]; Monica Morrow[6]; Nour Abuhadra[7]; George Plitas[8]; Stephanie Downs-Canner[9]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New-York, NY, US

INTRODUCTION: Pembrolizumab plus neoadjuvant chemotherapy (NAC+P) for patients with triple-negative breast cancer (TNBC) results in higher pathologic complete response (pCR) and longer event-free survival compared to neoadjuvant chemotherapy (NAC) alone. Alterations in the DNA damage response affect the tumor microenvironment and may influence response to immunotherapy. Our objective was to compare pCR rates between *BRCA1/2* carriers and noncarriers with TNBC undergoing NAC and NAC+P. **METHODS:** 341 women with stage II-III TNBC treated with NAC+P based on the KEYNOTE 522 regimen from 8/2021-5/2024 were compared to 433 consecutive patients who received NAC prior to 7/2021. pCR rates (ypT0/is

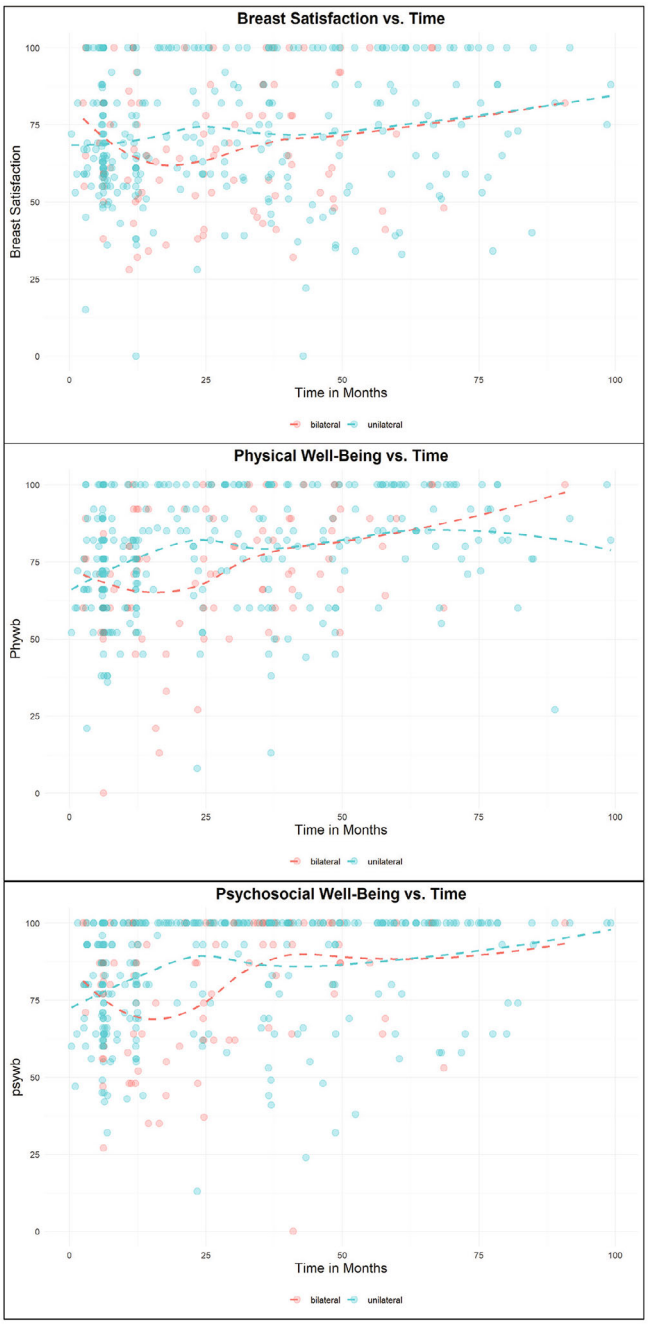
pN0) were compared between *BRCA1/2* carriers and noncarriers using Chi square tests. The association between *BRCA1/2* status and pCR was analyzed by logistic regression. **RESULTS:** 76 (18%) NAC patients and 56 (16%) NAC+P patients were *BRCA1/2* carriers. *BRCA1/2* carriers were younger, had lower BMI, and were more likely to self-identify as White. There was no difference in histology, grade, clinical T or N stage, or chemotherapy regimen between groups. pCR in the NAC group was 50% for *BRCA1/2* carriers and 36% for noncarriers (p=0.021). In the NAC+P group, pCR was 68% for *BRCA1/2* carriers compared to 55% for noncarriers (p=0.073). Among *BRCA1/2* carriers treated with NAC+P, pCR was 69% (31/45) for *BRCA1* and 60% (6/10) for *BRCA2* carriers. On multivariable analysis of the entire cohort, *BRCA1/2* status (OR 1.55, 95% CI 1.03-2.34, p=0.036), receipt of NAC+P (OR 2.13, 95% CI 1.71-3.12, p<0.001), younger age at diagnosis (OR 0.98, 95% CI 0.97-0.99, p=0.002), and high grade (OR 9.42, 95% CI 4.01-27.6, p<0.001) were associated with pCR. In the NAC+P group, only grade was associated with pCR (OR 17.4, 95% CI 5.03-110, p<0.001). **CONCLUSIONS:** Compared to noncarriers with TNBC, *BRCA1/2* carriers had better response to NAC and NAC+P (not statistically significant in NAC+P). Analysis of a larger sample size may further delineate differential response to NAC+P, which is important, as new therapeutic options (PARP inhibitors) are available to *BRCA1/2* carriers.

P238. Association of immediate symmetrizing oncoplastic surgery with patient-reported outcomes in patients with breast cancer – a retrospective cohort study

Martin Heidinger[1]; Gilles Bilfeld[2]; Nico Foege[3]; Julie M Loesch[4]; Nadia Maggi[5]; Fabienne D Schwab[6]; Christian Kurzeder[7]; Tibor A Zwimpfer[8]; Walter Paul Weber[9]

[1]University Hospital Basel, Basel, CH; [2]University Hospital Basel, Basel, CH; [3]Novustat GmbH, Wollerau, CH; [4]University Hospital Basel, Basel, CH; [5]University Hospital Basel, Basel, CH; [6]University Hospital Basel, Basel, CH; [7]University Hospital Basel, Basel, CH; [8]University Hospital Basel, Basel, CH; [9]University Hospital Basel, Basel, CH

INTRODUCTION: Oncoplastic breast surgery (OPS) with an immediate contralateral procedure for symmetry is commonly performed. However, its impact on the satisfaction and quality of life of patients with breast cancer (BC) remains uncertain. This study aimed to evaluate the association between unilateral versus bilateral OPS and patient-reported outcomes (PROs). **METHODS:** Patients with stage 0-III BC who underwent OPS (including oncoplastic breast conserving surgery (OBCS), as well as nipple- or skin-sparing mastectomy) at a Swiss university hospital between 01/2013-12/2023 with at least one prospectively collected postoperative BREAST-Q PRO questionnaire, were identified from a prospectively maintained institutional database. Outcomes included the identification of differences in PROs between those who underwent unilateral versus immediate symmetrizing surgery. A generalized linear model with backward-selection was used to detect such differences. **RESULTS:** Of 441 eligible patients, 333 (75.5%) underwent unilateral OPS, while 108 (24.5%) underwent bilateral OPS. The median time to PRO assessment was 35.1 months (Q1-Q3 13.4-49.5), without differences between the groups (p=0.426). No differences in any BREAST-Q domain were identified in postoperative PROs between patients who underwent unilateral versus bilateral OPS. Time-course analysis showed a non-significant reduction in BREAST-Q scores of breast satisfaction, physical and psychosocial well-being within the first 24 months postoperatively, which evened out thereafter (Figure). Short-term complications (unilateral: 21.0%; bilateral: 31.5%; p=0.036) and secondary surgeries due to complications (unilateral: 7.5%; bilateral: 16.7%; p<0.001) were more common in patients who underwent symmetrizing surgery, and negatively impacted physical well-being and breast satisfaction. **CONCLUSIONS:** The present study did not demonstrate any impact of immediate symmetrization on PROs. However, short-term surgical morbidity impacted physical well-being and breast satisfaction.



P239. Axillary Management after Neoadjuvant Endocrine Therapy

Laura D Leonard[1]; Min Yi[2]; Emma Wingate[3]; Puneet Singh, MD[4]; Abigail S Caudle, MD[5]; Rosa Hwang, MD[6]; Isabelle Bedrosian, MD[7]; Vicente Valero, MD[8]; Jennifer Litton[9]; Nuhad Ibrahim[10]; Kelly K. Hunt, MD, FSSO[11]

[1]MD Anderson Cancer Center, Houston, TX, US; [2]UT-MD Anderson Cancer Center, Houston, TX, US; [3]MD Anderson Cancer Center, Houston, TX, US; [4]UT-MD Anderson Cancer Center, Houston, TX, US; [5]UT-MD Anderson Cancer Center, Houston, TX, US; [6]UT-MD Anderson Cancer Center, Houston, TX, US; [7]UT-MD Anderson Cancer Center, Houston, TX, US; [8]MD Anderson Cancer Center, Houston, TX, US; [9]MD Anderson Cancer Center, Houston, TX, US; [10]MD Anderson Cancer Center, Houston, TX, US; [11]MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: In patients with hormone receptor-positive (HR+), Her2-negative breast cancer, neoadjuvant endocrine therapy (NET) has been shown to effectively increase breast conservation rates by downsizing the primary tumor. However, there is a lack of data available to define optimal axillary

management strategies after NET. We aimed to evaluate patterns of axillary management following NET and the association of post-NET nodal status with long-term oncologic outcomes. **METHODS:** A retrospective review of patients with clinical stage I-III, HR+ breast cancer who received 4-6 months of NET at a comprehensive cancer center between 2006 and 2019 was conducted. Patients were divided into 2 groups: clinically negative nodes (cN0) and biopsy-proven axillary nodal (cN1) disease at the time of diagnosis. Univariate analyses comparing clinicopathologic characteristics between 2 groups were performed. Proportions and means were compared using Fisher's exact test and T test, respectively. The local-regional recurrence (LRR) rates were compared between 2 groups. **RESULTS:** 165 patients were included (Table 1). 98 (59.4%) were cN0 while 67 (40.6%) were cN1. In the cN1 group, 4.5% had a pathologic complete response (pCR) in the nodes. 70.2% in the cN1 group underwent axillary lymph node dissection (ALND) as the initial axillary procedure and 92.5% underwent ALND overall. 98% (96/98) of those women with cN0 disease at diagnosis underwent sentinel lymph node dissection (SLND). 60% (15/25) of cN0 patients with a positive SLND underwent completion ALND regardless of the number of positive sentinel lymph nodes (median number of nodes 1; range 1-4). There were only 3 local-regional recurrences in the whole cohort at 7 years median follow-up (range 0.4-17.1). The 5-year LRR rate in cN0 patients was 1.1% while 5-year LRR rate in cN1 patients was 0. (P=0.96). **CONCLUSIONS:** The majority of patients with cN1 disease in our series underwent ALND. The nodal pCR rate was low, suggesting that the significance of nodal response to NET is negligible. Clinicians more frequently omitted ALND in patients with cN0 disease who had 1-2 positive SLNs similar to the upfront surgery algorithms in this population. The 5-year LRR rate was extremely low for the entire cohort suggesting that NET is an oncologically safe strategy for patients with HR+ disease even in the setting of large tumors and positive lymph nodes.

Table 1. Comparisons of demographic, clinical, pathological and treatment factors between different clinical nodal status (N=165)

Factors		Clinical node negative (N=98)	Clinical node positive (N=67)	P value^
Age at diagnosis				0.3
Mean	65	65	64	
Median (range)	63 (49-84)	64 (51-84)	63 (49-83)	
Race				0.1
White	114 (69.1)	73 (74.5)	41 (61.2)	
Hispanic	26 (15.8)	11 (11.2)	15 (22.4)	
Others	25 (15.2)	14 (14.3)	11 (16.4)	
Breast surgery				0.03
Segmental Mastectomy (SM)	94 (57)	63 (64.3)	31 (46.3)	
Total Mastectomy (TM)	71 (43)	35 (35.7)	36 (53.7)	
Margin re-excision				0.2
Yes	7 (4.2)	6 (6.1)	1 (1.5)	
No	158 (95.8)	92 (93.9)	66 (98.5)	
TM after SM				0.4
Yes	14 (8.5)	10 (10.2)	4 (6)	
No	151 (91.5)	88 (89.8)	63 (94)	
Initial Axillary Procedure				<0.0001
ALND	49 (29.7)	2 (2)	47 (70.2)	
Removal of Clipped Node Only	2 (1.2)	0 (0)	2 (3)	
SLND	108 (65.5)	96 (98)	12 (17.9)	
Targeted Axillary Dissection (TAD)	6 (3.6)	0 (0)	6 (9)	
Definitive Axillary Procedure				<0.0001
ALND	83 (50.3)	21 (21.4)	62 (92.5)	
SLND	81 (49.1)	77 (78.6)	4 (6)	
TAD	1 (0.6)	0 (0)	1 (1.5)	
Path LN status				<0.0001
Negative	73 (44.2)	70 (71.4)	3 (4.5)	
Positive	92 (55.8)	28 (28.6)	64 (95.5)	
Positive SLN				<0.0001
Yes	41 (24.9)	25 (25.5)	16 (23.9)	
No	71 (43)	69 (70.4)	2 (3)	
No SLND performed	53 (32.1)	4 (4.1)	49 (73.1)	
Histology				0.8*
IDC	88 (61.5)	53 (63.9)	35 (58.3)	
ILC with/without IDC	46 (32.2)	25 (30.1)	21 (35)	
Others	9 (6.3)	5 (6)	4 (6.7)	
Tumor grade				0.2*
1	20 (12.1)	14 (16.3)	6 (10.5)	
2	99 (60)	61 (70.9)	38 (66.7)	
3	24 (14.6)	11 (12.8)	13 (22.8)	
Unknown	22 (13.3)			
Lymphovascular invasion (LVI)				0.001*
Yes	74 (69.2)	54 (81.8)	20 (48.8)	
No	33 (30.8)	12 (18.2)	21 (51.2)	
Ki 67				0.6
Mean	20.6	21.4	19.6	
Multifocal				
Yes	22 (24.7)	11 (18.6)	11 (36.7)	
No	67 (75.3)	48 (81.4)	19 (63.3)	
Final margin status				0.04*
Positive	6 (8.6)	4 (8.3)	2 (9.1)	
Negative	59 (84.3)	43 (89.6)	16 (72.7)	
Close (< 2 mm)	5 (7.1)	1 (2.1)	4 (18.2)	
Adjuvant chemotherapy				<0.0001^
Yes	66 (40)	22 (26.8)	44 (72.1)	
No	77 (46.7)	60 (73.2)	17 (27.9)	
Unknown	22 (13.3)			
Adjuvant XRT				0.2*
Yes	107 (64.9)	59 (73.8)	48 (82.8)	
No	31 (18.8)	21 (26.3)	10 (17.2)	
Unknown	27 (16.4)			

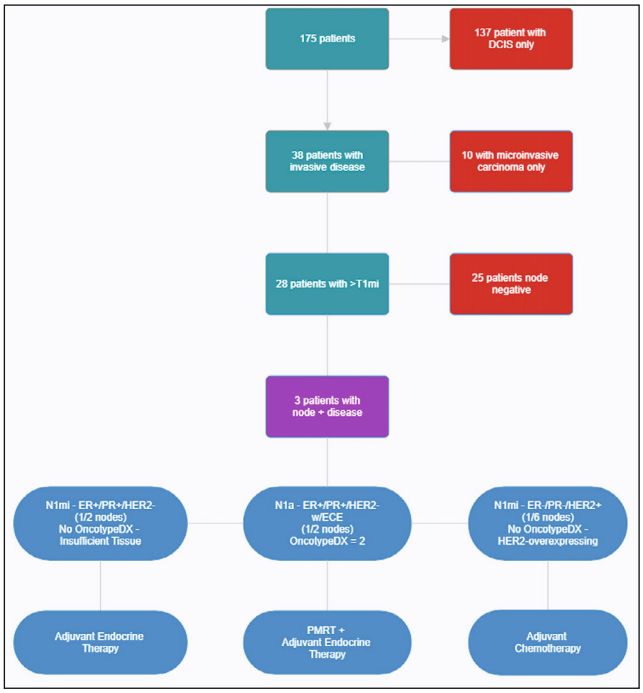
^ Fisher's exact test; *p value calculated after excluded Unknown category.

P240. Axillary staging outcomes in women undergoing mastectomy for ductal carcinoma in situ in the era of gene expression assays

Anna Levine, DO[1]; Jessica Thompson, MD[2]; G. Paul Wright, MD[3]; Amie Hop, MD[4]; Mariam Khan[5]; Hayden Wood[6]; Ibukunoluwa Omole[7]

[1]Corewell Health West, Grand Rapids, MI, US; [2]Corewell Health West, Grand Rapids, MI, US; [3]Corewell Health West, Grand Rapids, MI, US; [4]Corewell Health West, Grand Rapids, MI, US; [5]Corewell Health West, Grand Rapids, MI, US; [6]Michigan State University, Grand Rapids, MI, US; [7]Michigan State University, Grand Rapids, MI, US

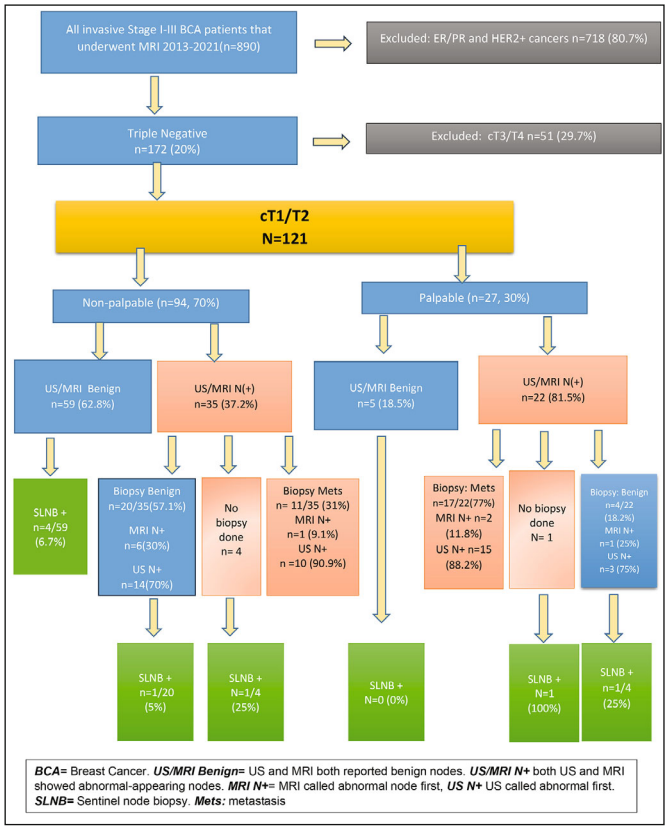
INTRODUCTION: Given that 20% of women diagnosed with ductal carcinoma in situ (DCIS) on core biopsy will be upstaged to invasive disease on final pathology and the potential inaccuracy of axillary mapping after mastectomy, a sentinel lymph node biopsy (SNB) is recommended as the standard of care at the time of the index surgery. In cases that are upstaged, the underlying invasive cancer is frequently of low grade with favorable biology. The primary study objective was to determine how often SNB at the time of mastectomy for DCIS alters adjuvant therapy recommendations. **METHODS:** A single institution cancer registry was utilized to retrospectively identify women treated with mastectomy for a preoperative diagnosis of DCIS between November 2017 and November 2023, excluding those with prior history of ipsilateral breast cancer. The impact of pathologic nodal status on adjuvant treatment was evaluated. **RESULTS:** The study population included 175 patients with a total of 38 (22%) invasive cancers identified. There were 9 cases of microinvasive disease, 1 occult cancer, and 28 patients with pT1 disease. Of those with pT1 malignancies, 3 had a positive sentinel node. However only 1 patient was recommended for additional adjuvant treatment, in the form of radiation therapy, as a result of axillary staging (Figure 1). One patient was recommended for adjuvant endocrine therapy based on hormone receptor status of the primary tumor, while the other patient was recommended for chemotherapy based on non-expression of estrogen or progesterone receptors and over expression of the HER2 receptor.Of the pT1 cancers, 15 (53.6%) were low grade, 8 (28.6%) were intermediate grade, and 5 (17.8%) were high grade; two-thirds were HR+ HER2-. Nine (5.2%) patients were perimenopausal, 64 (37%) premenopausal, and 100 (57.8%) postmenopausal. Eight patients received chemotherapy as a result of receptor subtype (7 HER2 amplified, 1 basal like). No patients were recommended for chemotherapy based solely on SNB results. Postoperative lymphedema was documented in 16 (9.1%) patients. **CONCLUSIONS:** Despite the prevailing recommendation to perform SNB in DCIS treated with mastectomy to account for the risk of undiagnosed underlying invasive cancer, our outcomes suggest nodal status has limited impact on adjuvant therapy offerings for this patient population. These findings indicate that SNB may not be requisite for every patient undergoing mastectomy for DCIS and its use in this setting should be reevaluated to avoid the potential morbidities of axillary staging.



P241. Beyond Conventional Imaging: Evaluating MRI's Role in Detecting Clinically Occult Nodal Metastasis in TNBC

Jessica A Bilz[1]; Shruti Mahale[2]; Firouzeh Arjmandi[3]; Bersu Ozcan[4]; Yin Xi[5]; Ann Marilyn Leitch[6]; Heather McArthur[7]; Basak Dogan[8]
[1]UTSW, Dallas, TX, US; [2]UTSW, Dallas, TX, US; [3]UTSW, Dallas, TX, US; [4]UTSW, Dallas, TX, US; [5]UTSW, Dallas, TX, US; [6]UTSW, Dallas, TX, US; [7]UTSW, Dallas, TX, US; [8]UTSW, Dallas, TX, US

INTRODUCTION: Evidence of nodal metastasis is a criterion used to identify patients with early-stage triple-negative cancers (TNBC) who are eligible for preoperative chemotherapy (NAC) with immunotherapy. We aimed to determine the rate of clinically occult nodal metastasis in patients with cT1-T2 TNBC identified on magnetic resonance imaging (MRI) and ultrasound (US). **METHODS:** All patients with newly diagnosed TNBC undergoing pre-operative breast MRI between 2013-2021 at our institution were identified through an institutional database. Patient and tumor clinicopathological features including radiologic nodal status by US and MRI, receipt of neoadjuvant chemotherapy, surgical pathology results, initial evaluation method (physical exam, US or MRI), abnormal vs benign axillary imaging findings (cN+ vs cN0), needle biopsy, and sentinel node biopsy (SLNB) results were collected. Mann Whitney-U and chi2 tests were used to assess the association between age/Ki67/tumor size and clinical tumor stage with imaging cN+ and needle biopsy result. **RESULTS:** Of the 171 TNBC patients identified, 121 (70.8%) had cT1-T2 disease. The mean age was 53±13 and mean tumor size was 27.1±10 mm. Of the 101 (83.5%) patients who received NAC, 40.6% (41/101) achieved pathologic complete response (pCR). At presentation nodes were non-palpable in 94/121 (77.7%) and palpable in 27/121 (22.3%). US and/or MRI assessed cN+ in 57/121(47.1%). On imaging, 22/27 (81.5%) of patients with palpable nodes were cN+, while 35 (37.2%) of 94 non-palpable were cN+ [first detected by US in 25/35 (71.4%) and MRI in 10/35 (28.6%)]. Needle biopsy confirmed metastasis in 11/35 (31.4%). Of these, 10/11(90.9%) were identified with US alone, and 1/11 (9.1%) with MRI+US for non-palpable only. SLNB revealed evidence of metastasis in 4(6.3%) of 64 patients with cN0 [1/4 (25%) upfront surgery, 3/6 (75%) following NAC]. Younger age (p<0.001), Black or Hispanic race (p=0.01), and larger tumor size (p=0.02) were associated with having cN+, while ki67% was not (p=0.24). Tumor stage (p=0.06), age (p= 0.48) and ki67 (p=0.77) were similar between biopsy+ and biopsy-negative groups. **CONCLUSIONS:** Ultrasound effectively detected nonpalpable nodal metastases in 9.1% of cT1-T2 TNBC, facilitating immunotherapy candidacy. MRI showed no significant added benefit in identifying nodal metastases.



P242. Breaking Barriers: Enhancing Access to Genetic Testing for All Breast Cancer (BC) Patients

Christine M Joliat, MD[1]; Jessica Bensenhaver, MD[2]; Ena Muhamedovic, DO[3]; Theresa Schwartz, MD[4]; Laura Dalla Vecchia, MD[5]; Laura Susick, PhD[6]; Lindsay Petersen, MD[7]; Anna Lehrberg, DO[8]
[1]Henry Ford Health System, Detroit, MI, US; [2]Henry Ford Health, Detroit, MI, US; [3]Henry Ford Health System, Detroit, MI, US; [4]Henry Ford Health System, Detroit, MI, US; [5]Henry Ford Health System, Detroit, MI, US; [6]Henry Ford Health System, Detroit, MI, US; [7]Henry Ford Health System, Detroit, MI, US; [8]Henry Ford Health System, Detroit, MI, US

INTRODUCTION: Revised genetic testing guidelines in 2019 recommended that all BC patients be eligible for testing. Our institution historically required a referral to a genetic counselor to have testing ordered. The 2019 guideline revision resulted in a larger number of patients referred, overwhelming our genetic counselling capacity. Further, there is a known disparity in minority population genetic testing and our metropolitan Detroit patient population has a significant proportion represented by black women (BW). Efforts were thus made in 2023 to improve access and testing rates by implementing an internal comprehensive genetic panel allowing cancer providers to directly order genetic testing. This study aims to define the rate of genetic testing before and after 2023, to assess the impact of these changes on testing completion rates and identify potential barriers to successful testing. **METHODS:** We used our institutional IRB-approved prospective BC registry to evaluate patients who were recommended for genetic testing from 2017 to 2024. Collected data points included patient race, genetic counselor referral, completion of consultation, and completion of genetic testing. **RESULTS:** Between 2017 and 2024, there were 2,437 women who consented to our registry, 1,656 were referred for genetic testing. Genetic referrals increased from 2017-2019 to 2020-2022 (61% to 72%, p< 0.0001). Genetic consultation completion also increased from 2017-2019 to 2020-2022 (76% to 86%, p< 0.0001). Analysis of 2017-2019, 2020-2022, and 2023-2024 patients showed a significant increase in completion of testing in the 2023-2024 cohort – 64% in 2017-2019, 60% in 2020-2022, 78% in 2023-2024 (p<0.0001). Univariate analysis by race between Caucasian women (CW, n=1029) and black women (BW, n=502) compared 2017-2022 and 2023-2024. Both groups significantly increased testing completion rates - 65% in 2017-2022 compared to 82% in 2023-2024 for CW (p<0.001) and 56% in

2017-2022 compared to 74% in 2023-2024 (p=0.01). BW had higher rates of not completing genetic consultation compared to CW (26% vs 18%), however this was not significant (p=0.21). **CONCLUSIONS:** Since the guidelines for genetic testing in patients with BC changed in 2019, we found a significant increase in the genetics counseling referral rate at our institution. However, providing direct access to panel testing in 2023 significantly improved completion of testing across all patients. Although not significant, the discrepancy trend toward testing completion for BW is worth noting and a second target for improvement.

P243. Breast Cancer in Pre- and Postmenopausal Patients: A Comparative Analysis

Gabriela Martinez, BS[1]; Melissa M Tempest, BS[2]; Taylor Garza, MD[3]; Francis Agcaoili, MD[4]; Abigail Beard, MD[5]
[1]University of South Florida, Tampa, FL, US; [2]University of South Florida, Tampa, FL, US; [3]University of South Florida, Tampa, FL, US; [4]University of South Florida, Tampa, FL, US; [5]University of South Florida, Tampa, FL, US

INTRODUCTION: The incidence of breast cancer in women under the age of 50 is on the rise worldwide. Specific patient populations and clinical characteristics may be more predictive than others with regards to disease diagnosis and treatment plans. Recent trends have shown an increasing trend of breast cancer amongst all racial groups. The aim of this study is to measure differences between postmenopausal and premenopausal patients receiving surgical treatment for their breast cancer at a Level 1 Center located in Tampa, Florida. **METHODS:** This retrospective chart review study includes data abstracted from a Level 1 Center located in Tampa, FL. Patients who were diagnosed with anatomic stage IA-IIIC breast cancer and received surgical intervention during 2023 were included. Patients were divided by menopause status. Comparative analysis was performed. **RESULTS:** 226 total patients received surgery in 2023 for stage IA-IIIC breast cancer. These patients were 63.7% White or Caucasian, 12.4% Black or African American, 2.2% Asian, 1.8% Multi-Racial, 19.9% Other. 25.2% of patients were Hispanic or Latino (H/L). 171 (75.7%) were postmenopausal (Post-M), 46 (20.4%) were premenopausal (Pre-M) and 9 (3.3%) were perimenopausal. There was no significant difference between races (p-value = 0.533); however, 41.3% of Pre-M patients were H/L, compared to only 21.1% of Post-M patients ($\chi 2$ = 7.99, p-value =0.005). The Pre-M group was 5 years older at the age of first birth compared to the Post-M group, with median age 28 and 23 respectively (p-value < 0.001). Both had similar amounts of nulliparous women (p-value = 0.248). In contrast, Pre-M women had a median of 1 birth, while Post-M women had 2 (p-value = 0.027). There was no difference in pathology, grade, ER status, PR status, HER2 status, or KI67 (p-values > 0.13). There was a mildly higher percentage of cells that expressed PR in the Pre-M group, with medians of 91% and 70% respectively (p-value = 0.08). Finally, Pre-M patients were more likely to elect for mastectomy as a surgical treatment at 56.5%, compared to 32.1% of Post-M patients ($\chi 2$ = 9.17, p-value = 0.002). **CONCLUSIONS:** The data demonstrates that premenopausal Hispanic patients could be more predisposed to breast cancer. Additionally, electing for a mastectomy is more popular among premenopausal patients. This study highlights how both racial and ethnic disparities and differential surgical preferences can influence the diagnosis and treatment of breast cancer.

P244. Can Chat GPT generate surgical plans for patient-specific breast cancer scenarios?

Jakob A Durden, MD[1]; George Burnet, MD[2]; Sarah Leslie, MPH[3]; Nicole Christian, MD[4]; Sarah Tevis, MD[5]
[1]University of Colorado School of Medicine, Aurora, CO, US; [2]University of Colorado School of Medicine, Aurora, CO, US; [3]University of Colorado Adult & Child Center for Outcomes Research & Delivery Science, Aurora, CO, US; [4]University of Colorado School of Medicine, Aurora, CO, US; [5]University of Colorado School of Medicine, Aurora, CO, US

INTRODUCTION: The advent of generative artificial intelligence models such as Chat GPT is shifting how patients seek medical advice. The accuracy of the output of these models, as well as their readability and references, is not well characterized. We used real world breast radiology and pathology results characteristic of five distinct clinical scenarios to interrogate Chat GPT's surgical decision making. **METHODS:** Breast radiology and pathology reports (n=5) were deidentified and submitted to Chat GPT 4.0mini with three identical repetitions (n=15) using the following prompt: "I am an (age) year old female patient. Answer as if you are a breast cancer specialist. What surgery do I need for my breast and lymph nodes? Tell me your references and provide links. Here are my test results:". The AI output was assessed for accuracy by two expert reviewers using a four-point Likert scale. Readability was assessed using the Flesh-Kincaid scale. Each citation was interrogated for hyperlink functionality and destination website. **RESULTS:** The mean accuracy score was 3.2 across all 15 responses. The scenario with the most accurate responses was Ductal Carcinoma In Situ in a 59-year-old female (4.0/4). The scenario with the least accurate responses was Invasive Ductal Carcinoma (hormone receptor positive) in an 82-year-old female (2.0/4) where none of the responses accounted for the fact that axillary surgery could be omitted based on current guidelines. Three of the 15 (20%) graded responses had blatant omissions of critical information regarding treatment options. Notable inaccuracies included one response for invasive ductal carcinoma that omitted mastectomy as an alternative to lumpectomy, and one response for a clinically positive lymph node that excluded any plans for axillary surgery. The mean Flesch-Kincaid readability score across all responses was 12.4, greatly exceeding the recommended sixth grade reading level of 6.0 for patient communications. The mean number of citations generated per prompt was 3.6. 74% of links were nonfunctional (invalid address/error message). 20.4% of links reached organizational homepages. 5.6% of citations did not include a hyperlink. No references reached diagnosis-specific webpages. **CONCLUSIONS:** Chat GPT is currently an unreliable source for patients seeking individualized treatment information regarding their breast cancer due to variability in responses, lack of nuance/contemporary guideline incorporation, lack of readability, and unclear references.

Clinical Scenario (patient age)	DCIS (59)	IDC; clinically negative axilla (59)	IDC; positive axillary node (52)	IDC [ER+/PR+], clinically negative axilla (82)	Inflammatory breast cancer (55)
Mean Accuracy	4	3.3	3.3	2	3.5
Mean Flesch-Kincaid Readability	11.0	13.1	12.5	12.1	13.2
Mean Citation Volume	3.0	3.7	3.3	3.3	3.0
Functional Reference Link	0%	33%	40%	40%	0%

DCIS: Ductal Carcinoma In Situ. IDC: Invasive Ductal Carcinoma. ER+: Estrogen Receptor Positive. PR+: Progesterone Receptor Positive.

Figure 1. Summary of results by clinical prompt.

P245. Clinical Correlates and Racial Disparities in Inflammatory Breast Cancer Survival, U.S. 2000-2020

Kameko Karasaki[1]; Brenda Hernandez[2]; Lenora Loo[3]; Hideko Yamauchi[4]; Toshi Iwase[5]; Yoko Takahashi[6]; Xiaoping Wang[7]; Teruo Yamauchi[8]; Naoto Ueno[9]; Ashley Marumoto, MD[10]
[1]University of Hawaii, Honolulu, HI, US; [2]University of Hawaii Cancer Center, Honolulu, HI, US; [3]University of Hawaii Cancer Center, Honolulu, HI, US; [4]University of Hawaii Cancer Center, Honolulu, HI, US; [5]University of Hawaii Cancer Center, Honolulu, HI, US; [6]University of Hawaii Cancer Center, Honolulu, HI, US; [7]University of Hawaii Cancer Center, Honolulu, HI, US; [8]University of Hawaii Cancer Center, Honolulu, HI, US; [9]University of Hawaii Cancer Center, Honolulu, HI, US; [10]University of Hawaii John A. Burns School of Medicine, Honolulu, HI, US

INTRODUCTION: Inflammatory breast cancer (IBC) is a rare and aggressive type of breast cancer for which survival has been shown to vary by race. A Surveillance, Epidemiology, and End Results (SEER) study between 1990-2004 demonstrated better survival in Asian and Pacific Islander (API) compared to non-Hispanic White (NHW) IBC patients while another SEER study between1973-2015 demonstrated worse survival for Blacks compared to NHW IBC patients. The objective of the current study was to evaluate overall survival (OS) of IBC patients by race and other clinical correlates in a more recent cohort (2000-2020). **METHODS:** The SEER database was retrospectively evaluated to assess 5-year OS in female IBC patients diagnosed between 2000-2020. IBC OS was compared by race as well as age, subtype, and first course treatment status using SEER*Stat and SAS software. Independent predictors of survival were evaluated using multivariate Cox proportional hazards regression. Non-overlapping 95% CI were considered significant. **RESULTS:** 6,113 female patients with IBC were identified between 2000-2020. The majority were NHW (73.8%, n=4,511), followed by Black (17.6%, n=1,075), then API/Other (8.6%, n=527). Most patients were ≥ 50 years of age (71.8%,390). The most common subtype was HR+/HER2- (42%, n=2,569), followed by HR-/HER2- (22.7%,386), HR+/HER2+ (18.9%,154), and HR-/HER2+ (16.4%,004). Black race relative to NHW race (Hazard Ratio1.43, 95% CI 1.30-1.57), age ≥50 relative to age <50 (Hazard Ratio 1.19, 95% CI 1.09-1.30), and no treatment relative to surgery, radiation, and/or systemic therapy (Hazard Ratio 3.38, 95% CI 3.03-3.78) were predictors of worse OS. HR+/HER2- (Hazard Ratio 1.53, 95% CI 1.36-1.73), HR-/HER2+ (Hazard Ratio 1.39, 95% CI 1.20-1.61), HR-/HER2-

(Hazard Ratio 3.23, 95% CI 2.84-3.66) compared to HR+/HER2+ subtypes were predictors of worse OS. API/Other race relative to NHW was not a significant predictor of OS (Hazard Ratio 0.92, 95% CI 0.79-1.07). (Table 1). **CONCLUSIONS:** Even in a more recent cohort, and despite treatment advances, Black race remains predictive of worse OS for patients with IBC compared to NHW race after adjusting for age, subtype, and treatment. API race was not associated with a significant survival advantage in our cohort which differs from prior studies. This may be secondary to small numbers though other aspects may also account for this finding. In addition to identifying underlying factors impacting survival for Black patients, future studies should focus on including underrepresented groups as there may be additional racial disparities not identified through SEER.

Table 1. Predictors of Worse IBC 5-year OS

	n	%	Hazard Ratio	LCI	UCI
Race					
White	4,511	73.8	^	^	^
Black	1,075	17.6	1.43	1.30	1.57
API/Other	527	8.6	0.92	0.79	1.07
Age					
<50	1,723	28.2	^	^	^
≥50	4,390	71.8	1.19	1.09	1.30
Treatment					
Yes	5,540	90.6	^	^	^
No	573	9.4	3.38	3.03	3.78
Subtype					
HR+/HER2+	1,154	18.9	^	^	^
HR+/HER2-	2,569	42	1.53	1.36	1.73
HR-/HER2+	1,004	16.4	1.39	1.20	1.61
HR-/HER2-	1,386	22.7	3.23	2.84	3.66

P246. Clinical alerts triggered by remote symptom monitoring are associated with increased 30-day surgical complications among patients undergoing lumpectomy for breast cancer

Solange Bayard, MD[1]; Melissa Assel[2]; Minji Kim[3]; Tracy-Ann Moo, MD[4]; Andrew Vickers, MD[5]; Sigrid Carlsson, MD[6]; Babak J Mehrara, MD[7]; Monica Morrow, MD[8]; Jonas Nelson, MD[9]; Audree Tadros, MD[10]

[1]Memorial Sloan Kettering, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New-York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Electronic patient-reported outcome measures (ePROMs) are utilized in the immediate postoperative setting to facilitate early detection of postoperative complications through real-time symptom monitoring. This study investigates whether symptom alerts triggered through the "Recovery Tracker" (RT), a postoperative ePROM, were predictive of 30-day readmission/reoperation among patients undergoing lumpectomy. **METHODS:** We performed a retrospective review of patients undergoing lumpectomy for breast cancer at a single institution from 8/2018- 5/2024. Patients responding to the RT on any day between postoperative days 1-5 were included. Symptoms reaching prespecified alert levels, red (urgent) and yellow (less urgent), were analyzed, using generalized additive models to assess trends in RT responses and univariable logistic regression to test the association between alerts and 30-day readmission or reoperation. **RESULTS:** 8,723 patients were included with 2,552 patients (29%) triggering at least one alert. Yellow alerts were more common than red alerts on all postoperative days. Most red alerts were triggered for pain severity or vomiting, while most yellow alerts were triggered for pain severity or wound redness. Patient reported symptom severity and interference downtrended over time (Figure 1). Rates of readmission and reoperations were low, the probability of resurgery or readmission was 1.1% among those with at least one day with an alert compared to 0.4% among those with no alerts. Triggering one or more alerts was associated with an increased likelihood for reoperation or readmission (OR 2.86; 95% CI 1.64-5.03; p<0.001). **CONCLUSIONS:** While rates of readmission and reoperation are low among breast cancer patients undergoing lumpectomy, triggering at least one ePROM alert is indicative of increased risk for readmission/reoperation.

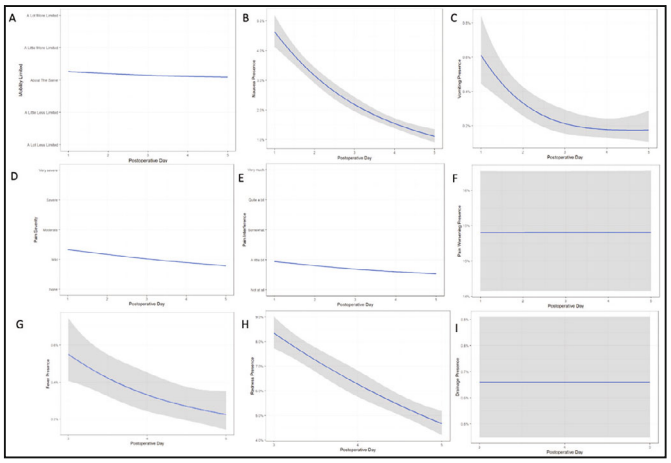


Figure 1. Recovery Tracker Response Trends

P247. Clinicopathologic Features and Oncologic Outcome of Encapsulated Papillary Breast Carcinoma

Lauren A. Gamble[1]; Thomas L. Amburn[2]; Giacomo Montagna[3]; Monica Morrow[4]; George Plitas[5]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Encapsulated papillary carcinoma (EPC) is a rare form of breast cancer which can exist as in situ or invasive forms. The diagnostic classification of EPC with invasion is considerably challenging, leading to inconsistent data reporting and disparate patient management. We sought to characterize clinicopathologic features and the oncologic outcome of EPC. **METHODS:** Data were collected prospectively at a single institution, and retrospective review was performed between 2001 and 2022. Data collection included patient demographics, tumor characteristics, and clinical outcomes. **RESULTS:** Over a 21-year period, 211 patients with papillary breast cancer were identified with 46 characterized as EPC. Patient and tumor characteristics are listed in Table 1. Median age of diagnosis was 68 years (range 39-86). The majority of tumors were classified as invasive (93%, 43/46). Invasive EPC were predominantly T1 (78%, 36/46) with the remaining being T2 (15%, 7/46). EPC was largely ER+ (97%, 45/46), with one tumor being triple negative (2%, 1/46), and none demonstrated HER2 amplification. Thirty women (65%) underwent breast conservation and the remaining mastectomy. Axillary staging with a sentinel node biopsy was performed in 73% (34/46) of women and only one patient had nodal micrometastasis (2%, 1/46). Following surgery, 39% (18/46) received adjuvant radiotherapy and 67% (31/46) endocrine therapy. Two patients (4%) received adjuvant chemotherapy; one for a pT2 tumor with triple negative receptor status and the other for nodal micrometastasis. At a median follow-up of 49 months (range 7-193) there have been no local or distant recurrences. **CONCLUSIONS:** Encapsulated papillary carcinoma is a rare sub-type of breast cancer, which demonstrates favorable clinicopathologic features and has an excellent prognosis. While the diagnosis of invasion represents a diagnostic challenge, our data suggest that axillary staging can be omitted regardless of invasion as regional nodal metastases are exceedingly uncommon.

Table 1. Characteristics of Patients with Encapsulated Papillary Carcinoma

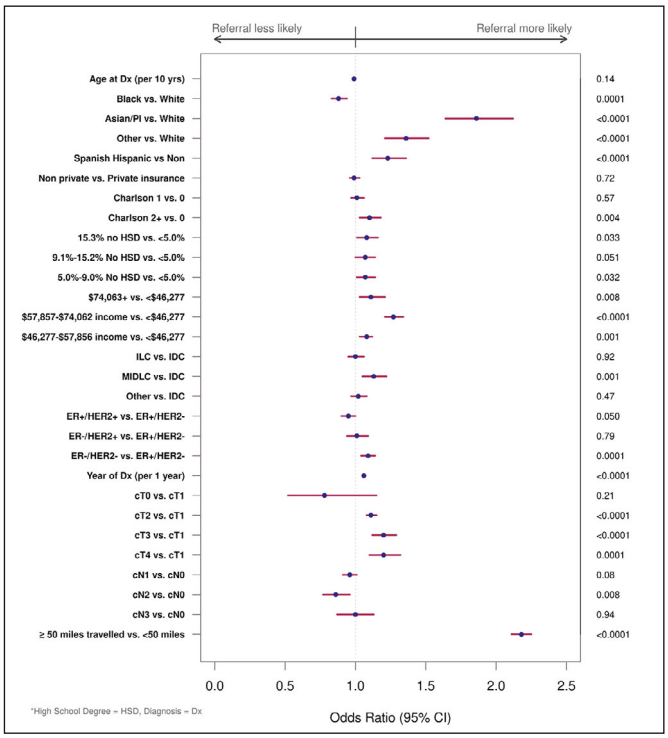
Clinicopathological features	n = 46
Age, median (range), y	68 (39-86)
Sex, female, N (%)	46 (100.0)
Tumor size	
In situ (Tis), n (%)	3 (6.5)
≤ 2 cm (T1), n (%)	36 (78.2)
> 2 and ≤ 5 cm (T2), n (%)	7 (15.2)
> 5 cm (T3), n (%)	0 (0.0)
Lymph nodes	
0 positive (N0), n (%)	45 (97.8)
Micrometastasis (N1mi), n (%)	1 (2.2)
1-3 positive (N1), n (%)	0 (0.0)
Receptor status	
ER positive, n (%)	45 (97.8)
PR positive, n (%)	42 (10.5)
HER2 positive, n (%)	0 (0.0)
TNBC, n (%)	1 (2.2)
Surgical procedure	
Partial mastectomy, n (%)	30 (65.2)
Mastectomy, n (%)	16 (34.8)
SLNB, n (%)	34 (73.9)
ALND, n (%)	4 (8.6)
Adjuvant therapy	
Chemotherapy, n (%)	2 (4.3)
Radiation therapy, n (%)	18 (39.1)
Endocrine therapy, n (%)	31 (67.4)

Abbreviations: ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; TNBC, triple negative breast cancer; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection

P248. Clinicopathologic and treatment differences between women in rural areas who are referred for breast cancer care compared to those treated locally

Christopher D Vetter, MD, MSc[1]; Courtney N. Day, MS[2]; Judy C. Boughey, MD[3]; Elizabeth B Habermann, PhD[4]; Dalliah M Black[5]
[1]Mayo Clinic, Rochester, MN, US; [2]Mayo Clinic, Rochester, MN, US; [3]Mayo Clinic, Rochester, MN, US; [4]Mayo Clinic, Rochester, MN, US; [5]Mayo Clinic, Rochester, MN, US

INTRODUCTION: Women residing in rural areas experience challenges across the continuum of breast cancer care. Referral to specialty care centers may improve outcomes but can introduce delays. We aimed to evaluate breast cancer treatment among rural women treated at their diagnosing institution (non-referred women, NRW) compared with those referred to another facility after diagnosis (referred women, RW). **METHODS:** Women from rural zip codes with stage I-III breast cancer were identified from the National Cancer Database, 2010-2021. Patient, tumor, and treatment characteristics were compared between RW and NRW using Chi-square or Wilcoxon tests where appropriate. A multivariable logistic regression model was used to evaluate predictors of referral. A multivariable Cox proportional hazards model was used to evaluate factors associated with death. **RESULTS:** Of 184,156 rural women, 89% were NRW and 11% were RW. Referral rate increased from 7% to 14% from 2010 to 2021 (p<.0001). On multivariable analysis (MVA), RW were less likely to be of black race and have ER+HER2+ or clinical N2 disease. RW were more likely to be of Asian race, Hispanic ethnicity, have larger clinical tumor size, or have ER-HER2- disease (Figure 1). RW were less likely to undergo breast conserving surgery (BCS) (52% vs 60%), receive post-BCS radiation (79% vs 86%), and receive endocrine therapy for ER+ disease (81% vs 85%) (all p<0.001). RW were more likely to have pre-operative systemic therapy (23% vs 19%), mastectomy with reconstruction (41% vs 32%), and travel ≥ 50 miles (45% vs 28%) (all p<0.001) compared to NRW. RW experienced longer time to first treatment (median 41 vs 32 days, p<0.0001) and more often had ≥ 60 days from diagnosis to first treatment (22% vs 13%, p<0.0001). On MVA, referral was not a significant predictor of mortality (HR 1.02, p=0.30). **CONCLUSIONS:** Referral of rural women with breast cancer is becoming more frequent. While rural women treated outside their diagnosing facility had longer time to first treatment, this did not impact survival. Differences exist between RW and NRW with regard to race, ethnicity, and tumor characteristics. It is not possible to determine whether these differences are due to lack of referral initiation vs socioeconomic limitations or patient preference which prevent referral completion. Further investigation into the underlying causes of these differences may identify opportunities to ensure optimal access to referral for rural women.



P249. Comparative Outcomes of Juvenile Breast Sarcomas: A Focus on Non – Phyllodes versus Phyllodes Variants

Sydney Smilen, DO[1]; Xiang Dong, MD[2]; Keerthivasan Vengatesan, MD[3]; Joyce L. Eum, DO[4]
[1]Nuvance Health, Danbury, CT, US; [2]Danbury Hospital, Danbury, CT, US; [3]Danbury Hospital, Danbury, CT, US; [4]Nuvance Health, Danbury, CT, US

INTRODUCTION: Phyllodes tumors are a rare fibroepithelial tumor that accounts for less than 0.5% of all breast tumors, and are even more rare in the pediatric population, presenting unique challenges in diagnosis and management. Although the dominant form of juvenile sarcomas of the breast is the phyllodes type sarcoma, in this paper, we demonstrate that non-phyllodes sarcomas of the breast are associated with worse outcomes compared to phyllodes. The rare and diverse presentation of these tumors, the management and the outcomes are highlighted. **METHODS:** We performed a retrospective review of the SEER research database that included 17 registries to examine patients ages 0-29 with soft tissue sarcomas of the breast over a 21-year span between 1990 and 2021. 256 patients were identified. Primary endpoints included overall survival, secondary endpoints included influences by ethnicity, age, histologic type and time from diagnosis to treatment on overall survival. **RESULTS:** Among the 256 patients with soft tissue sarcomas of the breast, the median overall survival rate exceeded 101 months (about 8 and a half years), with 85% of patients still alive at the time the data was collected. The Kaplan-Meier curve showed a significant difference in survival between patients with breast phyllodes tumors and other types (p<0.0001). The multivariate Cox regression analysis identified "Type of Sarcoma" as a significant predictor of survival (P=0.0489). The mean survival time is notably lower for patients treated ≥ 1 month group (44.5 months) compared to 0 months group (155.57). **CONCLUSIONS:** In conclusion, we found that phyllodes type breast sarcomas comprise over 72%

of Juvenile breast sarcomas in patients under 30 and that patients with phyllodes tumors show a better survival outcome compared to non-phyllodes tumors. We also demonstrated that there is a significant proportion of patients, about 25 percent who have a delay in treatment following diagnosis of juvenile onset breast sarcomas.

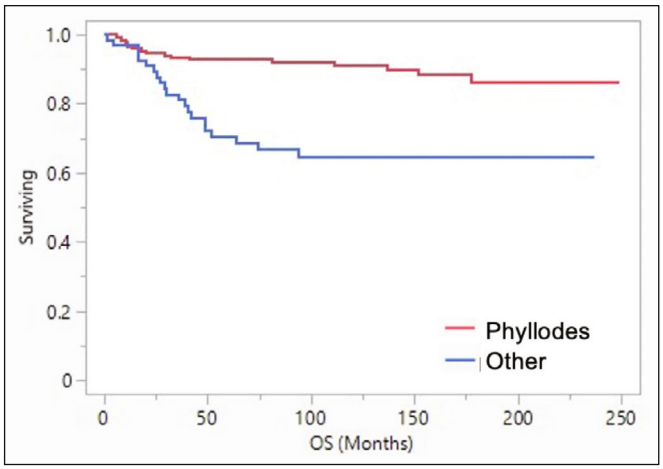


Figure 1. Kaplan-Meier Survival Estimates for Breast Sarcoma Patients Under 30 Years: Phyllodes Tumors vs Other Types

P250. Contemporary Nodal Management & Overall Survival in Older Patients with Triple Negative Breast Cancer

Adrienne N Cobb, MD MS[1]; Xiaowei Dong, MS[2]; Spencer Huang, PhD[3]; Amanda Kong, MD[4]; Chandler S. Cortina, MD, MS[5]

[1]Medical College of Wisconsin, Milwaukee, WI, US; [2]University of Wisconsin Milwaukee, Milwaukee, WI, US; [3]University of Wisconsin Milwaukee, Milwaukee, WI, US; [4]Medical College of Wisconsin, Milwaukee, WI, US; [5]Medical College of Wisconsin, Milwaukee, WI, US

INTRODUCTION: In 2016, the Choosing Wisely guidelines recommended omission of nodal surgery for patients age ≥70 years with early-stage cN0 HR+ HER2- breast cancer but excluded those with triple-negative breast cancer (TNBC). We aimed to investigate contemporary nodal management in patients ≥70 years with TNBC, identify factors associated with omission of nodal surgery, and examine overall survival (OS) by nodal surgery type.
METHODS: Women age ≥70 with stage I-III TNBC who underwent upfront surgery in the NCDB from 2017–2019 were included. Patients were separated into three surgical nodal management groups by number of nodes examined: omission (0), sentinel lymph node biopsy (SLNB, 1–5), and axillary lymph node dissection (ALND, >10). Descriptive statistics of patient characteristics and oncologic data were calculated and stratified by nodal surgery type. Multinomial logistic regression identified factors associated with nodal omission. The Kaplan-Meier method and a Cox proportional hazards model were performed to compare OS and factors associated with OS. **RESULTS:** Of the 9,098 eligible patients, most were age 70–75 (46.9%), non-Hispanic White (76.4%), had Medicare insurance (87.7%) and a Charlson Comorbidity index (CCI) of 0 (72.6%). The majority had stage I or 2 (87.5%) disease and underwent lumpectomy (62.5%). Regarding nodal surgery, 6,386 (70.2%) patients had SLNB, 955 (10.5%) had an ALND, and 850 (9.3%) had omission. Of the 850 patients with nodal omission, 55.2% were age >81, 69% had CCI of 0, 91.8% were cT1-2, 3.9% cT3, and 3.3% were cT4. When stratified by cT/N category, 14.8% of cT3N0 (n=26/176) and 31.7% of cT4N0 (n=20/63) patients had omission of nodal surgery. Additionally, 6.5% of cT3N+(n=7/107) and 8.4% of cT4N+ (n=8/95) omitted nodal surgery. (Table 1) Factors associated with nodal omission included age >81 (OR 4.5, 95% CI 3.7–5.3) and CCI of ≥3 (OR 1.5, 95% CI 1.1–2.0). Three-year OS was similar for those who underwent ALND (62%; 95% CI 59-66%) and had omission of nodal surgery (68%; 95% CI 65-72%) but improved for those who had SLNB (85%; 95% CI 84-86%) p<0.01. Compared to SLNB, patients with ALND had an HR of 1.3, (95% CI 1.2–1.5), and those with omission had an (HR of 1.6 (95% CI 1.4–1.9). **CONCLUSIONS:** In this cohort of patients ≥70 with TNBC, 9.3% omitted nodal surgery, including those with locally advanced and cN+ disease. Similar OS in the ALND and nodal omission groups suggests opportunity for better tools and guidelines to aid providers and patients in selecting which older patients with TNBC it may be reasonable to omit nodal surgery without compromising OS.

Table 1. Surgical nodal management by cT and cN category for women age ≥70 in the NCDB from 2017–2019 with Stage I-III TNBC.

AJCC Clinical T and N Category	Number of patients n	Omission of Nodal Surgery n (%)	SLNB n (%)	ALND n (%)
cT1-2 N0	6,877	750 (10.9%)	5,797 (84.3%)	330 (4.8%)
cT1-2 N+	590	25 (4.2%)	215 (36.4%)	350 (59.3%)
cT3 N0	176	26 (14.8%)	120 (68.2%)	30 (17%)
cT3 N+	107	7 (6.5%)	22 (20.6%)	78 (72.9%)
cT4 N0	63	20 (31.7%)	29 (46%)	14 (22.2%)
cT4 N+	95	8 (8.4%)	23 (24.2%)	64 (67.4%)

P251. Differences in Microbiome Composition in Breast and Stool Samples among Patients with HER2+ Breast Cancer

Diana Kantarovich, MD[1]; Olutayo Sogunro, DO, MS[2]; Christopher Umbricht, MD[3]; James Robert White, PhD[4]; Mehran Habibi, MD, MBA, FACS[5]

[1]Lenox Hill Hospital/Northwell Health, New York, NY, US; [2]Johns Hopkins University School of Medicine, Baltimore, MD, US; [3]Johns Hopkins University School of Medicine, Baltimore, MD, US; [4]Resphera Biosciences, College Park, MD, US; [5]Staten Island University Hospital/ Northwell Health, Staten Island, NY, US

INTRODUCTION: There is an estimated three trillion bacterial members that live in the human body. Their interaction with our body can play an important role in various physiological processes and even influence diseases such as cancer. The goal of our study was to explore potential differences in microbiome composition in breast tissue and stool samples in breast cancers with varying human epidermal growth factor receptor 2 (HER2) expression. **METHODS:** This is a single institution pilot study. After each patient completed their course of neoadjuvant chemotherapy, we obtained and analyzed samples of breast tissue, skin tissue, and stool specimens. To identify and exclude contaminants from breast tissue specimens, we initially analyzed 16S RNA sequencing data to detect skin-associated taxa, excluding those with an average skin abundance greater than 0.01% and a positivity rate of ≥10%. From this, 35 species were found to overlap with whole genome shotgun (WGS) data. Additionally, we identified taxa with high abundance (≥0.02%) in skin WGS samples and modest abundance (≥0.001%) in breast tissue, further expanding our contaminants list. In total, this resulted in the exclusion of 295 taxonomic members from the breast samples in the dataset. After exclusion, profiles were re-normalized to abundances among the remaining members. No taxa were excluded from stool. **RESULTS:** We analyzed samples from 11 female patients. Three patients were HER2 positive, two were HER2 ambiguous (IHC 2+; varying FISH results) and six patients were HER2 negative. All patients received neoadjuvant chemotherapy. Among the breast tissue samples there was a statistically significant difference in abundance of *Lactococcus lactis* among HER2- vs HER2 ambiguous ($p = 0.038$). In the stool samples there was a difference in abundance among *Alistipes putredinis* ($p = 0.023$), *Alistipes_u_s* ($p = 0.021$) and *Parabacteroides_u_s* ($p = 0.02$) in HER2- vs HER2+ breast cancer samples. There was also a difference in *Roseburia faecis* in stool samples from HER2- vs HER2+ ($p = 0.016$) and from HER ambiguous vs HER2+ ($p = 0.0081$) breast cancers. Finally, *Lachnospira eligens* species showed a significant difference in stool samples between HER2- vs HER2+ ($p = 0.0031$) and between HER2 ambiguous vs HER2+ ($p = 0.0019$) cancers. **CONCLUSIONS:** While our sample size is small, we show differences in the microbiome composition among breast tissue and stool samples in patients with breast cancers expressing HER2 receptors. This suggests that tumor characteristics can be reflected in the microbiome, which may help us better understand the underlying biology.

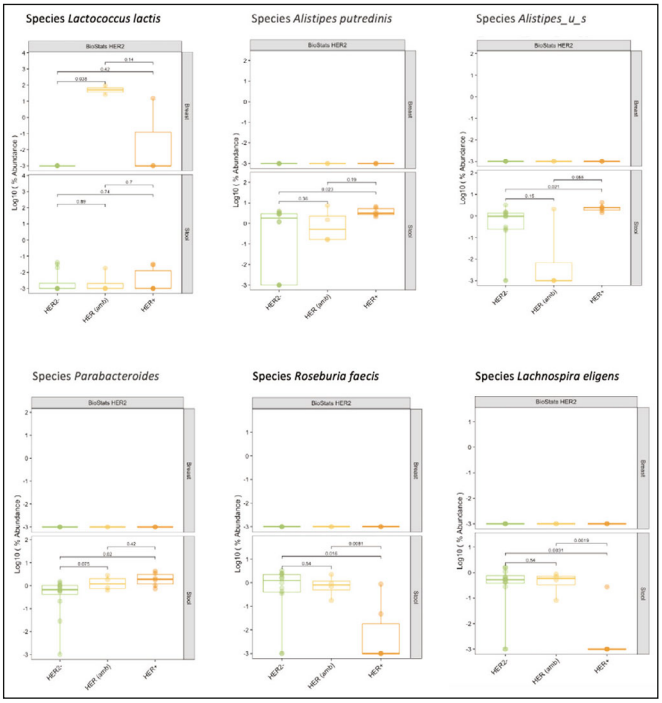
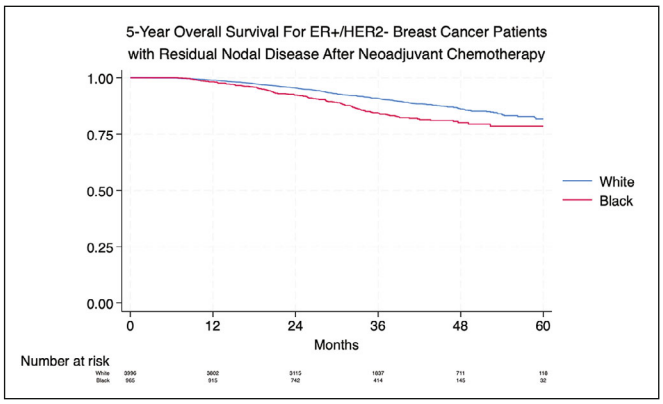


Figure 1. Individual Differences in Proportional Abundances of the Most Significantly Altered Microbial Communities in Breast and Stool Samples among Cancers with Varying HER2 Expression.

P252. Differential Utility of Genomic Assays in Predicting Nodal Response Across Racial Groups in Hormone Receptor-Positive Breast Cancer

Selena J An, MD, MSPH, MA[1]; Julia M. Selfridge, MD[2]; Katherine Reeder-Hayes, MD[3]; Chris B Agala, PhD[4]; Phillip Spanheimer, MD[5]
[1]University of North Carolina, Chapel Hill, NC, US; [2]The University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US; [3]University of North Carolina, Chapel Hill, NC, US; [4]University of North Carolina, Chapel Hill, NC, US; [5]University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US

INTRODUCTION: In patients with ER+/HER2- breast cancer (BC), genomic assays are increasingly used to guide systemic treatment decisions. However, racial differences in performance have been demonstrated and their utility in predicting nodal response is not well-elucidated in patients from diverse populations. We aimed to identify the ability of Oncotype Dx (ODX) to predict nodal pathologic complete response (npCR) after neoadjuvant chemotherapy (NAC) among different racial groups. **METHODS:** Adult women with stage 2-3 ER+/HER2- BC from 2010-2021 in the National Cancer Database who received NAC were included. Rates of npCR were compared between white and Black patients, stratified by risk of recurrence (ROR) based on ODX (low: 0-17, intermediate: 18-30, high: ≥ 31). Multivariable logistic regression was performed to assess for the association between npCR and ODX categories, stratified by race. Kaplan-Meier analyses were used to model overall survival for patients with and without npCR, stratified by race and ODX levels. **RESULTS:** 27,522 patients were included; 9,082 (33.0%, with 32.5% of white and 35.4% of Black patients) received ODX testing. Most patients in both groups had high ROR (91.0% white and 93.8% Black patients, p=0.001), reflecting the careful selection of patients for genomic testing. Overall, 19.6% (18.8% of white and 23.0% of Black patients, p<0.001) achieved npCR with a median age of 54 (interquartile range 45-63): 9.1% with low ROR, 9.7% with intermediate ROR, and 26.1% with high ROR. Stratifying by race, after adjusting for age, grade, histology, stage, comorbidity, treatment facility, and income, white patients with high ROR (odds ratio [OR] 1.96, 95% confidence interval [CI] 1.03-3.74) compared to Black patients (OR 6.39, 95% CI 0.84-48.5) were more likely to achieve npCR. Five-year overall survival did not differ by race among patients achieving npCR, but a difference was observed between white and Black patients who had residual nodal disease with high ROR (p<0.001, figure). **CONCLUSIONS:** Genomic assessment of recurrence risk in node-positive ER+/HER2- breast cancer was more predictive of npCR in white compared to Black patients after neoadjuvant chemotherapy. While Black patients had a higher rate of npCR, Black compared to white patients with residual nodal disease and high recurrence risk had worse survival. These findings suggest that prediction of chemosensitivity differs among racial groups, and that current genomic assays require further refinement in providing prognosis for different racial groups.



P253. Disparities among breast cancer patients in Appalachian Kentucky: Are we making progress?

Anna Reagan, MD[1]; Hannah McDonald, MD[2]; Sadie Junkins[3]; Kelsey Karnik, PhD[4]; Tony Mangino, PhD[5]; Veronica Jones[6]; Erin E Burke, MD, MS[7]
[1]University of Kentucky, Lexington, KY, US; [2]University of Kentucky Department of Surgery, Lexington, KY, US; [3]University of Kentucky School of Medicine, Lexington, KY, US; [4]University of Kentucky Department of Biostatistics, Lexington, KY, US; [5]University of Kentucky Department of Biostatistics, Lexington, KY, US; [6]University of Kentucky Department of Surgery, Lexington, KY, US; [7]Ohio State University, Columbus, OH, US

INTRODUCTION: Despite lower rates of breast cancer in Appalachian counties in Kentucky (KY) compared to the rest of KY, the mortality rate for Appalachian breast cancer patients has historically been significantly worse. We aimed to analyze differences in patient, tumor, and treatment factors in breast cancer patients from KY Appalachian counties compared to those from non-Appalachian counties. **METHODS:** The KY Cancer Registry, a population-based central cancer registry, was queried for all patients with a new diagnosis of stage I-IV breast cancer between 2010 and 2020. Demographic, clinicopathologic, treatment, and outcomes data were analyzed. **RESULTS:** Of the 4,100 KY patients with invasive breast cancer, 2,090 (50.98%) were from an Appalachian count. Appalachian patients were more likely to be white, have Medicaid/Medicare, have a higher BMI, and use tobacco (all p<0.05). They were less likely to present with local breast cancer (60.86% vs 63.98%) and more likely to present with locally advanced (30.19% vs 28.56%) or metastatic breast cancer (8.52% vs 7.36%) (p=0.038). Hormone receptor status was similar between groups. When stratified by stage, there were no significant differences in receipt of chemotherapy, endocrine therapy, or radiation for Appalachian versus non-Appalachian patients. Appalachian patients were significantly less likely to get surgery for localized disease (66.2% vs 69.4%) but more likely to get surgery for locally advanced (30.8% vs 28.6%) or metastatic disease (2.6% vs 2.1%) (p=0.021). Despite an increase in receipt of surgery in more advanced stages, Appalachian patients were not more likely to undergo more aggressive axillary surgery. The mastectomy rate was significantly higher in Appalachian patients (52.3% vs 45.7%, p < 0.0001). There was also a higher rate in the use of neoadjuvant chemotherapy in Appalachian patients (31.3% vs 23.8%, p < 0.001). Unadjusted survival analysis indicated that the risk of death was 17% higher for Appalachian patients (p=0.019); however, after adjusting for stage there was no significant survival difference between cohorts. **CONCLUSIONS:** Appalachian patients are more likely to present with advanced breast cancer. However, survival in this study population now matches those of patients in non-Appalachian counties when adjusting for stage suggesting some progress may have been made in the quality of treatment for Appalachian breast cancer patients. Further investigation into interventions that decrease the number of Appalachian patients presenting with advanced disease remains of great importance.

Table 1. Patient Demographics, Tumor Characteristics and Stage for Patients in Kentucky Diagnosed with Breast Cancer Between 2010 and 2020 by Appalachian and Non-Appalachian County.

Variable	Overall N = 4,100 (%)	Appalachian KY County N = 2,090 (%)	Non-Appalachian KY County N = 2,010 (%)	p-value
Age (years)				**0.016**
<50	998 (24.3)	513 (24.5)	485 (24.1)	
50-80	2,911 (71.0)	1,499 (71.7)	1,412 (70.2)	
80+	191 (4.6)	78 (3.7)	113 (5.6)	
Insurance Status				**< 0.001**
Insurance, NOS	1,857 (45.3)	858 (41.0)	999 (49.7)	
Medicaid	602 (14.7)	380 (18.2)	222 (11.0)	
Medicare	1,486 (36.2)	780 (37.3)	706 (35.1)	
Military/Govt	49 (1.19)	27 (1.3)	22 (1.1)	
Uninsured	90 (2.2)	39 (1.9)	51 (2.5)	
Unknown	16 (0.4)	6 (0.3)	10 (0.5)	
Marital Status				**< 0.001**
Married	2,315 (56.5)	1,247 (59.7)	1,068 (53.1)	
Other/Unknown	55 (1.3)	23 (1.1)	32 (1.6)	
Unmarried	1,730 (42.2)	820 (39.2)	910 (45.3)	
Ethnicity				**< 0.001**
Hispanic	57 (1.4)	11 (0.5)	46 (2.3)	
Non-Hispanic	4,036 (98.4)	2,075 (99.3)	1,961 (97.6)	
Unknown	7 (0.2)	4 (0.2)	3 (0.1)	
Race				**< 0.001**
Asian American Pacific Islander	45 (1.1)	4 (0.2)	41 (2.0)	
Black	230 (5.6)	25 (1.2)	205 (10.2)	
White	3,825 (93.3)	2,061 (98.6)	1,764 (87.8)	
Body Mass Index (kg/m2)				**< 0.001**
<25	738 (24.6)	303 (20.1)	435 (29.1)	
25-29.99	870 (29.0)	463 (30.8)	407 (27.3)	
30-39.99	1,070 (35.7)	559 (37.2)	511 (34.2)	
40+	318 (10.6)	179 (11.9)	139 (9.3)	
Charlson Comorbidity Index				**0.318**
<5	3,226 (85.3)	1,641 (85.6)	1,585 (84.9)	
5-10	503 (13.3)	244 (12.7)	259 (13.9)	
10-15	51 (1.3)	31 (1.6)	20 (1.1)	
15-20	3 (0.1)	1 (0.05)	2 (0.1)	
Tobacco Use Status				**< 0.001**
Never	2,235 (54.5)	1,084 (51.9)	1,151 (57.3)	
Tobacco use	1,210 (29.5)	700 (33.5)	510 (25.4)	
Unknown	655 (16.0)	306 (14.6)	349 (17.4)	
Distance to Hospital (miles)				**<0.001**
<30	1,830 (44.6)	306 (14.6)	1,524 (75.8)	
30-60	653 (15.9)	337 (16.1)	316 (15.7)	
60+	1,617 (39.4)	1,447 (69.2)	170 (8.4)	
Stage				**0.038**
Local	2,558 (62.4)	1,272 (60.9)	1,286 (64.0)	
Locally Advanced	1,205 (29.4)	631 (30.2)	574 (28.5)	
Metastatic	326 (7.9)	178 (8.5)	148 (7.4)	
Unknown	11 (0.3)	9 (0.4)	2 (0.1)	
ER Status				**0.351**
Negative	825 (21.6)	433 (22.2)	392 (20.9)	
Positive	2,999 (78.4)	1,519 (77.8)	1,480 (79.1)	
PR Status				**0.534**
Negative	1,174 (30.7)	608 (31.2)	566 (30.2)	
Positive	2,649 (69.3)	1,343 (68.8)	1,306 (69.8)	
HER2 Status				**0.053**
Negative	3,153 (82.8)	1,585 (81.6)	1,568 (84.0)	
Positive	656 (17.2)	357 (18.4)	299 (16.0)	

P254. Does Sarcopenia Matter? A Single-Institution Review on the Influence of Sarcopenia on Clinical Outcomes in Patients with Nonmetastatic Invasive Breast Cancer

Charlotte Burch[1]; Andrew Anthony Francis, MD, MS[2]; Xiaoyan Deng[3]; Dipankar Bandyopadhyay[4]; Kandace McGuire, MD[5]

[1]Virginia Commonwealth University, Richmond, VA, US; [2]Virginia Commonwealth University, Richmond, VA, US; [3]Virginia Commonweath University, Richmond, VA, US; [4]Virginia Commonwealth University, Richmond, VA, US; [5]Virginia Commonwealth University Medical Center, Richmond, VA, US

INTRODUCTION: Sarcopenia is recognized as a prognostic indicator in patients with cancer. It is associated with an increased risk of chemotherapy toxicity, postoperative complications, and poor quality of life and is an independent predictor of mortality. Evaluating sarcopenia is complex, and there remains debate about its definition and methods for measurement. Thus, the impact of sarcopenia on breast cancer outcomes has not been clearly elucidated. Utilizing skeletal muscle index (SMI), the most robust measurement of sarcopenia, we aim to investigate the effect of sarcopenia on survival in patients with nonmetastatic breast cancer. **METHODS:** We conducted a single-institution retrospective review of patients aged ≥18 diagnosed with invasive breast cancer between 2009-2023 who received abdominal computed tomography imaging within six months prior or up to 1 month after their breast cancer diagnosis. We excluded patients with metastatic disease, undergoing treatment for other primary cancers, or who declined standard of care. SliceOmatic Software version 5.0 (TomoVision) was used to measure SMI. Sarcopenia was defined as SMI < 41 cm2/m2. The primary outcomes were overall survival (OS), recurrence-free survival (RFS), and disease-specific survival (DSS). The chi-square and T-tests were performed to compare patients with and without sarcopenia. The Pearson correlation coefficient was used to determine the relationship between SMI versus BMI and age. Kaplan-Meier estimates and log-rank tests were used to assess our primary outcomes. **RESULTS:** We identified 108 patients who met our inclusion criteria. Thirty-three (31%) patients had sarcopenia. Patients with sarcopenia had significantly lower BMIs ($p < 0.01$) and were more often over 65 years of age ($p < 0.05$). There was a moderate correlation between SMI and BMI ($r = 0.43$, $p < 0.05$) and a weak correlation between age and SMI ($r = -0.30$, $p < 0.05$). Interestingly, in our cohort, nonsarcopenic patients had a significant decrease in OS ($p < 0.05$), and there were no differences in RFS ($p = 0.24$) or DSS ($p = 0.16$). **CONCLUSIONS:** Among patients with nonmetastatic breast cancer, sarcopenia neither influenced RFS and DSS nor led to decreased OS within our cohort, which may be due to our small sample size. Additionally, although there are significant differences in BMI and age of sarcopenia patients, there is a moderate to weak correlation between SMI versus BMI and age. As such, it remains unclear if sarcopenia should be considered a relevant risk factor in breast cancer prognosis.

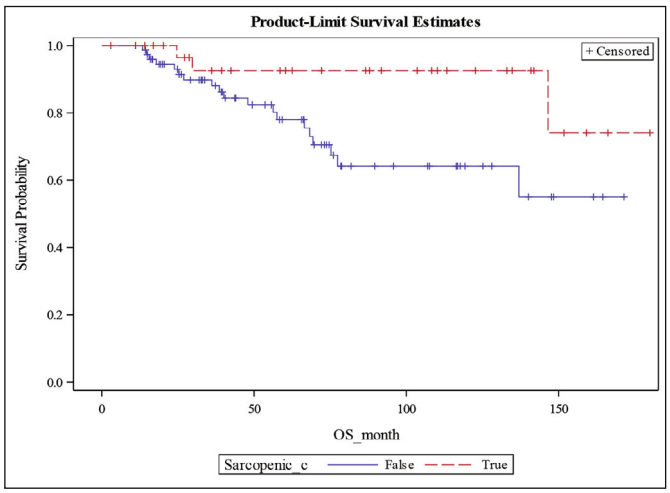


Figure 1. Kaplan-Meier curves comparing the overall survival of nonmetastatic breast cancer patients without (false) or with (true) sarcopenia. Log-rank test show a significant difference with p = 0.0323.

P255. Does Type of Axillary Surgery in Patients with Positive Nodes after Neoadjuvant Therapy Affect Outcomes?

Caitlin P Marsh, DO[1]; Anthony M Baez, DO[2]; Acacia Sharma[3]; Charles DiMaggio[4]; Alyssa Marmer[5]; Amber Guth[6]; Deborah Axelrod, MD[7]; Freya Schnabel[8]; Mary L Gemignani, MD[9]

[1]NYU, New York, NY, US; [2]NYU, New York, NY, US; [3]NYU, New York, NY, US; [4]NYU, New York, NY, US; [5]NYU, New York, NY, US; [6]NYU, New York, NY, US; [7]NYU, New York, NY, US; [8]NYU, New York, NY, US; [9]NYU, New York, NY, US

INTRODUCTION: The role of completion axillary node dissection (ALND) post neoadjuvant chemotherapy (NAC) for node-positive disease is well defined, however current data is unable to clarify when sentinel lymph node biopsy (SLNB) alone is an option. The aim of this study is to compare outcomes in patients with pN+ disease after NAC who had SLNB only or ALND. **METHODS:** Retrospective review of IRB-approved prospective database was performed to identify patients with invasive breast cancer treated with NAC from 01/01/2010 to 12/31/2023. Clinical, pathologic, treatment, and follow-up data was collected. Descriptive analyses were conducted in the R statistical software program and consisted of frequencies, proportions, standard deviations and associated 95% Confidence Intervals to compare patients with pN+ disease undergoing ALND vs. SLNB only. Comparisons of continuous variables were based on t tests and categorical variables were compared using Chi Square tests. Time to recurrence and death was estimated and compared using Kaplan Meier analysis. **RESULTS:** We identified 374 patients who received NAC, 148

(39.6%) of which had pN+ disease. Complete data was available for 137 patients and comprised our study group. Among these patients, 8 (5.8%) had SLNB only, and 129 (94.2%) underwent ALND. Clinical, pathologic, and treatment variables are included in Table1. Patients in the ALND group were younger (p=0.03) and were more likely to undergo mastectomy (p=0.006). There was no significant difference in use of radiation therapy or regional nodal irradiation between the groups (p=0.47 and 0.39). We found that although there was no difference in the number of positive sentinel nodes between the SLNB and ALND groups (1.2 vs 1.38, p=0.6), the SLNB group had a mean of 1.4 (SD 0.5) overall positive nodes compared to a mean of 4.4 (SD 4.2) in the ALND group, suggesting a larger burden of residual disease in the latter. Additionally, the SLNB group had a larger number of negative sentinel nodes (4.12 (0-18) vs. 1.09(0-33), p=0.01). With a median follow up of 5 years (range 0.1– 13 yrs), we noted no difference in breast cancer- specific or overall survival between the SLNB and ALND groups (BCSS was 100% vs. 88.4%; OS was 100% vs. 87.6%; p =0.44). **CONCLUSIONS:** In our study, the majority of patients with pN+ post NAC underwent ALND, and in the select number of patients treated with SLNB only, no difference in radiation therapy or outcomes was noted, supporting a less aggressive surgical approach. We await clinical trial results to help define best treatment approach in this setting.

Table 1. Clinical, Pathologic, and Treatment Variables in pN+ Patients Post NAC

Variable	ALND (N=129)	SLNB Only (N=8)	P-Value
Age (mean (SD))	**52 (12.6)**	**62(9.3)**	**0.03**
Histology (%)			0.19
IDC	118 (91.5)	6 (75.0)	
ILC	8 (6.2)	1 (12.0)	
Invasive Other	3 (2.3	1 (12.0)	
Tumor Size cm (mean (SD)	2.52 (2.2)	1.68 (1.1)	0.27
ER Positive (≥10%) (%)	97 (75.2)	6 (75.0)	1.00
PR Positive (≥10%) (%)	75 (58.1)	5 (62.5)	1.00
HER2 Positive (%)	43 (33.3)	2 (25.0)	0.92
Triple Negative (%)	16 (12.4)	0 (0.0)	0.62
Surgery			
Mastectomy (%)	**98 (24)**	**2 (25.0)**	**0.006**
Lumpectomy (%)	**31 (76)**	**6 (75.0)**	
Adjuvant Systemic Therapy (%)			0.30
No	5 (3.9)	1 (12.5)	
Yes	118 (91.5)	6 (75.0)	
N/A	6 (4.7)	1 (12.5)	
Radiation Therapy (%)			0.47
No	10 (7.8)	0 (0.0)	
Yes	113 (87.6)	7 (87.5)	
N/A	6 (4.7)	1 (12.5)	
Radiation Therapy Type (%)			**0.033**
PMRT	86 (66.7)	2 (25)	
WBRT	27 (20.9)	6 (75)	
Unspecified RT	1 (0.8)	0 (0.0)	
None	2 (1.6)	0 (0.0)	
Not Recorded	12 (9.3)	0 (0.0)	
Regional Nodal Irradiation (%)			0.39
Yes	109 (84.5)	7 (87.5)	
No	2 (1.6)	0 (0.0)	
Not Recorded	18 (14)	1 (12.5)	
Sentinel Nodes Positive (%)	1.20 (1.02)	1.38 (0.52)	0.64
Sentinel Nodes with ITC (mean (SD))	0.03 (0.17)	0.00 (0.00)	0.63
Sentinel Nodes Negative (mean (SD))	**1.09 (1.69)**	**4.12 (5.96)**	**0.01**
Axillary Nodes Positive (mean (SD))	3.74 (4.20)	N/A	N/A
Axillary Nodes with ITC (mean (SD))	0.12 (0.39)	N/A	N/A
Axillary Nodes Negative (mean (SD))	8.33 (6.44)	N/A	N/A
Overall Positive Lymph Nodes (mean (SD))	4.4 (4.2)	1.4 (0.5	
LVI (%)			0.52
No	38 (29.5)	4 (50.0)	
Yes	60 (46.5)	3 (37.5)	
Indeterminate	14 (10.9)	1 (12.5)	
Not Recorded	17 (13.2)	0 (0.0)	

P256. Does community-level distress correlate with the risk of developing breast cancer related lymphedema?

Yu Chen[1]; Fardeen Bhimani[2]; Andreina Giron[3]; Priyanka Parmar[4]; Susan L Jao, MD[5]; Gabriella Safian[6]; Kaiyu Tio[7]; Anna Lasak[8]; Sheldon Feldman[9]; Anjuli Gupta[10]; Jessica Pastoriza[11]; Maureen McEvoy[12]

[1]Breast Surgery Division, Department of Surgery, Montefiore Medical Center, Bronx, NY, US; [2]Breast Surgery Division, Department of Surgery, Montefiore Medical Center, Bronx, NY, US; [3]Breast Surgery Division, Department of Surgery, Montefiore Medical Center, Bronx, NY, US; [4]Breast Surgery Division, Department of Surgery, Montefiore Medical Center, Bronx, NY, US; [5]Breast Surgery Division, Department of Surgery, Montefiore Medical Center, Bronx, NY, US; [6]Albert Einstein College of Medicine, Bronx, NY, US; [7]Albert Einstein College of Medicine, Bronx, NY, US; [8]Department of Physical Medicine & Rehabilitation, Montefiore Medical Center, Bronx, NY, US; [9]Breast Surgery Division, Department of Surgery, Montefiore Medical Center, Bronx, NY, US; [10]Breast Surgery Division, Department of Surgery, Montefiore Medical Center, Bronx, NY, US; [11]Breast Surgery Division, Department of Surgery, Montefiore Medical Center, Bronx, NY, US; [12]Breast Surgery Division, Department of Surgery, Montefiore Medical Center, Bronx, NY, US

INTRODUCTION: Breast cancer related lymphedema (BCRL) significantly impacts the quality of life of breast cancer survivors and occurs in up to 60% of patients that undergo axillary surgery as part of their management. BCRL rates are two-fold higher in low-income and ethnic minority groups. While the risk of BCRL from breast cancer treatments is well known, the role of socioeconomic and geographic factors is less studied. The Distressed Communities Index (DCI), a validated socio-geographic measure of economic well-being, provides a comprehensive assessment of community-level distress. A recent study using a similar index found correlations between socioeconomic deprivation and BCRL risk. Our study thus investigates whether higher distressed communities, as measured by DCI quintiles, are associated with an increased risk of BCRL. **METHODS:** This retrospective study included breast cancer patients (age ≥ 18 years) treated at Montefiore Medical Center from 2011 to 2022. The study population was extracted from two databases: 1) patients referred to physical medicine for arm lymphedema therapy and 2) institutional tumor registry. Patients' zip codes were matched into the corresponding DCI quintiles and stratified into low distressed (quintiles 1-3) and high distressed (quintiles 4-5) groups. Chi-square tests and logistic regression were used to determine the association between DCI quintiles and BCRL. **RESULTS:** Out of 668 patients, 80.8% were from high distressed areas (DCI quintiles 4-5) and 19.2% were from low distressed areas (DCI quintiles 1-3). The chi-square test showed a significant association between DCI quintile and lymphedema when grouped into high and low distress groups (p = 0.004). After adjusting for race, ethnicity, and insurance, patients from high distress areas had a 20% increased risk of BCRL (OR 1.20, 95% CI [1.00, 1.44], p = 0.046). Ethnic minorities had twice the risk compared to white patients (OR 2.00, 95% CI [1.46, 2.72], p < 0.0001). Stratifying by race, patients who identified as black (p = 0.0003), "other" (p = 0.007), or "unknown" (p = 0.003) had higher risk compared to white patients. Patients with Medicaid (OR 0.648, 95% CI [0.444, 0.944], p = 0.03) or Medicare (OR 0.476, 95% CI [0.326, 0.696], p = 0.0002) had lower risk of BCRL compared to those with private insurance. **CONCLUSIONS:** Patients in higher distressed communities have a 20% increased risk of developing lymphedema compared to those in less distressed areas when controlling for race, ethnicity and insurance. Furthermore, race and insurance status also significantly impact BCRL risk.

Table 1. Descriptive statistics of socio-economic status and lymphedema in high and low distress group.

	Low Distress (DCI Quintile 1-3)	High Distress (DCI Quintile 4-5)
Age (Mean, SD)	56.3 (12)	59.0 (11.8)
BMI (Mean, SD)	28.2 (6.8)	30.8 (5.9)
Race		
Asian	15	17
Black	33	258
Other	5	27
White	74	216
Unknown	2	22
Ethnicity		
Hispanic	32	258
Non-Hispanic	96	282
Lymphedema		
Yes	55	311
No	73	229
Insurance		
Medicaid	33	164
Medicare	29	166
Private	60	199
Uninsured	3	1
Unknown	3	10
Total	128 (19.2%)	540 (80.8%)

P257. Evaluation of Axillary Ultrasound Performance on SOUND Trial Eligible Patients

Kyle R. Stephens, MD[1]; Megan Wilson, BS[2]; Manting Xu, BS[3]; Kelly McMasters, MD, PhD[4]; Nicolas Ajkay, MD, MBA[5]
[1]Division of Surgical Oncology, Department of Surgery, University of Louisville School of Medicine, Louisville, KY, US; [2]University of Louisville School of Medicine, Louisville, KY, US; [3]University of Louisville, Louisville, KY, US; [4]University of Louisville, Louisville, KY, US; [5]Division of Surgical Oncology, Department of Surgery, University of Louisville School of Medicine, Louisville, KY, US

INTRODUCTION: The SOUND trial suggested that sentinel lymph node biopsy (SLNB) could be omitted in small breast cancers with negative axillary ultrasound (AUS), despite 13.7% of preoperative AUS being falsely negative when validated on SLNB. Our aim was to evaluate the performance of AUS in our patient population using SOUND trial criteria. **METHODS:** A retrospective review of patients with T1 and T2 breast cancers who underwent preoperative AUS before lumpectomy and SLNB was conducted between 2015-2023. Demographic and tumor characteristics were collected. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of AUS were calculated. Two subgroup analyses, pathologic T classification group (T1mi/ T1a, T1b, T1c, and T2) and receptor status group (Luminal, Triple Negative, and HER2/neu positive) were performed comparing preoperative AUS performance metrics, demographics, and tumor characteristics. Univariate analyses and multivariate logistic regression were performed. **RESULTS:** Overall, this study was similar to the SOUND trial in terms of demographics and tumor characteristics, as well as falsely negative preoperative AUS (12.2%) (Table). The remaining performance metrics of preoperative AUS were: sensitivity (20%), specificity (90%), PPV (28%), NPV (86%). Subgroup analyses did not reveal significant differences in performance metrics in either case. Positive SLNB was significantly different (p-value .003) when comparing pathologic T group (38% T2, 14% T1c, 12% T1b, and 0% T1mi/T1a). Median age was significantly different (p-value .017) when comparing receptor status group (Luminal A 65, Triple (-) 62, and HER2/neu(+) 56). On multivariate logistic regression, increasing age (p= 0.035, OR .95) and increasing BMI (p= 0.002, OR .90) were significant predictors of decreased false negative AUS. **CONCLUSIONS:** The high specificity and negative predictive value of AUS suggests that foregoing SLNB in small breast cancers with negative pre-operative AUS is reasonable, especially in patients with T1mi/ T1a and T1b tumors.

Table. Descriotive Statistics. Current Studv vs SOUND

Variable	Current Study n=270	SOUND (SLNB) n=708
Age		
<40	1 (.4%)	10 (1.4%)
40-49	22 (8%)	128 (18.4%)
50-64	116 (43%)	298 (42.8%)
≥65	131 (49%)	261 (37.4%)
Median(IQR)	64 (58-71)	60(51-68)
Menopausal Status		
Premenopausal	50 (19%)	145 (20.6%)
Postmenopausal	220 (81%)	558 (79.4%)
Histology		
Ductal	233 (86%)	551 (77.8)
Lobular	19 (7%)	61 (8.6%)
Tubular	6 (2%)	27 (3.8%)
Other	12 (5%)	69 (9.7%)
pT Group		
pT1mi or pT1a	25 (9%)	71 (10%)
pT1b	87 (32%)	25(35.5%)
pT1c	126 (47%)	355 (50.1%)
pT2	32 (12%)	31 (4.4%)
No. of Positive LNs		
0	194 (84.3%)	599 (84.6%)
1-3	35 (15.3%)	93 (13.1%)
4-9	0 (0%)	2 (0.3%)
≥10	0 (0%)	2 (0.3%)
NA	1 (.4%)	12 (1.7%)
SLNB		
Yes	230 (85%)	708 (100%)
No	40 (15%)	
pN Group		
pN0	239 (89%)	584 (82.5%)
pN1mi	2 (.7%)	36 (5.1%)
pN1	28 (10%)	57 (8.1%)
pN2	1 (.4%)	4 (.6%)
ER status		
Yes	228 (84%)	652 (92.1%)
No	42 (16%)	56 (7.9%)
PR status		
yes	215 (80%)	600 (84.7%)
no	55 (20%)	108 (15.3%)
HER2 status		
yes	18 (7%)	48 (6.8%)
no	252 (93%)	660 (93.2%)
False Negative Axillary US	**28 (12.2%)**	**109 (13.7%)**

P258. Factors Associated with Locoregional Recurrence after Neoadjuvant Chemotherapy for Breast Cancer in a Safety-Net Medical Center

Danielle Brabender, MD[1]; Deena Hossino, MD[2]; Sean Kim, MS[3]; Margaret Jayich, MD[4]; Lauren Polyakov, MS[5]; David Gomez, MS[6]; Azadeh Carr, MD[7]; Stephen Sener, MD[8]
[1]Los Angeles General Medical Center, University of Southern California, Los Angeles, CA, US; [2]Los Angeles General Medical Center, University of Southern California, Los Angeles, CA, US; [3]Los Angeles General Medical Center, University of Southern California, Los Angeles, CA, US; [4]Los Angeles General Medical Center, University of Southern California, Los Angeles, CA, US; [5]Los Angeles General Medical Center, University of Southern California, Los Angeles, CA, US; [6]Los Angeles General Medical Center, University of Southern California, Los Angeles, CA, US; [7]Los Angeles General Medical Center, University of Southern California, Los Angeles, CA, US; [8]Los Angeles General Medical Center, University of Southern California, Los Angeles, CA, US

INTRODUCTION: The management of locally advanced breast cancer poses significant challenges, with contemporary strategies involving an approach that combines systemic and local treatment. Prior data published from this center on 102 patients treated with neoadjuvant chemotherapy (NAC) from 2015-2020 demonstrated that pathologic complete response (pCR), node-negative status after NAC, and triple negative biomarker subtype were associated with relapse-free survival (RFS). The current study was performed to validate the clinical impression that local and regional recurrences have become increasingly uncommon after a standardized multimodal treatment protocol. **METHODS:** A retrospective analysis was performed using a single institution database that included clinical, radiographic, and pathologic parameters for all non-metastatic and non-inflammatory breast cancer patients treated with NAC from 2015-2023. Uni- and multivariable analyses were performed to define associations between clinical factors, recurrence, and RFS. Kaplan-Meier method was used with log-rank test to evaluate differences in time-to-event distributions. Cox proportional hazards model included covariates in analyses. **RESULTS:** The median age was 51 years for 274 predominantly Hispanic (78%) patients included in the study. Median follow-up was 38.1 months; 206 (75%) patients had post-mastectomy chest wall radiation and 172 (63%) had regional node irradiation. The recurrence rates were 4% local, 2% regional, and 18% distant. Median time from surgery to local recurrence was 8.2 months and to regional recurrence was 9.7 months. Factors associated with local and distant recurrence can be seen in Table 1. There were no local or regional clinical recurrences in 92 (34%) patients who had pCR or in 85 (31%) patients who had radiological complete response after NAC. Locoregional recurrences were uncommon greater than 12 months after surgery. Five of 11 local recurrences occurred in patients who had a poor response to NAC (ypT4b). All of the 6 patients having regional recurrences had adjuvant radiation therapy, and only 2 occurred in patients who were pathologically node negative (ypN0) post NAC. **CONCLUSIONS:** Favorable responses to NAC were associated with excellent locoregional control rates. Results achieved for predominantly Hispanic patients at a safety net medical center were similar to those reported in prospective randomized clinical trials.

Table 1. Multivariable analysis of factors associated with clinical local and distant recurrences in 274 patients treated with neoadjuvant chemotherapy, 2015-2023.

		Local Recurrence N = 11 (14%)	Distant Recurrence N = 48 (18%)
Variable[1]	Total N (%)	*p*-value	*p*-value
cT4b	21 (8%)		**0.010**
cT2	156 (57%)		0.979
ypT2	49 (18%)	**0.013**	**0.002**
ypT3	19 (7%)		**0.003**
ypT4b	6 (2%)	**<0.001**	
ER+ ER-	155 (57%) 119 (43%)		**0.012**
HER2+ HER2-	108 (39%) 168 (61%)		**0.024**
ER+HER2-	94 (34%)		0.058
ypN0	167 (61%)	**0.003**	**<0.001**
pCR	92 (34%)	**0.016**	**<0.001**
rCR	85 (31%)	**0.023**	**<0.001**
RNI	172 (63%)		**0.024**

[1]The following factors possibly associated with local and distant recurrence were submitted to univariable models: biomarkers, type of surgical procedure, T-category before and after NAC, focality of tumor, response to NAC (ypN0, pCR, and rCR), and delivery of adjuvant radiation (RNI and CWRT). Factors with a p-value <0.05 were tested in multivariable models. Factors remaining significant are in bold.

Abbreviations: CWRT (chest wall radiation therapy), ER (estrogen receptor), HER2 (human epidermal growth factor receptor type 2), NAC (neoadjuvant chemotherapy), pCR (pathologic complete response), rCR (radiographic complete response), RNI (regional node irradiation).

P259. Factors Associated with Neoadjuvant Chemotherapy Utilization in Patients with Early-Stage HER2-Positive Breast Cancer in the Era of the KATHERINE Trial

Lauren N Cohen[1]; Christine Rogers[2]; Jan IC Lloren, RN, MPH[3]; Sailaja E Kamaraju, MD, MS[4]; Lubna N Chaudhary, MD, MS[5]; Chiang-Ching Huang, PhD[6]; Adrienne N Cobb, MD, MS[7]; Amanda L Kong, MD, MS, FSSO, FACS[8]; Puneet Singh, MD, MS, FSSO, FACS[9]; Mediget Teshome, MD, MPH, FSSO, FACS[10]; Chandler S Cortina, MD, MS, FSSO, FACS[11]

[1]Medical College of Wisconsin, Milwaukee, WI, US; [2]Medical College of Wisconsin, Milwaukee, WI, US; [3]Zibler School of Public Health, University of Wisconsin-Milwaukee, Milwaukee, WI, US; [4]Medical College of Wisconsin, Milwaukee, WI, US; [5]Medical College of Wisconsin, Milwaukee, WI, US; [6]Zibler School of Public Health, University of Wisconsin-Milwaukee, Milwaukee, WI, US; [7]Medical College of Wisconsin, Milwaukee, WI, US; [8]Medical College of Wisconsin, Milwaukee, WI, US; [9]UT-MD Anderson Cancer Center, Houston, TX, US; [10]UCLA Medical Center, Los Angeles, CA, US; [11]Medical College of Wisconsin, Milwaukee, WI, US

INTRODUCTION: Advancements in targeted therapy for HER2+ breast cancer (BC) have revolutionized clinical practice and outcomes. In the early-stage node-negative setting, the APT trial (2015) reported excellent outcomes for patients with pathologically confirmed ≤3cm pN0 HER2+ BC who received adjuvant paclitaxel/trastuzumab while the KATHERINE trial (2019) reported improved survival for those who received adjuvant T-DM1 for residual disease after neoadjuvant chemotherapy (NAC), thus expanding NAC indications beyond surgical de-escalation. We aimed to determine national rates of NAC in cT1–2 N0 HER2+ BC before and after the KATHERINE trial and identify factors associated with receiving NAC. **METHODS:** A retrospective cohort study was performed using the NCDB from 2016–21. Women age ≥18 with cT1–2 N0 M0 HER2+ BC were included. ANOVA, Kruskal-Wallis, Chi-square, and Fisher's Exact tests were used for univariable analysis, and a multivariable logistic regression analysis identified predictive variables of receiving NAC *vs* AC. **RESULTS:** 54,449 women met inclusion: 30,546 (56.1%) received AC, 19,562 (35.9%) received NAC, and 4,341 (8%) received no chemotherapy. Median age was 58 years (IQR 48–66), most were NH-White (71.5%) with unilateral (99%) tumors of ductal histology (92.8%) and underwent lumpectomy (62.7%). NAC utilization increased over time from 31% in 2016–17 to 43% in 2020–21 ($p<0.01$) and was primarily driven by patients with cT1c and cT2 disease. On regression analysis, women diagnosed in 2020–21 had a higher odds of receiving NAC *vs* those diagnosed in 2016–17 (OR 1.9, 95% CI 1.8–2.0) (Figure 1). NH-Black patients were less likely to receive NAC *vs* NH-White patients (OR 0.87, 95% CI 0.8–0.95) as well as those age ≥70 *vs* age 50–69 (OR 0.7, 95% CI 0.6–0.8). Patients with more comorbidities were less likely to receive NAC (OR 0.7, 95% CI 0.5–0.9) as well as those with Medicare compared to those with private insurance (OR 0.8, 95% CI 0.7–0.8). Women with cT1a-c tumors had lower odds of receiving NAC compared to women with cT2 tumors ($p<0.01$ for all). **CONCLUSIONS:** From 2016–21, national rates of NAC in women with cT1–2 N0 HER2+ BC increased after publication of the KATHERINE trial. Lower NAC rates for those with cT1 tumors reflect the influence of the APT trial while those related to race/ethnicity, age, and insurance status highlight disparities in care. Future studies are needed to understand the drivers of these disparities within the evolving clinical landscape of HER2+ BC, particularly given the implications of NAC on survival outcomes in poor responders.

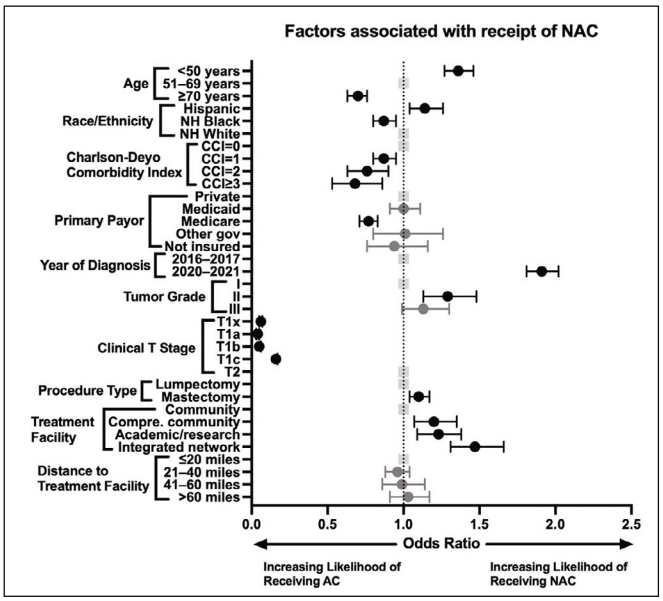


Figure 1. Factors associated with receipt of neoadjuvant chemotherapy vs adjuvant chemotherapy in cT1-2 N0 HER2+ breast cancer in the NCDB from 2016–2021.

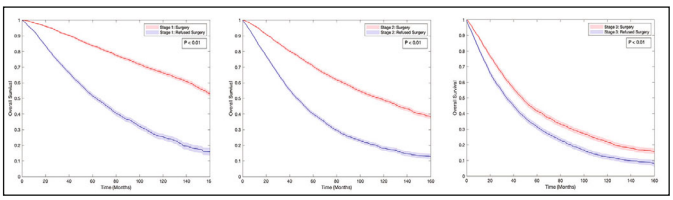
P260. Factors Associated with Refusal of Surgery in Stage I-III Breast Cancer and Their Effect on Survival

Gustavo Capo[1]; Malek Moumne[2]; Luke Guy[3]; Yagni Patel[4]; Carter Quinn[5]; Ryan Quisling[6]; Sohawm Sengupta[7]; Jonathan Palmer[8]; Danny Yakoub[9]; Alicia Arnold[10]

[1]Medical College of Georgia, Augusta, GA, US; [2]Medical College of Georgia, Augusta, GA, US; [3]Medical College of Georgia, Augusta, GA, US; [4]Medical College of Georgia, Augusta, GA, US; [5]Medical College of Georgia, Augusta, GA, US; [6]Medical College of Georgia, Augusta, GA, US; [7]Medical College of Georgia, Augusta, GA, US; [8]Medical College of Georgia, Augusta, GA, US; [9]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US; [10]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US

INTRODUCTION: Surgery remains a cornerstone of Breast Cancer (BC) treatment. Despite its survival benefit, some patients refuse surgery. We aim to identify factors influencing surgery refusal and their impact on median overall survival (OS). **METHODS:** The NCDB (2004-2020) was queried for stage I-III BC patients recommended for surgery. Patients who underwent surgery were compared to those who refused it. Logistic regression identified predictors of refusal. Propensity score matching (PSM) produced comparable groups. Kaplan Meir, Log Rank, and Cox models analyzed the effect of refusal on OS. Information on the type of surgery refused (lumpectomy or mastectomy) was unavailable. **RESULTS:** Of the 2,602,928 patients with BC recommended surgery, 16,003 (0.6%) refused it. The rate of surgery refusal increased from 0.25% in 2004 to 0.83% in 2020. Factors associated with an increased probability of surgery refusal include age >50 (OR=1.29), non-Hispanic Black (OR=2.10), tumor size 2-4.99cm (OR=1.56) and 5+cm (OR=2.33), radiation refusal (OR=91.70), chemotherapy refusal (OR=14.48) and TNM stage 2 (OR=1.74) and stage 3 (OR=3.04). Factors associated with a

decreased probability of surgery refusal include a Charleson comorbidity index (CCI) of 1 (OR=0.71), Private insurance (OR=0.29), Medicaid (OR=0.69), Medicare (OR=0.65), living in the South (OR=0.64) or West (OR=0.80), urban residence (OR=0.83), rural residence (OR=0.72), 50-200 mile commute to care center (OR=0.68), treatment in non-academic centers (HR=0.8) and triple-negative receptor status (OR=0.75). Kaplan Meir and Log Rank analysis of PSM groups showed decrease OS in surgery refusal groups across all stages (Fig. 1): Stage 1 [168 vs 63 mos. HR=3.86], Stage 2 [116 vs 46 mos. HR=2.63] and Stage 3 [47 vs 33 mos. HR=1.40]. Factors associated with decreased OS in patients who refused surgery include age >50 (HR=1.40), CCI 2+ (HR=1.71), Medicare insurance (HR=1.58), resided in the Midwest (OR=1.08), treatment at non-academic center (HR=1.2), tumor size >5cm (HR=1.31), enrollment in palliative care (HR=1.57), refusal of radiation (HR=1.25), refusal of chemotherapy (HR=1.54), triple-negative receptor status (HR=1.98), TNM stage 2 (HR=1.24) and stage 3 (HR=1.67). Factors associated with increased OS in patients who refused surgery include non-Hispanic Black (HR=0.80), Hispanic White (HR=0.77) and living in the West (HR=0.93). All variables met statistical significance (P<0.01). **CONCLUSIONS:** Surgery is associated with improved survival in stage I-III BC. Targeted intervention can mitigate factors associated with surgery refusal to improve outcomes.



P261. Frailty and Postoperative Complications in Older Adults with Non-Metastatic Breast Cancer

Eliza H Lorentzen, MD[1]; Yu-Jen Chen, MPH[2]; Claire Morton, MD[3]; Tari A. King, MD[4]; Elizabeth A Mittendorf, MD, PhD, MHCM[5]; Christina A Minami, MD, MS[6]

[1]Brigham and Women's Hospital/Dana-Farber Brigham Cancer Center, Boston, MA, US; [2]Brigham and Women's Hospital Center for Surgery and Public Health, Boston, MA, US; [3]Brigham and Women's Hospital Center for Surgery and Public Health, Boston, MA, US; [4]Brigham and Women's Hospital/Dana Farber Brigham Cancer Institute, Boston, MA, US; [5]Brigham and Women's Hospital/Dana-Farber Cancer Institute, Boston, MA, US; [6]Brigham and Women's Hospital/Dana Farber Brigham Cancer Center, Boston, MA, US

INTRODUCTION: Frailty, a condition marked by increased vulnerability to stressors, is associated with increased postoperative complication (POC) rates in major operations. However, the relationship between frailty and POCs after breast surgery, which is lower risk, remains unclear. We examined the association between frailty and POCs in older breast cancer patients undergoing upfront surgery. **METHODS:** Women ≥70 years with non-metastatic invasive breast cancer diagnosed 2013-2015 were identified in the SEER-Medicare dataset. Patients who had neoadjuvant treatment or reconstructive surgery were excluded. Frailty was defined by a validated claims-based measure. Systemic and local complications within 90 days of the index procedure were identified using claims data. Local complications included surgical site infection, seroma, hematoma, and other wound complications. Systemic complications included sepsis, pneumonia, urinary tract infection, myocardial infarction, deep vein thrombosis, and pulmonary embolism. Multivariable logistic regression was used to identify patient- and disease-specific covariates associated with POCs. **RESULTS:** Of 6,308 patients, 6.2% were frail. Compared to non-frail patients, a greater proportion of frail patients were ≥85 years (frail: 19.3% v. non-frail: 13.4%, p<0.001), had a Charlson Comorbidity Index ≥2 (frail: 64.7% v. non-frail: 16.5%, and underwent mastectomy (frail: 56.0% v. non-frail: 49.3%, p<0.001). A greater proportion of frail patients experienced systemic and local POCs (Table). On multivariable analysis, frailty was significantly associated with a higher odds of local POCs (OR 1.57, 95% CI [1.22 – 2.02]) and systemic POCs (OR 2.10, 95% CI [1.63 – 2.71]). Undergoing mastectomy compared to lumpectomy was also associated with a higher odds of local (OR 2.12, 95% CI [1.86-2.44]) and systemic (OR 1.19, 95% CI [1.02-1.49]) POCs. Chronological age was not significantly associated with a higher odds of local POCs, but age >80 years was associated with higher odds of systemic POCs compared to age 70-74 years (80-84 years: OR 1.40, 95% CI [1.13-1.72]; ≥85 years: OR 1.49, 95% CI [1.18-1.89]). **CONCLUSIONS:** The odds of local and systemic POCs was significantly greater in frail patients compared to non-frail patients, particularly among those undergoing mastectomy. These data suggest that both frailty and scope of surgery should be factored into treatment decision-making in older adults with breast cancer.

P262. Geographic Differences in Patient Experience after a Diagnosis of Lobular Breast Cancer

Alexis Graham-Stephenson, MD[1]; Esther Geven[2]; Jasmine Walker, MD, MPH[3]; Flora Migyanka[4]; Michelle Riba, MD[5]; Jacqueline Jeruss, MD, PhD[6]

[1]University of Michigan, Ann Arbor, MI, US; [2]European Lobular Breast Cancer Advocates, Netherlands, Utrecht, NL; [3]University of Michigan, Ann Arbor, MI, US; [4]The Dynami Foundation, Plymouth, MI, US; [5]University of Michigan, Ann Arbor, MI, US; [6]University of Michigan, Ann Arbor, MI, US

INTRODUCTION: Invasive lobular carcinoma (ILC) is a subtype of breast cancer with a distinct morphology and potential complex impact on clinical outcomes, including differences in detection, response to treatment, and tumor recurrence. Geographic disparities in breast cancer diagnosis and management may further contribute to the significant psychological stress encountered by ILC patients throughout their treatment course. The aim of our study was to identify factors that may negatively affect psychological wellbeing and highlight the unique experiences of ILC patients during diagnosis, treatment, and follow up. **METHODS:** A 31-item online questionnaire was created for distribution to three moderated patient groups whose members identified as having an ILC. The partially adaptive survey, consisted of demographic, Likert, multiple choice, and free response questions regarding patient experiences with ILC diagnosis, treatment, and follow up. Statistical analysis was performed using Chi-square, Mann-Whitney U, and unpaired two-sample t-testing. P-values <0.05 were considered significant. Free response answers were individually analyzed for identification of themes. **RESULTS:** A total of 902 participants from eighteen countries in Europe (n = 261) and North America (n = 614) responded to the survey. Mean age at diagnosis between the patient populations was similar (51.8 and 53.1, p = 0.075). Stage at diagnosis in European vs North American patients was I: 6 vs 33%, II: 15 vs 20%, III: 5 vs 11%, IV: 1 vs 3%. European patients had more advanced disease on presentation; as such, initial treatment recommendations were more likely to include chemotherapy (p <0.001) and radiation (p <0.001) in contrast to patients from North America. European respondents reported less emotional support from family (p = 0.003), employers, (p = 0.004), and healthcare providers (p <0.001) relative to their North American counterparts. Despite lower overall disease stage, North American respondents reported decreased confidence in medical follow up accuracy (p <0.001). Themes of anxiety, misinformation, lack of bodily autonomy, and perceived dismissal by healthcare providers were shared between groups, as was the concept of self-advocacy as a tool for empowerment and reestablishing a sense of control. **CONCLUSIONS:** While unique differences do exist between regions, certain negative psychological implications associated with an ILC diagnosis are universal. Results of this study offer insight into opportunities for global improvement in the management of ILC, including improved screening approaches and psychological support.

P263. Impact of Electronic (E-) Cigarette Vaping on Postoperative Wound Healing and Surgical Site Infections Following Mastectomy: A Propensity Score-Matched Analysis

Lauren T Kerivan, MD, MSc[1]; Terra M Hill, MD, MSc[2]; Diego R Mazzotti, PhD[3]; Kelsey E Larson, MD, FACS[4]

[1]University of Kansas Medical Center, Kansas City, KS, US; [2]University of Kansas Medical Center, Kansas City, KS, US; [3]University of Kansas Medical Center, Kansas City, KS, US; [4]University of Kansas Cancer Center, Overland Park, KS, US

INTRODUCTION: Cigarette smoking is an independent risk factor for postoperative wound complications. As electronic (E)-cigarettes gain popularity as "cleaner" alternatives to conventional cigarettes, there is a critical need for evidence on the risk profile of pre-procedural vaping. The aim of this study was to evaluate the impact of vaping on postoperative surgical site complications after mastectomy. **METHODS:** A retrospective, propensity score-matched cohort study of all women who underwent mastectomy without reconstruction at a single academic institution from 2020 to 2024 was performed. Patients with active vape use were matched with non-vaping patients in a 1:3 ratio based on demographic, clinical, and operative characteristics. Cohorts were compared using conditional logistic regression. The primary outcome was 30-day postoperative wound complications, including surgical site infection (SSI),

dehiscence, and necrosis. **RESULTS:** A total of 1,109 women were eligible for review, comprising 39 vapers and 1,070 non-vapers. Using propensity scores, 33 vapers were matched to 99 non-vapers. In the matched cohort, there was a significant positive association between pre-procedural vaping and 30-day postoperative wound complications (OR, 4.57; 95% CI, 1.48-14.13; P = 0.008). Vaping was associated with a significantly increased odds of SSI (OR, 6.60; 95% CI, 1.84-23.61; P = 0.004) and necrosis (OR, 6.96; 95% CI, 0.32-40.18; P = 0.03). No difference was found in the odds of dehiscence (OR 2.87; 95% CI, 0.64-12.83; P = 0.169). **CONCLUSIONS:** To our knowledge, this is the first cohort study to not only investigate the impact of perioperative vaping on surgical site complications, but also demonstrate an increased risk of 30-day complications in vapers who undergo mastectomy. Additional studies are needed to determine the impact of vaping on patients undergoing post-mastectomy reconstruction.

P264. Impact of screening mammography on breast cancer outcomes in women age 80 and over?

Siu-Yuan Huang, MD[1]; Makaelah Murray[2]; Angelique Rubio[3]; Nneoma Okoro[4]; Mina Sedrak[5]; Mediget Teshome, MD, MPH, FACS[6]; Susan A McCloskey, MD[7]; Nicholas J Jackson[8]; Nimmi S Kapoor, MD, FACS[9]

[1]University of California Los Angeles, Los Angeles, CA, US; [2]University of California Los Angeles, Los Angeles, CA, US; [3]University of California Los Angeles, Los Angeles, CA, US; [4]University of California Los Angeles, Los Angeles, CA, US; [5]University of California Los Angeles, Los Angeles, CA, US; [6]UCLA Medical Center, Los Angeles, CA, US; [7]University of California Los Angeles, Los Angeles, CA, US; [8]University of California Los Angeles, Los Angeles, CA, US; [9]University of California Los Angeles, Los Angeles, CA, US

INTRODUCTION: Age remains a significant risk factor for the development of breast cancer with implications on the aging population in the United States (US). While screening mammography is important for early detection, the US Preventive Services Task Force offers no specific screening mammography recommendations for women age>75 years of age given insufficient evidence. We sought to identify differences in outcomes among newly diagnosed breast cancer patients aged ≥80 years old based on receipt of screening mammography. **METHODS:** Retrospective review identified women with breast cancer diagnosed at ≥80 years of age from 2013-2020. Patients who received a screening mammogram within 2 years of diagnosis defined the screened cohort. Patients were excluded if they had a previous diagnosis of breast cancer. Data was collected on patient demographics, type and number of comorbidities, mammography timing, symptoms, tumor characteristics, treatment, and outcomes. Characteristics of the screened cohort were compared to the unscreened cohort with Chi-square and t tests. Kaplan-Meier survival analysis and log-rank testing was performed to compare overall survival and disease-free survival. **RESULTS:** Of 249 patients identified, 177 women met inclusion criteria, of which 74 (41.8%) were in the screened cohort and 103 (58.1%) were unscreened. Median age at diagnosis was 83 years (range 81-98), most patients were White (69%), had stage I or II tumors (73%), and most cancers were ER+HER2- (77%). The groups did not significantly differ in race/ethnicity, Area Deprivation Index, number of comorbidities, receptor status, axillary surgery, or receipt of endocrine therapy, adjuvant chemotherapy, or radiation. The unscreened cohort was more likely to have diabetes (25.6% vs 8.8%, p=0.025), palpable tumors (91% vs 9%, p<0.001), higher grade tumors (p < 0.001), and more advanced stage (p < 0.001). More patients in the screened cohort underwent breast conserving surgery (82.4% vs 60.6%), while more patients in the unscreened cohort either had mastectomy or did not undergo surgery (38.8% vs 17.6%, p = 0.009). With median follow-up of 55 months (range 1-146 months), the screened cohort had improved disease-free survival (DFS) (HR 0.53, 95% CI, 0.361-0.778, p = 0.001) and overall survival (OS) (HR 0.37, 0.170-0.804, p = 0.012). **CONCLUSIONS:** Women ≥ 80 years old diagnosed with breast cancer who received screening mammography presented with earlier stage disease and had improved DFS and OS compared to those who were not screened. In the context of an aging population, further studies to define specific guidelines for breast cancer screening in older women should be considered.

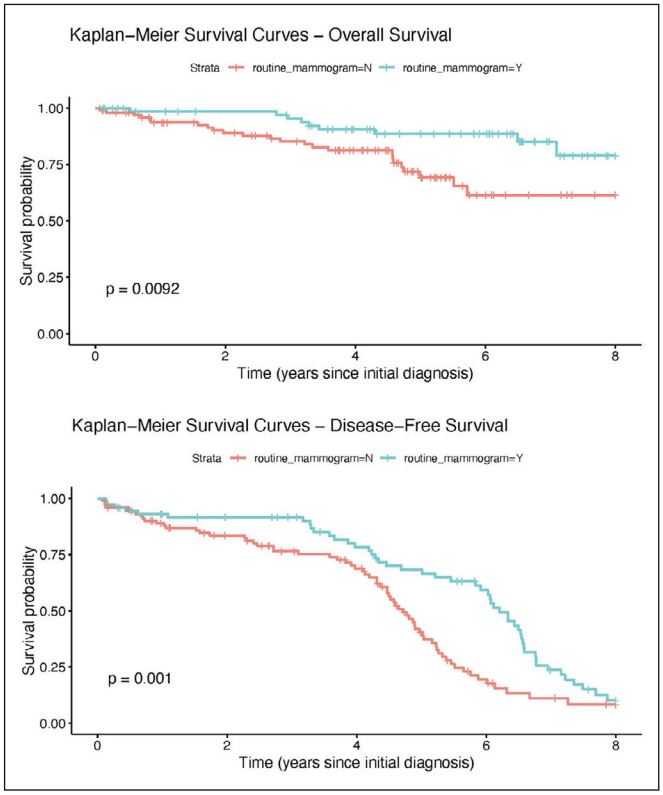


Figure. Impact of screening mammography on breast cancer outcomes in women aged 80 and over

P265. Intratumorally delivered conventional type I dendritic cells in de novo stage 4 HER2 breast cancer patients lead to reduction in primary breast cancer and metastasis

Paige Aiello, MD[1]; Aixa E Soyano, MD[2]; Robert J Weinfurtner, MD[3]; Nazanin Khakpour, MD[4]; Susan Hoover, MD[5]; John Kiluk, MD[6]; Carly Farrell, PA-C[7]; Brian Czerniecki, MD, PhD[8]

[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4]Moffitt Cancer Center, Tampa, FL, US; [5]Moffitt Cancer Center, Tampa, FL, US; [6]Moffitt Cancer Center, Tampa, FL, US; [7]Moffitt Cancer Center, Tampa, FL, US; [8]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Locoregional treatment of the breast primary in de novo metastatic breast cancer (dMBC) is controversial. Randomized controlled studies have shown no survival benefit, nor improvement in quality of life, with extirpative surgery of the primary tumor compared to systemic therapy. Intratumoral (IT) delivery of type I polarized dendritic cells (cDC1) pulsed with MHC class derived HER2 peptides combined with anti-HER2 antibodies has resulted in regression of primary tumors and metastasis in HER2 preclinical models and in early-stage breast cancer (BC) patients. We performed single patient exemption trials in several patients with HER2 dMBC using IT cDC1. **METHODS:** Newly diagnosed patients with HER2 dMBC were offered single patient FDA and IRB approved protocols with six weekly ultrasound-guided autologous intratumoral cDC1 injections (100 or 200 million cDC1 per injection). Patients were administered standard trastuzumab and pertuzumab (TP) every 3 weeks. Breast imaging with mammogram or MRI as well as systemic imaging was performed pre and post treatment to assess response to treatment. All patients received Taxotere, trastuzumab, pertuzumab (THP) following this regimen. **RESULTS:** Two female patients with dMBC, both <30 years old, have been treated prior to standard THP. Intratumoral cDC1 and TP was safe with little toxicity. Side effects included fevers, chills, headache, and injection site soreness typical of cDC1 injections. Both patients demonstrated significant reduction of primary breast cancer based on mammogram or MRI prior to standard therapy. Both patients also demonstrated systemic responses including bone, skull, spine and liver metastases as demonstrated by CT and MRI following the 6-week therapy. Both patients remain asymptomatic with minimal stable disease 9 months and 12 months following therapy. **CONCLUSIONS:**

Surgical resection of the primary tumor in dMBC does not improve mortality or quality of life. This study suggests the primary tumor can instead be used for delivery of intratumoral cDC1 to help control local disease while also impacting systemic disease. These encouraging results warrant further investigation of cDC1 in HER2 dMCB.

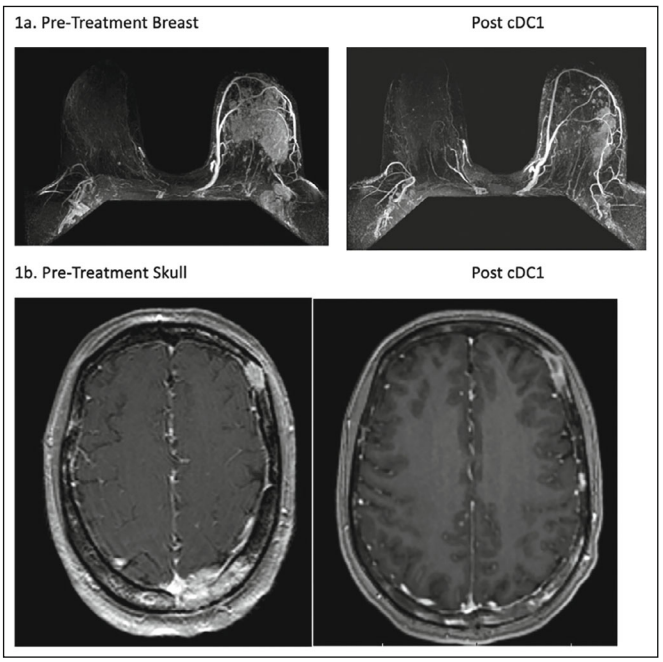


Figure 1a is a breast MRI of 30yo female pre and post treatment with cDCl vaccine treatment. Figure 1b is a brain MRI of 25 Y.52. female pre and post treatment with cDCl vaccine treatment.

P266. Is neoadjuvant chemotherapy justified in patients with TNBC or HER2+ disease presenting with a mammogram showing only calcifications spanning = 1 cm?

Max O. Meneveau, MD, MS[1]; Varadan Sevilimedu, MBBS, DrPH[2]; Sarah Eskreis-Winkler, MD, PhD[3]; Tiana Le[4]; Monica Morrow, MD[5]
[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Neoadjuvant chemotherapy (NAC) is recommended for patients with node-negative triple-negative (TN) or HER2+ breast cancer ≥ 2 cm in size (≥ T2) and is considered for those with 1-2 cm tumors (T1c). When the only mammographic finding is calcifications spanning ≥ 1 cm, it is unclear whether NAC is appropriate due to uncertainty regarding the invasive tumor size. We hypothesized that most of these patients do *not* have ≥ pT1c disease and should be treated with upfront surgery, and examined the utility of clinicopathologic/imaging features to identify patients suitable for NAC. **METHODS:** Women with TN or HER2+ invasive breast cancer presenting with a mammogram showing calcifications only spanning ≥ 1 cm were identified in our institutional database. Patients who received NAC were excluded. Extent of calcifications, US, and MRI findings were compared with final pathologic tumor size. **RESULTS:** The cohort included 126 patients with a median age of 54 years (IQR 47, 63); 83% (n = 104) had HER2+ tumors and 17% (n = 22) TN tumors. US and MRI were done in 83 (66%) and 52 (41%) patients, respectively. An US mass (median size 0.55cm, IQR 0.43, 0.80) was present in 26 (21%). 18 (14%) had an MRI mass (median size 0.8 cm, IQR 0.53, 1.00) and 36% had non-mass enhancement (NME) (median size 3.5 cm, IQR 1.80, 5.10). Median pathologic invasive tumor size was 0.6 cm (IQR 0.17, 1.00) and 9 patients (7.2%) had positive nodes. 27% (n = 34) had invasive tumors ≥ 1 cm. There were few differences in baseline characteristics (Table) between patients with invasion ≥ 1 cm and < 1 cm. Microinvasive disease on biopsy (n = 46, 37%) was more common among those with < 1 cm tumors (46% vs 12%, $p < 0.001$). Neither US nor MRI findings were associated with tumors > 1 cm. Among patients with more than microinvasion on biopsy, mass on MRI ($r = 0.65$, $p < 0.01$), but not extent of NME, US mass, or extent of calcifications was significantly correlated with invasive tumor size. Overall, 65% of patients received adjuvant chemotherapy. **CONCLUSIONS:** The majority of TN and HER2+ patients with calcifications > 1 cm on mammogram have invasive cancers < 1 cm in size. Extent of calcifications, US findings, and NME on MRI do not correlate with final invasive tumor size and should not be used in the decision to offer NAC. The size of a mass on MRI is significantly correlated with invasive tumor size, indicating this test is useful for clinical decision making when the biopsy shows more than microinvasion. The use of NAC in this population would have resulted in overtreatment of 35% of patients.

Characteristic	N	Invasive size < 1 cm (N = 92)[1]	Invasive size ≥ 1 cm (N = 34)[1]	p-value[2]
Age	126	54 (47, 63)	54 (51, 59)	0.9
Race	121			>0.9
Asian/other		14 (16%)	6 (18%)	
Black		8 (9.1%)	3 (9.1%)	
White		66 (75%)	24 (73%)	
Other		4 (4.3%)	2 (5.9%)	
Ethnicity	120			0.7
Not Hispanic		82 (93%)	29 (91%)	
Hispanic or Latino		6 (6.8%)	3 (9.4%)	
Peri/Postmenopausal	126	63 (68%)	25 (74%)	0.9
Microinvasive disease on biopsy	125	42 (46%)	4 (12%)	**<0.001**
Ductal histology	126	85 (92%)	30 (88%)	0.3
Receptor status	126			0.6
HER2+		77 (84%)	27 (79%)	
Triple Negative		15 (16%)	7 (21%)	
Span of calcifications (cm)	126	3.05 (1.98, 4.80)	3.60 (2.23, 7.00)	0.2
Ultrasound performed	126	60 (65%)	23 (68%)	0.8
Ultrasound mass size (cm)	26	0.55 (0.43, 0.80)	0.70 (0.55, 0.90)	0.3
MRI performed	126	41 (45%)	11 (32%)	0.2
MRI mass size	18	0.75 (0.53, 0.98)	1.90 (0.98, 2.55)	0.2
MRI NME size	45	3.90 (1.60, 5.15)	3.05 (3.00, 4.80)	>0.9
Invasive tumor size (cm)	126	0.30 (0.10, 0.70)	1.60 (1.20, 2.30)	**<0.001**
Operation	126			>0.9
Lumpectomy		47 (51%)	17 (50%)	
Mastectomy		45 (49%)	17 (50%)	
SLNB positive	126	4 (4.3%)	5 (15%)	0.054
Chemotherapy	126	52 (57%)	30 (88%)	**<0.001**
Mutation carrier	126	2 (2.2%)	2 (5.9%)	0.3

[1] n (%); Median (IQR)
[2] Fisher's exact test; Wilcoxon rank sum test; Pearson's Chi-squared test
Abbreviations: HER2, human epidermal growth factor receptor 2; NME, non-mass enhancement; SLNB, sentinel lymph node biopsy

P267. Is there a shift in standard axillary treatment of pathologic stage T3N1 breast cancer by US surgeons after the introduction of Z0011 and AMAROS?

Tiffany Nevill, MD[1]; Julie Peck, MBBS BAO[2]; Sindi Diko[3]; Ashley Stuckey, MD[4]; Micaela Weaver, DO[5]; Jamie Patterson, MD[6]; Stephanie Ng, MD[7]; Medhavi Gupta, MD[8]; Jennifer Gass, MD[9]; David Edmonson, MD[10]
[1]Women and Infants hospital, US; [2]Women and Infants hospital and Brown University, Providence, RI, US; [3]Wake Med hospital, US; [4]Women and Infants hospital, US; [5]Women and Infants hospital, US; [6]Women and Infants hospital, US; [7]Women and Infants hospital, US; [8]Women and Infants hospital, US; [9]Women and Infants hospital, US; [10]Women and Infants hospital, US

INTRODUCTION: Anecdotally there appears to be a shift in the standard treatment for breast cancer patients with pathologic stage T3N1 invasive disease after the introduction of Z011 and AMAROS trials. Currently the National Comprehensive Cancer Network (NCCN) recommends axillary dissection for breast cancer patients with pathologic T3N1 disease. We wanted to ascertain whether AMAROS and Z011 are being applied to upfront surgical candidates who subsequently had pathologic stage T3N1 disease versus the standard of axillary dissection. The primary goal is to assess whether there has been a de-escalation of surgical interventions within the axilla for this sub-group of patients. **METHODS:** We used the National Cancer Database (NCDB) to survey breast cancer patients who were clinically node negative and candidates for up-front surgery between 2012 and 2017. Baseline demographics, tumor characteristics and adjuvant treatments were analyzed with post Hoc Chi-Square comparisons were used with a Bonferoni adjustment for multiple responses where applicable using SPSS Version 28.0.1.1(15). **RESULTS:** We examined 723 patients who met our criteria and divided them into 4 groups: 1) those that underwent axillary dissection and nodal radiation, 2) those that underwent axillary dissection and no nodal radiation, 3) those that underwent sentinel lymph node biopsy and nodal radiation and 4) those that underwent sentinel lymph node biopsy without nodal radiation. We found that of the 723 people, 235 received axillary lymph node dissection with nodal radiation, 237 received axillary dissection without nodal radiation, 98 received sentinel lymph node biopsy with nodal radiation and 153 received sentinel lymph node biopsy without nodal radiation. A third of patients (34.72%)

received sentinel lymph node biopsy with or without nodal radiation with a final pathologic stage T3N1, which would not have been a surgical option before Z0011 and AMAROS were published and adopted. The mean age at diagnosis for all four groups was 62, with the youngest cohort, 57 years, being the axillary dissection with axillary nodal radiation group, this was statistically significant (p value 0.014). We also noted that although there was a change in the number of axillary dissections performed between 2012 and 2017, 109 versus 43, respectively, it was not statistically significant. There was a significant drop from 53 patients to 39 patients in Group 2 between 2013 and 2015 (p= 0.039). **CONCLUSIONS:** After the introduction and implementation of Z011 and AMAROS trials there was a change in surgical care of the axilla. The guideline to exclude complete axillary dissection for N1 patients has been associated with a reduction in axillary dissection for patients with or without the addition of axillary radiation to standard protocol. This standard is now being applied to upfront surgical candidates with pathologic T3 tumors reducing the use of axillary dissections and morbidity associated with this intervention.

P268. Locally Ablative Therapies in the Setting of Oligometastatic Breast Cancer: Therapeutic or Palliative?

Tori Chanenchuk[1]; Samantha M Thomas, MS[2]; Astrid Botty van den Bruele[3]; Ton Wang[4]; Laura H Rosenberger, MD[5]; Meghan R Flanagan, MD, MPH[6]; Gayle DiLalla[7]; E. Shelley Hwang, MD, MPH, FSSO[8]; Jennifer K Plichta, MD[9]
[1]Duke University Medical Center, Durham, NC, US; [2]Duke University, Durham, NC, US; [3]Duke University Medical Center, Durham, NC, US; [4]Duke University Medical Center, Durham, NC, US; [5]Duke University Medical Center, Durham, NC, US; [6]University of Washington, Seattle, WA, US; [7]Duke University Medical Center, Durham, NC, US; [8]Duke University, Durham, NC, US; [9]Duke University Medical Center, Durham, NC, US

INTRODUCTION: Current management of de novo metastatic breast cancer (dnMBC) focuses on symptom management, rather than cure. The potential benefits of surgical and/or ablative therapy for oligometastatic disease remain unclear. We aim to investigate the potential association of surgery and/or ablative therapy of the primary tumor and/or metastatic sites with overall survival (OS) among patients with dnMBC involving a single metastatic site. **METHODS:** Patients diagnosed with single site (brain, bone, liver, or lung) dnMBC who received at least one systemic therapy were selected from the National Cancer Database (2010-2021). Study groups were no locally ablative therapy/surgery (NLT), resection of breast primary only (BR), ablative therapy of distant mets only (MT), or resection of breast primary and ablative therapy of distant mets (BR+MT). Prognostic stage groups assigned as previously defined (PMID: 36944149). Logistic regression identified factors associated with treatment group; odds ratios (ORs) and 95% confidence intervals (CIs) reported. OS was estimated (Kaplan-Meier) and compared (log-rank tests). Cox proportional hazards estimated treatment group association with OS after adjustment for covariates; hazard ratios (HR) and CIs reported. **RESULTS:** Of the 22,433 patients included, median follow-up was 61.5 months. Bone-only mets were most common (68.8% vs lung-only 17%, liver-only 13.3%, brain-only 0.9%). Most had stage IVB disease (71.4% vs IVA 7.6%, IVC 13.1%, IVD 7.8%). Receiving surgery/locally ablative therapies was uncommon (BR+MT 6.4%, MT 10.6%, BR 15.3% vs NLT 67.7%). After adjustment, patients were more likely to receive NLT if they were older (Ref age <50 vs 70+, OR 2.49, 95% CI 2.24-2.76) or had a higher comorbidity score (Ref score 0 vs 2+, OR 1.36, 95% CI 1.16-1.60). Stratifying by stage, the unadjusted OS varied with those undergoing BR or BR+MT having the most favorable outcomes (all log rank p<0.001; Figure). Adjusting for demographic and clinical factors, treatment group was associated with survival, including better OS for those who received BR (Ref NLT vs BR, HR 0.62, 95% CI 0.58-0.67; BR+MT, HR 0.60, 95% CI 0.54-0.67) and worse OS for MT (HR 1.22, 95% CI 1.14-1.31). **CONCLUSIONS:** A minority of patients with dnMBC confined to a single site undergo surgical or ablative therapy, although BR+MT and BR-only were associated with improved OS. Our findings suggest that if invasive interventions are considered for patients with dnMBC and limited disease, resection of the breast primary may be beneficial.

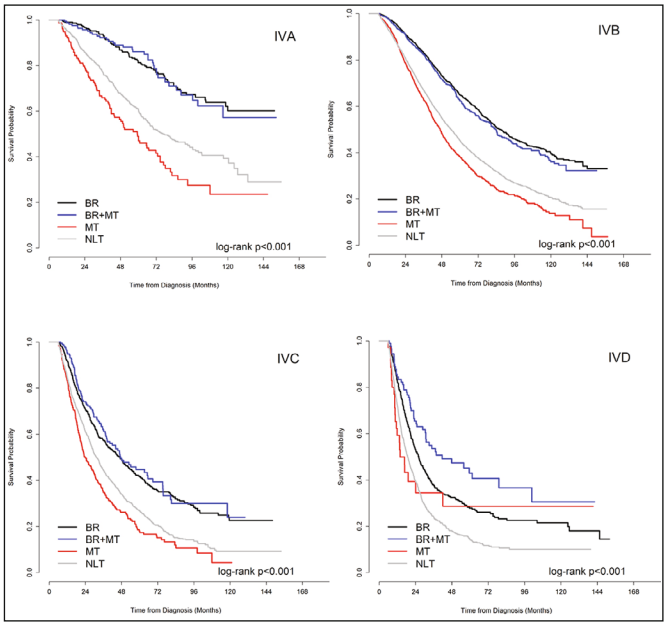


Figure. Overall Survival by Treatment Group within Stage (IVA-IVD)

P269. LumiSystem-guided lumpectomy enables informed customization of radiation therapy in select patients with breast cancer.

Brian Schlossberg, PhD[1]; Simona Shaitelman, MD[2]; Roberto Diaz, MD, PhD[3]; Kate Smith, MPH[4]; Jorge M Ferrer, PhD[5]; Kelly K. Hunt, MD, FSSO[6]; David Carr, MD[7]; Peter Blumencranz[8]; E. Shelley Hwang, MD, MPH, FSSO[9]; Irene Wapnir[10]; Barbara Smith, MD, PhD[11]
[1]Lumicell, Newton, MA, US; [2]MD Anderson Cancer Cneter, Houston, TX, US; [3]H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, US; [4]lumicell, newton, MA, US; [5]Lumicell, Newton, MA, US; [6]MD Anderson Cancer Center, Houston, TX, US; [7]Novant Health, Winston-Salem, NC, US; [8]Baycare Morton Plant Hospital, Clearwater, FL, US; [9]Duke University, Durham, NC, US; [10]Stanford Medical Cancer Center, Palo Alto, CA, US; [11]Massachusetts General Hospital, Boston, MA, US

INTRODUCTION: Adjuvant radiotherapy is standard of care (SOC) for most lumpectomy patients. There is an increasing emphasis on de-escalation/ omission of radiotherapy, so achieving the most complete tumor resection is critical to minimize the risk of recurrence. The LumiSystem has been shown to remove residual cancer missed by SOC and reduce the positive margin rate. We evaluated whether eligibility for de-escalation/omission of radiotherapy changed based on the LumiSystem intervention. **METHODS:** In this trial, we assessed margin status before and after LumiSystem-guided surgery for patients with stage 0-3 breast cancer. After surgeons completed SOC, patients were randomized 10:1 to receive additional LumiSystem-guided surgery. Eligibility for de-escalation/ omission of radiotherapy, both after SOC and after LumiSystem intervention, were retrospectively determined based on eligibility criteria from level I evidence and Practice Guidelines. **RESULTS:** A retrospective chart review was performed by two independent breast specialized radiation oncologists for the 166/357 (46.5%) patients that had additional LumiSystem-guided excisions taken. 77/166 (46.4%) patients (age: median - 66 yr., range - 51-82 yr.) were eligible for omission after SOC. 9/77 (11.7%) patients (age: median 51 yr., range 51-77 yr.) who were eligible for omission of radiotherapy following standard lumpectomy had residual tumor removed in subsequent LumiSystem-guided excisions. These residual tumor deposits included grade 3 histology and ranged from 1-11mm in size. 33/166 (19.9%) patients had a positive margin after standard lumpectomy, and 9/33 (27.3%) of these patients were converted to negative margins intraoperatively by LumiSystem-guided wider negative margins. 3/33 (9.1%) patients with positive SOC margins (age: median - 57 yr., range 54-73 yr.) had a change in eligibility for omission of radiotherapy based on LumiSystem-guided wider negative margins, and 2/33 (6.1%) patients also became eligible for smaller volumes of accelerated partial breast irradiation. **CONCLUSIONS:** LumiSystem-guided surgery altered radiation therapy recommendations in a subset of patients and resulted in removal of unsuspected residual tumor from patients who were eligible for

omission of adjuvant radiotherapy based on SOC negative margins. Using LumiSystem as an adjunct to standard lumpectomy may lead to the potential of the reducing targeted volume of radiation therapy and the option to omit radiation in additional patients.

P270. Mastectomy and Contralateral Prophylactic Mastectomy for Ipsilateral Breast Tumor Recurrence: Influence of Genetic Testing and Other Factors

Candice N. Santoro, DO[1]; Courtney N. Day, MS[2]; Jenna L. Sturz-Ellis, DO[3]; Tina J. Hieken, MD[4]; Mary M. Mrdutt[5]

[1]Mayo Clinic, Rochester, MN, US; [2]Mayo Clinic, Rochester, MN, US; [3]Mayo Clinic, Rochester, MN, US; [4]Mayo Clinic, Rochester, MN, US; [5]Mayo Clinic, Rochester, MN, US

INTRODUCTION: Surgical management of ipsilateral breast tumor recurrence (IBTR) is commonly mastectomy. No guidelines currently address contralateral prophylactic mastectomy (CPM) for patients (pts) with IBTR, and limited data exists on factors contributing to patient decision-making in this scenario. We assessed factors associated with CPM performed at time of mastectomy for IBTR. **METHODS:** With IRB approval, pts diagnosed with an IBTR undergoing mastectomy in 10/2008-5/2024 were identified from a prospective surgical database. Pts with synchronous distant disease or in whom IBTR was not the first recurrence were excluded. Pt demographics, genetic testing results, tumor characteristics of index cancer and IBTR, and operative details were assessed. Statistical analysis was performed with Chi-squared, Fisher's exact, Wilcoxon, and Cochran Armitage trend tests, as appropriate. **RESULTS:** We identified 405 pts with 406 IBTRs treated with mastectomy. 13 pts with prior contralateral mastectomy and 18 pts with contralateral mastectomy for contralateral cancer synchronous with IBTR were excluded. Of 375 remaining pts, 218 pts (58.1%) were treated with unilateral mastectomy (UM) and 157 (41.9%) with mastectomy and CPM. CPM pts were younger (median age 60.2 vs 69.4, p<0.0001) and more often had recurrent DCIS (30.1 vs 19.1%, p=0.0005), ER- invasive tumors (25.4% vs 15%, p=0.03), or HER2+ invasive tumors (15.1% vs 8.4%, p=0.08). CPM pts were more likely to undergo germline genetic testing (63.7% vs 41.7%, p<0.0001), but genetic testing results known prior to the IBTR operation were similar between the two groups (p=0.48). Immediate breast reconstruction (IBR) was twice as likely for CPM pts (p<0.0001). There were no differences in BMI, year of IBTR surgery, disease free interval (from index cancer to IBTR diagnosis), or prior contralateral breast cancer diagnosis. A contralateral cancer was diagnosed on operative pathology in 5 CPM pts (3.2%). Median follow up was 3.3 years for UM cohort and 4.9 years for CPM cohort. A subsequent contralateral breast cancer occurred in 6 UM pts (median 3.1 years post-IBTR surgery) and 1 CPM pt (4.9 years post-IBTR surgery). **CONCLUSIONS:** In our series of 375 pts treated with mastectomy for IBTR, 40% had a CPM. CPM patients were younger, more frequently underwent IBR, and commonly had recurrent DCIS. Interestingly, while genetic testing was performed more frequently among CPM pts, genetic testing results known at the time of surgery did not differ. Further investigation of the motivators for CPM in the setting of IBTR mastectomy is warranted.

Table 1. IBTR Patient and Tumor Characteristics

	Unilateral IBTR Mastectomy (N=218)	IBTR Mastectomy + CPM (N=157)	Total (N=375)	p value
Year of IBTR, median (range)	2016 (2007-2024)	2015 (2008-2024)	2016 (2007-2024)	0.3219[1]
Age at IBTR, median (range)	69.4 (40.5-92.3)	60.2 (23.7-80.0)	65.7 (23.7-92.3)	<0.0001[1]
BMI at IBTR, median (range)	28.0 (15.4-58.2)	27.7 (17.3-46.5)	27.9 (15.4-58.2)	0.4993[1]
Disease Free Interval, median (range) (yrs from index surgery to IBTR diagnosis)	10.2 (0.3-30.6)	10.3 (0.7-26.8)	10.2 (0.3-30.6)	0.4438[1]
Disease Free Interval (yrs from index surgery to IBTR diagnosis)				0.8171[2]
<3 years	47 (21.6%)	31 (19.7%)	78 (20.8%)	
3-5 years	20 (9.2%)	17 (10.8%)	37 (9.9%)	
>5 years	151 (69.3%)	109 (69.4%)	260 (69.3%)	
IBTR Clinical T Category (N=4 unk)				0.0005[2]
cTis	41 (19.1%)	47 (30.1%)	88 (23.7%)	
cT1/cT2	146 (67.9%)	103 (66.0%)	249 (67.1%)	
cT3/cT4	28 (13.0%)	6 (3.8%)	34 (9.2%)	
IBTR Clinical N Category (N=3 unk)				0.8227[3]
cN0	198 (91.7%)	144 (92.3%)	342 (91.9%)	
cN+	18 (8.3%)	12 (7.7%)	30 (8.1%)	
IBTR Biologic Subtype among Invasive Cancers (N=15 unk)				0.0109[3]
HR+HER2-	130 (77.8%)	73 (68.9%)	203 (74.4%)	
HR+HER2+	12 (7.2%)	6 (5.7%)	18 (6.6%)	
HR-HER2+	2 (1.2%)	10 (9.4%)	12 (4.4%)	
HR-HER2-	23 (13.8%)	17 (16.0%)	40 (14.7%)	
IBTR ER Status among DCIS Patients (N=1 unk)				0.7650[3]
Negative	11 (27.5%)	14 (30.4%)	25 (29.1%)	
Positive	29 (72.5%)	32 (69.6%)	61 (70.9%)	
Neoadjuvant Chemotherapy for IBTR Invasive Cancers (N=5 unk)	23 (13.1%)	22 (20.6%)	45 (15.9%)	0.0946[3]
Chemotherapy for IBTR Invasive Cancers (N=5 unk)	51 (29.0%)	48 (44.9%)	99 (35.0%)	0.0066[3]
Genetic Testing Completed (any time point)	91 (41.7%)	100 (63.7%)	191 (50.9%)	<0.0001[3]
Positive Mutation (any time point)	14 (15.4%)	18 (18.0%)	32 (16.8%)	0.6288[3]
Genetic Testing Results Known at Time of Surgery (N=29 unk)				0.4676[4]
Positive known at time of surgery	6 (8.0%)	13 (14.9%)	19 (11.7%)	
Negative known at time of surgery	39 (52.0%)	37 (42.5%)	76 (46.9%)	
VUS known at time of surgery	3 (4.0%)	3 (3.4%)	6 (3.7%)	
Not reported at time of surgery	27 (36.0%)	34 (39.1%)	61 (37.7%)	
Type of IBTR Mastectomy				<0.0001[3]
TM	166 (76.1%)	63 (40.1%)	229 (61.1%)	
SSM/NSM/ASM	52 (23.9%)	94 (59.9%)	146 (38.9%)	
History of Prior Contralateral BC	21 (9.6%)	12 (7.6%)	33 (8.8%)	0.5022[3]
Index Cancer Chemotherapy (N=1 unk)	56 (25.8%)	49 (31.2%)	105 (28.1%)	0.2511[3]
Index Cancer Radiation Therapy (N=1 unk)	176 (80.7%)	143 (91.7%)	319 (85.3%)	0.0032[3]

[1]Wilcoxon [2]Armitage Trend Test [3]Chi-Square [4]Fisher's exact

P271. Nipple Sensation and Nipple-Areolar Complex Outcomes After Oncoplastic Breast Surgery

Austin Olano, MD[1]; John Chou[2]; Emma Lampropoulos, MD[3]; Jeff Aalberg, MD[4]; Michael Jonczyk, MD[5]; Salvatore Nardello[6]; Sarah Persing[7]; Abhishek Chatterjee[8]

[1]Tufts Medical Center, Boston, MA, US; [2]Tufts University School of Medicine, Boston, MA, US; [3]Tufts Medical Center, Boston, MA, US; [4]Tufts Medical Center, Boston, MA, US; [5]Lahey Hospital and Medical Center, Burlington, MA, US; [6]Tufts Medical Center, Boston, MA, US; [7]Tufts Medical Center, Boston, MA, US; [8]Tufts Medical Center, Boston, MA, US

INTRODUCTION: Oncoplastic breast surgery (OBS) is a form of breast conservation surgery that often utilizes a breast reduction design to remove cancers along with immediate contralateral symmetry surgery. The breast with cancer typically then undergoes adjuvant radiation therapy. This study aimed to identify differences in nipple-areolar complex (NAC) outcomes comparing the oncologic breast (that also receives adjuvant radiation) to the contralateral symmetry breast following OBS. **METHODS:** Interviews containing validated nipple-focused questions were conducted on 28 patients (encompassing 56 breasts) who had undergone OBS with immediate contralateral symmetry surgery followed by adjuvant radiation. Outcomes were ranked on Likert scales between 1 and 4. A Wilcoxon signed-rank test was used to analyze the results for differences in nipple outcome rankings between the oncologic breast and the contralateral symmetry breast. **RESULTS:** There were no statistically significant differences in patient satisfaction with nipple height, NAC shape, or nipple sensation when comparing breasts having undergone oncoplastic resection with adjuvant radiation versus symmetry surgery. There was less patient satisfaction with the look of the NAC on the oncologic resection breast compared to the symmetry breast with a mean difference of -0.25±0.52 (p=0.03); however, a majority of patients (92.9%) reported being somewhat satisfied or very satisfied with the look of the NAC on the oncologic breast. Patients reported less sensation in their nipples on the oncologic resection breast compared to the symmetry breast with a mean difference of -0.36±0.73 (p=0.02). This did not, however, translate into a statistically significant difference in patient satisfaction with nipple sensation. **CONCLUSIONS:** For oncoplastic breast surgery, patient-reported NAC outcomes for the oncologic breast following oncoplastic resection and adjuvant radiation are comparable in terms of

sensation and appearance compared to the contralateral breast undergoing symmetry reduction surgery. These findings can enhance the pre-operative counseling of patients in the decision making process for breast cancer surgery.

Table 1. Average patient-reported nipple and NAC outcomes and differences in satisfaction and nipple sensation rankings when comparing breasts following oncologic resection/reduction (with adjuvant radiation) versus symmetry surgery (without radiation).

	Oncoplastic resection	Symmetry reduction	Mean Difference (SD)	p-Value
1(a). Nipple height	3.71	3.82	-0.11(±0.31)	0.25
1(b). Shape of NAC	3.61	3.82	-0.21(±0.50)	0.06
1(c). Look of NAC	3.46	3.71	-0.25(±0.52)	0.03
1(d). Satisfaction with sensation	3.21	3.50	-0.29(±0.90)	0.17
2. Amount of sensation	2.96	3.32	-0.36(±0.73)	0.02

(For items 1(a-d): 1="very dissatisfied", 2="somewhat dissatisfied", 3="somewhat satisfied", 4="very satisfied"; for item 2: 1="no sensation", 2="slight sensation", 3="some sensation", 4="normal sensation)

P272. Nodal Positivity Rates in Older Men with Hormone Receptor Positive Breast Cancer

Anthony M Baez[1]; Caitlin Marsh[2]; Charles DiMaggio[3]; Acacia Sharma[4]; Alyssa Marmer[5]; Freya Schnabel[6]
[1]NYU, New York, NY, US; [2]NYU, New York, NY, US; [3]NYU, New York, NY, US; [4]NYU, New York, NY, US; [5]NYU, New York, NY, US; [6]NYU, New York, NY, US

INTRODUCTION: The Society of Surgical Oncology's *Choosing Wisely* guidelines recommend against routine sentinel lymph node staging in clinically node-negative women aged 70 years and older with hormone receptor-positive breast cancer. Prior research has identified low-risk female patients with nodal positivity rates below 10%, to support the adoption of this guideline. Since male breast cancer management often follows paradigms derived from predominantly female studies, our objective is to identify a low-risk group among male breast cancer patients to support applying *Choosing Wisely* in this population. **METHODS:** In this retrospective study, the National Cancer Database (NCDB) was queried for men aged 70 years or older with invasive breast cancer. Demographic and tumor characteristic data were collected, and clinical T stage/tumor grade combinations were created to assess nodal positivity in patients who underwent sentinel lymph node biopsy (SLN), axillary lymph node dissection (ALND), or both. Statistical analysis included comparisons of nodal positivity between groups and the odds ratio for the association of nodal positivity with clinical T stage/tumor grade combinations. **RESULTS:** A total of 11,930 male breast cancer patients were included in this study. The average age was 77.9 years, and the mean tumor size was 23.9 mm. Estrogen receptor (ER) and progesterone receptor (PR) positivity rates were 95.7% and 87.7%, respectively. HER2 Neu positivity was observed in 9.7% of tumors. 13.4% of tumors were classified as grade 1, 49.9% as grade 2, 26.9% as grade 3, with the remainder unknown. Among patients with available data, the mean Ki67 score was 26.7%, and the mean Oncotype Recurrence Score was 15.6. Sufficient grade and clinical T stage information were available for 5,746 patients to calculate group nodal positivity rates. The groups with the lowest nodal positivity rates were: cT1mi/T1a-Grade1 (8.7%), cT1b-Grade1 (6.6%), and cT1mi/T1a-Grade3 (0%). Patients in these groups were 84% less likely to have a positive lymph node than those in other groups (Odds Ratio: 0.18, $p < 0.001$). Of note, only four patients were classified as cT1mi/T1a-Grade3. Nodal positivity rates for T1mi/T1a-Grade2 (18.4%), T1b-Grade2 (16.3%), and T1c-Grade1 (23%) were higher than those reported in female studies. **CONCLUSIONS:** This study supports applying Choosing Wisely guidelines in low-risk male breast cancer patients, particularly those with Grade 1 tumors measuring up to 1 cm. However, several T stage/grade combinations in our study showed higher nodal positivity rates compared to female data, indicating the need for caution when implementing these guidelines in men.

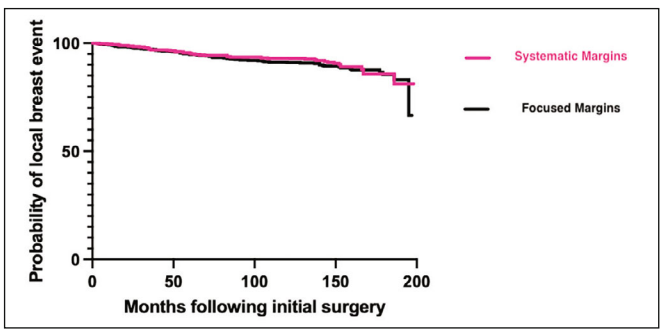
Table 1. Nodal Positivity Rates (% (n)) Across Various Clinical T Stage and Grade Combinations in Male Breast Cancer Patients

	Grade 1	Grade 2	Grade 3
cT1mi/T1a	**8.7** (*23*)	18.4 (*23*)	**0.0** (*4*)
cT1b	**6.6** (*61*)	16.3 (*129*)	18.5 (*27*)
cT1c	23.0 (*139*)	28.8 (*553*)	37.6 (*170*)
cT1 (*unspecified*)	11.0 (*127*)	25.5 (*412*)	32.5 (*166*)
cT2	29.7 (*340*)	40.4 (*1835*)	46.2 (*1157*)
cT3/T4	52.2 (*46*)	36.9 (*290*)	41.9 (*229*)

P273. Partial mastectomy for breast cancer: systematic or focused margins? A single center retrospective study after long-term follow up

Astrid M Heeren[1]; Lucas Sideris[2]
[1]Hôpital Maisonneuve-Rosemont, Université de Montréal, Montréal, QC, CA; [2]Hôpital Maisonneuve-Rosemont, Université de Montréal, Montréal, QC, CA

INTRODUCTION: Astrid M. Heeren, MD1, Mai-Kim Gervais, Pierre Dubé, MD, MSc1, Audrey Bélanger, Michaël Yassa, MD2, Peter Vavassis MD2, Marie-Christine GuilbertMD3, Marie-Hélène Ngo, MD3, Pierre Drolet, MD4, Cathy Menkarios, Evelyne Marchand, Jonathan Noujaim, MD5, Mikaël Soucisse, MD1, Guy Leblanc, and Lucas Sideris, MD1 From the departments of Surgery1, Radiation Oncology2, Pathology3, Anesthesiolgy4, and Medical Oncology4, Centre de Recherche, Hôpital Maisonneuve-Rosemont, Université de Montréal, QC, Canada. Positive margins after a partial mastectomy for breast cancer remain one of the more challenging complications of this surgery. Systematic cavity shaving is a well-known and widely debated strategy to reduce the percentage of positive margins. Although the technique of systematic shaving of margins is frequently performed, the question remains whether this reduces the return to the operating room (OR) and long-term local recurrences. This retrospective, single-center study compares two patient groups undergoing partial mastectomy with systematic or focused shaving of margins. **METHODS:** We retrospectively analyzed 1,083 patients who underwent partial mastectomy for breast cancer between 2008 and 2013. Four different surgeons performed the surgeries. The first group (n=464) underwent partial mastectomy with systematic resection of limited shaving margins, while the second group (n=619) either did not receive any shaving of margins or had a resection of focused margins. The primary outcome of this study was the rate of return to the OR. The secondary outcome was the long-term local recurrence rate. We conducted a univariate analysis of our data. **RESULTS:** Both groups were comparable in terms of demographic and clinicopathological characteristics. The median follow-up time was 12 years in both groups ($p = 0.3$). Final pathological analysis showed less multifocal disease (3.45%) and fewer node-positive cases (16.59%) in the systematic margins group compared to the focused margins group (12.76% of multifocal disease and 27.79% node-positive disease), respectively ($p = 0.0025$ and $p = 0.0119$). Data analysis revealed that the rate of definitive positive margins was slightly, but noticeably, lower in the systematic margins group (18.32%) compared to the focused margins group (19.06%) ($p = 0.0457$). There was no significant difference in the rate of return to the OR between the systematic margins group (16.59%) and the focused margins group (16.80%) ($p = 0.99$). Long-term follow-up showed that the rate of local recurrence was slightly lower in the systematic shaving group (9.27%) compared to the focused margins group (10.50%) ($p = 0.5392$). **CONCLUSIONS:** Systematic limited shaving of margins during partial mastectomy does not seem to reduce the need for reoperation. However, there is a slight, albeit not statistically significant, reduction in the local recurrence rate in the systematic margins group compared to the focused margins group.



P274. Perioperative Outcomes from the Pembrolizumab & Intraoperative Radiation Therapy Window of Opportunity trial for Early Stage Triple Negative Breast Cancer

Gabriela Doyle, Medical Doctorate[1]
[1]Columbia University/New York Presbyterian, New York, NY, US

INTRODUCTION: Triple-negative breast cancer (TNBC) is an aggressive subtype that creates challenges in treatment. The results of the KEYNOTE-522 trial support the use of neoadjuvant immunotherapy with pembrolizumab for Stage II/III TNBC. The utility of immunotherapy for earlier stage TNBC, however, is unclear. Additionally, the impact of intraoperative radiation therapy (IORT), utilized as a boost to the tumor bed given after neoadjuvant

immunotherapy is unknown. We present perioperative outcomes of TNBC patients treated with neoadjuvant pembrolizumab, followed by IORT and subsequent adjuvant chemotherapy and whole breast radiation. **METHODS:** Inclusion criteria were: tumors clinically <3cm, node-negative, hormone-receptor negative, and HER2-receptor negative breast cancer. Patients underwent two cycles of 200mg IV pembrolizumab at week 1 and week 4 followed by breast conserving surgery and sentinel lymph node biopsy with IORT (20Gy to surface). Tissue samples were obtained pre-radiation therapy and post-radiation therapy. Patients subsequently received adjuvant treatment with standard chemotherapy followed by whole breast radiation. **RESULTS:** Fifteen patients were included in the study. All patients were postmenopausal female nonsmokers. Demographics and tumor detection methods are presented in Table 1. Mean detected preoperative mammographic tumor size was 15.8mm. All patients had invasive ductal carcinoma. Surgical pathology mean tumor size was 15.9mm, statistically unchanged from mean clinical tumor size detected on preoperative mammogram (p=0.2419, CI -8.5, 2.24). Preoperative and postoperative Ki67% were mean 42.9% and 39.83%, statistically unchanged (p = 0.7896, CI = -20.6, 26.76). Majority of patients received taxotere and cyclophosphamide (TC), with dose-dense doxorubicin and cyclophosphamide (ddAC) as the second most common regimen. Mean time to initiation of adjuvant chemotherapy was 38.5 days. Two patients (13.3%) experienced thyroid-related toxicity post-treatment. Two patients (13.3%) had a documented postoperative seroma. **CONCLUSIONS:** Neoadjuvant pembrolizumab with intraoperative radiation therapy is a safe regimen in select patients with early triple-negative breast cancer that does not delay additional adjuvant treatment. A short course of single agent neoadjuvant immunotherapy did not reveal significant reductions in tumor size or proliferation markers. Study of long-term clinical outcomes is pending.

Table 1. Patient demographics and screening

Variables	
Age (years), mean	65.4 (49-81)
Ethnicity	
White	7 (47%)
Hispanic	5 (33%)
Black	1 (7%)
Other	2 (13%)
Body Mass Index, mean	32.3 (23.4-47.6)
Medical Comorbidities	
None	7 (47%)
Hypertension	6 (40%)
Hyperlipidemia	3 (20%)
Diabetes mellitus	2 (13%)
Cardiac	2 (13%)
Other	3 (7%)
Method of Tumor Detection	
Screening mammogram	13 (86%)
Screening magnetic resonance imaging	1 (7%)
Physical Exam	1 (7%)
Tumor Laterality	
Right	10 (67%)
Left	5 (33%)

P275. Predictors of Axillary Pathologic Complete Response After Neoadjuvant Systemic Therapy in Breast Cancer Patients Undergoing Targeted Axillary Dissection

Ariana Naaseh, MD, MPHS[1]; Grace Choi[2]; Olivia Galloway, MD[3]; Omolade O Sogade, MD[4]; Justin Dumrongkulraksa[5]; Benjamin Bowe, PhD[6]; Ashley Wilbers, MD[7]; Katherine Glover-Collins, MD, PhD[8]; Julie A Margenthaler, MD[9]; Rebecca L Aft, MD, PhD[10]

[1]Department of Surgery, Washington University in St. Louis School of Medicine, St. Louis, MO, US; [2]University of Missouri School of Medicine, Columbia, MO, US; [3]Department of Surgery, Washington University in St. Louis School of Medicine, St. Louis, MO, US; [4]Department of Surgery, Washington University in St. Louis School of Medicine, St. Louis, MO, US; [5]Department of Radiology, Washington University in St. Louis School of Medicine, St. Louis, MO, US; [6]Department of Surgery, Washington University in St. Louis School of Medicine, St. Louis, MO, US; [7]Department of Surgery, University of Missouri School of Medicine, Columbia, MO, US; [8]Department of Surgery, Washington University in St. Louis School of Medicine, St. Louis, MO, US; [9]Department of Surgery, Washington University in St. Louis School of Medicine, St. Louis, MO, US; [10]Department of Surgery, Washington University in St. Louis School of Medicine, St. Louis, MO, US

INTRODUCTION: Until recently, axillary dissection (AD) has been the standard surgical management for breast cancer patients with node positive disease who undergo neoadjuvant systemic therapy (NST). Targeted axillary dissection (TAD) has emerged as a less morbid alternative to AD and its feasibility has been demonstrated in multiple small cohorts. We sought to understand which pre and post-NST clinical, tumor, and imaging factors can be utilized to predict the likelihood of a pathologic complete response in the axilla (ax-pCR) to better select patients for TAD. **METHODS:** We conducted a retrospective cohort study of patients who had biopsy proven clinical N1 or N2 invasive breast cancer, received NST, and underwent TAD from 2017-2024 at our institution. TAD was defined as the removal of the sentinel lymph node (identified by blue dye and tracer) and the previously localized and biopsied positive node, which was confirmed to be part of the axillary specimen. Univariable and multivariable analyses were performed to analyze patient factors associated with ax-pCR, defined as ypN0. **RESULTS:** 159 patients were included, of which 60 (37.7%) had pathologic complete response (ypT0 or ypTis and N0) and 70 (44.0%) had ax-pCR (Table 1). Only 10 (5.5%) patients underwent further AD after TAD. After risk adjustment, patients with biomarker profiles of ER+/HER2+ (OR 9.50; 95% CI 3.35-26.91), ER-/HER2+ (OR 9.67; 9% CI 3.38-27.67), and triple negative (OR 6.49; 95% CI 2.61-16.11) had significantly higher odds of experiencing ax-pCR than patients who were ER+/HER2-. Patients with 3 imaging detected pre-NST lymph nodes were less likely to have ax-pCR than those with 1 (OR 0.21; 95% CI 0.05-0.85). For every additional residual breast lesion detected on post-NST imaging, patients were 53.8% less likely to have ax-pCR (p=0.02). Patients who were ycT1 (OR 0.21; 95% CI 0.07-0.64), ycT2 (OR 0.16; 95% CI 0.05-0.54), and ycT3 (OR 0.07; 95% CI 0.01-0.75). were less likely to have ax-pCR than those who were ycT0 by imaging post-NST. **CONCLUSIONS:** Number of lymph nodes detected on imaging pre-NST, post-NST breast staging, and hormone receptor status appear to be associated with ax-pCR in node-positive breast cancer patients without bulky lymphadenopathy and should be considered when selecting patients for TAD. In our cohort, post-NST axillary response was not associated with ax-pCR. Further studies are warranted to inform optimal patient selection for TAD.

Table 1. Imaging and oncologic characteristics of the cohort, before and after neoadjuvant systemic therapy (NST).

Characteristics	Pre-NST, n=159 (%)	Post-NST, n=159 (%)	P-value
Number of Breast Lesions Detected on Imaging, *mean (standard deviation)*	1.60 (0.98)	1.06 (0.75)	<0.001
Size of Largest Breast Lesion Detected on Imaging *(cm), mean (standard deviation)*	3.48 (2.06)	1.84 (1.43)	<0.001
Size of Largest Axillary Node Detected on Pre-Operative Imaging *(cm), mean (standard deviation)*	2.15 (1.11)	1.30 (0.72)	0.001
Cortical Thickness of Axillary Lymph Nodes, *mean (standard deviation)*	1.10 (1.46)	0.50 (0.65)	<0.001
Number of Abnormal Lymph Nodes Captured Imaging			<0.001
0	0 (0.0)	65 (40.9)	
1	69 (43.4)	59 (37.1)	
2	46 (28.9)	13 (8.2)	
3	15 (12.6)	2 (1.3)	
Multiple (≥4)	20 (12.6)	5 (3.1)	
Clinical T Stage			<0.001
TX	0 (0.0)	34 (21.4)	
T0	0 (0.0)	23 (14.5)	
T1	28 (17.6)	62 (39.0)	
T2	91 (57.2)	32 (20.1)	
T3	33 (20.8)	6 (3.8)	
T4	7 (4.4)	2 (1.3)	
Clinical N Stage			0.331
NX	2 (1.3)	0 (0.0)	
N1	148 (93.1)	147 (92.5)	
N2	9 (5.7)	10 (6.3)	
N3	0 (0.0)	2 (1.3)	

P276. Rate of neoadjuvant endocrine therapy use in estrogen receptor positive breast cancer before and after Covid-19

Sasha R Douglas, MD[1]; Samantha M Thomas, MS[2]; Astrid Botty van den Bruele, MD[3]; Ton Wang, MD[4]; Kendra Parrish, DO[5]; Laura H Rosenberger, MD[6]; Jennifer K Plichta, MD[7]; Maggie L Dinome, MD[8]; Akiko Chiba, MD[9]
[1]Duke University Medical Center, Durham, NC, US; [2]Duke University, Durham, NC, US; [3]Duke University Medical Center, Durham, NC, US; [4]Duke University Medical Center, Durham, NC, US; [5]Duke University Medical Center, Durham, NC, US; [6]Duke University Medical Center, Durham, NC, US; [7]Duke University Medical Center, Durham, NC, US; [8]Duke University Medical Center, Durham, NC, US; [9]Duke University Medical Center, Durham, NC, US

INTRODUCTION: For many hospital systems, operating room availability for non-emergent operations was restricted during the COVID-19 pandemic, leading to increased use of neoadjuvant therapies, such as neoadjuvant endocrine therapy (NET), for estrogen-receptor positive (ER+)/HER2- breast cancers as a bridge to surgery. The ACOSOG Z1031 trial showed 51% of patients who were originally deemed ineligible for breast conservation surgery (BCS) prior to therapy were able to successfully undergo BCS after NET. Despite this, the overall use of NET remains low. This study investigates NET utilization and related outcomes before, during, and after the pandemic. **METHODS:** Data from patients aged ≥18 with clinical T1-T4c, N0-3, ER+/HER2- non-metastatic breast cancer who underwent surgery were selected from the National Cancer Database. Patients were divided into two groups: those who received NET and those who underwent surgery first. The study analyzed trends from 2019 (pre-pandemic) to 2021 (post-pandemic) to assess changes in use of NET and subsequent BCS and chemotherapy use. Logistic regression was used to identify factors associated with NET versus surgery first. **RESULTS:** The study included 283,481 patients with 10,935 (3.9%) receiving NET and 272,546 (96.1%) undergoing surgery first. NET usage peaked in 2020 at 6.4% up from 2.3% in 2019, and though it declined to 3.2% in 2021, the rate remained higher than in 2019. This result held after adjustment (2020 vs. 2019: OR 2.95, 95% CI 2.67-3.26; 2021 vs 2019: OR 1.43, 95% CI 1.31-1.56). Median time to treatment from diagnosis was significantly shorter in the NET group (1.02 vs 1.35 months, p<0.001). Patients with T3-4 disease who received NET had equivalent or higher rates of BCS and were less likely to receive chemotherapy compared to surgery first. There was no clinically significant difference in survival between groups. **CONCLUSIONS:** NET use increased significantly during the onset of the COVID-19 pandemic in 2020 and remained higher than baseline in 2021. This was associated with decreased time to treatment and less use of chemotherapy. We should continue to consider use of NET in ER+ breast cancer patients especially in those with a possible delay to surgery, higher T category disease, and inability to tolerate chemotherapy.

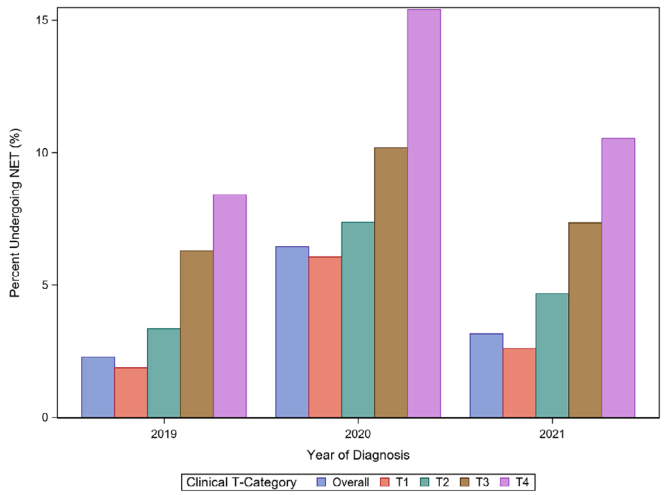
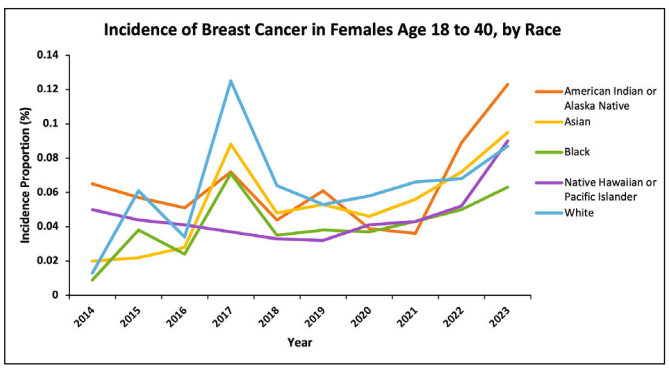


Figure. NET Use Rates by Clinical T-Category and Year of Diagnosis

P277. Rising Breast Cancer Incidence and Poor Outcomes in Young Women

Jennifer Den[1]; Nicole Nelson[2]; Kamil Khanipov[3]; Raj Vaghjiani[4]; Douglas Tyler[5]; Vicki S Klimberg[6]
[1]The University of Texas Medical Branch at Galveston, Galveston, TX, US; [2]University of Texas Medical Branch - Galveston, TX, Galveston, TX, US; [3]University of Texas Medical Branch - Galveston, TX, Galveston, TX, US; [4]University of Texas Medical Branch - Galveston, TX, Galveston, TX, US; [5]University of Texas Medical Branch - Galveston, TX, Galveston, TX, US; [6]University of Texas Medical Branch - Galveston, TX, Galveston, TX, US

INTRODUCTION: Recent studies have shown a troubling rise in breast cancer (BC) among young women. Our project evaluated BC incidence and trends among women aged 18-40 in the U.S. over ten years (2014-2023) by age, race, and ethnicity. We also compared the incidence and trend of overall survival (OS) and local recurrence (LR) in female patients aged 18-40 diagnosed with primary BC. **METHODS:** This retrospective study used data from the TriNetX Network. We first created a cohort of female patients aged 18-40 and evaluated the incidence of primary BC between January 2014 and December 2023. Of note, primary input of data into TriNetX began in 2017. We stratified these results by age, ethnicity, and race. We then created another cohort of female patients aged 18-40 with a primary BC diagnosis and evaluated the incidence of mortality and LR between January 2014 and December 2023. **RESULTS:** 18,250,987 female patients aged 18-40 were identified. From 2014 to 2023, the incidence of BC increased sixfold, from 635 cases (0.013%) to 4,475 (0.082%). Individuals aged 30-39 had the highest incidence. When stratified by race, white women had the most cases of BC, however, incidence of BC showed an uptrend in American Indians or Alaskan Natives (AI/AN), Asians, and Native Hawaiian or Pacific Islanders (NHPI) within the last four years. When stratified by ethnicity, non-Hispanic women initially had a higher incidence of BC but were surpassed by Hispanic women in 2022. We identified 38,683 female patients aged 18-40 in the U.S. with a primary BC diagnosis. From 2014 to 2023, these patients experienced a ninefold increase in overall mortality (0.09% to 0.851%) and local recurrence (0.3% to 2.9%). **CONCLUSIONS:** The incidence of BC among young women 18-40 years old has dramatically increased over the past decade, with the highest incidence in non-Hispanic white women 30-39 years old. However, an uptrend is being seen in young AI/AN, Asians, and NHPI, and Hispanic women. Overall mortality and LR have also experienced a significant increase. Our data underscores the importance of further research to understand these alarming trends and develop diagnostic and therapeutic approaches tailored to younger patients.



P278. Selective Use of Post-Lumpectomy Mammography

Carolyn Schnurr[1]; Danielle Hurst, MD[2]; Kristin LeMarbe, MD[3]; Elizabeth Ekkel, DO[4]; Sayee Kiran, MD[5]; Josh Dilworth, MD, PhD[6]; Thomas Quinn, MD[7]; Nayana Dekhne, MD[8]
[1]Corewell Health William Beaumont University Hospital, Royal Oak, MI, US; [2], US; [3], US; [4], US; [5], US; [6], US; [7], US; [8], US

INTRODUCTION: Post-lumpectomy mammography (PLM) may detect suspicious residual calcifications following breast-conserving surgery (BCS). However, PLM may lead to patient anxiety, delays in initiating adjuvant treatment, and increased costs. We aimed to identify predictors of suspicious residual calcifications that may be used to select patients for who PLM may be avoided. **METHODS:** A retrospective analysis was conducted of patients with breast cancer who underwent BCS and received PLM between May 2016 to June 2023 at a single institution. We recorded patient characteristics,

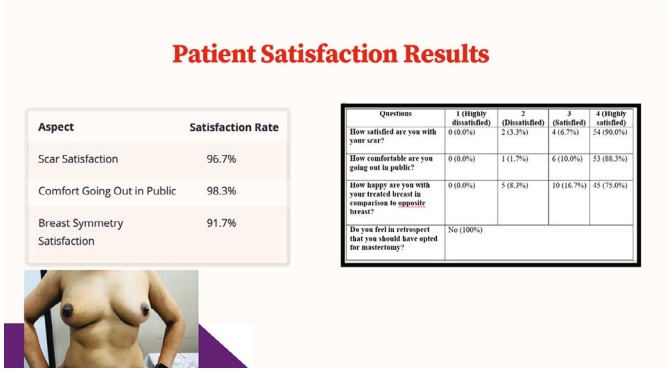
presence of suspicious calcifications on pre-operative and PLM, biopsy and surgical pathology, and if an additional procedure was performed. Wilcoxon Ranked-Sum and Fisher's Exact tests were used to compare outcomes between cohorts. Univariate (UVA) and multivariable analyses (MVA) identified potential predictors of residual calcifications on PLM, including clinical size of tumor and span of calcifications on imaging, microcalcifications on biopsy, size of invasive tumor and DCIS on final pathology, hormone receptor status, tumor grade, presence of lymphovascular invasion or an extensive intraductal component, and margin status (clear= ≥2 mm, close= <2 mm, or involved= tumor was on ink). **RESULTS:** We identified 463 patients with either pure DCIS (58%), invasive ductal carcinoma (37%), or invasive lobular carcinoma (4.5%) of whom 76 (16%) had residual suspicious calcifications on PLM and 70 (15%) underwent an additional procedure. Eleven patient's who underwent an additional procedure had clear initial surgical margins, and 5 (46%) of these had positive pathology. Forty patients who underwent an additional procedure had close initial margins, and 23 (58%) of these had positive pathology. Nineteen patients who underwent an additional procedure had involved margins, and 13 (68%) of these had positive pathology. On UVA, clinical tumor size (OR=1.85 [1.07,3.25], p=0.026), span of calcifications on pre-operative mammogram (OR=1.2 [1.05,1.37], p=0.007), microcalcifications on core-biopsy (OR=4.75 [1.42,29.5],p=0.034), extent of DCIS on surgical pathology (OR=1.17 [1.03,1.32], p=0.012), and close (OR=2.59 [1.39,5.10], p=0.004) or involved (OR=4.06 [1.86,9.01], p=<0.001) DCIS surgical margins predicted residual suspicious calcifications. Clinical tumor size (OR=2.38 [1.28,4.81], p=0.008) remained significant on MVA. **CONCLUSIONS:** Clinical tumor size predicted residual suspicious calcifications on PLM. Further investigation is needed to determine which tumor size threshold might be used to select patients with clear surgical margins who may avoid PLM.

P279. Surgical and aesthetic outcomes of chest wall perforator transposition flaps in partial breast reconstruction

Ashutosh Mishra, MCh, FACS[1]; SVS Deo, MS, FACS[2]; Ashutosh Mishra, MS[3]; Chinmay Bagla[4]; Ajay Gogia, MD, DM[5]; D N Sharma, MD[6]; Atul Batra, MD, DM[7]

[1]All India Institute of Medical Sciences, New Delhi, New Delhi, Delhi, IN; [2]AII India Institute of Medical Sciences, New Delhi, New Delhi, Delhi, IN; [3]All India Institute of Medical Sciences, New Delhi, Delhi, Delhi, IN; [4]All India Institute of Medical Sciences, New Delhi, New Delhi, Delhi, IN; [5]All India Institute of Medical Sciences, New Delhi, New Delhi, Delhi, IN; [6]All India Institute of Medical Sciences, New Delhi, New Delhi, Delhi, IN; [7]All India Institute of Medical Sciences, New Delhi, New Delhi, Delhi, IN

INTRODUCTION: Breast-conserving surgery (BCS) has become the standard of care for early, localized breast cancer. However, the main challenge is balancing the oncological and aesthetic outcomes. According to the location of the breast tumor, various flap procurement and placement techniques have been devised. However, there is limited evidence evaluating the outcomes of perforator-based oncoplastic breast reconstruction. Aim is to assess the surgical and aesthetic outcomes after partial breast reconstruction using chest wall perforator transposition flaps. **METHODS:** Sixty patients who had undergone partial breast reconstruction using chest wall perforator transposition flaps after January 2020 and completed one year of follow-up before June 2024 were included in the study. Data analysis was done from a prospectively maintained comprehensive database. Data on demographics, perioperative events, and surgical outcomes were recorded. Aesthetic outcomes reported by patients were collected using a Likert scale-based questionnaire. **RESULTS:** Mean age of study population was 46.1 years, and the body mass index was (24.7 kg/m2, SD 3.2). >50% of patients had breasts with small cup sizes (A&B) and mild ptosis (Non-ptotic and Grade 1 ptosis). Lateral intercostal artery perforator (LICAP), medial intercostal artery perforator (MICAP), and Anterior Intercostal Artery Perforator (AICAP) were performed in 54, 3, and 3 patients, respectively. The mean operative time for flap harvesting and insetting was 41, 23, and 25 minutes respectively. Postoperative surgical complications were graded according to the Clavien-Dindo classification. Six patients experienced minor wound dehiscence at the flap harvested site, three patients had marginal flap necrosis, two patients developed seroma and one patient developed post-operative hematoma. 96.7% of patients completed adjuvant radiation therapy. 96.7% reported that they were satisfied with the scar, 98.3% felt comfortable going out in public, and 91.7% felt that the symmetry of the breasts was satisfactory. **CONCLUSIONS:** Chest wall perforator transposition flaps for partial breast reconstruction are an excellent choice for immediate reconstruction offering quick recovery, low complication rates, high treatment compliance, and outstanding aesthetic outcomes. These flaps have very short learning curve and can be done without doppler.



P280. Temporal Trends in Mastectomy Election and Rationale in Young Patients With DCIS

Courtney Chen, MD[1]; Teodora Dumitra[2]; Rhea Rahimtoola[3]; Allison Nguyen, BSC[4]; Rayne Peerenboom, MD[5]; Marissa Boyle, MD[6]; Alice Chung, MD[7]; Catherine Dang, MD[8]; Scott Karlan, MD[9]; Armando E. Giuliano, MD[10]; Farin Amersi, MD[11]

[1]Cedars Sinai Medical Center, Los Angeles, CA, US; [2]Cedars-Sinai Medical Center, Los Angeles, CA, US; [3]Cedars-Sinai Medical Center, Los Angeles, CA, US; [4]CedarsSinaiMC, Los Angeles, CA, US; [5]Cedars-Sinai Medical Center, Los Angeles, CA, US; [6]Cedars Sinai, West Hollywood, CA, US; [7]Cedars-Sinai Medical Center, Los Angeles, CA, US; [8]Cedars-Sinai Medical Center, Los Angeles, CA, US; [9]Cedars-Sinai Medical Center, Los Angeles, CA, US; [10]Cedars-Sinai Medical Center, Los Angeles, CA, US; [11]Cedars-Sinai Medical Center, Los Angeles, CA, US

INTRODUCTION: Managing young (≤50 years old (yo)) ductal carcinoma in situ (DCIS) patients is complex, balancing risk reduction, treatment effects, and quality of life. Recent studies note an increase in bilateral mastectomy (MTX) over breast conserving surgery in young DCIS patients. We hypothesize this progressive trend is from personal preference. We analyzed DCIS patients ≤50yo undergoing MTX, their decision making, reconstruction, and oncologic outcomes. **METHODS:** Retrospective review of prospectively collected data on DCIS patients from 01/2007-12/2022 treated at a single academic institution was performed. Biennial MTX rates and clinical factors were analyzed using Student T-tests (continuous variables, regression slopes for rates) and Pearson's X-square for categorical variables. Surgical decision-making was extracted by review of pre-operative provider clinical documentation in medical records. **RESULTS:** Of 1138 DCIS patients, 391 (34.4%) were ≤50yo (25-50), and 747 (65.6%) were >50 (51-86). Overall, 208 (18.2%) patients underwent MTX; per group, 26% (102 of 391) were ≤50yo and 14.2% (106 of 747) were >50yo (p<0.01). Groups were similar in grade (grades I-III, p=0.98), tumor size (avg 2.7cm both, p=1.00), and receptor status (ER- 85.3% vs 74.5%, PR- 77.5% vs 64.2% for ≤50 vs >50 respectively, p=0.06 both). Both had similar clinically significant genetic mutations rates (≤50 – 17.5% vs >50 – 11%, p=0.13). Biennial MTX rates increased significantly overall; for ≤50 yo patients, rates went from 11.4% (9 of 79) to 54.9% (28 of 51) and 5.5% (6 of 109) to 27.7% (26 of 94) in patients >50yo from 2007-2009 to 2019-2022 (p<0.01). More patients ≤50yo received nipple sparing mastectomies (NSM) (≤50- 56.9% vs >50 - 31.1%, p<0.01) and reconstruction (≤50- 94.1% vs>50yo- 69.8%, p<0.01). Recurrence rates were similar (p>0.05). 1/5th of patients (≤50- 22 of 102 vs >50- 19 of 106) didn't have identifiable MTX rationale, but ≤50yo patients commonly cited personal preference (avoidance of tamoxifen, radiation, concern for future risk of cancer, cosmesis) (≤50 – 23.5% vs > 18.9%) for electing for mastectomy, whereas for >50yo patients cited prior radiation/breast cancer (≤50- 4.9% vs >50- 22.6%). **CONCLUSIONS:** DCIS patients appear to be shifting towards mastectomy, most significantly in ≤50yo patients despite similar tumor characteristics and recurrence outcomes, though the receipt of NSM strongly differs based on age. Further investigation regarding decision making and counseling on best practice is needed, as younger patients are increasingly opting for more aggressive surgical intervention without oncologic benefit/ indications.

Table 1. Mastectomy rationale for DCIS patients over and under 50 years old

Reported Rationale for Mastectomy	≤50 yo N (%)	>50 yo N (%)
Not available	22 (21.6)	19 (17.9)
Multifocal/centric disease	8 (7.8)	9 (8.5)
Extent of disease	15 (14.7)	20 (18.9)
Known genetic mutation	18 (17.6)	11 (10.4)
Strong family history	10 (9.8)	3 (2.8)
Prior history of radiation and/or breast cancer	5 (4.9)	24 (22.6)
Personal preference (concern for recurrence, avoidance of radiation/, hormone therapy/ surveillance, cosmesis)	24 (23.5)	20 (18.9)

P281. The Use Of Neoadjuvant Immunotherapy Is Associated With Increased Surgical Complications In Women With Breast Cancer

Danielle Graham, MD, PhD[1]; Ariana Kassam[2]; Yuan Yuan[3]; Alisa Blumenthaler[4]; Marissa Boyle[5]; Alice Chung[6]; Armando E. Giuliano[7]; Farin Amersi, MD[8]
[1]Cedars-Sinai Medical Center, Los Angeles, CA, US; [2]Cedars Sinai, West Hollywood, CA, US; [3]Cedars Sinai, West Hollywood, CA, US; [4]Cedars Sinai, West Hollywood, CA, US; [5]Cedars Sinai, West Hollywood, CA, US; [6]Cedars-Sinai Medical Center, Los Angeles, CA, US; [7]Cedars-Sinai Medical Center, Los Angeles, CA, US; [8]Cedars-Sinai Medical Center, Los Angeles, CA, US

INTRODUCTION: Immunotherapy has revolutionized the treatment of cancer in recent decades. The KEYNOTE-522 trial demonstrated the importance of immunotherapy in the treatment of early triple-negative breast cancer (TNBC). However, the impact of neoadjuvant immunotherapy on surgical complications is not well understood. The purpose of this study was to determine the association between the use of neoadjuvant immunotherapy and surgical complications in patients with TNBC. **METHODS:** Patients with Stage I-III TNBC who were treated with neoadjuvant systemic therapy at a single institution from July 2016 through July 2024 were evaluated. Patient and tumor characteristics, treatment details, and surgical complications were compared between patients treated with and without neoadjuvant immunotherapy. Complications including cellulitis and abscess were considered minor complications, whereas hematoma requiring reoperation, flap or nipple areola necrosis requiring reoperation, and expander/implant removal were considered major complications. Fisher exact and Wilcoxon tests were used to compare characteristics between groups. Univariate and multivariate logistic regression were performed to identify factors associated with surgical complications. **RESULTS:** 197 patients with TNBC were included in the final analysis. Of these, 131 (66.5%) were treated with neoadjuvant immunotherapy plus chemotherapy and 66 (33.5%) were treated with neoadjuvant chemotherapy alone. The use of immunotherapy was associated with higher cN and higher Ki67 (p <0.02). Patients who were treated with neoadjuvant immunotherapy underwent reconstruction after mastectomy less frequently (n=49, 37.4%) than patients who were not treated with neoadjuvant immunotherapy (n=37, 56.0%, p=0.02). The overall complication rate was 16.2% (32/197); the complication rates in patients treated with and without immunotherapy were 18.3% (24/131) and 12.1% (8/66), respectively. The major complication rate was 7.1% (14/197) in the overall cohort, 9.2% (12/131) in patients treated with immunotherapy, and 3.0% (2/66) in patients treated without immunotherapy. The majority of complications occurred within 30 days of the operation. On univariate analysis, BMI >30, mastectomy, and reconstruction with tissue expander and/or implant were associated with increased complications. On multivariate analysis, BMI >30 (OR 5.80, CI 2.00-18.18, p<0.01), neoadjuvant immunotherapy (OR 3.00, CI 1.16-8.80, p=0.03), and mastectomy (OR 3.88, CI 1.04-15.64, p=0.05), were significantly associated with increased complications. There were more complications with the use of tissue expander and/or implant reconstruction (OR 3.04, CI 0.95-11.17, p=0.07), but this did not reach statistical significance. **CONCLUSIONS:** The use of neoadjuvant immunotherapy is associated with increased surgical complications and increased major surgical complications in women with breast cancer. Increased BMI and mastectomy were also associated with increased overall and major surgical complications. More overall surgical complications after reconstruction with tissue expander and/or implant were observed, though this was not statistically significant.

Table 1. Multivariate analysis examining factors associated with surgical complications in women with breast cancer after treatment with neoadjuvant systemic therapy.

	Any complication			Major complication		
Characteristic	OR	95% CI	p value	OR	95% CI	p value
Age	1.01	0.98-1.05	0.39	0.98	0.93-1.04	0.61
BMI >30 (ref = BMI ≤30)	5.80	2.00-18.18	<0.01	7.94	1.41-61.52	0.02
Neoadjuvant immunotherapy (ref = no)	3.00	1.16-8.80	0.03	8.07	1.64-75.08	0.03
Mastectomy (ref =partial mastectomy)	3.88	1.04-15.64	0.05	1.58	1.37-445.27	0.05
Reconstruction						
None	Ref	Ref	Ref	Ref	Ref	Ref
Tissue expander and/or implant	3.04	0.95-11.17	0.07	3.31	6.03-31.67	0.22
Flap-based	2.06	0.23-13.11	0.47	6.80	0.53-82.04	0.12

P282. The Use of Hemostatic Agents to Decrease Drain Time in Breast Cancer Surgery Procedures

Austin Olano, MD[1]; Saman Namazian[2]; Alexander Martin[3]; Caroline King, MD[4]; Salvatore Nardello[5]
[1]Tufts Medical Center, Boston, MA, US; [2]Tufts University School of Medicine, Boston, MA, US; [3]Tufts University School of Medicine, Boston, MA, US; [4]Tufts Medical Center, Boston, MA, US; [5]Tufts Medical Center, Boston, MA, US

INTRODUCTION: Drains can be used in oncoplastic surgery and after mastectomy given the extensive undermining of tissue. Our primary goal was to investigate whether hemostatic agents used during breast cancer surgery could decrease drain time length. Secondary goals were to investigate whether hemostatic agents decreased seromas and hematomas. **METHODS:** A retrospective chart review that included oncoplastic breast surgery (OBS), mastectomy without reconstruction, and tissue expander (TE) exchange was performed. Data collected included use of hemostatic agent (fibrin sealant [FS, EVICEL] or combination powder [CP, HEMOBLAST Bellows]), time to JP drain removal, and postoperative complications (seroma, hematoma, and operating room [OR] reintervention). Statistical analyses included t-tests and Fisher's exact test where appropriate. **RESULTS:** A total of 412 patients were included. For all operations, there were statistically significant reductions in JP drain duration with CP compared to no hemostatic agent (Table 1). Following OBS and TE exchange, there were statistically significant reductions in JP drain duration with CP compared to FS – 7.0 versus 11.0 days for OBS (p<0.001), 4.6 versus 17.3 days for TE exchange (p=0.042). There were no statistically significant differences in incidence of hematomas, seromas, or OR reintervention among any groups. **CONCLUSIONS:** The use of hemostatic agents, particularly combination powder (HEMOBLAST Bellows), in breast cancer surgery significantly reduces the duration of JP drain use; regardless of the type of breast cancer operations being used.

Table 1. Postoperative outcomes following surgery for breast cancer comparing no hemostatic agent, fibrin sealant (Evicel), or combination powder (HEMOBLAST Bellows)

	Oncoplastic Surgery			Mastectomy			Expander Exchange		
	No agent (n=87)	HEMOBLAST (n=102)	*p-value*	No agent (n=15)	HEMOBLAST (n=55)	*p-value*	No agent (n=39)	HEMOBLAST (n=11)	*p-value*
Follow-up (weeks)	7.9	19.6	-	15.3	11.5	-	6	11.5	-
Seroma	2 (2.3%)	2 (2.0%)	1	4	6	0.465	2	0 (0.0%)	1
Hematoma	5 (5.7%)	3 (2.9%)	0.474	1	2	1	0 (0.0%)	0 (0.0%)	-
JP drain duration (days)	11.4 ± 4.5	7.0 ± 3.9	**<0.001**	20.3 ± 8.7	12.5 ± 6.1	**<0.001**	12.1 ± 6.2	4.6 ± 3.4	**0.019**
Return to OR	2 (2.3%)	0 (0.0%)	0.211	3	4	0.409	1	0 (0.0%)	1
	Evicel (n=73)	HEMOBLAST (n=102)	*p-value*	Evicel (n=25)	HEMOBLAST (n=55)	*p-value*	Evicel (n=5)	HEMOBLAST (n=11)	*p-value*
Follow-up (weeks)	7.4	19.6	-	8.5	11.5	-	5.4	11.5	-
Seroma	4 (5.5%)	2 (2.0%)	0.237	4	6	0.725	1 (20.0%)	0 (0.0%)	0.312
Hematoma	0 (0.0%)	3 (2.9%)	0.266	1	2	1	0 (0.0%)	0 (0.0%)	-
JP drain duration (days)	11.0 ± 5.3	7.0 ± 3.9	**<0.001**	12.9 ± 5.1	12.5 ± 6.1	0.829	17.3 ± 10.7	4.6 ± 3.4	**0.042**
Return to OR	0 (0.0%)	0 (0.0%)	-	2	4	1	0 (0.0%)	0 (0.0%)	-

P283. The relationship amongst stage IV triple negative breast cancer and regional lymph node metastases

Jenny Bui, MD, MPH[1]; Saul Nathanson, MD[2]; Jessica Bensenhaver, MD[3]; Theresa Schwartz, MD[4]; Lindsay Petersen, MD[5]; Anna Lehrberg, DO[6]; Laura Dalla Vecchia, MD[7]; Kylie Springer, MS[8]; Laura Susick, PhD[9]
[1]Henry Ford Health, Detroit, MI, US; [2]Henry Ford Health, Detroit, MI, US; [3]Henry Ford Health, Detroit, MI, US; [4]Henry Ford Health System, Detroit, MI, US; [5]Henry Ford Health System, Detroit, MI, US; [6]Henry Ford Health System, Detroit, MI, US; [7]Henry Ford Health System, Detroit, MI, US; [8]Henry Ford Health-Department of Public Health Sciences, Detroit, MI, US; [9]Henry Ford Health System, Detroit, MI, US

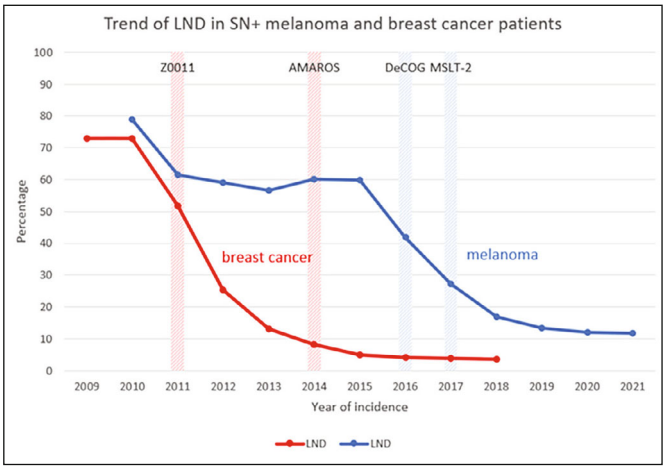
INTRODUCTION: Clinical, pathological, and genetic evidence indicates that breast cancer (BC) typically invades peri-tumoral vessels, spreading first to regional lymph nodes (LNs) before metastasizing to systemic sites. However, some patients develop systemic metastases without LN

involvement. Observing a trend of fewer LN metastases in triple-negative breast cancer (TNBC) patients, we hypothesized that stage IV TNBC may represent a subtype in which the pathway to systemic metastasis bypasses the LNs entirely. **METHODS:** We examined all TNBC and ER+/PR+/HER2/neu negative BC patients with lymphovascular invasion (LVI) within our vertically integrated healthcare system. Data were drawn from a long-term, prospectively maintained database from 1995–2022. Patients excluded from the study included men, BC recurrences, and instances of missing pathological or molecular information. All clinicopathologic and molecular categorical data, including histologically confirmed ALN and systematic metastases, were analyzed statistically using both parametric and non-parametric tests, as appropriate for each variable. Statistical significance was set at $p < 0.05$. **RESULTS:** A total of 446 patients with LVI: 91 (20%) TNBC and 355 (80%) ER+/PR+/HER2/neu negative were compared. The median age (interquartile range) of the study cohort was 60 (51-70). Patients were predominantly white (228, 59%). 19 (21%) of TNBC patients developed systemic metastases compared to 37 (10%) of ER+/PR+/HER2/neu negative patients (p=0.003). Patients with TNBC and LVI were less likely to have LN metastasis than ER+/PR+/HER2/neu negative patients with LVI (OR: 0.456, 95% CI: 0.284-0.73, p=0.001). 34 (37%) TNBC patients developed LN metastases compared to 199 (57%) ER+/PR+/HER2/neu negative patients. These patients were also more likely to have systemic metastasis compared to the ER+/PR+/HER2/neu negative patients with LVI (OR: 3.730, 95% CI: 1.545-9.006, p=0.003). **CONCLUSIONS:** Patients with TNBC whose tumors display LVI are significantly less likely to have ALN metastases but have an increased risk of systemic metastasis. If we could identify molecular, genetic, or biochemical markers in primary tumors that predict which patients are more prone to systemic metastasis without LN involvement, we could potentially avoid sentinel LN biopsy in this subgroup.

P284. The trend of lymph node dissection in sentinel node-positive melanoma and breast cancer patients

Thijs Van Dalen[1]; Eline Verreck[2]
[1]Surgical Oncology, Erasmus MC, US; [2]Erasmus MC, Rotterdam, NL

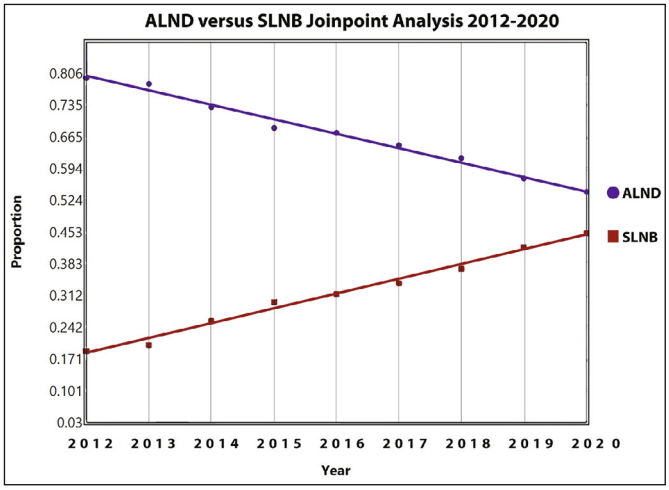
INTRODUCTION: In both breast cancer- and melanoma patients, surgical treatment of regional lymph nodes de-escalated in the past decade following the results of clinical trials obviating the need of lymph node dissection (LND) in patients with involved sentinel lymph nodes (SN+): Z0011 (2011) and AMAROS (2014) for breast cancer, DeCOG-SLT (2016) and MSLT-II (2017) for melanoma. We evaluated and compared national trends of LND over the past decade and studied factors influencing these trends aware that LNDs in both breast cancer and melanoma are commonly executed by the same surgeons. **METHODS:** Data were derived from the nationwide Netherlands Cancer Registry. Data of cT1-3 breast cancer patients undergoing surgery and sentinel lymph node biopsy (SLNB) between 2009-2018 and melanoma patients diagnosed between 2010-2021 undergoing primary surgery SLNB were collected. Patients were included if the SLNB contained metastases. **RESULTS:** Over the study period, performance of LND in SN+ breast cancer patients decreased from 73% in 2009 to 4% in 2018, and for the main part this decrease was observed in the three years since the first trial was published in support of 'no LND' (2011). LND in melanoma patients decreased from 79% to 12% (figure 1) and the starkest decrease was observed in the year before the first clinical trial was published (2016). Factors associated with higher chance of performing LND both in breast cancer- and melanoma patients were low patient age, more extensive lymph node involvement and treatment in low volume hospitals. The proportion of patients receiving LND over the study period varied between regions in the Netherlands: ranging from 15% to 66% in breast cancer patients and from 17% to 38% in melanoma patients. These regional differences do not correspond evenly between the two tumour types. **CONCLUSIONS:** In both breast cancer- and melanoma patients a decreasing trend is observed that started in close relation with publication of randomized trials in support of 'no LND'. Comparable patient, tumour and institutional characteristics influencing the decreasing trend were observed in the two tumour types. Regional differences were observed but were unevenly distributed comparing breast cancer to melanoma.



P285. Trends in Axillary Lymph Node Dissection for Clinically Node Positive Triple Negative Breast Cancer

Hannah Trembath, MD, MS[1]; Chase E Cox, MD, MSW.[2]; Jessica R Schumacher, PhD[3]; Phillip Spanheimer, MD[4]
[1]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [2]University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US; [3]University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US; [4]University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US

INTRODUCTION: Triple negative breast cancer (TNBC) is an aggressive subtype of breast cancer with worse overall survival. Recent advances with chemoimmunotherapy have significantly improved patient outcomes including clearance of axillary disease potentially facilitating avoidance of the morbidity of axillary lymph node dissection (ALND). We evaluated practice changes in rates of ALND in node positive TNBC patients treated with neoadjuvant chemotherapy. **METHODS:** Women ≥ 18 years of age with cT1-4, N1-3, M0 TNBC who received neoadjuvant chemotherapy prior to surgery between 2012-2020 were selected from the National Cancer Database (NCDB) (n=25,059). The annual percent change (APC) and trend in sentinel lymph node biopsy (SLNB) and ALND utilization over time was estimated by joinpoint analysis. We assessed the relation between sociodemographic and clinical factors and ALND using logistic regression. **RESULTS:** Within our cohort, average age was 53, majority of patients were white (67%), majority of patients had T2 (49%), N1 (77%) disease, type of surgery was similarly divided between lumpectomy (35.6%), unilateral mastectomy (37.7%), and bilateral mastectomy (26.7%). The incidence of ALND significantly decreased over time (80% in 2012 to 54% in 2020; APC=-3.2%, p<0.001) with a commensurate increased use of SLNB (18% to 45%; APC=3.3%, p<0.001). Factors associated with ALND include the following: ALND: age (OR 1.01, CI 1.01, 1.01), Black race (*ref.* White, OR 1.11, CI 1.04, 1.2), no insurance (*ref.* private insurance, OR 1.3, CI 1.09, 1.56), Charlson comorbidity index of 1 (*ref.* 0, OR 1.2, CI 1.1, 1.32), T4 stage (*ref.* T1, OR 1.42, CI 1.26, 1.61), increasing cN stage (*ref.* N1, N2 OR 1.7, CI 1.54, 1.88)(N3 OR 1.51 CI 1.36, 1.69), inflammatory histology (*ref.* Ductal, OR 1.79, CI 1.19, 2.68), mastectomy (*ref.* lumpectomy, unilateral OR 2.7, CI 2.5, 2.91)(bilateral OR 2.08, CI 1.92, 2.25), received radiation (OR 1.34, CI 1.24, 1.45). Patients who underwent immunotherapy were less likely to have undergone ALND (OR 0.88, CI 0.79, 0.996). **CONCLUSIONS:** The rates of ALND in clinically node positive TNBC patients receiving neoadjuvant chemotherapy have decreased over time showing steady adoption of axillary de-escalation. Omission of ALND was more likely for patients who received immunotherapy demonstrating improvement in a key neoadjuvant metric; omission of ALND was less likely for patients with more advanced disease and for black and uninsured patients. Further studies are needed to determine racial and socioeconomic drivers of persistent ALND use in these patients.



P286. Trends in axillary management for clinically node-positive breast cancer patients with pathologically node-positive disease after neoadjuvant chemotherapy

Nicole Rademacher, MD[1]; Kristy K. Broman, MD, MPH[2]; Lily A. Gutnik, MD[3]
[1]University of Alabama at Birmingham (UAB), Birmingham, AL, US; [2]University of Alabama at Birmingham, Birmingham, AL, US; [3]University of Alabama at Birmingham, Birmingham, AL, US

INTRODUCTION: For clinically node-positive (cN+) breast cancer patients with residual disease after neoadjuvant chemotherapy (NAC), standard of care is axillary lymph node dissection (ALND). For patients that convert to clinically node negative, SLN (sentinel lymph node) or targeted axillary dissection (TAD) is also acceptable. We evaluated temporal trends in surgical axillary management across cancer center types for cN+ patients found to be pathologically node-positive (pN+) on surgery after NAC. **METHODS:** The study included patients identified using the National Cancer Database diagnosed with T1-T4, cN1-cN3 breast cancer from 2016-2021 who received NAC and were pN+ on axillary surgery. Clinical node status between NAC and surgery was unknown. Extent of axillary surgery was defined as SLN, SLN followed by ALND, or ALND. Variation in the extent of axillary surgery across Commission on Cancer facility types over time was analyzed with multinomial logistic regression (reported as relative risk with 95% confidence intervals) and adjusted for sociodemographic factors, receptor status, stage, breast surgery, and receipt of radiation. **RESULTS:** Among 38,584 patients, axillary interventions were ALND (n=17,190, 44.55%), SLN followed by ALND (n=14,255, 36.95%), and SLN (n=7,139, 18.50%). Across all facility types, the proportion of patients who underwent SLN or SLN followed by ALND increased over time while ALND declined (Figure 1). In the adjusted analysis, relative to community cancer programs, patients who received treatment at integrated network (RR 1.69, 95% CI 1.50-1.90), research/academic (RR 1.38, 95% CI 1.23, 1.54), and comprehensive community programs (RR 1.21, 95% CI 1.08, 1.35) were more likely to undergo SLN followed by ALND than ALND. The likelihood of SLN compared to ALND was lower at academic/research programs (RR 0.84, 95% CI 0.73, 0.96) and greater at integrated network programs (RR 1.26, 95% CI 1.10,1.45). **CONCLUSIONS:** An appropriate rise in SLN followed by ALND reflects de-implementation of upfront ALND for clinically node-positive breast cancer patients found to be pN+ on surgery after NAC. There was also a rise in SLN in this population which is not yet an evidence-based strategy suggesting a spillover effect whereby practices such as ALND are de-implemented in populations for which it has not yet been studied. This highlights the importance of multidisciplinary discussion given the nuanced management of breast cancer and to assure best available evidence is appropriately applied.

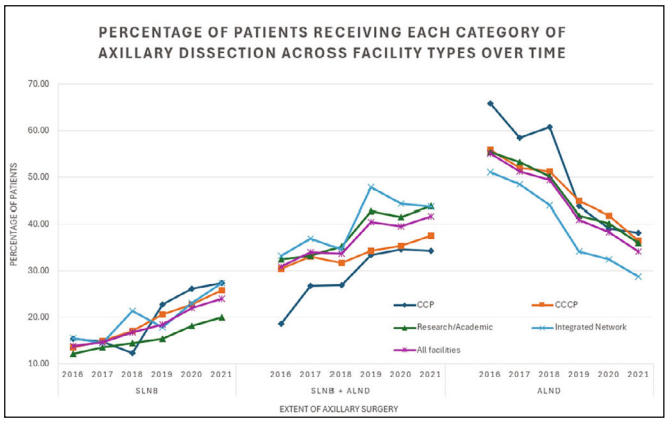


Figure 1. Percentage of patients by facility type undergoing surgery (SLN dissection alone, SLN dissection followed by ALND, and ALND alone).

P287. Volumetric Lumpectomy Specimen Image Visualization for Intraoperatively Directing Cavity Shaves (VIVID), a Phase II Study

Swati A Kulkarni[1]; Padraig Carolan[2]; Denise Scholtens[3]; Nikolaj Reiser[4]; Danielle Kline[5]; Yasmin Pina[6]; Michelle Guo[7]; Natalie H Friedman[8]; Rebecca L Aft, MD, PhD[9]; Stephanie Valente[10]; Xiaoqin Jennifer Wang[11]; Christian Wietholt[12]; Xiao Han[13]
[1]Northwestern University, Chicago, IL, US; [2]Northwestern University, City, IL, US; [3]Northwestern University, Chicago, IL, US; [4]Clarix Imaging, Chicago, IL, US; [5]Northwestern University, Chicago, IL, US; [6]Northwestern University, Chicago, IL, US; [7]Northwestern University, Chicago, IL, US; [8]Northwestern University, Chicago, IL, US; [9]Department of Surgery, Washington University in St. Louis School of Medicine, St. Louis, MO, US; [10]Cleveland Clinic, Cleveland, OH, US; [11]University of Kentucky College of Medicine, Lexington, KY, US; [12]Clarix Imaging, Chicago, IL, US; [13]Clarix Imaging, Chicago, IL, US

INTRODUCTION: Specimen radiography is an important tool to assess margin status after lumpectomy for breast cancer (BC). Volumetric Specimen Imaging (VSI) is a new specimen imaging technology that gives full 3D, micro-CT images of lumpectomy specimens in real time. We conducted a multicenter, Phase II prospective single-arm study in patients with BC undergoing localized lumpectomy. The main objective was to determine if intraoperative use of VSI allowed surgeons to accurately identify margin status, such that ≤10% of patients have positive margins not identified by VSI. Other objectives included 1) sensitivity and specificity; 2) volume of tissue excised, final positive margin rate and re-operation rate compared with historical controls. **METHODS:** Patients ≥18 years of age diagnosed with BC were eligible. Standard of care (SOC) lumpectomy was performed; the specimen was imaged with VSI. Images were reviewed intraoperatively to identify close/positive margins. "VSI directed shaves" were taken followed by additional shaves per SOC. Interim analyses was performed after 20, 40, 60 and 80 patients were enrolled according to the Bayesian optimal phase II (BOP2) design. Data was collected on whether re-excision was recommended based on the final pathology of the lumpectomy and VSI-directed shaves and if re-excision occurred within 2 months. Volume excised, positive margin rate and re-operation rate were calculated using multiple regression and compared to historical matched controls collected from each site. **RESULTS:** One hundred patients were recruited, and 400 controls were identified from 4 sites. The median age was 62 years; 80 patients were diagnosed with invasive breast cancer and 20 patients with DCIS. Median lesion size was 51mm. Nine patients (9%) had positive margins on the main specimen unidentified by VSI. Sensitivity and specificity were 37% and 78% respectively. Of the 599 evaluable margins, 21 (3.5%) had positive margins compared to 4% (96/2400) in the controls. The median excision volume was 49 cm3 compared to 62cm3 in the controls. The reoperation rate was 10% in the VIVID study and 8.8% in the controls (p=0.49). **CONCLUSIONS:** Using VSI resulted in missing ≤ 10% of positive lumpectomy margins. The volume of tissue excised in the VIVID study was less, with a lower positive margin rate compared to historical controls. Sensitivity and specificity were lower than expected but evidenced by retrospective review of intraoperative images, they would significantly improve after additional training and use of the novel VSI imaging technology.

P288. "Missed" Rectal Organ Preservation with Pathologic Complete Response following Total Neoadjuvant Treatment: Why did they undergo mesorectal excision?

Apeksha Dave[1]; Amalia Stefanou[2]; Sophie Dessureault[3]; Julian Sanchez[4]; Iman Imanirad[5]; Tiago Biachi[6]; Sarah Hoffe[7]; Jessica Frakes[8]; Seth Felder[9]
[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4]Moffitt Cancer Center, Tampa, FL, US; [5]Moffitt Cancer Center, Tampa, FL, US; [6]Moffitt Cancer Center, Tampa, FL, US; [7]Moffitt Cancer Center, Tampa, FL, US; [8]Moffitt Cancer Center, Tampa, FL, US; [9]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Rectal organ preservation in locally advanced rectal cancer (LARC) following total neoadjuvant treatment (TNT) may approach 50%. Patient selection is imperfect and relies on MRI and endoscopic restaging. This series examines factors influencing the decision to proceed with total mesorectal excision (TME) following TNT and re-staging MRI/endoscopy in cases of pathologic complete response (pCR). **METHODS:** A retrospective single institution review of 35 patients with LARC, treated with TNT followed by TME with pCR between 2017-2024 is reported. Twenty patients were excluded because restaging MRI or endoscopy after TNT was missing. Clinical restaging completeness of MRI and endoscopic tumor response (complete cCR, near-complete nCR, incomplete iCR utilizing the OPRA tumor regression schema) was retrieved from records and annotated descriptively. **RESULTS:** 15 patients were included, 67% were male, and average age was 52.8 years. Initial MRI indicated T2 (1), T3 (11), and T4a (3) disease, with 80% N+. TNT sequence was induction chemoradiation (CRT) + consolidation chemotherapy (CT) in 40%; induction CT + consolidation CRT in 53%; and 1 patient received short course radiation with consolidation CT. Average time from TNT completion to restaging MRI, endoscopy, and TME was 31, 33, and 84 days, respectively. 87% underwent low anterior resection and the remaining abdominoperineal resections. Factors leading to TME are described in Table 1. Either an MRI or endoscopic response was designated as an incomplete response in 9 (60%) of the patients. The only patient with a cCR on both modalities pursued TME due to patient preference. Other reasons for TME included inability to tolerate neoadjuvant therapy and a synchronous distal sigmoid tumor. **CONCLUSIONS:** Selection of LARC patients following TNT for rectal organ preservation remains imperfect, with the risks of missing local residual disease being a primary concern. However, post TNT MRI and endoscopic restaging may reflect an incomplete tumor response based on standardized regression schema yet demonstrate a pCR. Here we highlight the challenges in tumor response assessment, underscoring the need for improved response evaluation and considerations for over-staging of presumed residual tumor.

Table 1. Factors leading to TME

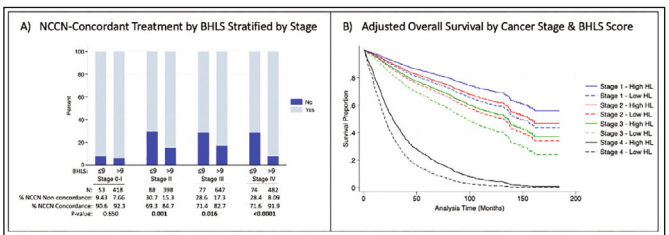
Patient	MRI	Endoscopy	Other
1	iCR, restaged T1/T2N0	iCR, visible tumor	
2	iCR, restaged T3N0	iCR, ulcerated lesion	
3	cCR	iCR, ulcerated mass	
4	cCR	cCR	Patient preference
5	cCR	High grade stricture	
6	cCR	nCR, mucosal irregularity	Patient preference
7	iCR, restaged T1/T2N0	iCR, visible tumor	
8	iCR, restaged T3Nx w/ persistent extracellular mucin	iCR, fungating mass	
9	cCR	nCR, mucosal irregularity	Patient preference
10	nCR, intermediate T2 signal	iCR, ulcerated lesion	
11	iCR, restaged T2NX	iCR, visible tumor	
12	nCR, intermittent T2 signal	iCR, ulcerated lesion	
13	iCR, restaged T1/2N0	nCR, mucosal irregularity and adenoma	Incomplete neoadjuvant treatment
14	nCR w/ 6mm nodule	High grade stricture	
15	cCR	nCR, erythema and nodule	Synchronous sigmoid cancer

cCR- Complete Clinical Response, nCR- Near-Complete Clinical Response, iCR- Incomplete Clinical Response

P289. Association of Patient Health Literacy with NCCN-Concordant Colorectal Cancer Treatment and Survival

Emma Bradley, MD[1]; Sobia Siddiqui[2]; Alexander Hawkins[3]; Aimal Khan[4]; Kamran Idrees[5]
[1]Vanderbilt University Medical Center, Nashville, TN, US; [2]Vanderbilt University Medical Center, Nashville, TN, US; [3]Vanderbilt University Medical Center, Nashville, TN, US; [4]Vanderbilt University Medical Center, Nashville, TN, US; [5]Vanderbilt University Medical Center, Nashville, TN, US

INTRODUCTION: Low health literacy has been associated with poor health outcomes in many chronic diseases as well as poorer use of health care services. As cancer care becomes increasingly complex, the role of health literacy in empowering patients to successfully navigate their care becomes more critical. Although health literacy has been shown to play a role in colorectal screening, its impact on oncologic outcomes is less well defined. Our objective is to explore the association between patient health literacy and receipt of guideline-concordant colorectal cancer treatment, as well as subsequent survival outcomes. **METHODS:** We performed a retrospective analysis of 2241 patients with newly diagnosed colorectal cancer from 2010-2023 from a single tertiary referral institution. Patients who died within 30 days of diagnosis or surgery were excluded. Health literacy level was assessed by the Brief Health Literacy Screen (BHLS). Low health literacy was defined as BHLS ≤9. Treatment concordance with National Comprehensive Cancer Network (NCCN) guidelines was determined based on cancer stage and type. Univariate, multivariate and survival analyses were performed. **RESULTS:** A total of 1413 patients with colon cancer and 828 patients with rectal cancer were included. There were 292 (13%) patients with low HL and 1949 (87%) patients with adequate HL. Patients with low HL were more likely to be older (median age 66 vs 59 years), federally insured (68.2% vs 42%) and have higher Elixhauser comorbidity scores (1.6 vs 1.16). Patients with low health literacy were less likely to receive NCCN-concordant treatment in both unadjusted (217/292 (74.3%) vs 1701/1945 (87.5%), p<0.0001) and adjusted analyses (OR 0.52 [95% CI 0.38-0.72]) compared to patients with adequate health literacy. Stratified by stage, lower health literacy was associated with a decreased odds of receiving NCCN-concordant treatment in patients with Stage II, Stage III and Stage IV cancer (Figure 1A). Lower health literacy was also associated with higher hazard of all-cause mortality in unadjusted and adjusted analyses (HR 1.42 [95% CI 1.19-1.71]; (Figure 1B). **CONCLUSIONS:** In patients with colorectal cancer, lower health literacy was independently associated with decreased likelihood of receiving NCCN-concordant treatment and worse overall survival. Further attention to patient health literacy is valuable in oncologic treatment of patients with colorectal cancer. Future directions include exploration of reasons for non-concordance with treatment guidelines, as well as implementation of health literacy targeted interventions in colorectal cancer treatment.



A) Univariate analysis demonstrating percentage who did not receive a NCCN-concordant treatment course represented in dark blue, in patients with BHLS score S9 and >9 stratified by cancer stage. B) Multivariate cox proportional hazards regression adjusted overall survival in colorectal cancer patients with low HI (BHLS S9) compared to BHLS>9 stratified by cancer stage.

Figure 1. NCCN-Concordant Treatment and Survival by BHLS

P290. Avoiding Right Hemicolectomy after Appendectomy for Appendiceal Cancer- External Validation of a Predictive Model for Nodal Metastases

Po Hong Tan, MBBS[1]; Richard M Miller, BS[2]; Andrew Saleeb[3]; Hoe Yan Hor[4]; Melody Pi Yin Tu[5]; Sanjay Bagaria, MD[6]; Travis E. Grotz, MD, FSSO[7]; Emmanuel Gabriel[8]; Zhi Ven Fong, MD, MPH, DrPH[9]; Chee-Chee H. Stucky, MD[10]; Nabil Wasif, MD, MPH[11]

[1]Mayo Clinic, Phoenix, AZ, US; [2]Mayo Clinic, Phoenix, AZ, US; [3]Mayo Clinic Arizona, Phoenix, AZ, US; [4]Mayo Clinic Arizona, Phoenix, AZ, US; [5]Mayo Clinic Arizona, Phoenix, AZ, US; [6]Mayo Clinic Florida, Jacksonville, FL, US; [7]Mayo Clinic, Rochester, MN, US; [8]Mayo Clinic Florida, Jacksonville, FL, US; [9]Mayo Clinic Arizona, Phoenix, AZ, US; [10]Mayo Clinic Arizona, Phoenix, AZ, US; [11]Mayo Clinic Arizona, Phoenix, AZ, US

INTRODUCTION: Appendiceal cancer (AC) is a rare tumor with varied histologic subtypes, each exhibiting a different propensity for metastasis to regional lymph nodes (LNM). We previously developed a risk prediction model for LNM in AC utilizing population data to inform surgical decision-making regarding completion right hemicolectomy. The primary objective of this study is to externally validate this model for LNM using an institutional dataset. **METHODS:** Patients treated for Neuroendocrine tumors, Mucinous Adenocarcinoma (MA), Non-mucinous Adenocarcinoma, Signet ring cell carcinoma (SRC), and Goblet cell carcinoma (GCC) of the appendix from 1976-2024 were included. The National Cancer Database based risk prediction model was applied to estimate the likelihood of LN metastasis. Discrimination was assessed using the concordance statistic (C-statistic) and Brier score, while calibration was evaluated with curve intercept and slope. **RESULTS:** During the study period, 539 patients met eligibility criteria. The median age of the population was 57.9 and 48.2 % were male. The most common histologic subtype was MA at 41.9% and the least common was SRS at 5.9%. The most common T stage was T4, seen in 49.9% of patients, and the most common tumor grade was grade 2, present in 35.1%. The overall incidence of LNM was 35.8%. Our validation cohort demonstrated a C-statistic of 0.77. Calibration analysis showed a Brier score of 0.18, with an intercept of -0.25 and slope of 1.11 for the calibration curve, suggesting slight overprediction for low-risk patients but overall good model calibration (Figure). **CONCLUSIONS:** External validation of this risk prediction model for LNM in AC showed reasonable calibration and discrimination. This model can serve as a clinical decision aid for completion right hemicolectomy following appendectomy. Other pathologic or genetic markers should be investigated to further improve model performance.

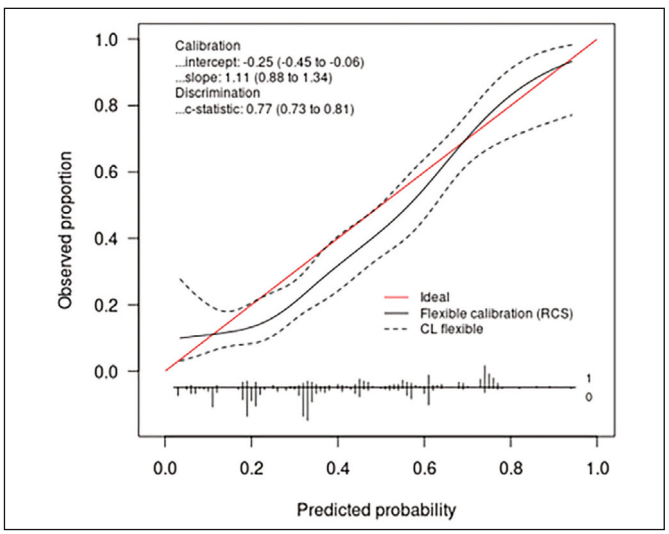


Figure. Calibration Curve estimated by Restricted Cubic Spline (RCS)

P291. Evaluation of risk factors for outlet obstruction in robot-assisted rectal cancer surgery with ileostomy : A single institution retrospective study

Yutaka Ochi[1]; Masayuki Hiraki[2]; Asami Arita[3]; Kiminori Yanagisawa[4]; Taishi Hata[5]; Yoshiro Yukawa[6]; Shinsuke Katsuyama[7]; Go Shinke[8]; Mitsuru Kinoshita[9]; Yoshifumi Iwagami[10]; Keijiro Sugimura[11]; Yutaka Takeda[12]; Kohei Murata[13]

[1]1 Department of Surgery, Kansai Rosai Hospital, Amagasaki, JP; [2]Department of Surgery, Kansai Rosai Hospital, Amagasaki, JP; [3]Department of Surgery, Kansai Rosai Hospital, Amagasaki, JP; [4]Department of Surgery, Kansai Rosai Hospital, Amagasaki, JP; [5]Department of Surgery, Kansai Rosai Hospital, Amagasaki, JP; [6]Department of Surgery, Kansai Rosai Hospital, Amasgasaki, JP; [7]Department of Surgery, Kansai Rosai Hospital, Amagasaki, JP; [8]Department of Surgery, Kansai Rosai Hospital, Amagasaki, JP; [9]Department of Surgery, Kansai Rosai Hospital, Amagasaki, JP; [10]Department of Surgery, Kansai Rosai Hospital, Amagasaki, JP; [11]Department of Surgery, Kansai Rosai Hospital, Amagasaki, Hyogo, JP; [12]Department of Surgery, Kansai Rosai Hospital, Amagasaki, JP; [13]Department of Surgery, Kansai Rosai Hospital, Amagasaki, JP

INTRODUCTION: With the recent increase in robot-assisted rectal cancer surgeries, more and more patients are undergoing ileostomy to reduce the risk of anastomotic leakage. However, there are a wide variety of complications associated with ileostomy, which can delay the start of postoperative food intake and the introduction of adjuvant chemotherapy. Various factors such as age, gender, and thickness of the rectus abdominis have been reported as risk factors for outlet obstruction, but no consensus has yet been reached. In this study, we investigated the risk factors to prevent outlet obstruction after ileostomy. **METHODS:** Sixty-six patients who underwent robot-assisted surgery with ileostomy for rectal cancer between January 2022 and March 2024 were included in this study. The subjects were divided into two groups: 13 patients with outlet obstruction (Clavian Dindo ? Grade I) (OO group) and 53 patients without outlet obstruction (non-OO group), and risk factors were retrospectively analyzed. **RESULTS:** In terms of patient background, there were significantly more males in the OO group (p=0.022). There were no significant differences in surgical or tumor factors between the two groups. Postoperative hospital stay (p=0.0005) and postoperative days on diet (p=0.0015) were predominantly longer in the OO group. There was no significant difference in the thickness of the thickest part of the rectus abdominis (p=0.36), but there was a significant difference in the thickness of the rectus abdominis at the site of ileostomy (p=0.047). The angle of passage of the ileostomy through the rectus abdominis was also significantly smaller in the OO group (p=0.0021). The ratio of the diameter of the intestinal canal of the ileostomy to the shortest diameter of the hole at the rectus abdominis was also significantly different between the two groups (p=0.020). **CONCLUSIONS:** In our hospital, the risk factors for outlet obstruction were male, the thickness of the rectus abdominis muscle at the site of the ileostomy, the angle of passage through the rectus abdominis muscle, and the ratio of the diameter of the intestinal canal of the ileostomy to the shortest diameter of the hole in the rectus abdominis. Based on the above risk factors, it is desirable to construct the ileostomy in an area where the rectus abdominis muscle is thin and, to make the hole as large as possible so that it is perpendicular to the rectus abdominis muscle. However, there is a possibility of other complications, such as parastomal hernia, and further study is needed.

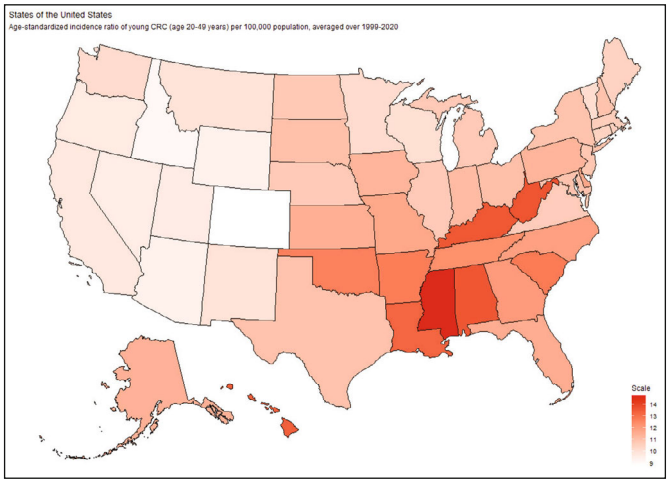
P292. Geographical Disparity in Incidence of Young Colorectal Cancer across States in the United States

Swati Sonal[1]; M Harshvardhan[2]; Paul Richardson[3]; Hiroko Kunitake[4]; Robert N. Goldstone[5]; Sophia K McKinley[6]; David L Berger[7]

[1]University of Minnesota, Minneapolis, MN, US; [2]University of Tennessee, Knoxville, Knoxville, TN, US; [3]Massachusetts General Hospital, Boston, MA, US; [4]Massachusetts General Hospital, Boston, MA, US; [5]Massachusetts General Hospital, Boston, MA, US; [6]Massachusetts General Hospital, Boston, MA, US; [7]Massachusetts General Hospital, Boston, MA, US

INTRODUCTION:
Incidence of colorectal cancer (CRC) in young population is rising in the United States (US). This study describes the disparities in incidence of young CRC across states in US. It also elucidates the association of clinical, sociodemographic and behavioral factors with state-wide incidence of young CRC. **METHODS:** The age-standardized incidence ratios of young CRC (age 20-49 years per 100,000 population) for 51 states including Washington D.C. were obtained for years 1999-2020 from CDC-WONDER database. Variables for each state such as sex, race, ethnicity, household income, health expenditure, incidence of diabetes in young adults (per 100 population, age 18-44 years), percent of young adults with obesity (age 18-44 years), smoking, alcohol use, fruit & vegetable intake, and outpatient antibiotic usage were obtained from various national databases. Pearson correlation coefficient (r) was used to assess the univariable correlation of factors with incidence of young CRC and inter-factor correlation to assess for multicollinearity. Variables with r >0.7 were excluded from multivariable analysis. Multivariable analysis was performed using linear regression. **RESULTS:** Southeastern states had a higher incidence of young CRC compared to other states, with

highest incidence noted in Mississippi (14.76 per 100,000 population). On univariable analysis, antibiotic usage (r=0.75), no exercise (r=0.73), low fruit intake (r=0.67), incidence of young diabetes (r=0.66), and obesity (r=0.64) were most strongly associated with young CRC incidence. On multivariable regression, diabetes (Beta coefficient, b=3.35), obesity (b=0.11), Hispanic ethnicity (b=-0.04), and White race (b=-0.04) were significantly correlated with incidence of young CRC ($p<0.05$). **CONCLUSIONS:** There is a clear geographic disparity in incidence of young colorectal cancer, highest in Southeastern states. Diabetes and obesity in young adults strongly correlate with rising incidence of CRC in young adults. These associations may be valuable for developing targeted investigations and health policies which will hopefully help curb the rising incidence of CRC under 50 years of age.



P293. HIPEC and Neoadjuvant Chemotherapy for T4 Colon Cancer: Who Is a Candidate?

Mina M Ayad, MD[1]; Logan Harper[2]; Ronald Charles, MD[3]; Sakti Chakrabarti, MD[4]; Luke D. Rothermel, MD, MPH[5]; John B Ammori[6]; Richard S Hoehn, MD[7]
[1]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [2]Case Western Reserve University School of Medicine, Cleveland, OH, US; [3]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [4]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [5]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [6]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [7]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US

INTRODUCTION: Surgical resection and adjuvant chemotherapy remain the mainstay of managing early-stage Colon Cancer (CC), including those with locally advanced T4 lesions. While the HIPECT4 trial suggested hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC) may improve disease control for patients who present with T4 CC, and the FOXTROT study showed benefit with neoadjuvant chemotherapy, many of these patients present urgently due to bleeding, obstruction, or perforation, which may preculde implementation of these therapies. Our aim was to identify the proportion of T4 CC at our institution that would be amenable to neoadjuvant therapy and/or HIPEC during initial CC presentation. **METHODS:** This was a retrospective database review of patients with T4 CC treated at our regional hospital system between 2018 and 2022. Chart review encompassed patient demographics, preoperative details, operative information, and postoperative course. Determination of T4 disease was based on surgical pathology. Patients were divided into three groups based on whether they presented for surgery in an elective, urgent (surgery within 7-10 days), or emergent manner (surgery typically within 24 hours). Basic descriptive statistics helped ascertain differences between the three groups: one-way ANOVA for quantitative variables and Pearson's Chi-squared test for categorical variables, with significance determined on a threshold of $p<0.05$. **RESULTS:** In total, 208 patients were identified: 128 underwent elective surgery, 67 had urgent surgery, and 13 required emergent surgery. There were no significant differences between the groups with respect to baseline characteristics, but urgent and emergent cases were more likely to occur at our main tertiary center as opposed to a satellite hospital. Elective cases were more often performed laparoscopically, but less likely to involve fecal diversion or experience exhibit peri-operative complications (19% vs 30% and 46%) (all $p<0.05$). Interestingly, elective cases had the highest rate of disease recurrence (38% vs 21% and 30%, $p<0.05$). Peritoneal recurrence occurred in 39%, 55%, and 66% of elective, urgent, and emergent cases, respectively, although this was not significant. **CONCLUSIONS:** In this analysis, 94% of patients with T4 CC undergo surgery with sufficient notification to allow arrangement for HIPEC, and 62% may be candidates for neoadjuvant therapy. Given the high risk for disease recurrence, many of these T4 CC patients may benefit from a multidisciplinary approach to treatment.

P294. Initial Trends in the Implementation of Commission on Cancer Standard 5.7 on Total Mesorectal Excision: An Analysis of Compliance Data from 2022 and 2023

Alison S Baskin, MD[1]; Elizabeth C Funk, MSW[2]; Amanda B Francescatti, MS[3]; Brandy R Sinco, MA, MS[4]; Bryan E Palis, MA[5]; Matthew H.G. Katz, MD[6]; Tina J. Hieken, MD[7]; Judy C. Boughey, MD[8]; Ronald J Weigel, MD, MBA, PhD[9]; Daniel J Boffa, MD, MBA[10]; Lesly A Dossett, MD, MPH[11]
[1]University of California, San Francisco, San Francisco, CA, US; [2]American College of Surgeons, Chicago, IL, US; [3]American College of Surgeons, Chicago, IL, US; [4]University of Michigan, Ann Arbor, MI, US; [5]American College of Surgeons, Chicago, IL, US; [6]MD Anderson Cancer Center, Houston, TX, US; [7]Mayo Clinic, Rochester, MN, US; [8]Mayo Clinic, Rochester, MN, US; [9]American College of Surgeons, Chicago, IL, US; [10]Yale School of Medicine, New Haven, CT, US; [11]University of Michigan, Ann Arbor, MI, US

INTRODUCTION: To reduce variation and improve quality in rectal cancer surgery, in 2021 the American College of Surgeons (ACS) Commission on Cancer (CoC) implemented Operative Standard 5.7, which requires a complete or near-complete total mesorectal excision (TME) for all curative-intent resections of mid-to-low rectal cancers. CoC site reviewers recently began evaluating synoptically formatted pathology reports for hospital compliance with CoC Standard 5.7. We analyzed compliance data from site reviews to assess the early implementation status of CoC Standard 5.7. **METHODS:** Hospital compliance rates with CoC Standard 5.7 were abstracted from documentation of site reviews conducted in 2022 and 2023. Each site review comprised of up to seven randomly sampled cases meeting criteria for CoC Standard 5.7 per hospital. **RESULTS:** Overall, 652 site visits occurred including 329 in 2022 and 323 in 2023. Of these, 175 (27%) sites had no cases eligible for review, primarily because rectal cancer cases were referred to other facilities or were ineligible due to tumor location (e.g., above the anterior peritoneal reflection), no evidence of residual tumor after neoadjuvant treatment, or surgical intent. Among the 477 sites reviewed, 419 (88%) were compliant, 57 (12%) were non-compliant, and one received a "deficiency resolved" designation (Table). Of non-compliant sites, the median percentage case compliance was 57% (IQR, 33-67%). Compliance rates were similar across the different types of CoC sites (e.g., Academic Comprehensive Cancer Program, Comprehensive Community Cancer Program, Integrated Network Cancer Program, etc.). **CONCLUSIONS:** CoC site review documentation indicates most CoC hospitals perform curative-intent rectal cancer surgery, qualifying them for evaluation of compliance with CoC Standard 5.7. The majority of hospitals in this early assessment were compliant, however 1 in 8 were not. While non-compliance rates did not improve between 2022 and 2023, most non-compliant hospitals were close to achieving compliance, often needing just one or two additional compliant cases. Efforts to support improved compliance with CoC Standard 5.7 should be broadly applicable to all types of CoC sites.

Table. Site Characteristics by Compliance Status

	All visited CoC sites with eligible cases[1]	Compliant	Non-compliant	P-value[2]
	N=477	N=419 (87.8%)	N=57 (11.9%)	
Site Review Year				P=0.19
2022	237	214 (90.3%)	23 (9.7%)	
2023	240	205 (85.4%)	34 (14.2%)	
Type of CoC Site				P=0.46
ACAD	100	91 (91.0%)	9 (9.0%)	
CCCP	213	185 (86.9%)	28 (13.2%)	
CCP	55	46 (83.6%)	9 (16.4%)	
HACP	1	1 (100%)	0 (0%)	
INCP	76	65 (85.5%)	10 (13.2%)	
NCIP	29	28 (96.6%)	1 (3.5%)	
NCIN	3	3 (100%)	0 (0%)	
Number cases reviewed[3]				
Mean [SD]	5.6 [11.7]	5.1 [4.9]	8.5 [29.0]	
Median [IQR]	5.0 [2.0-7.0]	5.0 [2.0-7.0]	3.0 [2.0-6.0]	P=0.13
Number cases compliant[3]				
Mean [SD]	4.8 [8.2]	4.8 [4.5]	5.3 [19.5]	
Median [IQR	4.0 [2.0-6.0]	5.0 [2.0-7.0]	2.0 [1.0-3.0]	P<0.001
Percentage of cases compliant[3]				
Mean [SD]	90.0% [20.1%]	95.4% [10.9%]	48.2% [25.1%]	
Median [IQR]	100% [85.7-100%]	100% [100-100%]	57.1% [33.3-66.7%]	P<0.001

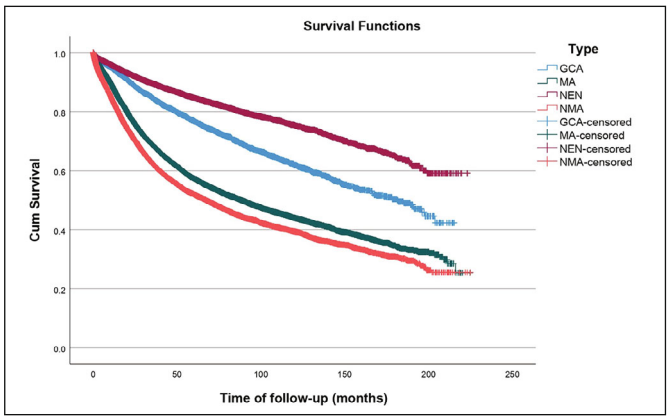
[1]One site received a "deficiency resolved" designation and is not included in comparisons between compliant and non-compliant sites. [2]Statistical Tests: Pearson chi-square test for site review year percentages, Fisher's exact test for type of CoC site percentages, and Wilcoxon rank sum test for medians. [3]Number of cases reviewed and/or number of cases compliant was not provided in all site review documentation.

Abbreviations: CoC (Commission on Cancer), ACAD (Academic Comprehensive Cancer Program), CCP (Community Cancer Program), CCCP (Comprehensive Community Cancer Program), HACP (Hospital Associate Cancer Program), INCP (Integrated Network Cancer Program), NCIP (National Cancer Institute-Designated Comprehensive Cancer Center Program), NCIN (National Cancer Institute Network Cancer Program)

P295. Management and Outcomes of Different Types of Appendiceal Cancer: A National Cancer Database Study

Ali Esparham[1]; Jennifer Whittington[2]; Zahra Shafaee[3]
[1]Mashhad University of Medical Sciences, Mashhad, Iran, Mashhad, IR; [2]Department of Surgery Elmhurst Hospital Center, Icahn School of Medicine, New York, NY, US; [3]Department of Surgery Elmhurst Hospital Center, Icahn School of Medicine, New York, NY, US

INTRODUCTION: Appendiceal tumors encompass a variety of histological types that exhibit different behaviors. This study aims to investigate and compare overall survival, predictive factors for overall survival, and management trends of histological variations of appendiceal tumors. **METHODS:** The National Cancer Data Bank (NCDB) database (2004–2020) was evaluated to include patients with appendiceal tumors histologies including goblet cell adenocarcinoma (GCA), neuroendocrine neoplasm (NEN), non-mucinous adenocarcinoma (NMA), and mucinous adenocarcinoma (MA). Univariate and multivariate analyzes were performed. **RESULTS:** The GCA, MA, NEN, and NMA groups consist of 6,111, 16,471, 19,199, and 11,065 patients, respectively. The NMA and NEN groups had significantly lowest and higher overall survival compared to other types (p<0.001 for both) (GCC: 143.27 (140.23-146.30), MA: 111.91 (109.996-113.832), NEN: 170.88 (168.56-173.20), and NMA: 101.399 (99.132-103.666) months). The independent predicting factors of overall survival were age (HR: 1.03 (1.03-1.04)), black race (HR: 1.24 (1.08-1.43), ref: white race), fourth median income (HR: 0.84 (0.74-0.96), ref: first median), Charleson index comorbidity score (HR: 1.3 (1.22-1.38)), lymphovascular invasion (HR: 1.28 (1.15-1.42)), pathologic stage 2 (HR: 1.32 (1.12-1.57)), stage 3 (HR: 1.99 (1.66-2.40)), stage 4 (HR: 4.20 (3.47-5.07)), ref: stage 1, intraoperative systemic therapy (HR: 0.52 (0.39-0.70)), positive surgical margin (1.55 (1.39-1.73)), number of positive lymph nodes (HR:1.06 (1.05-1.07)), moderately differentiated tumors (HR:1.43 (1.25-1.63)), poorly differentiated (HR: 1.94 (1.69-2.24)), undifferentiated (HR: 1.48 (1.14-1.91)), ref: well differentiated, and NMA type (HR:1.30 (1.10-1.55)). Furthermore, in terms of type of surgery, significantly higher patients of GCA (54.6%) and NMA (55.2%) groups underwent subtotal colectomy compared to other groups. Regarding systemic therapy, significantly higher patients of MA group received intraoperative, and both neoadjuvant and adjuvant therapy compared to other groups. Also, NEN group had significantly higher patients who underwent surgery with laparoscopic approach compared to others. Figure 1 shows Kaplan-Meier curve of overall survival of GCA, and NMA groups. **CONCLUSIONS:** This study reveals that different types of appendiceal tumors have distinct signals with regard to overall survival and treatment approaches. NENs showed the highest rates of overall survival, while NMAs had the lowest. These results underscore the need for personalized treatment strategies for each tumor type to improve patient outcomes.



P296. NCDB analysis of total mesorectal excision quality after implementation of Commission on Cancer Operative Standard 5.7

Kelley Chan, MD, MS[1]; Amanda B Francescatti, MS[2]; Bryan E Palis, MA[3]; Steven D Wexner, MD, PhD[4]; Sameh H Emile, MD[5]; Elizabeth C Funk, MSW[6]; Bell Pastore[7]; Peter Carpenter, MHA[8]; Matthew H.G. Katz, MD[9]; Tina J. Hieken, MD[10]; Timothy J Vreeland, MD[11]
[1]Loyola University Medical Center, Maywood, IL, US; [2]American College of Surgeons, Chicago, IL, US; [3]American College of Surgeons, Chicago, IL, US; [4]Cleveland Clinic Florida, Weston, FL, US; [5]Cleveland Clinic Florida, Weston, FL, US; [6]American College of Surgeons, Chicago, IL, US; [7]American College of Surgeons, Chicago, IL, US; [8]American College of Surgeons, Chicago, IL, US; [9]MD Anderson Cancer Center, Houston, TX, US; [10]Mayo Clinic, Rochester, MN, US; [11]Mercy, O'Fallon, MO, US

INTRODUCTION: Complete or near complete total mesorectal excision (TME), compared to incomplete TME, are associated with decreased local recurrence and improved survival for patients with rectal cancer. However, despite this, approximately 1/3 of resections are reported to have incomplete TME. To improve the quality of rectal cancer care, in 2020, the Commission on Cancer (CoC) adopted TME as an operative standard (5.7) for patients with mid/low rectal cancer with implementation beginning the following year. The objective of this study was to evaluate TME quality among patients treated at CoC-accredited hospitals in the early adoption period of CoC Operative Standard 5.7. **METHODS:** This retrospective cohort study queried the National Cancer Database for patients with stage I-III rectal adenocarcinoma who underwent curative surgery in 2022. TME status was abstracted from pathology reports and defined as high-quality (complete or near complete TME) or low-quality (incomplete TME). Patients were excluded if they did not receive TME or if their TME quality was unknown. Chi-squared tests compared patient sociodemographic, tumor, treatment, and hospital characteristics by TME quality. Significant variables were included in adjusted multivariable glimmix models, with hospital as a random effect, to investigate associations with low-quality TME. **RESULTS:** Of 4,118 patients, 60.0% were male, median age was 61 years (IQR 51-70), and 90.8% received high-quality TME. Compared to patients with high-quality TME, a higher proportion of patients with low-quality TME were age ≥70 years old (34.8% vs 25.1%, p=0.001), had stage II disease (28.2% vs 23.4%, p=0.032), had fewer than 12 lymph nodes examined (19.0% vs 12.5%, and had a positive circumferential resection margin (20.8% vs 6.9%, p<0.001). After adjustment, age ≥70 years old (OR 1.56; 95% CI 1.03 – 2.38), uninsured status (OR 3.22; 95% CI 1.53 – 6.77), Medicaid insurance status (OR 1.83; 95% CI 1.15 – 2.90), and treatment at an integrated network hospital (OR 1.74; 2.65) were associated with low-quality TME. **CONCLUSIONS:** In the early adoption period of CoC Operative Standard 5.7, 90.8% of patients at CoC-accredited hospitals received high-quality TME; however, disparities exist across patient sociodemographic and hospital characteristics.

Table. Multivariable adjusted odds ratios for receipt of incomplete total mesorectal excision.

Variable	Receipt of Incomplete Total Mesorectal Excision, OR (95% CI)	p-value
Age (years)		
18-49	0.91 (0.64 – 1.31)	0.613
50-59	Ref.	
60-69	0.90 (0.63 – 1.29)	0.571
≥70	1.56 (1.03 – 2.38)	**0.038**
Insurance status		
Uninsured	3.22 (1.53 – 6.77)	**0.002**
Private insurance	0.99 (0.69 – 1.43)	0.959
Medicaid	1.83 (1.15 – 2.90)	**0.011**
Medicare	Ref.	
Other/Unknown	1.52 (0.75 – 3.08)	0.241
Geographic region		
Midwest	Ref.	
North	0.90 (0.57 – 1.43)	0.663
Northeast	0.83 (0.54 – 1.27)	0.388
South	0.71 (0.44 – 1.17)	0.181
Southeast	1.08 (0.70 – 1.67)	0.725
West	0.60 (0.36 – 1.01)	0.054
Program Type		
Academic	Ref.	
Community	2.09 (0.94 – 4.63)	0.069
Comprehensive community	1.47 (0.97 – 2.22)	0.067
Integrated network	1.74 (1.15 – 2.65)	**0.009**
NCI	1.40 (0.83 – 2.34)	0.206
Surgery		
Abdominoperineal resection	Ref.	
Low anterior resection	0.23 (0.17 – 0.30)	**<0.001**
Pull through coloanal	0.28 (0.15 – 0.52)	**<0.001**
Total proctocolectomy	0.42 (0.26 – 0.70)	**0.001**
Surgical Approach		
Open	Ref.	
Laparoscopic	0.69 (0.47 – 1.01)	0.055
Robotic	0.65 (0.48 – 0.87)	**0.005**
Laparoscopic or robotic converted to open	1.64 (1.03 – 2.61)	**0.036**
Neoadjuvant therapy		
No neoadjuvant therapy	Ref.	
Received neoadjuvant chemotherapy or radiotherapy	1.29 (0.99 – 1.67)	0.056

P297. Prognostic factors for young patients with colorectal liver metastases following surgical resection: a SEER population-based study

Gabrielle Grob, BA[1]; Fang Fang[2]; Matvey Karpov, MPH[3]; Winifred M Lo, MD[4]
[1]Eastern Virginia Medical School, Norfolk, VA, US; [2]Old Dominion University, Norfolk, VA, US; [3]Old Dominion University, Norfolk, VA, US; [4]Eastern Virginia Medical School, Norfolk, VA, US

INTRODUCTION: Colorectal cancer (CRC) has been on the rise in adults under the age of 50 since the 1990s, and these patients are more likely to present with metastatic disease. Among patients with colorectal liver metastases (CRLM), approximately one-third present with isolated liver metastases, and surgical resection is a potentially curative treatment option. The aim of this study was to understand factors associated with disease-specific survival in young patients (<45 years old) vs older patients (≥45 years and older). **METHODS:** The SEER database was queried for patients with CRLM who underwent primary tumor resection and liver metastasectomy from 2000-2023. Patients under age 20, with metastases beyond the liver, or who had not had surgery for liver metastases were excluded. Chi-square test was used to compare differences by age group. Kaplan-Meier analysis was used to calculate disease-specific and overall survival. Cox regression analysis analyzed prognostic factors. **RESULTS:** 3196 patients were identified. 41.2% were female. 76.7% were white. Between groups, there was no significant difference in sex, race, income, rural location, T staging or pre-op CEA. Younger patients had slightly more positive regional lymph nodes from primary resection (3.8 vs 3.2, p=0.032) and chemotherapy than older patients. There was no significant difference in overall or disease-specific survival between age groups. In the overall cohort, neoadjuvant chemotherapy (HR 1.73, CI 1.3-2.3, p<0.001), perioperative chemotherapy (HR 1.83, CI 1.38-2.43, and elevated pre-operative CEA (HR 1.16, CI 1.04-1.29, p <0.01) were associated with improved disease-specific survival. The presence of positive regional lymph nodes was associated with decreased survival (HR 0.98, CI 0.96-0.99, p <0.01). For younger patients, those with higher household income had higher disease-specific survival (HR 1.08, HR 1.03 – 1.13, p>0.01), but no other factor had prognostic impact. Limitations include lack of liver surgery-specific information. **CONCLUSIONS:** For young patients with colorectal liver metastases undergoing liver metastasectomy, usual factors associated with disease-specific survival in older patients do not appear to be prognostic. Further study is warranted to better understand patient and tumor selection for surgical resection of colorectal liver metastases in young patients.

P298. Social Vulnerability Predicts State-Level Racial and Ethnic Disparities in Receipt of Treatment for Early-Onset Colorectal Cancer Patients with Metastatic Disease

Tracey Pu, MD[1]; Alexandra Gustafson, MD[2]; Kendra N Coleman, BS[3]; Joal Beane, MD[4]; Andrew M Blakely, MD[5]; Rebecca A. Snyder, MD, MPH[6]; Oliver S Eng[7]
[1]National Cancer Institutes/National Institutes of Health, Bethesda, MD, US; [2]National Cancer Institute, Bethesda, MD, US; [3]NCI/NIH, Bethesda, MD, US; [4]Ohio State University, Columbus, OH, US; [5]National Institutes of Health, Bethesda, MD, US; [6]MD Anderson Cancer Center, Houston, TX, US; [7]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US

INTRODUCTION: Racial and ethnic disparities persist in both incidence and outcomes for early-onset colorectal cancer (EO-CRC). Although public health initiatives are largely funded by state-policy, little is known how geographic vulnerability affects receipt of care in minoritized populations. Social determinants of health may further contextualize these inequalities and identify possible targets for intervention via state-level policy. **METHODS:** EO-CRC was defined as patients who were diagnosed <50 years old and patients with diagnosis years 2010-2020 were extracted from the SEER database. Aggregated state level population-weighted median percentile rankings were calculated for Social Vulnerability Index (SVI) for U.S. counties represented in the SEER database. Scores were stratified into tertiles, where the third tertile (TR3) represents the most vulnerable. **RESULTS:** 15,864 EO-CRC patients with metastatic disease were analyzed including 8580 (54.2%) Non-Hispanic White (NHW), 3479 (22.0%) Hispanic, 2318 (14.6%) Non-Hispanic Black (NHB), 1328 (8.4%) Non-Hispanic Asian or Pacific Islander (NHAPI), and 125 (0.8%) Non-Hispanic American Indian/Alaskan Native (NHAIAN) patients. EO-CRC patients residing in SVI TR1 states were more likely compared to TR2 and TR3 to receive chemotherapy (90.2% vs. 84.3% and 84.1%, all p<0.01) or combination chemotherapy and surgery (51.9% vs. 45.1% and 44.4%, all p<0.01). When stratifying by race, NHW patients had a higher percentage of patients residing in SVI TR1 states compared to Hispanic and NHB patients (6.2% vs. 1.3% and 0.7%, respectively, all p<0.01). Hispanic and NHB patients also had a higher percentage of patients residing in SVI TR3 states (41.1% and 42.5%, respectively) compared to NHW patients (40.8%, all p<0.01). No differences in receipt of treatment were observed between racial and ethnic groups residing in SVI TR1 regions. In SVI TR3 regions, Hispanic (80.7%) and NHB patients (80.6%) were less likely than NHW patients (85.8%) to receive chemotherapy (all p<0.001). Hispanic (40.5% vs. 45.7%, p=0.02) and NHB patients (41.2% vs 45.7%, p<0.01) were also less likely than NHW patients to receive combination chemotherapy and surgery. **CONCLUSIONS:** Disparities in receipt of treatment in EO-CRC patients is highly correlated with SVI, with Hispanic and NHB patients within lower tertile SVI regions receiving less treatment. Further investigation is warranted to guide public health policy in mitigating disparities to increase access of care.

Table. Receipt of Treatment of EO-CRC Patients Stratified By State-Level Social Vulnerability Index Tertiles

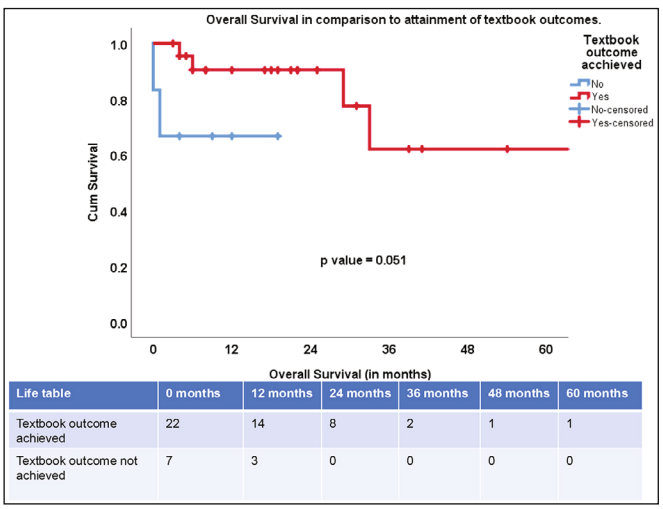
			Chemotherapy	Surgery	Combination Chemotherapy + Surgery
			Yes	Yes	Yes
Social Vulnerability Index	Tertile 1	**ALL RACES**	**533 (90.2%)**	**326 (55.3%)**	**307 (51.9%)**
		(A) NHW	438 (90.3%)	261 (54.0%)	246 (50.7%)
		(B) NHB	12 (85.7%)	8 (57.1%)	7 (50.0%)
		(C) NHAPI	34 (89.5%)	22 (57.9%)	22 (57.9%)
		(D) NHAIAN	10 (90.9%)	9 (81.8%)	9 (81.8%)
		(E) Hispanic	37 (90.2%)	25 (61.0%)	22 (53.7%)
	Tertile 2	**ALL RACES**	**6728 (84.3%)**	**4109 (52.3%)**	**3595 (45.1%)**
		(A) NHW	3555 (85.5%)$^{B(0.04), E}$	2258 (55.2%)$^{B, E}$	2003 (48.2%)$^{B, C}$
		(B) NHB	985 (81.3%)$^{A(0.04), C}$	572 (48.0%)^{A}	480 (39.6%)^{A}
		(C) NHAPI	589 (88.6%)$^{B, E}$	339 (51.5%)	306 (46.0%)
		(D) NHAIAN	68 (78.2%)	41 (48.2%)	33 (37.9%)
		(E) Hispanic	1516 (82.6%)$^{A, C}$	891 (49.4%)^{A}	767 (41.8%)^{A}
	Tertile 3	**ALL RACES**	**5000 (84.1%)**	**3046 (51.8%)**	**2639 (44.4%)**
		(A) NHW	2741 (85.8%)$^{B, E}$	1659 (52.5%)	1460 (45.7%)$^{E(0.07)}$
		(B) NHB	729 (80.6%)$^{A, C}$	443 (49.6%)$^{C(0.048)}$	372 (41.2%)^{C}
		(C) NHAPI	449 (88.2%)$^{B, E}$	289 (57.5%)$^{B(0.048), E(0.02)}$	261 (51.3%)$^{B, E}$
		(D) NHAIAN	17 (89.5%)	10 (52.6%)	10 (52.6%)
		(E) Hispanic	1057 (80.7%)$^{A, C}$	639 (49.5%)$^{C(0.02)}$	531 (40.5%)$^{A(0.02), C}$

*All p-value <0.01 unless otherwise states. Superscript ^{A}=Significance compared to Non-Hispanic White, Superscript ^{B}=Significance compared to Non-Hispanic Black, Superscript ^{C}=Significance compared to Non-Hispanic Asian or Pacific Islander, Superscript ^{D}=Significance compared to Non-Hispanic American Indian/Alaskan Native, Superscript ^{E}=Significance compared to Hispanic
**Abbreviations: MHI = Median Household Income, NHW = Non-Hispanic White, NHB = Non-Hispanic Black, NHAPI= Non-Hispanic Asian or Pacific Islander, NHAIAN = Non-Hispanic American Indian/Alaska Native

P299. Textbook Outcomes in Colorectal Cancer Surgery for Septuagenarians and Octogenarians: A Reality Check on Feasibility and Influence on Survival.

Preethi Santhosh Shetty, Associate Professor[1]
[1]Kasturba Medical College, Manipal, Karnataka, IN

INTRODUCTION: The elderly comprising of patients over 70 years, often present with colorectal cancers in the advanced stages needing extensive surgeries and multi-modal treatment. The co-existing illnesses and their frail nature often preclude attainment of textbook outcomes measures. This study evaluates the feasibility of obtaining textbook outcomes in such patients and also its influence on long term survival. **METHODS:** A retrospective analysis of prospectively maintained electronic database was done for the period between March 2019 to January 2024. All elderly patients i.e. 70 years and above who underwent curative colorectal surgery were included in the study. The textbook outcome measures were defined by the Dutch Colorectal Audit group i.e. 1) In-hospital mortality, 2) Re-interventions, 3) R0 resection, 4) Post-operative complications, 5) Length of hospital stay ≥14 days & 6) Re-admission within 30 days. These were compared to the survival outcomes using Kaplan Meier curves and Cox- regression analysis was performed to determine the factors influencing the survival outcomes. **RESULTS:** Between March 2019 to January 2024, 29 patients above 70 years of age underwent curative colorectal surgeries. The median age was 74 years ± 4 years. Nearly three-fourths were male. Low anterior resections (31%) and anterior resections (38%) were the main surgeries performed. One patient underwent total pelvic exenteration and another liver metastatectomy in the same setting. Minimally invasive procedure was performed in 41% of the patients. The textbook outcomes were achieved in 76% of the patients. R0 resections were performed in all patients. Two patients had in-hospital mortality. The estimated overall survival (OS) was 34.5 ± 4.3; CI 26.1 – 42.9 months. There was trend towards better OS when textbook outcomes were attained (34.9 ± 4.6; CI 24.9-44.0 months vs. 25.7 ± 6.1; CI 13.6-37.7 months, p value =0.645). **CONCLUSIONS:** The attainment of textbook outcomes in the elderly during colorectal cancer surgeries is always a possibility and should be striven for, since it positively correlates with the survival outcomes.



Life table	0 months	12 months	24 months	36 months	48 months	60 months
Textbook outcome achieved	22	14	8	2	1	1
Textbook outcome not achieved	7	3	0	0	0	0

P300. The Association of CDH1 Germline Variants and the Rate of Endoscopic Diagnosis of Colon Adenomas: A Single-Institution Experience

Adrienne B Shannon, MD[1]; Christine Laronga[2]; Marie C Lee, MD[3]; Julian Sanchez, MD[4]; Jose M Pimiento, MD[5]; Seth Felder, MD[6]; Andrew J Sinnamon, MD[7]
[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4], US; [5]Moffitt Cancer Center, Tampa, FL, US; [6], US; [7]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Germline CDH1 variants result in increased risk of gastric (GC) and invasive lobular (ILC) carcinoma with high penetrance. Limited data suggests a higher incidence of colorectal neoplasia in CDH1 mutation patients, but data remains limited on the risk of colon adenoma formation and the role of colonoscopy in this population. **METHODS:** Adult patients who underwent next generation sequencing 2012-2023 revealing a pathogenic mutation (PM) or variant of unknown significance (VUS) in CDH1 were identified and seen in consultation within a surgical clinic at a single institution were identified. Clinical and treatment characteristics were analyzed using univariate analyses. **RESULTS:** Thirty-eight patients with CDH1 PM or VUS were identified at a single high-volume cancer center. Median age of CDH1 mutational analysis was 42 (interquartile range (IQR) 35-58) years. The majority of patients had deletion (N=15, 39.5%) or nonsense (N=6, 15.8%) mutations or VUS (N=7, 18.4%). Twenty-six (68.4%), 20 (52.6%), and 11 (29%) patients had a family history of ILC, GC, and colon cancer, respectively. Twelve (31.6%) patients had GC on final specimen following gastrectomy, and 12 (31.6%) patients had ILC on final specimen following mastectomy. Eighteen (47.4%) patients underwent screening colonoscopy in addition to screening for GC and ILC; the median age at screening colonoscopy was 51.5 (IQR 46-58) years and 4 (22.2%) patients were <45 years of age at the time of colonoscopy. Among patients <45 years of age, the rate of adenoma detection was 50%. Adenomas were identified in 8 (44.4%) patients, and of these patients, 6 (75%) had right-sided, 4 (50%) had left-sided, and 2 (25%) had both right- and left-sided adenomas, respectively. No patients were identified on colonoscopy to have colorectal cancers. When examining only patients with CDH1 PM (N=31), 16 (51.6%) patients underwent screening colonoscopy, and 8 (50%) patients had adenomas detected. Conversely, of the 2/6 CDH1 VUS patients who underwent screening colonoscopy, neither patient had adenomas detected. **CONCLUSIONS:** The association of CDH1 variants and colorectal neoplasia remains undefined, but the rate of colorectal adenoma detection in this population of patients is greater than three-fold higher than the general population. Consideration of earlier colonoscopy of CDH1 variant patients and insurance approval may be warranted.

Table. Colonoscopy characteristics and endoscopic findings of CDH1 pathogenic mutation and variant of unknown significance patients who underwent colonoscopy screening at a single institution.

Patients who Underwent Colonoscopy Screening **N=18, 50%**	**N (%)**
Age at screening colonoscopy, years (median, IQR)	51.5 (46-58)
Number of polyps found on colonoscopy (mean, SD)	1.2 (1.5)
Non-adenomatous polyps identified	4 (22.2)
Adenomatous polyps identified	8 (44.4)
Right-sided	6 (75.0)
Left-sided	4 (50.0)

P301. A Systematic Review of Surgical Care for Persons Experiencing Homelessness with Cancer

Harris Allen[1]; Wendy Feng[2]; Caroline Falker[3]; Cynthia Brandt[4]; Victor Agbafe[5]; James Allen[6]; Jayson Esdaille[7]; Vikram Reddy[8]; Anne Mongiu[9]; Nikki Civitella[10]; Haddon Pantel[11]; Melissa Perkal[12]; Shilpa Murthy, MD, MPH[13]
[1]Yale-New Haven Health, New Haven, CT, US; [2]Yale-New Haven Health, New Haven, CT, US; [3]Yale-New Haven Health, New Haven, CT, US; [4]Yale-New Haven Health, New Haven, CT, US; [5]Yale-New Haven Health, New Haven, CT, US; [6]Yale-New Haven Health, New Haven, CT, US; [7]Yale-New Haven Health, New Haven, CT, US; [8]Yale-New Haven Health, New Haven, CT, US; [9]Yale-New Haven Health, New Haven, CT, US; [10]West Haven VA Medical Center, West Haven, CT, US; [11]Yale-New Haven Health, New Haven, CT, US; [12]West Haven VA Medical Center, West Haven, CT, US; [13]Yale School of Medicine, New Haven, CT, US

INTRODUCTION: Over 3.5 million people experience homelessness (PEH) in the US annually and cancer related deaths are twice as high in PEH compared to the general population. Oncologic management of PEH is influenced by social determinants of health (SDOH) including lack of health insurance, housing, and unreliable transportation as cancer care requires multimodal diagnostic workups and therapies by a multidisciplinary team. To improve cancer related mortality, SDOH and their influence on surgical cancer outcomes should be a focus for surgeons. However, there is a paucity of literature examining surgical cancer care in PEH. The objective of this review is to examine disparities in surgical access, treatment, and cancer outcomes for PEH. **METHODS:** A systematic review was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. An initial search used terms of homelessness, cancer, and surgery. References were identified in databases including OVID MEDLINE, OVID Embase, Web of Science- Core Collection, Scopus, Healthcare Administration Database,

Cochrane CENTRAL, as well as Google Scholar and grey literature. Papers were selected in 3 phases: two reviewers (HA/WF) independently screened abstracts, and assessed full text articles for eligibility, and discrepancies were reviewed by SSM. **RESULTS:** A total of 1073 papers were generated, and 26 papers met inclusion criteria -13 case studies, 9 cohort studies, 2 op eds and 2 reviews. Articles included 22 to over 2 million patients and included cancers of the lung, colorectal, breast, and melanoma. Significantly more PEH presented with advanced cancers compared to the general population, and few received surgical treatment. Moreover, studies suggested PEH have inconsistent primary medical care, which may play a role in delayed diagnoses, advanced stage presentation, reduced access to surgeons, and treatments at non-specialist sites. Many PEH patients were ultimately lost to postoperative follow-up and long-term cancer surveillance. **CONCLUSIONS:** Although cancer-related deaths are higher in PEH compared to the general population, there are few studies examining challenges faced by PEH when receiving surgical cancer care. This literature review provides insight into major barriers, including reduced access to surgeons, delays in diagnosis, and treatment at non specialist sites. Further work focused on solutions is warranted, such as developing routine screening programs and pathways for PEH cancer patients to readily access surgical care.

P302. Analyzing MyChart Use in Surgical Oncology Care

Shay Behrens, MD[1]; Andy Kaempf, PhD[2]; Thomas Sutton, MD[3]; Ranish Patel, MD[4]; Tanuj Devara[5]; Jeff Gold, MD[6]; Brett Sheppard[7]
[1]Oregon Health and Sciences University, Portland, OR, US; [2]Oregon Health and Sciences University, Portland, OR, US; [3]Oregon Health and Sciences University, Portland, OR, US; [4]Oregon Health and Science University, Portland, OR, US; [5]Oregon Health and Sciences University, Portland, OR, US; [6]Oregon Health and Sciences University, Portland, OR, US; [7]Oregon Health and Science University, Portland, OR, US

INTRODUCTION: Electronic medical records (EMRs) and electronic health record (EHR) systems are now widely adopted, serving patients, providers, and healthcare systems. Patient portals within EHRs, like "MyChart," can improve care, enhance patient understanding, and boost outcomes. Given the complexity of healthcare disparities in cancer treatment and their impact on oncological outcomes, we aimed to explore how surgical oncology patients utilize MyChart during cancer treatment. **METHODS:** Patients with five types of cancer from 2015 to 2022 were included in the study. The cancer sites were breast, colorectal, skin, hepatobiliary, and pancreas. Exclusions applied to patients without first-course treatment at OHSU, those with dual cancer diagnoses on the same day, or those missing key data, including cancer diagnosis date, first contact at OHSU date, or last follow-up/death date. An Epic health record query was conducted to extract MyChart-related metrics from the date of diagnosis to the last follow-up or death date. **RESULTS:** Of 6,326 cancer patients who underwent surgery during their first course of treatment, 71.5% (n=4,524) had an active MyChart account. The median follow-up from cancer diagnosis was 42 months. Breast cancer patients had the highest activation rate (86.7%), followed by colorectal (72.6%), skin (72.7%), pancreatic (65.4%), and hepatobiliary (56.0%) cancers. Colorectal, skin, hepatobiliary, and pancreatic cancer patients were more likely to activate MyChart after their diagnosis, with most doing so within one month. Skin cancer patients had the fewest log-ins (0.9/month), while breast cancer patients had the highest usage, particularly for scheduling appointments, averaging 1.0 messages per month (IQR: 0.2–4.6). Patients frequently used the admissions, visits, and test results tabs, while features like account details, payments, immunizations, insurance, problem lists, questionnaires, and result graphs were rarely used. Interestingly, the web platform was the primary method of access. **CONCLUSIONS:** Cancer patients are using MyChart to engage with the healthcare system, with a high activation rate within the first month of diagnosis. Increased use for tasks like appointment scheduling and accessing test results suggests that MyChart may improve communication, care coordination, and outcomes. Future research should explore disparities between MyChart users and non-users and identify ways to optimize its use to enhance cancer care and outcomes.

P303. Association of social determinants of health diagnosis codes with survival in Medicare-insured patients with cancer

Joshua Herb, MD, MSCI[1]; Chung-Yuan Hu, PhD[2]; Sharon Giordano, MD MPH[3]; George J Chang, MD, MS[4]; Rebecca A. Snyder, MD, MPH[5]
[1]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [4]MD Anderson Cancer Center, Houston, TX, US; [5]MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Social determinants of health (SDOH) impact treatment and long-term outcomes among patients with cancer. Since 2015, the Centers for Medicare & Medicaid Services have recommended using ICD diagnosis codes Z55-Z65 to document specific SDOH. These diagnosis codes refer to various SDOH domains such as education and literacy (Z55), housing (Z59), employment (Z56), and social environment (Z60) (Table). We examined national trends in utilization of Z-codes and their association with survival in patients with cancer. **METHODS:** Patients ≥ 66 years of age with breast, colorectal, lung, prostate, or pancreatic cancer were identified in the SEER-Medicare database (2016-2019). The primary exposure was a Z-code claim in the 12 months before or 3 months after cancer diagnosis. The primary outcome was overall survival. Multivariable Cox regression was performed to examine the association of Z code claims with overall survival, controlling for demographic/clinical covariates. **RESULTS:** Of 209,811 patients, 3,638 (1.7%) had at least one Z code claim, and use increased slightly over the study period (1.5% in 2016 and 1.9% in 2019). Patients with a Z-code claim, compared to patients without a Z code claim, were older (23.1% vs 12.9% 85+ years old), more frequently female (61.7% vs 47.2%), more likely dual eligible (4.8% vs 2.1%) and had higher Charlson Comorbidity Scores (28.3% vs 18.3% 3+) (all P<0.01). Of patients with a Z-code, the most common codes were Z60 (problems with social environment, 44%) and Z63 (problems with primary support group, 33%), and were submitted most often by home health agencies (55.2%) and least often by inpatient facilities (1.4%). On adjusted analysis, having any SDOH Z-code claim was associated with worse survival (HR 1.89; 95% CI 1.80-1.97), however, associations varied by specific Z-code (Table). **CONCLUSIONS:** To date, SDOH Z-codes are rarely submitted among Medicare patients with cancer, particularly for inpatient care. Thus, it remains unclear if Z-codes accurately reflect the social needs of patients with cancer. Based on current coding, having any SDOH Z-code claim is associated with worse survival in patients with cancer, but individual Z-codes are not consistently associated with survival. If usage increases, further studies should determine if SDOH Z-codes enable effective risk-adjustment.

Table. Association of Z-code claim with overall survival among Medicare insured patients with cancer.

Z code	Definition – "Problems related to. .":	Adjusted HR	95% CI
Any Z code		1.14	(1.09-1.19)
Z55	Education/Literacy	1.08	(0.73-1.59)
Z56	Employment	0.87	(0.55-1.37)
Z57	Occupational exposures	1.09	(0.92-1.29)
Z59	Housing/Economic circumstances	1.36	(1.17-1.58)
Z60	Social Environment	1.09	(1.03-1.16)
Z62	Upbringing	0.76	(0.46-1.24)
Z63	Primary support group	1.05	(0.95-1.16)
Z64	Certain psychosocial circumstances	-	-
Z65	Other psychosocial circumstances	1.36	(1.21-1.53)

- Z64 not evaluable due to low number of Z-code claims

P304. Association of socioeconomic status and neighbourhood ethnic diversity with failure to rescue in curative-intent stage I-III colorectal cancer surgery: a population-based cohort study

Adom Bondzi-Simpson[1]; Tiago Ribeiro, MD, MSc[2]; Andrea Covelli, MD, PhD[3]; Aisha Lofters, MD, PhD[4]; Rinku Sutradhar, PhD[5]; Rebecca A. Snyder, MD, MPH[6]; Callisia Clarke, MD, MS, FSSO[7]; Natalie G Coburn, MD, MPH[8]; Julie Hallet, MD, MSc, FSSO[9]
[1]University of Toronto, Toronto, ON, CA; [2]University of Toronto, Toronto, ON, CA; [3]Sinai Health System - Mount Sinai Hospital, Toronto, ON, CA; [4]University of Toronto, Toronto, ON, CA; [5]University of Toronto, Toronto, ON, CA; [6]MD Anderson Cancer Center, Houston, TX, US; [7]Medical College of Wisconsin, Milwaukee, WI, US; [8]University of Toronto, Toronto, ON, CA; [9]Sunnybrook Health Sciences Centre, Toronto, ON, CA

INTRODUCTION: Failure to rescue (FTR) is a quality indicator reflecting the ability of care structures to detect and treat patients with declining clinical status. Though frequently reported in aggregate for entire populations, quality indicators may vary by social determinants of health, further contributing to an inability to detect health disparities. We examined the association between patient's neighbourhood socioeconomic status (SES) and neighbourhood ethnic diversity on FTR after curative-intent colorectal cancer (CRC) resection. **METHODS:** We conducted a population-based retrospective cohort study of adults undergoing resection for stage I-III CRC (2007-2020). Exposures were SES and ethnic diversity defined by ecologic measures from census data, measured in quintiles. Using postal codes, quintiles were ordered from the 1st quintile, representing highest SES and lowest ethnically diverse

neighbourhoods, to the 5th, representing the lowest SES and most ethnically diverse neighbourhoods. The primary outcome was FTR, as *the number of patients with a major complication who died in-hospital*. Logistic regression examined the association between each exposure and outcome while adjusting for confounders. **RESULTS:** Of 60,470 patients included, FTR occurred in 1,158 (1.9%). Among those with FTR, 289 (25.0%) were from the lowest SES neighborhoods versus 196 (16.9%) in the highest (p <0.001), whereas 214 (18.5%) were from the highest ethnically diverse neighbourhoods versus 245 (21.2%) in the lowest (p= 0.12). After adjusting for age, sex, surgical approach, comorbidity burden, cancer type, and year, residing in the both the lowest SES (Odds Ratio, OR 1.26; 95% confidence interval, CI 1.05-1.52) and highest ethnically diverse neighborhoods (OR 1.53, 95%CI 1.26-1.85) was associated with higher odds of FTR. When considering only colon cancer (n=42,755), the findings remained for patients residing in the highest ethnic diversity neighborhoods OR 1.37 (95%CI 1.37-2.11), but not for those in the lowest SES neighborhoods (OR 1.23, 95% CI 1.00-1.52). When considering only rectal cancer (n =17,715), no independent association was observed with either exposure. **CONCLUSIONS:** Patients from the lowest SES neighborhoods had a 26% increase in the odds of FTR compared to those from the highest SES neighborhoods. Furthermore, patients from the most ethnically diverse neighborhoods had 53% increase in the odds of FTR compared to those from the least diverse neighborhoods. These findings outline the need to report quality indicators stratified by social determinants of health to identify inequalities that warrant intervention to improve access to care for at-risk populations.

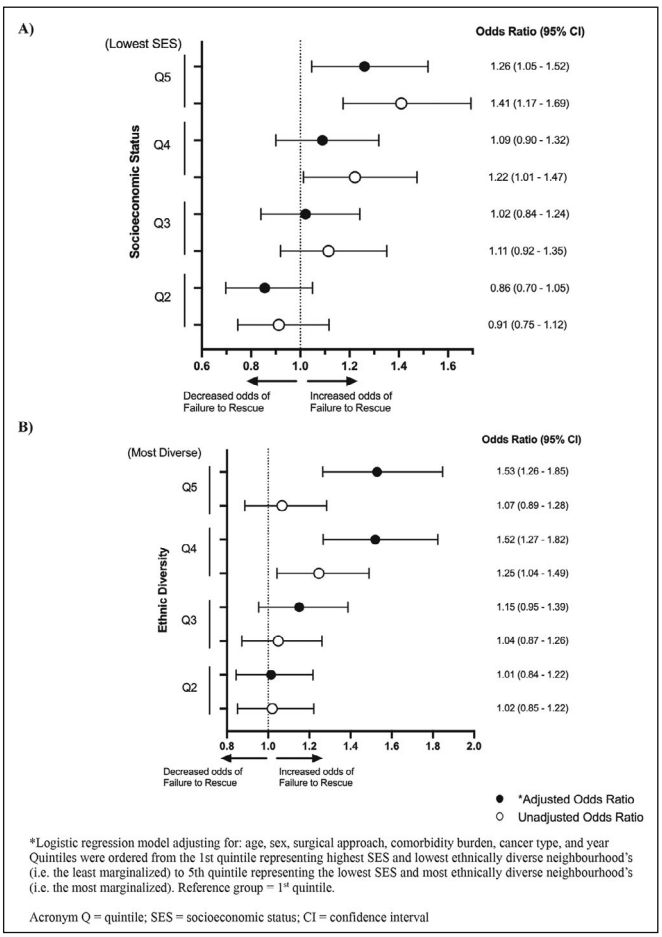


Figure 1. Forest plot of odds ratios examining the association between neighbourhood-level dimensions of marginalization (SES and ethnic diversity) and failure to rescue after curative-intent surgery for stage I-III colorectal cancer in Ontario (2007-2020). Unadjusted and adjusted association of A) SES and B) neighborhood ethnic diversity with failure to rescue. Uni and multivariable logistic regression models were fitted reporting odds ratios with 95% confidence intervals.

P305. Awareness of hereditary breast cancer and genetic testing among breast cancer patients in Nigeria: A multi-center study

Funmilola Wuraola[1]; Jenine Ramruthan, MSc[2]; Nneka Sunday[3]; Isaac Olusegun Alatise[4]; Agodirin Olaide[5]; Mary Ogunyemi[6]; Olawale Boladuro[7]; Saheed Lawal[8]; Emma Reel, MSW[9]; Tulin D Cil, MD, MEd[10]

[1]Obafemi Awolowo University Teaching Hospital, Ife, Osun, NG; [2]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, CA; [3]Alex-Ekwueme Federal University Teaching Hospital, Abakaliki, Ebonyi, NG; [4]Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Osun State, NG; [5]University of Ilorin, Ilorin, Kwara, NG; [6]African Research Group for Oncology, Ife, NG; [7]Alex Ekwueme Federal University Teaching Hospital, Abakaliki, NG; [8]African Research Group for Oncology, Ife, NG; [9]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, CA; [10]Princess Margaret Cancer Centre, University Health Network, Toronto, ON, CA

INTRODUCTION: Breast cancer remains a major public health concern in Nigeria, often diagnosed at advanced stages due to delayed presentation and limited awareness. Understanding patient knowledge of breast cancer is essential to improve early detection and outcomes. This study aimed to assess the demographic and clinical characteristics of breast cancer patients across three Nigerian hospital centers and evaluate their knowledge of breast cancer risk factors, hereditary breast cancer, and genetic testing. **METHODS:** A cross-sectional study was conducted among 230 newly diagnosed breast cancer patients attending Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife; University of Ilorin Teaching Hospital (UITH), Ilorin; and Federal Teaching Hospital Abakaliki (FETHA), Ebonyi in Nigeria. Data on demographics, tumor characteristics, and molecular subtypes, were collected. Knowledge of breast cancer symptoms, risk factors and hereditary breast cancer was assessed using a structured questionnaire. Univariable and multivariable linear and logistic regression analyses identified factors associated with knowledge scores. **RESULTS:** The mean age of participants was 48.3 years; the majority were female (99.1%); Most patients were traders (51.1%) and of low socioeconomic status (66.5%). Educational levels varied, with 33.0% having tertiary education. A large proportion presented at advanced stages (Stage III: 51.7%, Stage IV: 21.3%), with 64.3% having triple-negative breast cancer. Knowledge of risk factors was low, with higher knowledge associated with tertiary education (p = 0.004) and higher socioeconomic status (p = 0.020), while older age (≥65) was linked to lower scores (p = 0.091). Participants from UITH, Ilorin had lower knowledge of breast cancer symptoms than those from OAUTHC Ile-Ife (p < 0.001). Regarding hereditary breast cancer, only 11 patients (4.8%) had heard of BRCA genes, of these most had a tertiary education. Willingness to undergo BRCA1/2 genetic testing was high (95.7%), with 93.9% willing to inform siblings and 96.5% willing to encourage genetic testing for family members. **CONCLUSIONS:** Awareness of hereditary breast cancer was low, despite high willingness for genetic testing. Higher educational level and socioeconomic status remained strong predictors linked to higher knowledge of breast cancer risk factors. Knowledge gaps were more pronounced among older, less educated, and disadvantaged patients, highlighting the need for targeted education to improve understanding of hereditary breast cancer and genetic testing in this setting.

P306. Curative-Intent Therapies for Colorectal Liver Metastases: Estimating Survival Impact by Difference-In-Difference Analysis of SEER-Medicare

Vasileios Tsagkalidis, MD[1]; Elizabeth A. Handorf, PhD[2]; Benjamin A. Bates, MD[3]; David G. Brauer, MD, MPHS[4]; Patrick M. Boland, MD[5]; Charu Verma, MPH[6]; Mariam F. Eskander, MD[7]; Miral S. Grandhi, MD[8]; Haejin In, MD, MBA, MPH[9]; Hari S. Iyer, ScD[10]; Timothy J. Kennedy, MD[11]; Russell C. Langan, MD[12]; Jason C. Maggi, MD[13]; Henry A. Pitt, MD[14]; Elisa V. Bandera, MD, PhD[15]; Alexander A. Parikh, MD, MPH[16]; Brett L. Ecker, MD[17]

[1]Banner MD Anderson Cancer Center, Gilbert, AZ, US; [2]Rutgers School of Public Health, Piscataway, NJ, US; [3]Institute for Health, Health Care Policy & Aging Research, New Brunswick, NJ, US; [4]University of Minnesota, Minneapolis, MN, US; [5]Rutgers Cancer Institute, New Brunswick, NJ, US; [6]Institute for Health, Health Care Policy & Aging Research, New Brunswick, NJ, US; [7]Rutgers Cancer Institute, New Brunswick, NJ, US; [8]Rutgers Cancer Institute, New Brunswick, NJ, US; [9]Rutgers Cancer Institute, New Brunswick, NJ, US; [10]Rutgers School of Public Health, Piscataway, NJ, US; [11]Rutgers Cancer Institute, New Brunswick, NJ, US; [12]Rutgers Cancer Institute, New Brunswick, NJ, US; [13]Rutgers Cancer Institute, New Brunswick, NJ, US; [14]Rutgers Cancer Institute, New Brunswick, NJ, US; [15]Rutgers School of Public Health, Piscataway, NJ, US; [16]University of Texas Health Science Center San

Antonio MD Anderson Cancer Center, San Antonio, TX, US; [17]Rutgers Cancer Institute, New Brunswick, NJ, US

INTRODUCTION: For patients with colorectal cancer liver metastasis (CRCLM), curative-intent liver therapies are associated with improved survival. However, randomized data are lacking and individual-level retrospective data are limited by selection bias. We aimed to quantify the survival impact of these therapies by analyzing how regional variation in liver therapy rates influence survival outcomes within health service areas (HSA). **METHODS:** The SEER-Medicare database (2000-2020) was analyzed for patients ages 66-85 with liver-isolated CRCLM who underwent curative-intent liver therapy (i.e, hepatectomy, ablation, or transplantation). Rates of resection within HSAs for each year were calculated. A modified difference-in-differences risk-adjusted analysis was performed for two eras (Era 1: 2002-2004; Era 2: 2013-2015) to quantify the impact of changing rates of curative-intent liver therapy on HSA-level survival. **RESULTS:** A total of 34,781 patients were included. The majority had synchronous CRCLM (65.8%) and received chemotherapy (63.1%); a minority (10.9%) underwent curative-intent liver therapy (hepatectomy, 74.3%; ablation alone, 24.9%; transplantation 0.8%). Fifty-six (34%) HSAs had the rate of curative-intent liver therapy increase (≥5%) across eras, 58 (36%) HSAs had the rate remain constant, and 49 (30%) HSAs experienced a rate decrease (≥5%). Each 5% increase in the rate of curative-intent liver therapy was associated with a 1.2% (95% CI 0.4%-2.0%) increase in the risk-adjusted 1-year survival rate (p=0.003). **CONCLUSIONS:** Health service area changes in rates of curative-intent therapy for CRCLM lead to population-level changes in cancer survival. Efforts to increase patient access to and subsequent completion of curative-intent therapies can meaningfully improve outcomes for CRCLM.

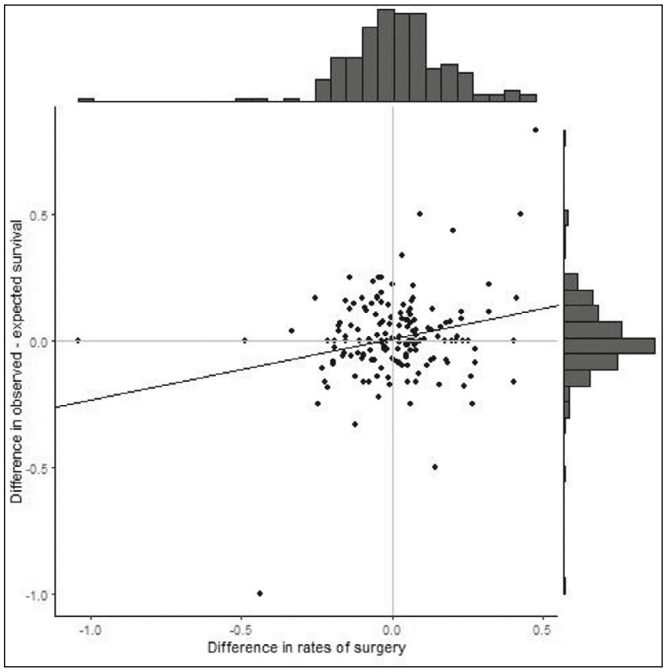


Figure 1. Graphical representation of the modified difference-in differences analysis. Each point on the scatterplot represents an HSA. The x-axis measures the change in rates of surgery between the two time periods (Era 1: 2002-2004; Era 2: 2013-l5). The y-axis measures the change in the observed – expected 1-year survival between the two time periods. The fitted regression line shows the relationship between these measures. The marginal histograms sliow the distribution of the changes.

P307. Disparities in Surgical Care of Colorectal Liver Metastases

Ashley E Martinez[1]; Alexis Webber, MD[2]; Carter Larrance, BS[3]; Sandra R. DiBrito, MD, PhD[4]
[1]Albany Medical College, Albany, NY, US; [2]Albany Medical Center, Albany, NY, US; [3]Albany Medical Center, Albany, NY, US; [4]Albany Medical Center, Albany, NY, US

INTRODUCTION: Up to 25% of colorectal cancer patients present with liver metastases (CRLM) and 50% develop metastases over time. Surgical management of CRLM can be curative, but certain demographic and socioeconomic factors disproportionately hinder vulnerable patient populations from receiving advanced surgical care. **METHODS:** We queried the 2011-2021 National Cancer Database for cases of CRLM. We explored patient and facility characteristics associated with receipt of surgery vs. no surgery for metastatic liver lesions. **RESULTS:** Out of 67225 cases, 18.0% underwent hepatectomy. Surgery rates were higher among Non-Hispanic White (NHW) patients compared to Non-Hispanic Black (NHB) and Hispanic/Latino (HL) patients (Table 1, p<0.001). Surgery rates declined with lower income and education quartiles, and were lower for patients with no insurance or government insurance compared to those with private insurance (Table 1). Academic programs had higher surgery rates than community cancer programs (p<0.001). Patients receiving surgery traveled farther than non-surgery care (Table 1). Controlling for patient and center level factors, multivariable analysis showed NHB and HL patients were less likely to undergo liver surgery compared to NHW patients (OR:0.81, 95%CI [0.77-0.87]; OR:0.90, 95%CI [0.83-0.97]). Patients treated at academic programs had significantly higher odds of surgery compared to community cancer programs (OR:2.3, 95%CI [2.11-2.50]). Patients with private or government insurance had higher odds of surgery compared to uninsured patients (OR:2.0, 95%CI [1.79-2.23], OR:1.60, 95%CI [1.43-1.80]). Highest income quartile patients were more likely to have surgery than the lowest quartile (OR:1.18, 95%CI [1.09-1.28]). **CONCLUSIONS:** Surgical management of CRLM is necessary to achieve cure for appropriately selected patients. However, access to surgical care is not equally distributed amongst patient populations. Significant socioeconomic and demographic disparities exist in access to surgical care amongst CRLM patients and require further exploration to improve resource allocation.

Table 1. Description of patient and program characteristics for cases of colorectal liver metastases treated with or without liver surgery from 2011-2021.

	Surgery (n=12093)	No Surgery (n=55132)	P-value
Age, mean (SD)	61.4 (11.5)	65.9 (12.3)	< 0.001
Sex, n (%)			0.2
Male	6814 (17.8)	31383 (82.2)	
Female	5279 (18.2)	23749 (81.8)	
Race/Ethnicity, n (%)			< 0.001
Non-Hispanic White	9526 (18.6)	41658 (81.4)	
Non-Hispanic Black	1721 (15.4)	9438 (84.6)	
Hispanic/Latino	846 (17.3)	4036 (82.7)	
Median Income Quartiles*, n (%)			< 0.001
<$46,277	2085 (15.4)	11485 (84.6)	
$46,277 - $57,856	2759 (17.3)	13157 (82.7)	
$57,857 - $74,062	2874 (18.3)	12808 (81.7)	
$74,063+	4375 (19.8)	17682 (80.2)	
No High School Degree Quartiles *, n (%)			< 0.001
15.3%+	2467 (15.4)	13553 (84.6)	
9.1% - 15.2%	3504 (17.6)	16362 (82.4)	
5.0% - 9.0%	3571 (19.0)	15189 (81.0)	
<5.0%	2551 (20.3)	10028 (79.7)	
Insurance Status, n (%)			< 0.001
Not insured	407 (12.8)	2777 (87.2)	
Government Issued	5820 (14.7)	33777 (85.3)	
Private	5866 (24.0)	18578 (76.0)	
Facility Type, n (%)			< 0.001
Community Cancer Program	728 (11.9)	5389 (88.1)	
Comprehensive Community Cancer Program	3716 (13.9)	22965 (86.1)	
Academic/Research Program	5332 (24.7)	16223 (75.3)	
Integrated Network Cancer Program	2317 (18.0)	10555 (82.0)	
Mean Distance Traveled, miles (SD)	33.0 (93.5)	20.5 (67.8)	< 0.001

*reported 2016-2020

P308. Disparities in Surgical Intervention for Metastatic Colorectal Cancer: A Population Based Evaluation of the SEER Database

Hector J Garcia-Navas, MD[1]; Denise Danos[2]; Andrea Fa[3]; Kristen Limbach, MD[4]; James Watson, MD[5]; Mary Maluccio, MD[6]; Omeed Moaven, MD[7]; Kevin Sullivan, MD[8]

[1]LSU HSC, New Orleans, LA, US; [2]LSU HSC, New Orleans, LA, US; [3]LSU HSC, New Orleans, LA, US; [4]Tulane University School of Medicine, New Orleans, LA, US; [5]LSU HSC, New Orleans, LA, US; [6]LSU HSC, New Orleans, LA, US; [7]LSU Health, New Orleans, LA, US; [8]LSU HSC, New Orleans, LA, US

INTRODUCTION: Cytoreduction and liver resection have been demonstrated to improve survival for peritoneal and liver metastases in patients with colorectal cancer (CRC). However, studies have shown surgical intervention rates as low as 10% in CRC patients with liver metastases. This project aims to identify patient populations and healthcare disparities that undergo surgery at inequitable rates. **METHODS:** Cases of metastatic colon cancer diagnosed from 2016 to 2020 were retrospectively identified in the Surveillance, Epidemiology, and End Results (SEER) database. Cases diagnosed in individuals younger than 18, unknown treatment, or sociodemographic data were excluded. Categorical case characteristics were compared using Chi-square tests. Overall survival was analyzed with Cox proportional hazards models. **RESULTS:** 11,069 patients with metastatic CRC were identified. The metastatic site was liver only (LO) in 40.6% of patients, peritoneum only (PO) in 12.6% of patients, and either multiple/other 43.3%. 2,326 patients (9.1%) received multimodal therapy (MT). 12.4% of LO metastases received MT versus 11.9% of PO. In CRC metastatic to LO, older age, Hispanic, non-Hispanic Black, and counties with median income <$85,000 were associated with reduced likelihood of receiving surgery in addition to chemotherapy (all p<0.05, Table 1). In patients with PO metastases, increased age and male sex were associated with reduced likelihood of undergoing surgery in addition to chemotherapy (p<0.05), but race/ethnicity and income were not associated with the addition of surgery to chemotherapy (Table 1). A Cox proportional hazard model that included age, sex, race, ethnicity, income, and tumor characteristics demonstrated that non-Hispanic Black race was significantly associated with worse survival in LO metastases (HR 1.20, 95% CI 1.10-1.31, p<0.0001), but there was no survival difference for race in patients with PO metastases. **CONCLUSIONS:** In a large national database, we demonstrate aggressive MT including both chemotherapy and distant site surgery at rates of 12.4% for LO metastatic CRC and 16.6% in PO metastatic CRC. Data demonstrates a racial disparity in reduced likelihood of non-Hispanic Black patients of undergoing surgery in addition to chemotherapy of LO metastases, as well as reduced survival for non-Hispanic Black LO metastases. This racial disparity is not demonstrated for PO metastases. Efforts should also be focused on patient and provider education to improve surgical rates for colorectal liver metastases in Black patient populations

Table 1. Adjusted odds ratios and 95% confidence intervals from logistic regression of having surgery to the distant site in cases of metastatic colon cancer with chemotherapy, SEER 2016-2020.

	Liver Metastases		Peritoneum Metastases	
	RR (95% CI)	p-value	RR (95% CI)	p-value
Age at diagnosis (ref= 20-44)				
45-64	0.76 (0.62,0.93)	0.0066	0.70 (0.50,0.98)	0.0394
65-74	0.57 (0.46,0.71)	<.0001	0.53 (0.36,0.78)	0.0013
75 and older	0.39 (0.30,0.50)	<.0001	0.56 (0.36,0.85)	0.0073
Sex (ref= Female)				
Male	0.97 (0.86,1.10)	0.6366	0.35 (0.28,0.45)	<.0001
Race/Ethnicity (ref= White)				
Non-Hispanic Black	0.66 (0.55,0.80)	<.0001	0.86 (0.59,1.25)	0.4330
Non-Hispanic Asian or Pacific Islander	0.90 (0.73,1.12)	0.3588	0.76 (0.49,1.16)	0.2048
Hispanic (All Races)	0.69 (0.58,0.84)	0.0001	1.07 (0.78,1.47)	0.6845
Median income (ref=$85,000 or greater)				
Less than $45,000	0.83 (0.69,1.00)	0.0475	1.00 (0.70,1.42)	0.9874
$45,000-$84,999	0.87 (0.75,1.00)	0.0447	0.88 (0.67,1.15)	0.3477
Metropolitan (ref='Yes')				
No	0.93 (0.75,1.16)	0.5053	0.98 (0.65,1.47)	0.9040
Tumor sequence (ref=First)				
Subsequent	1.07 (0.89,1.28)	0.4740	0.88 (0.62,1.24)	0.4616
Histology (ref= Adenocarcinoma)				
Mucinous	1.19 (0.85,1.67)	0.3091	1.17 (0.85,1.62)	0.3330
Signet Ring Cell	0.64 (0.14,2.84)	0.5563	0.87 (0.55,1.38)	0.5523
Colon site (ref= Left)				
Right	1.04 (0.91,1.18)	0.5838	1.29 (1.01,1.65)	0.0438
Not Otherwise Specified	0.34 (0.23,0.50)	<.0001	0.73 (0.48,1.10)	0.1329

P309. Disparities in postoperative outcomes for cancer patients with limited English proficiency: a systematic review

Nensi M Ruzgar[1]; Anusha Jayaram[2]; Carolina Vigna Saade[3]; Anays Murillo[4]; Anne Fladger[5]; Tara Kent[6]
[1]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, US; [2]Beth Israel Deaconess Medical Center, Boston, MA, US; [3]University of Connecticut School of Medicine, Farmington, CT, US; [4]Beth Israel Deaconess Medical Center, Boston, MA, US; [5]Harvard Medical School, Boston, MA, US; [6]Beth Israel Deaconess Medical Center, Boston, MA, US

INTRODUCTION: Limited English proficiency (LEP) has been associated with disparate access to healthcare in surgical patients at points of diagnosis, treatment, and postoperative follow up. However, studies involving patients with cancer have been limited by the low numbers of patients with LEP compared to English proficient (EP) counterparts. Here we aimed to synthesize literature comparing postoperative outcomes for patients with cancer based on LEP. **METHODS:** OVID Medline, EMBASE, Web of Science, and CINAHL were systemically searched from database inception through 2/1/2023 to identify investigations in which primary language, English proficiency, or interpreter use were used to compare postoperative outcomes. A subgroup analysis was conducted on completed studies on patients who had undergone surgery for cancer. Study quality was assessed using the Oxford Center of Evidence Based Medicine Levels of Evidence. **RESULTS:** Of 3,688 identified unique records, 60 completed and 30 ongoing studies met inclusion criteria for surgical patients; 14 met the subgroup criterion of oncology patients undergoing surgery. Breast cancer was the most studied (6/14, Table), followed by colorectal cancer (4/14). Eleven studies were based in USA and 3 in Australia. In total, 63,672 participants were studied and 6,936 had LEP (10.9%). Determination of LEP varied: 6 studies defined groups by patients' primary language, 2 by medical interpreter use, 2 by patient-reported languages spoken at home, and 4 by a mixture. Length of stay (LOS), readmissions, and malignancy-specific measures were the most studied postoperative outcomes (5 of 14 studies). Patients with LEP had longer LOS than EP patients in 3 of the 5 studies, with these differences remaining significant in two studies after adjusting for race, income and comorbidities. LEP cohorts had statistically significant increases in readmissions in 2 of 5 studies, higher complication rates in 1 of 3 studies, increased ED visits in 1 of 2 studies, and increased discharge to rehab over home in 2 of 2 studies. Mortality and postoperative ICU need were similar between language groups. **CONCLUSIONS:** Research on postoperative outcomes for cancer patients with LEP is limited by inconsistent definitions of LEP. While cancer patients with LEP have longer LOS, adjusted models show that race and socioeconomic status contribute to these language-based disparities. Further efforts are needed to standardize the definition of LEP to appropriately assess linguistic needs and barriers experienced by cancer patients seeking surgical care.

Table. Studies on comparing postoperative length of stay (LOS) for patients with cancer based on limited English proficiency (LEP).

Study (n)	*Site of malignancy*	*LOS variable*	*Comparison of unadjusted measures*	*P value*	*Adjusted models*
Ahmad 2019 (n=1894)	Cervix, ovaries, uterus	Postoperative LOS >1 day for minimally invasive or >3 days for open	Not reported	Not reported	Multivariate logistic regression: IRR not reported, p>0.05
Feeney 2019 (n=37531)	Pancreas, breast, thyroid, adrenal gland, stomach, liver, biliary tract	Total LOS in days (median [IQR])	**ES: 3.00 (1-7)** **SS: 4.00 (1-8)** **NENSS: 4.00 (1-8)**	**<0.001**	Negative binomial regression: IRR for SS vs ES: 1.02 (0.98-1.06) IRR for NENSS vs. ES: 1.03 (0.99-1.07)
Feeney 2020 (n=2467)	Thyroid, breast, pancreas, liver, biliary tract, gastrointestinal tract, skin/soft tissue	LOS in days (median [IQR])	EP: 1.5 (0.7-1.7) LEP: 1.5 (0.7-1.7)	0.68	Negative binomial regression: IRR for LEP vs. English proficient: 0.99 (0.88-1.10)
Manuel 2022 (n=2232)	Brain	Postoperative LOS in days (median [IQR])	**EP: 3.0 (2.0-5.0)** **LEP: 5.0 (3.0-8.0)**	**<0.001**	Negative binomial regression: **IRR for LEP vs. EP: 1.11 (1.00-1.24, p=0.04)**
Will 2021 (n=7324)	Brain	Total LOS in days (median [IQR])	**EPL: 6 (3-9)** **SPL: 7 (3-10)** **NENSPL: 7 (4-11)**	**<0.001**	Negative binomial regression: IRR for SPL vs. EPL: 1.02 (0.96-1.09, p=0.561) IRR for NENSPL vs. EPL: 1.04 (0.98-1.11, p=0.198)
		Postoperative LOS (median [IQR])	**EPL: 4 (3-6)** **SPL: 4 (3-6)** **NENSPL: 4 (3-7)**	**<0.001**	Negative binomial regression: IRR for SPL vs. EPL: 1.01 (0.92-1.10, p=0.860) **IRR for NENSPL vs. EPL: 1.10 (1.03-1.18, p=0.008)**

(EPL: English primary language. SPL: Spanish primary language. NENSPL: Non-English/Non-Spanish Primary Language. ES: English-speaking. SS: Spanish speaking. NENSS: Non-English/Non-Spanish Speaking. EP: English proficient. IRR: Incidence rate ratio. Results with p<0.05 bolded).

P310. Evaluation of Social Support, Discrimination, and Perceived Health in Patients with Gastrointestinal Tract Cancers

Samuel David Butensky, MD[1]; Jihoon Kim[2]; Elizabeth L Godfrey[3]; David G su, MD[4]; Daniel Kerekes, MD[5]; Nita Ahuja, MD, MBA, FACS[6]; Caroline H. Johnson, PhD[7]; Sajid Khan, MD, FACS[8]

[1]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [2]Yale University Department of Biomedical Informatics and Data Sciences, New Haven, CT, US; [3]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [4]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [5]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [6]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [7]Yale School of Public Health, New Haven, CT, US; [8]Yale University School of Medicine, Department of Surgery, New Haven, CT, US

INTRODUCTION: Health-related social conditions affect cancer outcomes. Gastrointestinal cancers (GIC) comprise of a large proportion of cancers diagnosed in the United States. We hypothesized that a diagnosis of GIC negatively impacts Social Determinants of Health (SDOH) and perceived health (PH). **METHODS:** Prospectively collected data from The All of Us database was queried for GIC patients who completed SDOH and PH surveys. Healthy, non-cancer (NC) participants were matched to GIC based on age, race, sex, deprivation index, and Charlson Deyo comorbidities using Propensity Score Matching. Regression was used to analyze the relationship between cancer status and survey scores. **RESULTS:** A total of 231,033 patients met the criteria: 14,032 GIC and 217,001 NC. The majority of patients were white (69%%), female (59.2%), and non-Hispanic (97.2%). Colorectal cancer was most represented (81%), followed by anus (12%), stomach (3%), and pancreatic (1%) cancers. The median time between cancer diagnosis and survey response was 3.4 years (IQR 1.4-6.5 years). With respect to SDOH, GIC patients perceived more social support (β 0.07 [95% CI: 0.04, 0.10]), more neighborhood positivity (β 0.07 [95% CI: 0.05, 0.10]) and less healthcare discrimination (β -0.03 [95% CI: -0.06, -0.01]) (Table 1, NC is reference). GIC surveyed < 1 year after their diagnosis scored higher on social support than those surveyed > 1 year (β 0.13 [95% CI: 0.05, 0.21]). For PH, GIC were 15% more likely to report better mental health and 33% more likely to report better quality of life (QOL). Those diagnosed < 1 year before their survey had no difference in perceived physical and general health compared to NC, although their QOL (OR 1.3 [95% CI: 1.2-1.4]) and mental health (OR 1.1[95% CI: 1.0-1.2]) were similar to those surveyed > 1 year after the diagnosis. Chemotherapy-treated GIC patients reported better PH in all four domains, including QOL (OR 1.3, [95% CI: 1.2-1.5]) and mental health (OR 1.2, [95% CI: 1.1-1.4]). **CONCLUSIONS:** Findings of this survey study reveal that a GI cancer diagnosis has a favorable impact on SDOH and PH - GIC feel more supported, less discriminated, and perceive better health compared to NC, and time of cancer diagnosis and chemotherapy impact outcomes. A concerted societal effort is required to improve health related social conditions for individuals with and without cancer.

Table 1. Effect of cancer status on perceived health and social determinants of health

Social Determinants of Health*	Beta (95% CI)	P Value
Social Support	0.074 (0.04, 0.10)	< 0.001
Neighborhood Positive	0.074 (0.05, 0.10)	< 0.001
Healthcare Discrimination	-0.034 (-0.06, -0.01)	< 0.001
UCLA Loneliness	-0.013 (-0.03, 0.01)	0.196
Perceived Health Domain*	**Odds Ratio (95% CI)**	**P Value**
Quality of Health	1.32 (1.27, 1.38)	< 0.001
Physical Health	1.27 (1.21, 1.32)	< 0.001
Mental Health	1.15 (1.10, 1.20)	< 0.001
General Health	1.26 (1.21, 1.32)	< 0.001

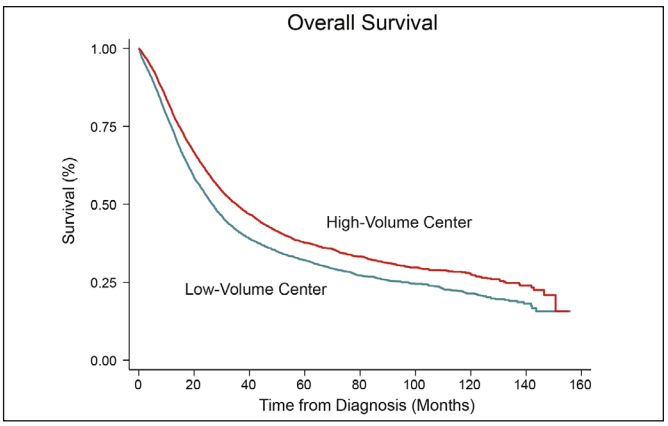
* Comparison is GIC vs. NC, with NC as the reference group.

P311. Examining Surgical Volume and Outcomes for Pancreas Surgery: A Propensity Matched Analysis

Noah Brown, MD[1]; Joshua Horns[2]; Courtney Scaife[3]

[1]University of Utah, Salt Lake City, UT, US; [2]University of Utah, Salt Lake City, UT, US; [3]Huntsman Cancer Institute, Salt Lake City, UT, US

INTRODUCTION: Despite many advances in nonsurgical treatment of pancreatic adenocarcinoma, resection remains the only curative intent treatment. For pancreaticoduodenectomy, it has been demonstrated time and again that there is an inverse relationship between the number of operations performed per year and mortality. Using the NCDB pancreas dataset with surgical information from 2010-2021, we sought to examine the volume-outcome relationship using a propensity-matched analysis. **METHODS:** We calculated propensity scores for treatment at a high-volume center against patient demographic, comorbidity, and treatment characteristics and then performed one-to-one, nearest neighbor matching with replacement. This resulted in a matched cohort of 10,876 patients with no statistically significant difference in age, sex, ethnicity, race, insurance status, community status, Charlson-Deyo Score, histology, stage, and rate of neoadjuvant chemotherapy. We defined a high-volume center as any center performing at least ten procedures (pancreaticoduodenectomies and total pancreatectomies combined) in a calendar year. Descriptive statistics were used to compare the groups, Cox proportional hazards models were used to calculate hazard ratios, and a logit matched analysis was used to calculate affect of the treatment on the treated (ATT). **RESULTS:** Using a Cox proportional hazards model, we found a hazard ratio of 0.754 (95% CI 0.709-0.802, p= <0.001) for patients treated at high volume centers. Median survival improved from 26.6 months (95% CI 25.5-27.7 mo) at low-volume centers to 35.3 months (95% CI 33.4-37.2 mo) at high-volume centers. We found significant differences in 30- and 90-day mortality in both the raw percentage (30-day mortality: high-volume center 2.81%, low-volume center 5.04%, p= <0.001; 90-day mortality: high-volume center 5.93%, low-volume center 9.14%, p= <0.001) and matched analysis (30-day mortality: ATT difference 2.57% (SE: 0.372%); 90-day mortality: ATT difference 3.62% (SE: 0.501%)). Length of stay after definitive surgical management was longer for low-volume centers (median: 9 days, IQR 6-14 days vs. 8 days, IQR 6-11 days). R0 resection rate was lower at low-volume centers as well (78.9% vs 83.1%, p= <0.001). **CONCLUSIONS:** While our data suggests that there are clear racial and socioeconomic disparities that exist between patients treated at low volume centers and those treated at high-volume centers, controlling for these variables does not eliminate the outcomes disparity. This suggests that fundamental differences exist in the quality-of-care patients are receiving and points to a need for expanded access to high volume centers for these often-disadvantaged patients.



P312. Feasibility of a Symptomatic Screening Tool for Early Detection of Gastric Cancer in Roatán, Honduras

Jade Tso[1]; Susana Galeas[2]; Brendalee Martinez[3]; Kallie Vallecillo[4]; Mustafa Faleh Abidalhassan[5]; Natan Webster[6]; Heidy Leiva[7]; Mustafa Al-Qaraghli[8]; Cameron E Gaskill[9]

[1]University of California, Davis, Sacramento, CA, US; [2]Clinica Esperanza, Sandy Bay, Roatan, HN; [3]Clinica Esperanza, Sandy Bay, Roatan, HN; [4]Clinica Esperanza, Sandy Bay, Roatan, HN; [5]Northwell Health, Department of Surgery, New Hyde Park, NY, US; [6]Clinica Esperanza, Sandy Bay, Roatan, HN; [7]Clinica Esperanza, Sandy Bay, Roatan, HN; [8]University of California, Davis, Department of Surgery, Sacramento, CA, US; [9]University of California, Davis, Division of Surgical Oncology, Department of Surgery, Sacramento, CA, US

INTRODUCTION: Gastric cancer (GC) is the leading cause of cancer death in Central Latin America, with late-stage diagnosis common due to nonspecific early symptoms. The National Institute for Health and Care Excellence (NICE) developed symptomatic screening guidelines validated in high-income settings to identify patients requiring urgent referral for upper gastrointestinal endoscopy. We piloted this tool to assess feasibility of early GC detection in Roatán, Honduras. **METHODS:** A screening tool was adapted from NICE guidelines for Roatán. Patients screened positive if they had dysphagia or were over 55 with weight loss and upper abdominal pain,

acid reflux, or dyspepsia. This study took place at the region's main primary care clinic. Nonpregnant adults were consecutively screened during usual care. If positive, they were referred to endoscopy and approached for study enrollment. Enrolled patients were contacted monthly to collect information on demographics, GC risk factors, barriers to endoscopy, and timing and findings of endoscopy. Endoscopy capacity and perceived patient barriers were assessed via a provider questionnaire. **RESULTS:** 500 patients were screened over 12 months. Nine screened positive, with seven screenings being clinically relevant to GC. Of these, four (57%) were female, average age was 49 years (IQR: 18), average years lived in Roatán was 29 (IQR: 34), and hypertension (57%) and hyperlipidemia (29%) were the most common comorbidities. Two (29%) had a family history of cancer, four (57%) had a previous H. pylori infection, six (71%) took acid reflux medication, and four (57%) had dietary risk factors for GC. All patients cited cost as a barrier to endoscopy, while two (29%) each reported difficulty traveling to a facility, lack of knowledge about endoscopy facilities, and uncertainty about needing the procedure. One of seven patients received endoscopy, facilitated by an outside medical brigade 6 months after their positive screening, with diagnosis non-malignant findings. For a population of 109,000 people, there is one permanent endoscopy provider with capacity for two to three endoscopies weekly at a private center with one working endoscope for 8100 lempiras ($327) per procedure. There is no local pathology capacity for diagnosing GC; samples are sent to an outside facility for 1500 lempiras ($60) each. **CONCLUSIONS:** While NICE criteria are feasible for screening GC in Honduras, limited endoscopy access and capacity hinder early diagnosis. Our findings highlight the need to expand local diagnostic capacity and address financial barriers to endoscopy and pathology services.

P313. Financial Toxicity in Oncologic Care: Analysis of Accommodation Cost at National Cancer Institute Cancer Centers

J. Asher Jenkins, MD[1]; Gaurav Jategaonkar[2]; Cece Chen[3]; Dillon Cheung, MD[4]; Chee-Chee H. Stucky, MD[5]; Nabil Wasif, MD, MPH[6]; David Etzioni, MD, MHS[7]; Barbara Pockaj, MD[8]; Zhi Ven Fong, MD, MPH, DrPH[9]
[1]Mayo Clinic Arizona, Phoenix, AZ, US; [2]Mayo Clinic Arizona, Phoenix, AZ, US; [3]Mayo Clinic Arizona, Phoenix, AZ, US; [4]Mayo Clinic Arizona, Phoenix, AZ, US; [5]Mayo Clinic Arizona, Phoenix, AZ, US; [6]Mayo Clinic Arizona, Phoenix, AZ, US; [7]Mayo Clinic Arizona, Phoenix, AZ, US; [8]Mayo Clinic Arizona, Phoenix, AZ, US; [9]Mayo Clinic Arizona, Phoenix, AZ, US

INTRODUCTION: The increasing push for regionalization of complex cancer care has resulted in many patients traveling for their care. However, traveling for care is associated with economic stressors that are underappreciated, including accommodation cost that falls on patients and their caregivers, and poses a significant financial barrier. This study aims to examine accommodation cost at National Cancer Institute (NCI) Designated Cancer Centers in the United States. **METHODS:** Accommodation cost per night was assessed for each of the 74 identified NCI cancer centers by averaging the lowest nightly rate of at least three hotels with vacancy within a 20-minute driving distance from the treatment facility. Cancer center websites were queried for information regarding discounted/free lodging. Linear regression was used to correlate price per night and availability of discounted/free lodging with cost-of-living index (COLI, 100 is national average). **RESULTS:** The median cost per night across all 74 NCI centers was $108 (IQR 78.5-141.5), and median COLI was 102.1 (IQR 95.8-126.3). Discounted accommodation was offered at 42/74 (57%), while 18/74 (24%) offered free accommodation. No correlation was observed between COLI and cost per night (R2=0.0880), between COLI and discounted (R2=0.0375) or free (R2=0.0000) lodging, or between average cost per night and discounted (R2=0.0004) or free (R2=0.0003) lodging. Accommodation cost was significantly higher in the Northeast (median $132, IQR 93-158), followed by Pacific (median $126, IQR 98-149), Southeast (median $104, IQR 75-137), Midwest (median $102, IQR 78-131) and West (median $65, IQR 59-100) (p=0.001). **CONCLUSIONS:** Given the often longitudinal nature of cancer treatment and follow up, the cumulative cost of accommodation can pose a significant barrier to cancer care at NCI centers. Just over half of NCI centers offer discounted accommodation options, and the vast majority do not offer free accommodation. Patients were not any more likely to be offered discounted or free lodging in high COLI cities where many cancer centers are located, with a median cost of $108 per night and statistically significant higher prices in the Northeast and Pacific regions. Regionalization of cancer care to high-volume centers may further disadvantage rural and low-income patients and their families when required to stay near their treatment center. Payor reimbursement for lodging expenses, as well as other unanticipated costs such as food and transportation, may facilitate care delivery and improve access to NCI centers.

Table 1. Median price per night stay listed by U.S. Geographic Region with overall p-value.

Region	Median Cost Per Night (IQR)	P-value
Northeast	$132 ($93-$158)	0.001
Southeast	$104 ($75-$137)	-
Midwest	$102 ($78-$131)	-
West	$65 ($59-$100)	-
Pacific	$126 ($98-$149)	-

P314. Impact of Insurance Patterns on Survival in Patients with Solitary Fibrous Tumors

Belain Eyob[1]; Bima J Hasjim[2]; Amy Y Li[3]; Warren Chow[4]; Michael O'Leary[5]; Maki Yamamoto[6]; Oliver S Eng[7]
[1]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [2]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [3]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [4]Division of Hematology/Oncology, Department of Medicine, University of California Irvine Medical Cen, Orange, CA, US; [5]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [6]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [7]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US

INTRODUCTION: Solitary fibrous tumors (SFTs) are rare, indolent sarcomas which are primarily treated surgically but often recur and/or metastasize. Although disparities in the treatment of rare tumors have been reported, there is a paucity in the literature of SFTs, outcomes, and associations with the evolving national insurance coverage landscape (e.g., Medicaid expansion in 2014). Thus, we explored factors associated with survival in a national cohort of patients with SFTs. **METHODS:** The National Cancer Database (NCDB) was queried to identify adult patients (≥18 years) diagnosed with retroperitoneal and peritoneal SFTs between 2004 and 2019. Univariable and Multivariable Cox proportional hazard regression analyses were used to identify independent prognostic risk factors associated with post-operative survival (POS) following surgical resection. **RESULTS:** A total of 141 patients were diagnosed with SFTs from 2004-2019. 72 (51%) were male and 115 (82%) were of non-Hispanic White race. Median age was 64 (IQR 55-74) years, and 7 (5%) had evidence of metastasis at time of diagnosis. 74 (52%) had government insurance (Medicaid/Medicare), whereas 64 (45%) had private insurance. There were 132 (94%) patients treated with surgical resection, of which 33 (23%) underwent surgical debulking. Of patients treated surgically, those with private insurance traveled farther as compared to patients with Medicare/Medicaid (median: 12.70 [IQR 6.70-35.55] miles vs. 8.90 [IQR 3.90-20.50] miles, p=0.001). On multivariable analysis, tumor size >20cm was independently associated with worse POS (HR: 5.40, 95% CI: 1.57-18.58, p=0.008), while private insurance was protective (HR:0.21, 95% CI: 0.06-0.74, p=0.014). Among patients diagnosed after Medicaid expansion (≥2014), insurance status was no longer an independent predictor of POS (p=0.13). **CONCLUSIONS:** Privately insured patients with SFTs traveled longer distances to care and private insurance was associated with a 79% lower risk of death following surgical resection compared to those with government insurance. However, after the expansion of Medicaid in 2014, the differences in rates of mortality between government and private insurance was mitigated. Although health disparities between patients with private and government insurance continue to be widely reported in cancer literature, further research is required to explore the potential survival benefits of expanding national health insurance plans for patients with rare tumors, such as SFTs.

P315. Impact of Social Determinants of Health on Adherence to Cancer Screening in Patients with High-Risk Genetic Mutations

Ashley W Quinn[1]; Sacha Finn[2]; Stevany Saxon-Filipe, MPH[3]; Ang Gao, MS[4]; Stephanie Serres[5]; Shruti Zaveri[6]; Anthony Froix[7]; Rachel Wooldridge[8]; Deborah Farr[9]; Anvy Nguyen[10]; Ann Marilyn Leitch[11]
[1]UT Southwestern, Dallas, TX, US; [2]University of Texas Southwestern, Dallas, TX, US; [3]UT Southwestern Medical Center, Dallas, TX, US; [4]UT Southwestern, Dallas, TX, US; [5]The University of Texas Southwestern Medical Center, Dallas, TX, US; [6]The University of Texas Southwestern Medical Center, Dallas, TX, US; [7]The University of Texas Southwestern Medical Center, Dallas, TX, US; [8]The

University of Texas Southwestern Medical Center, Dallas, TX, US; [9]The University of Texas Southwestern Medical Center, Dallas, TX, US; [10]The University of Texas Southwestern Medical Center, Dallas, TX, US; [11]UTSW, Dallas, TX, US

INTRODUCTION: Social determinants of health (SDOH) contribute to cancer care disparities, including screening rates. Patients with genetic mutations that increase the risk of cancer are advised to undergo more rigorous screening. We examined the association of neighborhood-level SDOH and individual demographic factors with adherence to recommended cancer screening in patients with high-risk genetic mutations. **METHODS:** Retrospective review of a prospectively maintained institutional genetics database was completed to identify patients with at least one known pathogenic high-risk mutation (Table 1). Adherence to gene-specific National Comprehensive Cancer Network screening guidelines (3.2024) was assessed using the electronic health record between August 26, 2019 and August 26, 2024. Patients were linked to neighborhood SDOH data from the American Community Survey and assigned an Area Deprivation Index (ADI) using residential address. Stepwise logistic regression was used to evaluate the association of SDOH and other demographic factors with adherence to screening. **RESULTS:** 441 patients were eligible for mutation-specific screening. 53.5% of these patients had lapses in screening. Increased likelihood of screening lapses was seen in those who were uninsured (OR 4.52 [95% CI 1.95-10.44]) or living in areas with a higher percentage of single-parent households (OR 1.06 [95% CI 1.02-1.11]). Non-English speakers were less likely to have screening lapses (OR 0.36 [95% CI 0.16-0.86]). 306 patients were eligible for risk-reducing mastectomy (RRM) and 327 patients were eligible for risk-reducing salpingo-oophorectomy (RRSO). 69.0% of eligible patients did not undergo RRM and 63.9% of eligible patients had not undergone RRSO. Older patients were slightly more likely to undergo RRM (Mean age: Yes, 43.9 [±10.26]; No, 39.7 [±13.77]; OR 1.03 [95% CI 1.01-1.04]) and RRSO (Mean age: Yes, 50.9 [±11.53]; No, 36.9 [±11.40]; OR 1.10 [95% CI 1.08-1.13]). **CONCLUSIONS:** Over half of the patients with high-risk mutations were found to have lapses in screening. Uninsured patients and those living in areas with more single-parent households were more likely to experience these lapses. Additionally, most patients did not undergo risk-reducing surgery, further highlighting the need to prevent screening lapses. Identifying factors that increase the risk of screening gaps in patients with high-risk mutations can enable healthcare systems to implement interventions to improve adherence to screening regimens.

Table 1. Neighborhood-Level SDOH and Individual Demographic Variables

Individual Factors	p Values	Neighborhood-Level Factors	p Values
Age†,‡	RRM: 0.0110 RRSO: < 0.0001	National ADI†	RRM: 0.0218
Gender		State ADI	
Race		% w/ Crowded Housing	
Ethnicity		% w/ Housing Cost Burden	
Language*	Lapses: 0.0207	% of Single-Parent Households*	Lapses: 0.0049
Insurance*	Lapses: 0.0004	% Unemployed	
Multiple Mutations		% Living Below 150% of Poverty Level	
Mutation (% with mutation)		% w/o Broadband Internet	
ATM: 111 (15.83%)		% w/o HS diploma	
BARD1: 12 (1.71%)		% w/ Minority Status	
BRCA1: 137 (19.54%)		% Aged ≥ 65 y/o	
BRCA2: 185 (26.39%)			
CDH1: 11 (1.57%)			
CHEK2: 130 (18.54%)			
NF1: 6 (0.86%)			
PALB2: 62 (8.84%)			
PTEN: 4 (0.57%)			
RAD51C: 19 (2.71%)			
RAD51D: 16 (2.28%)			
STK11: 2 (0.29%)			
TP53: 6 (0.86%)			

*Statistically significant in screening lapses, †statistically significant in RRM, ‡statistically significant in RRSO

P316. Impact of Sociodemographic and Clinical Factors on Postoperative Outcomes Following Post-Mastectomy Flap-Based Reconstruction

Ariana Naaseh, MD, MPHS[1]; Alice Bewley, MS[2]; Terence M Myckatyn, MD[3]; Julie A Margenthaler, MD[4]

[1]Department of Surgery, Washington University in St. Louis School of Medicine, St. Louis, MO, US; [2]Department of Medicine, Washington University in St. Louis School of Medicine, St. Louis, MO, US; [3]Department of Surgery, Washington University in St. Louis School of Medicine, St. Louis, MO, US; [4]Department of Surgery, Washington University in St. Louis School of Medicine, St. Louis, MO, US

INTRODUCTION: Post-mastectomy flap-based reconstruction (FBR) is an important component of comprehensive breast cancer care, shown to be feasible and safe, although not without risk of complications. Prior research suggests the existence of sociodemographic disparities in complications after FBR, but the literature is largely limited to 30-days post-surgery. We sought to examine the impact of sociodemographic and clinical factors on 30-day and 90-day FBR postoperative outcomes. **METHODS:** We performed a retrospective cohort study of adults undergoing FBR in the Healthcare Cost and Utilization Project Florida State Inpatient Database (2015-2021). FBR included deep inferior epigastric perforator (DIEP), transverse rectus abdominis muscle (TRAM), and latissimus dorsi (LD) flaps. Data elements were abstracted using ICD 10 codes and comorbidities defined using the Elixhauser classification. Univariate and multivariate analyses were performed to analyze patient factors associated with 30-day and 90-day postoperative complications and readmissions. **RESULTS:** We identified 3,537 women admitted for mastectomy with FBR (Table 1). In total, 483 (13.7%) patients experienced complications within 30 days of surgery, while 529 patients (15.0%) experienced complications within 90 days. Similarly, 224 patients (6.3%) were readmitted within 30 days, while 368 (10.4%) were readmitted within 90 days. After risk-adjustment, patients living in smaller metropolitan areas (OR 1.28; 95% CI 1.03-1.60) or with ≥4 comorbidities (OR 1.42; 95% CI 1.05-1.91) had increased odds of experiencing complications. Patients on Medicaid (OR 3.09; 95% CI 1.89-5.05), Medicare (OR 1.83; 95% CI 1.15-2.92), or with ≥2 comorbidities (OR 1.90; 95% CI 1.32-2.73) were more likely to experience hospital length of stay (LOS) ≥7 days. LD flap patients were less likely to experience prolonged LOS (OR 0.38; 95% CI 0.23-0.61). Residing in smaller metropolitan areas (OR 1.39; 95% CI 1.01-1.90), having ≥2 comorbidities (OR 1.57; 95% CI 1.16-2.12), or having Medicare (OR 1.86; 95% CI 1.29-2.66) were associated with increased odds of 30-day and 90-day readmission. **CONCLUSIONS:** Disparities exist in outcomes after FBR and are most pronounced in patients with public insurance, in smaller metropolitan areas, and with multiple comorbidities. These findings highlight sociodemographic and clinical factors associated with worse postoperative outcomes and suggest a need to target post-operative interventions to reduce disparities through standardized pathways and post-discharge care coordination

Table 1. Patient demographics and outcomes of interest by flap type.

	DIEP Flap Patients (n=2427)	LD Flap Patients (n=729)	TRAM Flap Patients (n=381)	P value
Age Group				<0.001
20-35	128 (5.3%)	29 (4.0%)	20 (5.2%)	
36-50	935 (38.5%)	163 (22.4%)	120 (31.5%)	
51-65	1186 (48.9%)	369 (50.6%)	168 (44.1%)	
66-80	178 (7.3%)	161 (22.1%)	71 (18.6%)	
81+	Unable to report*	Unable to report*	Unable to report*	
Race				0.045
White	1490 (61.4%)	458 (62.8%)	208 (54.6%)	
Black	388 (16.0%)	100 (13.7%)	75 (19.7%)	
Hispanic	438 (18.0%)	145 (19.9%)	76 (19.9%)	
Other	111 (4.6%)	26 (3.6%)	22 (5.8%)	
Expected Primary Payer				<0.001
Medicare	281 (11.6%)	244 (33.5%)	100 (26.2%)	
Medicaid	72 (3.0%)	52 (7.1%)	57 (15.0%)	
Private insurance	1953 (80.5%)	400 (54.9%)	198 (52.0%)	
Other	121 (5.0%)	33 (4.5%)	26 (6.8%)	
Income Quartile				<0.001
First quartile	400 (16.5%)	142 (19.5%)	107 (28.1%)	
Second quartile	533 (22.0%)	178 (24.4%)	92 (24.1%)	
Third quartile	679 (28.0%)	187 (25.7%)	89 (23.4%)	
Fourth quartile	815 (33.6%)	222 (30.5%)	93 (24.4%)	
Rurality				<0.001
Metropolitan areas of >= 1 million population	1760 (72.5%)	503 (69.0%)	240 (63.0%)	
Counties in metropolitan areas of 50,000-999,999 population	545 (22.5%)	202 (27.7%)	133 (34.9%)	
Micropolitan and rural counties	122 (5.0%)	24 (3.3%)	Unable to report*	
Comorbidities				0.046
0-1	1260 (51.9%)	400 (54.9%)	175 (45.9%)	
2-3	854 (35.2%)	230 (31.6%)	145 (38.1%)	
4-5	256 (10.5%)	73 (10.0%)	48 (12.6%)	
6+	57 (2.3%)	26 (3.6%)	13 (3.4%)	
Complications	354 (14.6%)	101 (13.9%)	74 (19.4%)	0.031
Surgical Site Infection	Unable to report*	Unable to report*	Unable to report*	0.513
Flap Necrosis	20 (0.8%)	12 (1.6%)	Unable to report*	0.061
Wound complications	56 (2.3%)	21 (2.9%)	14 (3.7%)	0.246
Seroma	90 (3.7%)	15 (2.1%)	20 (5.2%)	0.017
Hematoma	16 (0.7%)	Unable to report*	Unable to report*	0.614
Mechanical Complications	79 (3.3%)	33 (4.5%)	17 (4.5%)	0.184
Flap Revision	Unable to report*	Unable to report*	Unable to report*	0.512
Return to the operating room	79 (3.3%)	12 (1.6%)	Unable to report*	0.013
Microvascular complications	49 (2.0%)	Unable to report*	Unable to report*	0.002
Transfusion	108 (4.4%)	14 (1.9%)	23 (6.0%)	0.001
Prolonged length of stay	150 (6.2%)	23 (3.2%)	47 (12.3%)	<0.001
Readmission within 30 days	151 (6.2%)	41 (5.6%)	32 (8.4%)	0.182
Readmission within 90 days	232 (9.6%)	89 (12.2%)	47 (12.3%)	0.052

*Unable to report due to the HCUP data use agreement which does not allow the publication of any data points with values less than or equal to 10 to be reported to preserve patient anonymity

P317. Income-Based Disparities in Survival for Metastatic Gastrointestinal Stromal Tumor are Worsening Following Introduction of Generic Imatinib: A National Cancer Database Analysis

Thomas L Sutton, MD MCR[1]; Teodora Dumitra[2]; Timothy DiPeri, MD[3]; Rayne Peerenboom[4]; Marco Ventin[5]; Alexandra Gangi, MD, FSSO[6]
[1]Cedars-Sinai Medical Center, Los Angeles, CA, US; [2]Cedars-Sinai Medical Center, Los Angeles, CA, US; [3]Cedars-Sinai Medical Center, Los Angeles, CA, US; [4]Cedars-Sinai Medical Center, Los Angeles, CA, US; [5]Cedars-Sinai Medical Center, Los Angeles, CA, US; [6]Cedars-Sinai Medical Center, Los Angeles, CA, US

INTRODUCTION: In 2001, imatinib fueled a paradigm shift in the treatment of metastatic gastrointestinal stromal tumors (mGIST), adding years to survival and facilitating multidisciplinary care, such as metastasectomy for disease that is stable on therapy. Imatinib's cost in the United States rapidly increased, exceeding $10,000 a month in 2013 compared to a manufacturing cost of less than $40. In 2016, a generic equivalent of imatinib became available, however no data have been reported on whether this has affected outcomes. **METHODS:** We performed an analysis of the National Cancer Database (NCDB) for patients with synchronous mGIST diagnosed from 2010-2021. Patients were grouped into "low" and "high" income by median income quartiles (1st and 2nd versus 3rd and 4th), and analyzed by insurance status and year of diagnosis (2010-2015 versus 2016-2021). Overall survival (OS) was evaluated with Kaplan-Meier analysis and multivariable Cox proportional hazards modeling. **RESULTS:** 4058 patients were identified, with n=2381 (58.7%) within the upper two quartiles of estimated median income. The majority of patients had either Medicare (n=1849, 45.6%) or private (n=1551, 38.2%) insurance. Patients pre- and post-2016 were clinicopathologically similar, and similar proportions received primary and distant-site surgery. Median follow-up was 65.7 months. For patients with private insurance there was a 31-month difference in median OS for low versus high income patients (70.9 months vs. 102.1, P<0.001). This disparity was driven by worsened survival for low-income patients post-2016 (median OS 49.9 months vs. not reached, P<0.001, Figure), while there was no difference in survival pre-2016 (median OS 77.8 vs 94.9 months, P=0.07). In contrast, patients with Medicare, Medicaid, and other insurance types had no difference in OS by income group either pre- or post-2016 (all P>0.3). On multivariable analysis adjusting for age, comorbidities, and receipt of primary/distant site surgery, the combination of private insurance and low income was independently associated with worse OS compared to private insurance and high income (HR 2.06, P<0.001). **CONCLUSIONS:** Income-based disparities in OS for patients with mGIST and private insurance are clinically significant and are paradoxically increasing following the availability of generic imatinib. Pharmaceutical and insurance company practices that may be contributing to this outcome have been well-described. A combination of legislative and private interventions is needed to ensure that access to highly effective oncologic therapies that enable multidisciplinary oncologic care, such as metastasectomy, is not restricted.

P318. Insurance Status and Treatment Patterns in Newly Diagnosed Gastric Cancer

Rebecca M. Platoff, MD MSc[1]; Kelly McGovern[2]; Aidan Aicher[3]; Brijesh Rana[4]; Alexandra E Adams, MD[5]; Ray Ramirez[6]; Theodore Wang[7]; Jacinto Saenz[8]; Sorasicha Nithikasem[9]; Sruti Cheruvu[10]; Lia Kwak[11]; Sarah Bueno Motter[12]; Mariam F. Eskander, MD[13]; Miral S. Grandhi, MD[14]; Brett L. Ecker, MD[15]; Timothy J. Kennedy, MD[16]; Sara Heinert[17]; Elizabeth A. Handorf, PhD[18]; Hari S. Iyer, ScD[19]; Antoinette Stroup[20]; Haejin In, MD, MBA, MPH[21]
[1]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, US; [2]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, US; [3]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, US; [4]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, US; [5]Atlantic Health System, Morristown, NJ, US; [6]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, US; [7]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, US; [8]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, US; [9]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, US; [10]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, US; [11]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, US; [12]Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, BR; [13]Rutgers Cancer Institute, New Brunswick, NJ, US; [14]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, US; [15]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, US; [16]Rutgers Cancer Institute, New Brunswick, NJ, US; [17]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, US; [18]Rutgers School of Public Health, Piscataway, NJ, US; [19]Rutgers School of Public Health, Piscataway, NJ, US; [20]Rutgers Cancer Institute, New Brunswick, NJ, US; [21]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, US

INTRODUCTION: Outcomes for gastric cancer outcomes appear to be related to sociodemographic factors. We aim to evaluate the impact of socioeconomic and clinical factors including patients' insurance status on treatment patterns including time to treatment after new diagnosis of gastric cancer. **METHODS:** Retrospective chart review was performed for patients with gastric cancer, identified via institutional cancer registry, from a single institution from 2016-2022. Time to treatment was defined as days from diagnosis to treatment initiation (chemotherapy, surgery, or radiation). Univariable and multivariable analyses were performed to evaluate the association between insurance status and other sociodemographic factors and a delay in time to treatment (defined as greater than 60 days) as well as ultimate lack of treatment. Logistic regression modelling was performed to control for significant variables. Statistical analysis was performed using SAS 9.4. **RESULTS:** Three hundred and nineteen patients were included, of which median age was 67.28 (IQR 58.0-76.2) and 60.2% were male. Sixty-three patients (19.7%) did not undergo cancer treatment after diagnosis. Not receiving treatment was associated with age >75 (OR 5.79, CI 2.07 – 16.21), female gender (OR 3.18, CI 1.64 – 6.17), histology other than adenocarcinoma (OR 3.30, CI 1.42 – 7.71), and diagnosis in the emergency department (OR 2.17, CI 1.1 – 4.27). Of the 255 patients who did undergo treatment, the median time to treatment was 41 days and there were 65 (25.5%) who experienced delay in treatment >60 days. Treatment delay was associated with increasing age (OR 7.45, CI 2.13 – 26.11), symptoms of abdominal pain or bleeding as opposed to nausea/vomiting (OR 6.87, CI 1.25 – 37.72, OR 8.06, CI 1.12 – 58.26), and having no insurance or Medicaid (OR 5.67, CI 2.04 – 15.73). **CONCLUSIONS:** Delays to treatment initiation and ultimate lack of treatment for patients with newly diagnosed gastric cancer appears to be affected by sociodemographic factors including insurance status. Further study will help us to deepen our understanding of the modifiable risk factors that can help us to target these disparities to improve outcomes for gastric cancer.

P319. Integration of social determinants of health in quality indicators for colorectal cancer surgery: a scoping review

Adom Bondzi-Simpson, MD, MSc[1]; Tiago Ribeiro, MD, MSc[2]; Alice Zhu, MD, MSc[3]; Aisha Lofters, MD, PhD[4]; Rinku Sutradhar, PhD[5]; Andrea Covelli, MD, PhD[6]; Rebecca A. Snyder, MD, MPH[7]; Callisia Clarke, MD, MS, FSSO[8]; Natalie G Coburn, MD, MPH[9]; Julie Hallet, MD, MSc, FSSO[10]
[1]University of Toronto, Toronto, ON, CA; [2]University of Toronto, Toronto, ON, CA; [3]University of Toronto, Toronto, ON, CA; [4]University of Toronto, Toronto, ON, CA; [5]University of Toronto, Toronto, ON, CA; [6]Sinai Health System - Mount Sinai Hospital, Toronto, ON, CA; [7]MD Anderson Cancer Center, Houston, TX, US; [8]Medical College of Wisconsin, Milwaukee, WI, US; [9]University of Toronto, Toronto, ON, CA; [10]Sunnybrook Health Sciences Centre, Toronto, ON, CA

INTRODUCTION: Quality indicators (QIs) are standardized measures that allow healthcare systems to track performance, identify gaps, and inform areas of priority for strategic planning. However, how cancer systems integrate the social determinants of health (SDoH) into the development, reporting and measurement of QIs is unclear. We conducted a scoping review to explore the use of SDoH in QIs for colorectal cancer (CRC) surgery, with the intent to assess gaps in knowledge and develop practical considerations for integrating SDoH into QIs. **METHODS:** Following Arksey and O'Malley frameworks, we searched MEDLINE, EMBASE, HealthSTAR databases for all studies examining QIs for stage I–III CRC surgery, from database inception to January 2023. Two authors independently reviewed titles, abstracts, and full texts. An integrated conceptual framework for understanding SDoH for cancer health equity was utilized to structure data extraction, interpretation and reporting. **RESULTS:** Of 113 studies included, 70 (61.9%) reported QIs for healthcare systems, 33 (29.2%) measured factors associated with QIs, and 10 (8.9%) developed QIs. SDoH were assessed in 65 (58%) studies. There was heterogeneity in terminology. Common SDoH studied were: age, sex, race, geography, and insurance, with fewer studies exploring education, family structures, and healthcare funding (private/public systems). SDoH were integrated as descriptive analysis only in 14/65 (21.5%) of studies, while the others examined adjusted associations. Of 32 studies examining associations between SDoH and QI, 18 (56.2%) described the variable selection strategy and 4 (12.5%) explored interactions. All studies reported relative effect estimates, with none reporting additive effects. The direction of the reported associations varied considerably across studies. **CONCLUSIONS:** We identified gaps in integrating SDoH into the development, reporting and measurement of QIs including lack of consideration of SDoH; lack of examination of associations

between SDoH and QIs accounting for appropriate confounders and interactions; and lack of assessment of additive effects. To support equity and equality in quality care monitoring, future research on QIs could consider reporting by SDoH and developing benchmarks for acceptable/unacceptable variation across SDoH, using social frameworks for modelling inequalities reporting additive and relative effect estimates, and testing interactions.

P320. Lymphatic Complications in Patients Undergoing Melanoma Surgery in a Developing Country

Jessica J Farzan[1]; Gabriel A De la Cruz Ku[2]; Jiddu A Guart[3]; Anshumi Desai[4]; Camila Franco[5]; Jessica Mroueh[6]; Vanessa Mroueh[7]; Camille Briskin[8]; Nichita Kulkarni, MD[9]; Otto Ziegler Rodriguez[10]; Gonzalo Ziegler Rodriguez[11]
[1]University of Massachusetts Medical School, Worcester, MA, US; [2]University of Massachusetts Medical School, Worcester, MA, US; [3]University of Massachusetts Medical School, Worcester, Worcester, MA, US; [4]University of Miami Miller School of Medicine, Miami, FL, US; [5]University of Texas Medical Branch at Galveston, Texas, Galveston, TX, US; [6]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, US; [7]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [8]University of Massachusetts Medical School, Worcester, MA, US; [9]University of Massachusetts Medical School, Worcester, MA, US; [10]Clinica Ziegler, Lima, PE; [11]Instituto Nacional de Enfermedades Neoplasicas, Lima, PE

INTRODUCTION: Surgical intervention, particularly sentinel lymph node and lymph node dissection, is essential in managing melanoma, targeting locoregional disease, and preventing metastasis. Key complications necessitate a thorough understanding to optimize patient care and minimize morbidity. Our aim was to elucidate risk factors for post-operative lymphatic complications in melanoma patients undergoing lymph node surgery. **METHODS:** A retrospective cohort study was conducted, reviewing records of melanoma patients who underwent lymphatic surgery at the Instituto Nacional de Enfermedades Neoplasicas (INEN) from 2010-2019. Descriptive statistics and univariate/multivariate logistic regression analyses were performed to identify predictors of lymphatic complications. **RESULTS:** The study included 699 melanoma patients (mean age 60.70 years, 51.4% female). Surgical interventions included wide local excision (56.9%), sentinel lymph node surgery (67.7%), and lymph node dissection (32.3%). Complications included lymph node dehiscence (1.6%), infection (6.2%), lymphedema (2.7%), and lymphoceles (5.7%). Lymphatic complications were associated with greater age (64.76y vs. 59.91y, p=0.002), anatomic site (lower extremity, 97.2% vs. 74.8%, p<0.001), clinically positive lymph nodes (55.3% vs. 29.9%, p=0.004), lymph node dissection (47.8% vs. 29.4%, ulceration (78.8% vs. 68.0%, p=0.027), number of mitosis per mm2 (8.26 vs. 6.43, p=0.025), positive lymph node (74.1% vs. 49.7%, higher N stage (p<0.001), adjuvant chemotherapy (20.0 vs. 11.6%). Multivariate analysis identified lymphatic invasion (OR=2.601, 95%CI: 1.232-5.491) and positive lymph node pathology (OR=2.066, 95%CI: 1.034-4.127) as risk factors, while primary lesion location in the upper extremity (OR=0.055, 95%CI: 0.007-0.408) and trunk (OR=0.106, 95%CI: 0.014-0.818) were protective factors. **CONCLUSIONS:** Key risk factors for postoperative lymphatic complications in melanoma patients undergoing lymph node surgery in a developing country were lower extremity involvement, lymph node dissections, lymphatic invasion, and positive lymph nodes. Understanding these risk factors can aid clinicians in optimizing management strategies to minimize postoperative lymphatic complications.

P321. National Cancer Database Representation of United States Cancer Cases

Anays Murillo, MD, MPH[1]; Kelsey S Romatoski, MD[2]; Sophie H Chung, MD[3]; Elizabeth S Davis, MSPH[4]; Veer S Sawhney, BA[5]; Kelly Kenzik, MS, PhD[6]; Sing Chau Ng, MS[7]; Jennifer F Tseng, MD, MPH[8]; Teviah E Sachs, MD, MPH[9]
[1]Boston Medical Center, Boston, MA, US; [2]Boston Medical Center, Boston, MA, US; [3]Boston Medical Center, Boston, MA, US; [4]Boston Medical Center, Boston, MA, US; [5]Boston Medical Center, Boston, MA, US; [6]Boston Medical Center, Boston, MA, US; [7]Boston Medical Center, Boston, MA, US; [8]Boston University Chobanian & Avedisian School of Medicine, Boston, MA, US; [9]Boston Medical Center, Boston, MA, US

INTRODUCTION: The National Cancer Database (NCDB) is a robust oncology dataset, providing large-scale data for tracking trends, outcomes, and disparities in cancer care in the US. Though widely used in cancer outcomes research, its reliance on only Commission on Cancer approved hospitals can lead to underrepresentation of certain populations, skewing of data, and may limit generalizability of findings. We sought to identify the percentage of incidence cancer cases represented in the NCDB as compared to the US cancer population. Our data can be used by all those conducting research utilizing the NCDB to more accurately interpret data on a national level. **METHODS:** Incident cancer cases in the NCDB from 2016-2020 were compared to incident cases in the United States Cancer Statistics (USCS) database, a registry providing nearly 100% coverage of new US cancer cases. NCDB case coverage was defined as percentage of cases the NCDB represents of USCS cases. This analysis was performed for the entire cohort (age 20+ years) and sub-analyses were performed for: age, sex, race, ethnicity, location of residence, and specific cancer sites. **RESULTS:** From 2016-2020, a total of 6,515,675 cancer cases were newly diagnosed in the NCDB and 9,311,593 in the USCS, resulting in NCDB case coverage of 70% over the 5 years. Case coverage increased from 68% in 2016 to 73% by 2020. When examining sex, age, race, and ethnicity, NCDB captured the most US cancer cases among women, ages 20 to 44 years, people identified as other/without race data, and patients identified as non-Hispanic/non-Latino (respective case coverage: 74%, 75%, and 71%). The lowest case coverage was among men, 85+ year-olds, American Indian/Alaskan Native people, and Hispanic/Latino individuals (65%, 59%, 42%, and 55%). By region, with data restricted to ages 40+, the New England cancer population was most represented (82%) while the Mountain region (49%) was least represented. Similar underrepresentation was seen within top cancer sites and missingness of data was captured when examined by cancer system in the NCDB. **CONCLUSIONS:** The NCDB's US cancer case representation is improving, though there remain gaps by age, sex, race/ethnicity, and residence location. Further exacerbating this are unknown variables. Prior studies have demonstrated the association of missingness with worse outcomes. While some large registries offer calculators to extrapolate study sample size, the NCDB does not, and therefore our data can offer researchers the opportunity to better adjust their data, especially that of the underserved populations, to the US population at large.

Table: Sociodemographics of National Cancer Database (NCDB) and United States Cancer Statistics (USCS) database

	Sociodemographics	NCDB count (n)	USCS count (n)	Case Coverage (%)
Sex$^{\Delta}$	Male	2,987,266	4,566,415	65%
	Female	3,528,409	4,745,178	74%
Age$^{\Delta}$	20-44	529,614	704,238	75%
	45-64	2,468,695	3,356,925	74%
	65-84	3,131,515	4,591,203	68%
	85+	385,851	659,227	59%
Race$^{\Delta}$	White	5,392,989	7,738,967	70%
	Black	724,252	994,672	73%
	American Indian/Alaska Native	24,113	57,342	42%
	Asian/Pacific Islander	228,646	326,144	70%
	Unknown/Other	145,675	194,441	75%
Ethnicity$^{\Delta}$	Hispanic/Latino	415,971	752,242	55%
	Non-Hispanic/Non-Latino	5,972,953	8,353,946	71%
	Unknown/Other	126,551	205,405	62%
Region^{+}	New England	371,446	452,100	82%
	Middle Atlantic	957,035	1,272,087	75%
	East North Central	1,055,687	1,321,188	80%
	West North Central	477,561	615,913	78%
	South Atlantic	1,346,015	1,918,287	70%
	East South Central	411,690	553,447	74%
	West South Central	529,952	920,255	58%
	Mountain	277,088	561,664	49%
	Pacific	765,101	1,261,823	61%
Location^{+}	Metro	5,108,371	7,285,952	70%
	Non-Metro	911,658	1,415,131	64%
	Unknown	171,546	175,681	98%

Δ Case coverage is calculated using n=6,515,675 for NCDB and n=9,311,593 for UCSC
+ Case coverage is calculated using n=6,191,575 for NCDB and n=8,876,764 for UCSC given age restriction to 40 years and above for residency variable

P322. Neighborhood Disadvantage and Postoperative Outcomes: A Study of PDAC Patients in a Tertiary Urban Center

Karim Koussa, MD[1]; George Nassif, MD[2]; Julie Clark, PhD[3]; Kyra Langley[4]; Divya Kanumuri[5]; Erykah Murphy[6]; Katherine S. Cools, MD, MSCR[7]; Rupen Shah, MD[8]; David Kwon, MD[9]
[1]Henry Ford Hospital, Detroit, MI, US; [2]Department of Surgery, Henry Ford Hospital, US; [3]Henry Ford Pancreatic Cancer Center, US; [4]Henry Ford Pancreatic Cancer Center, US; [5]Henry Ford Pancreatic Cancer Center, US; [6]Henry Ford Pancreatic Cancer Center, US; [7]Henry Ford Hospital, US; [8]Henry Ford Health, US; [9]Henry Ford Health, Detroit, MI, US

INTRODUCTION: Lower socioeconomic status (SES) has been linked to worse cancer outcomes, higher mortality rates and lower survival probabilities. The Area Deprivation Index (ADI), a validated measure of neighborhood-level SES, captures socioeconomic disparities and provides a better understanding of how social determinants of health impact cancer care and outcomes. Our Multidisciplinary Pancreas Clinic – comprising nurse navigation, medical, surgical, radiation oncologists, psychologists, and nutritionists – aims to provide equitable and efficient care to all patient demographics in our integrated health system. We sought to explore the association between neighborhood disadvantage and postoperative outcomes in patients undergoing pancreatectomy for Pancreatic Ductal Adenocarcinoma (PDAC). **METHODS:** A retrospective analysis of PDAC patients diagnosed between 2016 and 2024 was conducted. To measure neighborhood disadvantage, the cohort was categorized into ADI tertiles: Q1 (1-44), Q2 (45-74) and Q3 (75-100) with 1 and 100 being the least and most disadvantaged groups, respectively. Logistic Regression and Kaplan-Meier method were used to assess the association between ADI and our outcomes of interest which included post-surgical pancreatic complications, unplanned readmission within 30 days and mortality. **RESULTS:** 413 patients underwent a pancreatectomy for PDAC between 2013 and 2024. The mean age at diagnosis was 64.9 ± 10 years and median ADI was 61. Patients in Q3 (highest disadvantage) were almost 3 times more likely to be readmitted within 30 days after surgery when compared to those in Q1 (OR: 2.81, 95% CI [1.02 ; 7.76], p-value= 0.04). There were no significant differences between ADI groups in pancreatic fistula, gastroparesis, post-surgical bleeding (all $p > 0.05$) and in mortality (log-Rank p=0.551). **CONCLUSIONS:** Patients from more disadvantaged neighborhoods, as indicated by higher ADI, had significantly higher 30-day readmission rates following surgery. These results highlight the need to implement targeted strategies that address and improve social determinants of health, and its role in affecting post-surgical outcomes, for it is becoming increasingly more evident that their role is nearly as important in oncologic care and postoperative recovery.

P323. Neighborhood Disinvestment and Healthcare Utilization in Surgical Patients with Breast Cancer

JC Chen, MD[1]; Yevgeniya Gokun, MS[2]; Jesse Plascak, PhD[3]; Mohamed I Elsaid, MPH, PhD[4]; Joal Beane, MD[5]; Eric Schupp, MD[6]; Samilia Obeng-Gyasi, MD[7]
[1]Ohio State University, Columbus, OH, US; [2]Ohio State University, Columbus, OH, US; [3]Ohio State University, Columbus, OH, US; [4]Ohio State University, Columbus, OH, US; [5]Ohio State University, Columbus, OH, US; [6]Parkview Health, Fort Wayne, IN, US; [7]The Ohio State University Medical Center, Columbus, OH, US

INTRODUCTION: In patients with breast cancer, neighborhood disinvestment (ND), a measure of physical deterioration in the built environment, has been linked to more aggressive tumor characteristics and poorer overall survival. The objective of this study was to examine the association between ND and healthcare utilization in patients with breast cancer who underwent surgery. **METHODS:** Females aged 18+ with stages I-III breast cancer who underwent surgical treatment between 2012 and 2020 were retrieved from the Ohio State University cancer registry. Previously validated methods including virtual neighborhood audits of six disinvestment indicators, item response theory, and spatio-temporal visualization were used to estimate ND scores at patient addresses on date of diagnosis. Higher scores signified greater ND. Healthcare utilization was defined as having either emergency department (ED) visits and/or hospital admissions within the first year of initiating cancer treatment. Admissions linked to the day of surgery were excluded. Generalized estimating equation models of binary healthcare utilization outcomes were used to generate odds ratios (OR) and 95% confidence intervals (CI) for levels of ND (high > median ND, low ≤ median ND). Multivariable models adjusted for age, race, health insurance, marital status, presence of reconstructive surgery, and type of breast and axillary surgery. **RESULTS:** Among 1,443 patients with non-missing data, higher proportions of patients living in high ND identified as Black (30.75% vs. 10.82%, p=0.018), were single (28.25% vs. 13.18%, p=0.001), and were Medicaid-insured (17.87% vs. 4.16%, p=0.005). Patients residing in neighborhoods with greater disinvestment had higher risk of having at least one ED visit (21.19% vs. 14.29%, p=0.002) and/or at least one hospital admission (14.82% vs. 10.96%, p=0.032) than individuals living in areas with continued investment. High ND trended toward a higher risk of developing postoperative complications (11.36% vs. 8.74%, p=0.075), but there were no differences in ICU admissions (p=0.233) or unplanned procedures (p=0.427) between high vs low ND. On multivariable analysis, each unit increase in ND was associated with greater odds of healthcare utilization (aOR 1.44, 95% CI 1.09-1.90). **CONCLUSIONS:** In this cohort of surgical patients with breast cancer, residing in neighborhoods with significant physical deterioration was independently linked to higher healthcare utilization during the first year of cancer treatment.

P324. Practice Patterns of Complex General Surgical Oncology Diplomates

Joshua M.V. Mammen, MD, PhD, MBA, MEd[1]; Anne Larkin, MD[2]; Peter Angelos, MD PhD[3]; Bridget Fahy[4]; Collin Dougherty[5]; Lawrence Kim[6]
[1]University of Nebraska, Omaha, NE, US; [2]University of Massachusetts Medical Center, Worcester, MA, US; [3]University of Chicago, Chicago, IL, US; [4]University of New Mexico Comprehensive Cancer Center, Albuquerque, NM, US; [5]University of Nebraska, Omaha, NE, US; [6]University of North Carolina Chapel Hill, Chapel Hill, NC, US

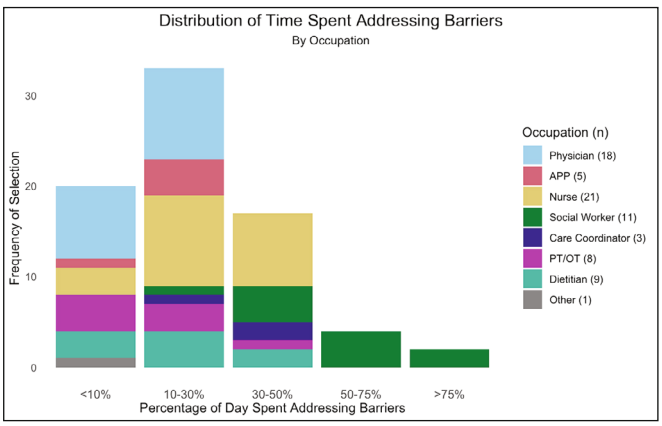
INTRODUCTION: Complex General Surgical Oncology (CGSO) certification was first awarded in 2014. CGSO training includes a comprehensive range of areas. The independent practice of CGSO diplomates has not been studied. The breadth of CGSO diplomate practice could impact training, certification, and re certification models. Therefore, the CGSO Board endeavored to better understand current practice patterns. **METHODS:** A survey was sent to CGSO diplomates awarded certification from 2014-2023. Multivariate ANOVA was used to compare differences in practice percentages. Tukey's HSD test was used to identify differences in individual practice areas. For non-normally distributed variables, Wilcoxon tests were used to compare ideal and current practice differences. **RESULTS:** 490 eligible subjects, 190 diplomates responded (39%). 38% were female and 62% male. The racial and ethnic distribution was 69% white, 19% Asian, 3% Black/African American, and 9% Hispanic. 65% reported being university employees with another 18% reporting academic affiliation. The largest practice pattern was broad-based surgical oncology (43%). 31% reported practice limited to a few closely related disease sites while 20% reported a practice limited to a small number of disease sites not closely related. Only 5% reported a practice limited to a single disease type. The most common individual practice area reported was pancreatic cancer (23%) followed by hepato-biliary (20%). The least common practice area was palliative care (1%). Correlation modeling defined practice models with greater than 50% of a practice being within these disease groups led to creation of five groups (1. GI/HIPEC/HPB 2. Breast 3. Endocrine/Palliative/Other 4. Colorectal 5. Melanoma/Sarcoma) and Generalists (those who did not have focused practices). The largest groups were GI/HIPEC/HPB (39.7%) and Generalist (32.2%). Respondents hoped to increase the proportion of HPB patients in their ideal practices ($p < 0.001$). Early (2014-2018) and later (2019-2023) cohort of diplomates certified were analyzed for practice differences. The largest numerical differences were in HPB (early 38.1% versus later 47.9%, p = 0.20) and Breast (early 16.6% versus later 11.2%, p = 0.99), but none were statistically significant. **CONCLUSIONS:** While practice patterns of CGSO diplomates vary, most have a broad practice. HPB malignancies is a major component and area of interest for most CGSO diplomates. The findings support maintaining a training paradigm that is broadly inclusive of surgical oncology areas, but with an enhanced emphasis on HPB malignancies.

P325. Provider perspectives of barriers to GI cancer care

Trisha Lal[1]; Anand Kathardekar[2]; Christina S Boutros, DO[3]; Sarah Koopman-Gonzalez, PhD[4]; Natalie N Chakraborty, MD[5]; Luke D. Rothermel, MD, MPH[6]; Jordan Winter[7]; Richard Hoehn, MD[8]
[1]Case Western Reserve/University Hospitals, Cleveland, OH, US; [2]The University of Akron, Akron, OH, US; [3]Univerisity Hospitals, Cleveland Medical Center, Cleveland, OH, US; [4]Case Western Reserve Univeristy, Cleveland, OH, US; [5]University Hospitals, Cleveland Medical Center, Cleveland, OH, US; [6]University Hospitals, Cleveland Medical Center, Cleveland, OH, US; [7]University Hospitals, Cleveland Medical Center, Cleveland, OH, US; [8]University Hospitals, Cleveland Medical Center, Cleveland, OH, US

INTRODUCTION: Disparities in care for patients with gastrointestinal (GI) cancers are well-documented, yet solutions remain elusive. Understanding barriers faced by healthcare providers is essential to improving care equity. This study explored the perceptions of healthcare providers at a regional academic health system regarding barriers to GI cancer care. We hypothesize that these barriers play a critical role in shaping care delivery. **METHODS:** A cross-sectional survey was conducted among healthcare providers, including physicians, advanced practice providers (APPs), nurses, dieticians, social workers, care coordinators, and physical/occupational therapists who care for GI cancer patients. Survey items assessed barriers encountered in practice and suggestions for improving care. Descriptive statistical analysis evaluated the

quantitative data from closed-ended questions across professional roles, while thematic analysis identified perceived barriers from open-ended responses. **RESULTS:** Seventy-nine healthcare providers responded to the survey out of 120 possible responses. Initial treatment planning had the most significant barriers across all disciplines. Health literacy was cited as the most critical barrier to diagnosis, while insurance coverage, financial constraints, geographic location, lack of transportation, and social support were the primary obstacles to treatment. Barriers varied by profession: physicians noted geographic and transportation limitations, while nurses and social workers emphasized gaps in health literacy, insurance, and social support. Systemic issues such as limited access to specialized care and healthcare personnel shortages were also noted. Notably, 55% of physicians spent 10-30% of their time addressing non-medical barriers to treatment, while 38% of nurses spent 30-50% (Figure 1). Care coordination across disciplines was commonly cited as a challenge, with many calling for improved communication and establishing multidisciplinary clinics. Food insecurity, housing stability, and language/cultural barriers were less prominent concerns. **CONCLUSIONS:** Oncology providers at a large regional cancer center spend significant time addressing non-medical barriers to treatment for GI cancer patients, particularly during initial treatment planning. The most common challenges reported were insurance, transportation, health literacy, and social support. These findings, with their potential to guide the development of team-based, equity-focused interventions, offer hope for enhancing patient navigation and reducing inefficiencies and disparities in care delivery.



P326. Racial Disparities in Receipt of Adjuvant Chemotherapy for High-Grade Metastatic Soft Tissue Sarcoma

Noor Habboosh[1]; Katia Papalezova[2]
[1]Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY, US; [2]Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY, US

INTRODUCTION: Undifferentiated pleomorphic sarcoma (UPS) and Myxofibrosarcoma (MFS) represent the most common histologic subtypes of extremity and truncal soft tissue sarcomas (STS). Patients experience high rates of local recurrence given the peripheral infiltrative growth pattern, and patients with high grade tumors are at risk for developing distant lung metastases. Targeted therapies remain elusive given the genomic complexity of these tumors, yet adjuvant and neoadjuvant radiation and adjuvant anthracycline-based chemotherapy have shown promise in improving survival. Given prior studies' demonstration of racial disparities in metastatic STS clinical outcomes, this study seeks to evaluate racial disparities in receipt of these adjunct therapies as a potential contributing factor to these outcomes. **METHODS:** A retrospective cohort of patients who were diagnosed with UPS/MFS from 2010-2020 with complete staging information was identified from the Surveillance, Epidemiology, and End Results Program (SEER) database (n=10,042). Univariate analysis was performed with chi-squared tests, and multivariable analysis was performed with Cox regression. **RESULTS:** 184 (1.83%) patients developed distant lung metastases. Of these patients, 61% were Male, 39.6% were diagnosed with high-grade STS at age 60-79 years, 25.5% age 40-59, 27.2% age >80, 7.7% age <40. 66.3% of patients self-identified as White, 14.1% Black, 13.6% Hispanic, 5.5% Asian/Pacific Islander, 0.54% American Indian. Overall mortality in this cohort was 85.3%, with 78.3% of cases attributed to disease-specific death (DSD). While race was not associated with overall mortality, Black (aRR 1.84, %95CI 1.76-1.99, p< 0.01), Hispanic (aRR 1.92, %95CI 1.83-1.96, and Asian/Pacific Islander (aRR 1.60, %95CI 1.551.65, p< 0.01) race was associated with higher DSD. Race was not significantly associated with rate of surgical resection or receipt of neoadjuvant/adjuvant radiation. Black (aRR 1.77, %95CI 1.70-1.80, p<0.01) and Hispanic (aRR 1.81, %95CI 1.77-185, p<0.01) patients who underwent surgical resection and radiation were more likely to experience DSD than their White counterparts. White race was associated with higher rate of chemotherapy administration (35%, aRR 1.55, %95CI 1.46-1.57, p<0.01) than for Black (14.1%) and Hispanic (12.4%) patients. **CONCLUSIONS:** UPS/MFS represent high-grade STS with a high rate of local recurrence and potential for lung metastasis, contributing to significant morbidity and mortality for patients, with Black and Hispanic patients historically suffering greater DSD despite comparable rates of lung metastasis to their White counterparts. While there is no statistically significant correlation between race and treatment with surgical resection or radiation, this analysis identifies racial disparities in receipt of adjuvant chemotherapy; This analysis highlights the importance of further characterizing disparities in access to comprehensive cancer care, as lack of access to these emerging therapies may contribute to observed differences in DSD.

P327. Racial and Ethnic Differences in Physical & Mental Health After Cancer Diagnosis

Brittany C. Fields, MD, MPH[1]; Kaiping Liao, PhD[2]; Joshua Herb, MD, MSCI[3]; Jessica E. Maxwell, MD MBA[4]; Naruhiko Ikoma, MD, MS[5]; Michael P. Kim, MD[6]; Jeffrey E. Lee, MD[7]; Ching-Wei D. Tzeng, MD[8]; Matthew H.G. Katz, MD[9]; Rebecca A. Snyder, MD, MPH[10]
[1]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [4]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [5]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [6]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [7]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [8]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [9]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [10]MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Racial and ethnic disparities in the treatment and survival of patients with gastrointestinal (GI) and hepatopancreatobiliary (HPB) malignancies are well-established; however, differences in health-related quality of life (QoL) are understudied. The purpose of this study was to compare changes in physical and mental health following GI or HPB cancer diagnosis by race and ethnicity. **METHODS:** Patients diagnosed with GI or HPB malignancies after 1998, and who completed surveys within 2 years pre- and post-diagnosis were identified from a 70,000-patient cohort of Medicare beneficiaries in the NCI SEER-Medicare Health Outcomes Survey (MHOS) database. Validated Physical Component Summary Scores (PCS12) and Mental Component Summary Scores (MCS12) of VR-12 or SF-36 Health Surveys were normalized to a 0-100 scale. Paired T-test was used to compare the change in scores between baseline and follow-up surveys. **RESULTS:** Of 2105 identified patients, 70.1% (1476) self-identified as Non-Hispanic White (White), 9.8% (207) Non-Hispanic Black (Black), 10.6% (223) Hispanic, and 9.5% (199) Other race or ethnicity. Most patients had colorectal (75.7%, 1594) or pancreatic cancer (7.8%, 165). Racial and ethnic differences in social risk factors were observed, with more White patients reporting college education, home ownership, and household income ≥$30,000 compared to Black or Hispanic patients. Pre-cancer diagnosis, more Black patients rated their general health worse and had lower mean PCS and MCS scores than White patients. White patients, however, were more likely than Black patients to report worsened general health after cancer diagnosis (38.5% vs. 30.9%, p<0.001). After diagnosis, mean (SD) PCS significantly decreased across all groups (Figure 1A), most notably among White patients (-4.2 [SD 10.7], p<0.01) and patients of Other race or ethnicity (-5.0 [SD 11.8], p<0.01). Decline in mean MCS was greatest for patients of Hispanic ethnicity (-4.2 [11.9], p<0.01) or Other race or ethnicity (-5.0 [11.8], p<0.01; Figure 1B). There was no difference in post-diagnosis timing of follow-up surveys by race (p=0.08). **CONCLUSIONS:** While Black patients report worse pre-cancer health status and QoL scores, they are less likely to report a decline in physical or mental health scores following GI or HPB cancer diagnosis. This may be explained by worse baseline health status, improved access to care post-diagnosis, differences in reporting, or improved community support. Qualitative research is necessary to understand the differential physical and mental health needs among patients with GI and HPB malignancies.

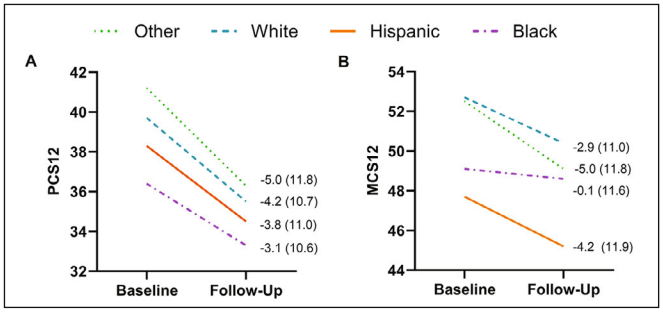


Figure 1. Mean (standard deviation) changes in (A) Physical Component Summary Scores (PCS 12) and (B) Mental Component Summary Scores (MCS 12) between baseline (pre-cancer diagnosis) and follow-up (post-cancer diagnosis) SEER-MHOS surveys for patients of varying races and ethnicities with a gastrointestinal or hepatopancreatobiliary cancer diagnosis.

P328. Racial disparities in receipt of guideline concordant pancreatic cancer care among older adults in the U.S.

Joshua Herb, MD, MS[1]; Kaiping Liao, PhD[2]; Kever A Lewis, MD[3]; Sharon Giordano, MD MPH[4]; Matthew H.G. Katz, MD[5]; John Lin, MD MSHP[6]; Rebecca A. Snyder, MD, MPH[7]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [4]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [5]MD Anderson Cancer Center, Houston, TX, US; [6]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [7]MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Patients racialized as Black experience a higher incidence and mortality from pancreatic cancer. The aim of this study was to examine differences in receipt of guideline concordant care (GCC) among older adults with pancreatic cancer racialized as Black, White, or Hispanic ethnicity. **METHODS:** Patients aged 65 years and older with incident pancreatic cancer racialized as White, Black, or Hispanic ethnicity were identified in the SEER-Medicare database from 2004-2019. The primary outcome was receipt of stage-specific GCC (stage I/II: surgery+chemotherapy+/-radiation; stage III: chemotherapy+/-surgery+/-radiation; stage IV: chemotherapy+/-radiation). Multivariable logistic regression was used to identify factors associated with GCC. Oaxaca-Blinder decomposition was used to examine the contribution of measured and unmeasured variables to racial disparities in receipt of GCC. **RESULTS:** Of 12,772 patients included, 85.5% of patients racialized as White (n=10,915), 7.8% Black (n=992), and 6.8% Hispanic ethnicity (n=865). Patients of Hispanic ethnicity and racialized as Black were more often dual-eligible for Medicare/Medicaid than patients racialized as White (38.6%, 26.9%, and 7.5%, respectively). In total, 56.3% received GCC. On adjusted analysis, patients racialized as Black were less likely to receive GCC for early stage (stage I/II) disease compared to patients racialized as White (OR 0.66; 95% CI 0.53-0.83), but not for stage III (OR 0.65; 95% CI 0.41-1.01) or stage IV (OR 0.87; 95% CI 0.66-1.14) disease. No difference in GCC was observed among patients of Hispanic ethnicity when compared to patients racialized as White. Increased age and dual-eligibility were associated with decreased likelihood of GCC across stages. Differences in receipt of GCC among patients racialized as Black and White remain largely unexplained. Of the measured factors, comorbidities, dual-eligibility, and area level poverty contributed most to the disparity in GCC (Table). **CONCLUSIONS:** Just over half of an insured population with pancreatic cancer receive GCC. Despite an increased focus on equity in cancer care, Black-White racial disparities in receipt of GCC are prevalent, particularly among patients with early-stage disease. Further studies are critical to identify and address the unmeasured factors driving treatment disparities.

Table: Contributing Factors for Racial Disparities in Guideline Concordant Care for Patients with Pancreatic Cancer.

	Stage I/II	Stage III	Stage IV
Difference (White-Black)	11.6%	9.4%	4.1%
Explained			
Age	-3.0%	-2.0%	-1.0%
Sex	0.1%	0.8%	0.1%
Dual-Eligibility	2.0%	3.1%	0.8%
Charlson Comorbidity Index	1.3%	0.2%	0.7%
Area Level Poverty	2.2%	-0.8%	0.7%
Hospital/Practice Volume	1.2%	-0.3%	-0.03%
Region	0.4%	0.9%	-0.2%
Year of Diagnosis	-0.1%	0.5%	0.1%
Unexplained	7.5%	7.0%	3.0%

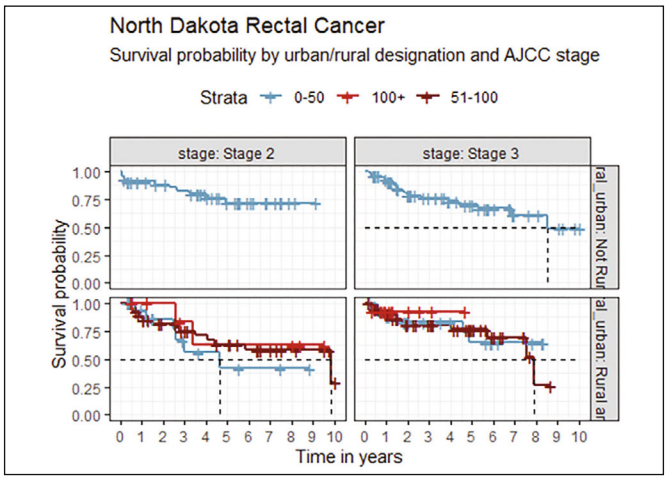
Positive values indicate racial differences in these factors increased the measured disparity, while negative values indicate that racial differences decreased the measured disparity.

P329. Rural-Urban Disparities in Multidisciplinary Access to Care for Stage II-III Rectal Adenocarcinoma in North Dakota

Kajsa Anderson, BS[1]; Hilla I. Sang, PhS[2]; Robert P. Sticca, MD[3]; Sabha Ganai, MD, PhD, MPH, FACS, FSSO[4]

[1]University of North Dakota School of Medicine, Fargo, ND, US; [2]Sanford Fargo Medical Center, Fargo, ND, US; [3]University of North Dakota School of Medicine, Fargo, ND, US; [4]University of North Dakota School of Medicine, Fargo, ND, US

INTRODUCTION: Treatment of rectal cancer requires a multimodal approach including chemotherapy, radiation, and surgery. There is an assumption that rural populations have poorer outcomes due to less access to treatment. We hypothesize that rural patients have increased time to treatment and decreased survival. **METHODS:** We performed a retrospective review of tumor registry data from an integrated health system across North Dakota from 2013 - 2022. We included 284 patients who had clinical stage II or III rectal adenocarcinoma. Rural-urban location was classified based on zip code of patients using USDA Rural Urban Commuting Area (RUCA) codes designating RUCA 1-3 as urban and 4-10 as rural. Rural travel distance was calculated with ArcGIS. Cox proportional hazard models were utilized to compare overall survival after confounding control. **RESULTS:** The majority of patients were male (65%) and white (92%) with the next largest ethnicity being Indigenous American (6.3%). 169 patients were classified as rural and 115 as urban. Indigenous Americans comprised a greater proportion of rural (8.9%) compared to urban (2.6%) counties ($p<0.05$). Stage II patients were 72% male and 28% female, while Stage III patients were 60% male and 40% female ($p<0.05$). There was no significant difference in proportion of early-onset rectal cancer (under 50 years), comprising 11% of urban and 14% of rural patients. Average time from diagnosis to chemoradiation was similar between groups at 55 days ($p=0.10$). Average time to surgery was similar at 129 days for urban patients compared to 126 days for rural patients ($p=0.57$). Average time to surgery differed between stage II disease at 112 days versus stage III disease at 137 days ($p=0.024$). On multivariate analysis, there was no significant difference in survival when comparing patients by proximity of treating facility while controlling for age, gender, race, pT stage, and pN stage. Stage II patients had a 5-year overall survival estimate of 64% compared to 72% for Stage III patients ($p>0.05$). **CONCLUSIONS:** Rural patients are assumed to have worse cancer treatment outcomes, however we have identified that there is no significant difference in survival for patients in this study based on rural or urban status. Surprisingly, there was no difference in survival of stage II or stage III patients managed in the state. This suggests that both rural and urban patients with clinical Stage II adenocarcinoma may be doing worse than expected, and warrants further study.



P330. Skin Deep: Racial Disparities in Patients with Acral Lentiginous Melanoma

Andrew Anthony Francis, MD, MS[1]; Bassam Dahman, Phd[2]; Benjamin Schmidt, MD, FACS[3]; Raphael Louie[4]
[1]Virginia Commonwealth University, Richmond, VA, US; [2]Virginia Commonwealth University, Richmond, VA, US; [3]Virginia Commonwealth University, Richmond, VA, US; [4]Virginia Commonwealth University, Richmond, VA, US

INTRODUCTION: Acral lentiginous melanoma (ALM) is a rare subtype of cutaneous melanoma, accounting for 2-3% of melanoma cases in the United States. While the overall incidence of ALM remains low, it constitutes the majority of melanoma cases among black patients, accounting for 19-36% of melanoma diagnoses. Given the impact of ethnic and racial disparities on cancer outcomes and Virginia's high diversity index, we aim to investigate regional population trends and racial disparities in outcomes between black and white patients. **METHODS:** We performed a single-institution retrospective review of patients 18 or older with ALM from 2010-2023. Our primary outcomes were overall survival (OS) and recurrence-free survival (RFS). We used two-tailed t-tests and Fisher's exact test for statistical analysis. OS and RFS were evaluated with Kaplan-Meier estimates and the log-rank test. **RESULTS:** We identified 41 patients with ALM, 30 were white (73.2%) and 10 were black (24.4%). One patient was Middle Eastern (2.4%) and excluded from further statistical analysis. Age, sex, BMI, medical comorbidities, tumor location, and primary treatment modalities were similar between groups. 20% of black patients had clinically positive nodes at presentation vs 3.3% of white patients. Initial biopsy underestimated final Breslow depth in a significantly greater proportion of black patients (60% vs. 23%, p <0.05). Black patients had thicker tumors (7.9 mm vs. 4.8 mm) and more aggressive pathological features: mitotic rate, regression, ulceration, and lymph vascular invasion (all p < 0.05). Black patients had significantly higher rates of locoregional disease on final pathology (60% vs. 16.7%). Melanoma-specific mortality was higher among black patients (30% vs 6.7%, p = 0.09). Kaplan Meier estimates of OS and RFS were not statistically different (p = 0.66 and 0.87). **CONCLUSIONS:** ALM is a rare subtype of melanoma with proportionally higher mortality than other subtypes. This is one of the largest single-institution series in the current era evaluating the epidemiology and disparities of ALM among black patients. Despite advances in systemic therapy, disparities among black patients with ALM persist. Further efforts are needed to better understand social, medical, and biologic factors that may impact ALM outcomes among black patients.

P331. Socioeconomic and Institutional Factors Affecting the Receipt of Neoadjuvant Therapy in Locally Advanced Gastric Cancer: A National Cancer Database Analysis

Sumaya Ghaffar, MD[1]; Andrii Khomiak, MD[2]; Ana L. Gleisner, MD, PhD[3]; Martin D McCarter, MD[4]; Steven Ahrendt, MD[5]; Richard Schulick, MD MBA[6]; Marco Del Chiaro, MD PhD[7]; Benedetto Mungo, MD[8]
[1]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [2]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [3]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [4]University of Colorado School of Medicine, Aurora, CO, US; [5]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [6]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [7]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [8]University of Colorado School of Medicine, Aurora, CO, US

INTRODUCTION: Neoadjuvant therapy (NAT) is currently among the recommendations by the NCCN guidelines for Locally Advanced Gastric Cancer (LAGC). This study aims to evaluate the use of NAT among LAGC patients, focusing on socioeconomic characteristics related to its receipt and its impact on outcomes. **METHODS:** The National Cancer Database was leveraged from 2004 to 2020. We included all adenocarcinoma LAGC patients with an indication to receive NAT according to the NCCN Guidelines (≥ cT2, M0) who underwent surgical resection. We compared patients who received NAT to those who did not (non-NAT). Differences in categorical variables were assessed using the Chi-Square test. Kaplan-Meier survival analysis was performed to estimate survival probabilities, and Cox regression analysis was employed to calculate Hazard Ratios (HR). **RESULTS:** We identified 34,036 patients within the inclusion criteria. Median age was 66 years, with 70% being males. 62% of patients received NAT, the only systemic therapy in 46.9% of cases. Only 15.0% of the population received both NAT and adjuvant treatment. The group who received NAT was significantly younger (64 vs 70 years, p<0.001), and composed of a white population (81.8% vs 70.9%, p<0.001). A lower Charlson-Deyo Comorbidity (CC) score was noticed in NAT recipients, which more often had a CC 0 (71% vs 65.1%, p < 0.001). Most patients receiving NAT were treated at an Academic/Research Program, (51.9% vs 42.7%, p<0.001). There was a higher proportion of privately insured in the NAT group (44.6% vs 29.8%, and a higher proportion of Medicare patients in the non-NAT group (56.4% vs 42.7%, p<0.001). When evaluating urban versus rural areas, there was no difference in NAT receipt, except when evaluating urban areas with over a million inhabitants, where patients received NAT more often (61.1% vs 54.8%, p<0.001). NAT group had lower levels (< 7%) of no high-school completion (25.6% vs 19.9%, p<0.001) and more often were in the higher end of household income (35.8% vs 31.5%, p<0.001). NAT receipt was associated with better overall 5-yr survival (HR 0.63 [95%CI 0.60-0.65], p <0.0001) when adjusted for age, sex, Charlson-Deyo Score, histology, AJCC T stage, type of surgery, and receipt of adjuvant therapy. Patients who received NAT had better survival outcomes when compared to those who received only adjuvant or no systemic therapy (56.9 months for both NAT and adjuvant, 47.3 months for only NAT, vs 40.4 months for adjuvant only and 31.1 months for no systemic therapy, p<0.001). **CONCLUSIONS:** Patients with LAGC who did not receive NAT despite having the indication had different socioeconomic characteristics, which may configure a barrier to access. The receipt of NAT was associated with better survival outcomes in this cohort.

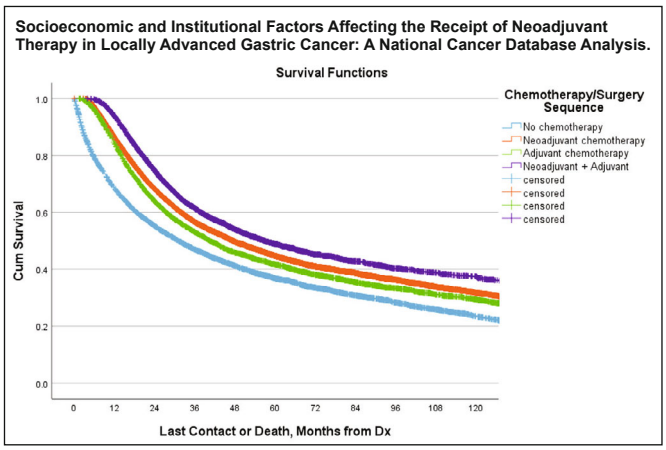


Figure 1. Kaplan-Meier Survival Curve: Comparative Outcomes of NAT and Systemic Therapy Strategies in Patient Survival (p<0.001).

P332. Using Granular Patient-Specific Data to Understand Predictors of Clinical Trial Enrollment

Weichuan Dong[1]; Jamie Shoag[2]; Deb Bruno[3]; John Shanahan[4]; Johnie Rose[5]; Siran Koroukian[6]; Richard Hoehn, MD[7]
[1]Case Western Reserve University, Cleveland, OH, US; [2]Cleveland Clinic, Cleveland, OH, US; [3]University Hospitals Cleveland Medical Center, Cleveland, OH, US; [4]University Hospitals Cleveland Medical Center, Cleveland, OH, US; [5]Case Western Reserve University, Cleveland, OH, US; [6]Case Western Reserve University, Cleveland, OH, US; [7]University Hospitals Cleveland Medical Center, Cleveland, OH, US

INTRODUCTION: Overall rates of cancer clinical trial enrollment are too low, and significant racial and socioeconomic inequities exist regarding access and participation. We analyzed all cancer patients at our institution using a novel social determinants of health (SDOH) data linkage to identify unique predictors of trial enrollment. **METHODS:** We analyzed patients aged 18-75 years diagnosed with cancer in our regional hospital system between 2018-2021, categorized based on enrollment in interventional clinical trials. Independent patient variables included standard demographics along with data from the LexisNexis Socioeconomic Health Attributes dataset, which provides hundreds of variables related to income, education, social support, and other SDOH. Multi-step variable selection was performed with a combination of manual, statistical, and machine-learning methods. Propensity score matching was performed using age, gender, and cancer type. Variable importance was assessed using Classification and Regression Tree (CART), Boruta machine learning algorithm, and stepwise logistic regression. **RESULTS:** Of the 12,645 cancer patients identified, 652 (5.2%) participated in clinical trials. Age, gender, and cancer type were strongly correlated with trial enrollment, so a propensity-matched 7:1 cohort of non-trial:trial patients was created to account for these characteristics. In this cohort, trial patients were more often White (84.5% vs 77.5%), with private insurance (54.3% vs 49.4%), higher annual income ($51,000 vs $43,000), higher home value ($173,000 vs $140,000) and historic property count (median: 2 vs 1; all $p<0.01$). Education, marital status, and driving distance were not significant. The Boruta and CART analyses found that clinical trial enrollment was predicted by health insurance, income, and property ownership. Finally, stepwise logistic regression found that race was initially a predictor of trial enrollment, but lost significance after adjustment for income and insurance. **CONCLUSIONS:** Compared to prior studies, which focus on populations of clinical trial patients, this is a robust analysis of a large population of cancer patients along with granular patient-specific socioeconomic data. Through multiple analytic methods, these findings suggest financial resources are the largest predictors of clinical trial enrollment and should be the focus of initiatives to increase access to novel treatments for all cancer patients.

P333. Local recurrence patterns in surgically treated stage III and IV oral squamous cell carcinoma: A Prospective Observational Study

Kush Shah[1]; Ridham Shah[2]; Niket Shah[3]
[1]KD Hospital, Ahmedabad, Gujarat, IN; [2]KD Hospital, Ahmedabad, Gujarat, IN; [3]KD Hospital, Ahmedabad, Gujarat, IN

INTRODUCTION: Oral squamous cell carcinoma (OSCC) is a significant health issue, especially in stages III and IV, with high recurrence rates despite advances in treatment. While factors such as tumor size, differentiation, surgical margins, and lymphovascular invasion have been studied, predictors of early local recurrence remain unclear. This study aims to identify high-risk clinical and pathological variables associated with recurrence and to examine demographic patterns. **METHODS:** We analyzed 260 OSCC patients, evaluating parameters including tumor staging, nodal stage, lymph node ratio, cell differentiation, margin status, depth of invasion, extracapsular extension, lymphovascular invasion, perineural invasion, radiation type, radiotherapy completion status, and the interval between surgery and radiation. The goal was to identify correlations with local recurrence and determine significant high-risk variables and demographic trends. **RESULTS:** In stage III and IV OSCC patients, no significant correlation was found with local recurrence for parameters such as primary staging ($p = 0.771$), nodal staging ($p = 0.27$), group staging ($p = 0.211$), cell differentiation ($p = 0.518$), margin status ($p = 0.229$), depth of invasion ($p = 0.469$), radiation type ($p = 0.996$), radiotherapy completion ($p = 0.964$), and the time between surgery and radiation ($p = 0.358$). Significant predictors of local recurrence included lymph node ratio ($p < 0.00001$), perineural invasion (PNI) ($p < 0.00001$), lymphovascular invasion (LVI) ($p = 0.003$), and extracapsular extension (ECE) ($p < 0.00001$). **CONCLUSIONS:** Lymph node ratio, PNI, LVI, and ECE are significant predictors of early local recurrence in advanced OSCC.

P334. Oncological safety, efficacy and Quality of Life of patients undergoing transaxillary gasless endoscopic hemithyroidectomy for the treatment of thyroid cancer less than 4 cm

Sanjay Kumar Yadav, MCH, FACS, FSSO[1]
[1]NSCB Medical College, Jabalpur, IN

INTRODUCTION: The aim of this study was to report the safety and efficacy and quality of life (QoL) of endoscopic hemithyroidectomy (ETx) in patients with selected differentiated thyroid cancer as compared to conventional open hemithyroidectomy (OTx). **METHODS:** This was a single-institution observational study. The clinical records of patients with a histopathological diagnosis of differentiated thyroid cancer who were candidates for hemithyroidectomy were reviewed. Demographic, clinical, and histopathological data were collected. Health related quality of life was evaluated using validated ThyPRO39Hin questionnaire at baseline, 1 month and 6 months. **RESULTS:** During the study period, 94 patients underwent hemithyroidectomy for DTC. Eleven patients (11/134) were lost to follow-up and 14 patients underwent completion thyroidectomy based on definitive pathology. The final study group was composed of 69 patients, who had a median follow-up of 2 years. 28 patients underwent ETx and 45 underwent OTx. The average tumor size was 3+/-1 cm in the ETx group and 3.6+/- 0.8 cm in OTx group. The mean operative time was 80+/-35 minutes in ETx group and 44+/-28 minutes in OTx group. There was no difference in perioperative complications and hospital stay. For the ETx group, there was a lower neck pain score on the third postoperative day and higher cosmetic satisfaction at 3 months. The mean preoperative ThyPRO39 scores were comparable in all domains. Mean ThyPRO scores for all domains 1 month post-surgery were significantly better in ETx group having medium effect sizes. The difference in ThyPRO scores between the two groups became comparable at 6 months. **CONCLUSIONS:** ETx for thyroid cancer is safe and feasible option. However, long term QoL is similar to open conventional surgery.

P335. Predictive Value of Preoperative TSH Levels for Thyroid Hormone Supplementation Post- Thyroid Lobectomy: A 200-Patient Retrospective Cohort Study

Andres Tame-Elorduy[1]
[1]MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Background: A thyroid lobectomy is a commonly indicated procedure for a wide variety of thyroid pathologies; however, the decisions between a total thyroidectomy vs a lobectomy requires counseling of lifelong dependence on thyroid hormone supplementation. However, the need for thyroid supplementation following lobectomy can vary significantly among patients. This study aims to evaluate whether preoperative Thyroid-Stimulating Hormone (TSH) levels can help predict the requirement for thyroid hormone replacement therapy (THRT) postoperatively in patients undergoing thyroid lobectomy. **METHODS:** Methods: 1281 patients who received thyroid lobectomies for benign and malignant disease at MD Anderson Cancer Center from 2016 to February 2024 were screened. The exclusion criteria were a hyperactive nodule, undifferentiated thyroid carcinoma, age <18 years-old, no follow up at 6 months, and preoperative hypothyroidism. Post operative TSH values were obtained early in the post-op period (6-8 weeks) and late in the post-op period (6-12 months). The primary outcome was the requirement for THRT at their follow up at 6-12 months post-op, using logistic regression analysis and ROC curve analysis to evaluate the predictive value of preoperative TSH levels. **RESULTS:** Results: Of the 1281 patients screened, 200 met the inclusion criteria with a gender distribution of distribution of 74.37% female and 25.63% male with a median age of 50 ranging from 18 to 86 years old. Preoperative TSH levels varied among patients. Logistic regression analysis demonstrated that pre-op TSH levels were a significant predictor of the need for levothyroxine supplementation at 6-12 months post-op (Odds Ratio [OR] = 3.65, 95% Confidence Interval [CI] = 2.25-5.93, P < 0.001). Higher preoperative TSH levels increased the risk of needing THRT in the postoperative setting. Early post-op TSH (6-8 weeks post-op) (OR = 2.00, 95% CI = 1.48-2.70, P & 0.001) and late post-op TSH (6-12 months post-op) (OR = 1.21, 95% CI = 1.04-1.41, P = 0.016) were also significant predictors. A pre-op TSH cut-off value of 1.5 mIU/L was identified as the optimal threshold, with sensitivity and specificity at this cut-off being 66% and 75%, respectively. The Negative Predictive Value. (NPV) was 63.5 while the Positive Predictive Value (PPV) was 76.8%. **CONCLUSIONS:** Conclusion: The study demonstrates a significant correlation between preoperative TSH levels and the necessity for postoperative thyroid hormone supplementation. Patients with preoperative TSH levels above 1.5 mIU/L were more likely to require THRT at 6-12 months. These findings suggest that preoperative TSH could serve as a predictive marker for post-op thyroid function, aiding in preoperative patient counseling and management planning. This information is crucial for better counseling patients on the potential outcomes of thyroid lobectomy versus total thyroidectomy, helping them make informed decisions regarding their surgical options.

P336. Risk Factors and Prognosis of Peritoneal Metastases in Small Bowel Neuroendocrine Tumor Patients

Jeremy Chang, MS MD[1]; Luis C Borbon[2]; Scott K. Sherman, MD[3]; Chandrikha Chandrasekharan, MBBS[4]; Po H Ear, PhD[5]; Andrew M Bellizzi, MD[6]; Joseph S Dillon, MD[7]; James R Howe, MD[8]

[1]University of Iowa Hospitals and Clinics, Iowa City, IA, US; [2]University of Iowa Hospitals and Clinics, Iowa City, IA, US; [3]University of Iowa Hospitals and Clinics, Iowa City, IA, US; [4]University of Iowa Hospitals and Clinics, Iowa City, IA, US; [5]University of Iowa Hospitals and Clinics, Iowa City, IA, US; [6]University of Iowa Hospitals and Clinics, Iowa City, IA, US; [7]University of Iowa Hospitals and Clinics, Iowa City, IA, US; [8]University of Iowa Hospitals and Clinics, Iowa City, IA, US

INTRODUCTION: Small bowel neuroendocrine tumors (SBNETs) demonstrate indolent growth despite 25-50% of patients presenting with metastases at diagnosis. Surgical resection and cytoreduction may improve survival even with metastatic disease. The peritoneum is the second most common metastatic site after the liver, and while studies suggest that peritoneal metastases (PM) are associated with worse overall survival (OS), limited data exist on risk factors and outcomes of these patients post resection. **METHODS:** A single-institution review of a prospective database identified patients from 2013-2024 with histopathologic diagnosis of SBNET who underwent surgical intervention (primary resection and/or metastasis cytoreduction). Demographics, disease characteristics, treatments, and outcomes were abstracted. The Lyon staging system defined the extent of PM. Primary outcome measures were OS and progression-free survival (PFS), estimated by Kaplan Meier Method and compared by Log Rank Test. Cox multivariable analysis was performed to identify variables independently associated with PM. **RESULTS:** Of 282 patients with SBNET undergoing surgical resection, 84 (29.8%) had synchronous or metachronous PM. Patients with PM were more often female (59.5% vs 44.4% with no PM, p=0.02; Table) and more likely to have synchronous liver metastasis (85.7% vs 64.1% with no PM, p<0.01). Primary tumors in PM patients were larger in size and more often T4 stage. Most PM patients had intraoperative Lyon stage 3 or 4 (i.e. diffuse) peritoneal disease (82.1%). In multivariable analysis, female sex and liver metastases were positively associated with PM (p<0.01 for both). Patients with PM had worse median PFS than those without (40 vs 76 months, p=0.03) and were more likely to receive peptide receptor radiotherapy (PRRT). There was no significant difference in median OS between patients with and without PM post resection. Patients with PM had similar rates of postop Clavien-Dindo Grade 3- 4 complications (p=0.09), but higher rates of bowel obstruction in follow-up after resection (19.0% vs 2.5%, p<0.01; median follow up 59 months). **CONCLUSIONS:** Peritoneal metastases occur in 30% of patients with SBNETs and are more common in females and patients with liver metastases. Post-resection/cytoreduction, OS was similar between those with and without PM, but PM patients had worse PFS, increased use of PRRT, and more bowel obstructions. Similar OS in SBNET patients with and without PM suggests that PM should not dissuade surgeons from resection/cytoreduction for these patients when feasible.

Table. Study Characteristics and Associated variables with PM Incidence

	PM (n=84)	No PM (n=198)	p-value	Association with PM Incidence OR [95% CI]	P-value
Median Age	61.0 ± 2.4	59.7 ± 1.8	0.44	---	---
Gender			**0.02**		
Male	34 (40.5%)	110 (55.6%)		Ref	
Female	50 (59.5%)	88 (44.4%)		**1.17 [1.06 – 1.30]**	**<0.01**
ASA Class				**---**	**---**
1	1 (1.2%)	2 (1.0%)			
2	39 (46.4%)	82 (41.4%)			
3	32 (38.1%)	104 (52.5%)			
4	5 (6.0%)	3 (1.5%)			
NA	7 (8.3%)	7 (3.5%)			
Synchronous Liver Metastasis	72 (85.7%)	127 (64.1%)	**<0.01**	**1.20 [1.07 – 1.35]**	**<0.01**
Grade			0.23		
1	27 (32.1%)	84 (42.4%)		Ref	
2	51 (60.7%)	102 (51.5%)		0.99 [0.89 – 1.11]	0.91
3	6 (7.1%)	10 (5.1%)		0.96 [0.76 – 1.21]	0.75
NA	0	2 (1.0%)			
Primary Tumor Size			**<0.01**		
<1 cm	9 (10.7%)	17 (8.6%)		Ref	
1 – 2 cm	23 (27.4%)	106 (53.5%)		0.82 [0.66 – 1.01]	0.06
>2 cm	47 (55.9%)	63 (31.8%)		0.98 [0.79 – 1.22]	0.84
NA	5 (6.0%)	12 (6.1%)		---	
T stage			**<0.01**		
0	0	2 (1.0%)		---	
1	2 (2.4%)	6 (3.0%)		Ref	
2	4 (4.8%)	35 (17.7%)		0.94 [0.65 – 1.37]	0.76
3	34 (40.5%)	103 (52.0%)		1.03 [0.72 – 1.48]	0.87
4	37 (44.0%)	42 (21.2%)		1.24 [0.86 – 1.80]	0.24
NA	7 (8.3%)	10 (5.1%)		---	
N Stage			0.08		
0	2 (2.4%)	9 (4.5%)		Ref	
1	42 (50.0%)	117 (59.1%)		1.01 [0.76 – 1.35]	0.91
2	38 (45.2%)	61 (30.8%)		1.09 [0.81 – 1.47]	0.57
NA	2 (2.4%)	11 (5.6%)			
Received PRRT	28 (33.3%)	32 (16.2%)	**<0.01**		
Median Overall Survival (Months [95% CI])*	226 [226 - NA*]	Not reached [161 – NA*]	0.15		
5 YR Overall Survival	82.10%	88.40%	0.16		
Median Progression Free Survival (Months, 95% CI)	40 [28 - 60]	76 [61 - 100]	**0.03**		
Minor complication[1]	9 (10.7%)	23 (11.6%)	0.82		
Major Complication [2]	7 (8.3%)	7 (3.5%)	0.09		
30-Day Mortality	2 (2.4%)	1 (0.5%)	0.16		
Bowel Obstruction	16 (19.0%)	5 (2.5%)	**<0.01**		

PM=peritoneal metastases; OR=observed risk; NA=not available; *not enough events to calculate median survival; [1]Clavien Dindo Grade 1 or 2; [2]Clavien Dindo Grade 3 or 4

P337. Surgical management of locoregionally recurrent left-sided adrenocortical carcinoma

Shruthi R Perati, MD[1]; Alyssa Eade, MD[2]; Aaron Dinerman, MD[3]; Kate Barrows, MD[4]; Rachael Lowney, MD[5]; Tracey Pu, MD[6]; Leila Sarvestani, MD[7]; Carolina Larrain, MD[8]; Lindsay Friedman, MD[9]; Ashley Rainey[10]; Andrew M Blakely, MD[11]; Jeremy L. Davis, MD[12]; Naris Nilubol, MD[13]; Jonathan M Hernandez, MD[14]

[1]National Institutes of Health/National Cancer Institute, Bethesda, MD, US; [2]National Institutes of Health, Bethesda, MD, US; [3]National Institutes of Health, National Cancer Institute, Bethesda, MD, US; [4]National Cancer Institute, Bethesda, MD, US; [5]National Institutes of Health/National Cancer Institute, Bethesda, MD, US; [6]National Cancer Institutes/National Institutes of Health, Bethesda, MD, US; [7]National Institutes of Health/National Cancer Institute, Bethesda, MD, US; [8]National Institutes of Health, Bethesda, MD, US; [9]National Institutes of Health, National Cancer Institute, Bethesda, MD, US; [10]National Institutes of Health/National Cancer Institute, Bethesda, MD, US; [11]National Institutes of Health, Bethesda, MD, US; [12]National Institutes of Health, National Cancer Institute, Bethesda, MD, US; [13]National Institutes of Health, National Cancer Institute, Bethesda, MD, US; [14]National Institutes of Health, Bethesda, MD, US

INTRODUCTION: The management of recurrent adrenocortical carcinoma (ACC) is complicated and not well-defined, owing to the difficulties surrounding the re-operative field and often multifocal nature of disease recurrence. We sought to examine the results of en bloc multivisceral resections to achieve complete tumor extirpation for patients with locoregionally recurrent left-sided ACC. **METHODS:** Ten patients underwent aggressive multi-visceral en bloc resection of recurrent left-sided ACC between 2018-2024. Oncologic treatment history, operative data, 30-day post-operative outcomes, locoregional recurrence-free survival and quality of life (QOL) were assessed. **RESULTS:** The mean age of patients with recurrent ACC was 51 years (median 57, range 20-68) at time of operation and 90% of patients had undergone prior lines of systemic therapy. Patients had undergone a median of one prior operation (mean 1.5, range 1-4) before undergoing surgery at our center. Size of local

recurrence(s) on pre-operative imaging averaged 5.9cm (range 1.9-12.2cm) at largest diameter, with patients having a median of 3 (range 1-8) foci of locoregional disease recurrence. All patients had R0 resections. Of the en bloc resections, 8 (80%) involved distal pancreatectomy, 6 (60%) splenectomy, 7 (70%) left nephrectomy, 8 (80%) partial diaphragm resection (of which 5 (62.5%) required mesh repair), 5 (50%) partial hepatectomy, 5 (50%) partial gastrectomy, and 5 (50%) partial descending colectomy. Post-operatively, 2 patients (20%) developed a pancreatic fistula (Grade B). The majority of complications were minor/Clavien-Dindo I-II (n=6). The median duration of post-operative hospitalization was 17 days. Only one patient was readmitted within 30 days after surgery (10%), and there were no peri-operative mortalities. Eight patients had sufficient follow-up (median of 18 months and IQR 15.5-44.0 months) to evaluate locoregional recurrence-free survival. Four patients developed locoregional recurrence at a mean of 14.8 months post-operatively. One patient recurred and died from progression of disease within one year (Figure). 60% of QOL survey respondents reported feeling recovered and back to baseline activity level within 4 months of surgery. 100% of respondents reported that they would choose to undergo the operation again if they could go back. **CONCLUSIONS:** R0 resections can be obtained for locoregional control of left-sided ACC with acceptable morbidity and impact on QOL. Patient selection for these aggressive resections is paramount.

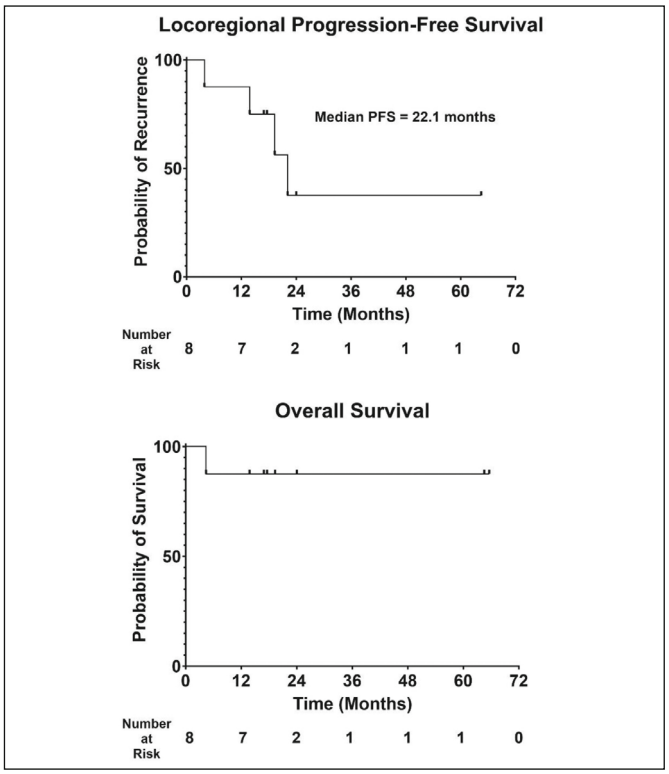


Figure. Locoregional Recurrence-Free (top) and Overall (bottom) Survival

P338. Survival Differences of Anaplastic Thyroid Cancer after Total Thyroidectomy between Radiation and Chemotherapy: A SEER Database Analysis

Laura M Cogua[1]; Connor J Tupper[2]; Peter T Silberstein[3]; Kathryn E Coan[4]
[1]Creighton University School of Medicine, Phoenix, AZ, US; [2]Hofstra/Northwell Zucker School of Medicine, New Hyde Park, NY, US; [3]Creighton University School of Medicine, Omaha, NE, US; [4]Creighton University School of Medicine, Phoenix, AZ, US

INTRODUCTION: Anaplastic thyroid cancer (ATC) is an aggressive endocrine malignancy. There is limited data on survival based on treatment for ATC, especially concerning the use of chemotherapy and/or radiotherapy. The aim of this study is to investigate survival differences by extent of treatment in ATC. **METHODS:** ATC patients from the Surveillance, Epidemiology, and End Results (SEER) were selected from 2000-2020. Treatment was divided into total thyroidectomy (TT) alone, TT plus radiation (TT-R), TT plus chemotherapy, TT (TT-C), and TT plus radiation and chemotherapy (TT-RC). Covariates included age, gender, race, stage, tumor size, median household income, and population size of the patient's home area. Cox regression analyses were completed to compare survival. **RESULTS:** A total of 403 patients were included. The median survival of the cohort was 4 months with TT, 8 months with TT-R, 9 months with TT-C, and 13 months with TT-RC. Cox regression results showed worse survival for patients who received a TT only (p's<0.001) while no differences were found between TT-RC and TT-R or TT-C. Age over 65 years (p=0.049), regional (p=0.020) and distant stage (p<0.001), and rural communities (p<0.001) were associated with worse survival. **CONCLUSIONS:** Although survival for ATC is poor, these results demonstrated there is increased survival in patients that received TT-RC, which supports the current American Thyroid Association guidelines for ATC management. Patient age, stage and living in rural communities may decrease survival, which should be considered in the management of ATC.

P339. The influence of calcium and PTH in glucose metabolism on patients with and without diabetes: A National Health and Nutrition Examination Survey study

Kailey Oppat[1]; Frances J. Bennett[2]; Loreski Collado[3]; Vignesh Jayaraman Muralidharan[4]; Anee S. Jackson[5]; Snehal Patel[6]; Neil Saunders[7]; Collin Weber[8]; Jyotirmay Sharma[9]; Thomas Szabo Yamashita[10]
[1]Emory University, Atlanta, GA, US; [2]Emory University, Atlanta, GA, US; [3]Emory University, Atlanta, GA, US; [4]Emory University, Atlanta, GA, US; [5]Emory University, Atlanta, GA, US; [6]Emory University, Atlanta, GA, US; [7]Emory University, Atlanta, GA, US; [8]Emory University, Atlanta, GA, US; [9]Emory University, Atlanta, GA, US; [10]Emory University, Atlanta, GA, US

INTRODUCTION: Primary hyperparathyroidism (PHPT) is characterized by elevated serum calcium (Ca) and inappropriately elevated/normal parathyroid hormone (PTH). Although often asymptomatic, PHPT can have severe metabolic consequences. Ca is involved in the regulation of insulin secretion. Effects of PHPT on glucose metabolism have not been well studied and presently, diabetes status is not considered when selecting patients (pts) for surgical management of PHPT. **METHODS:** Using the National Health and Nutrition Examination Survey (NHANES) database, a program that assesses the health status of Americans (2003-2016), we identified pts with and without PHPT (±PHPT), defined as either PTH ≥65 with a Ca 10.2 or, for pts without an available PTH, as vitamin D>30 and Ca 10.2. We then assessed for diagnosis of type 2 diabetes mellitus (±,serif">DM), defined as blood glucose (BG)>126, glycated hemoglobin (A1c)>6.5, or self-reported. Our primary aim was to explore the relationship of Ca and PTH with BG and A1c among pts ±,serif">DM based on PHPT status. **RESULTS:** 7895 (8.0%) of NHANES pts were included in +DM cohort, while 88,479 (92.0%) were included in -DM cohort. When comparing pts ±DM, +DM pts have significantly higher mean PTH than DM pts (50.9 vs. 43.1, p<.001). Of +DM pts, 45 (0.6%) were included in +DM/+PHPT cohort and 7850 (99.4%) were included in +DM/PHPT cohort. Of DM pts, 357 (0.4%) were included in DM/+PHPT cohort and 88122 (99.6%) were included in DM/PHPT cohort. When comparing the +DM/+PHPT and DM/+PHPT cohorts, PTH was not significantly different (116.8 vs. 106.8, p=.54). Although not statistically significant, there is a negative linear relationship between Ca and BG in +DM/+PHPT cohort (p=.82). There is a positive linear relationship between Ca and BG (p=0.01) in -DM/+PHPT cohort. In contrast, among -PHPT cohort, Ca demonstrates a negative linear relationship with both BG (p<.001) and A1c (p<.001). Mean BG was significantly higher in +DM/-PHPT than +DM/+PHPT cohort (135.2 vs. 151.6, p=.05). Interestingly, among +DM/The NHANES data suggests that there is linear relationship between PTH and Ca with glucose metabolism, which differs based on DM and PHPT status. Further studies are needed to assess the clinical implication of impaired glucose metabolism in PHPT and how this may impact surgical management of this disease.

P340. The risk of hepatic abscess in patients with metastatic pancreatic neuroendocrine tumors and bilioenteric anastomosis

Jace P Landry[1]
[1]UT MD Anderson Cancer Center, Houston, LA, US

INTRODUCTION: Patients with pancreatic neuroendocrine tumors (PNETs) who undergo resection for curative intent often recur distally (about 40%). The most common site of metastasis is the liver and liver-directed therapies (LDT) can offer improved progression-free survival. Patients who have undergone pancreatoduodenectomy (PD) are at risk for LDT-related complications due to the presence of a bilioenteric (BE) anastomosis. We sought to determine the rates and risks of LDT-related complications in this population. **METHODS:** A retrospective review of clinicopathologic data of patients with resected PNETs

from 2000-2021 who developed metachronous hepatic metastasis were collected from a single institution, prospectively collected database. Outcomes after LDT were determined and compared between patients having undergone PD vs distal pancreatectomy (DP). Patients with synchronous pancreatectomy and LDT were excluded (N=25). **RESULTS:** Of 463 resected PNET patients (154 PD; 309 DP), 18 PD (12%) and 35 DP (11%) patients subsequently developed hepatic metastases and underwent LDT. In the PD group, 8 patients underwent major hepatectomies, 12 minor hepatectomies, 1 ablation, 1 chemoembolization, and 1 peptide receptor radionuclide therapy (PRRT). Post-LDT complications included: 4 hepatic abscesses (22%), 1 BE anastomotic stricture (6%), and 1 left hepatic duct stricture (6%). In the DP group, 19 patients underwent major hepatectomies, 17 minor hepatectomies, 10 ablations (5 in IR, 4 in OR, 1 both), 6 PRRT, and 2 bland embolizations. In this group, one hepatic abscess (3%) was observed following partial hepatectomy. Hepatic abscess occurred more frequently post-PD than DP following LDT (p=0.04); there was no difference between the number of hepatectomies following DP (94%) vs PD (91%; p=0.9). Time from last LDT to hepatic abscess ranged from 1 week to 5 years following LDT. No deaths were associated with post-LDT complications. **CONCLUSIONS:** BE anastomosis is associated with a significantly higher risk for post-LDT hepatic abscess, compared to LDT after DP. Careful consideration is necessary when planning intervention for hepatic metastasis following PD for PNETs. Further research is needed to determine the optimal perioprocedural antimicrobial approach and to evaluate the quality of life and management impact of post LDT hepatic abscesses.

P341. What happens next? Follow up of incidental adrenal masses

Lauren Kelz[1]; Jesse Passman, MD[2]; Lily Owei, MD[3]; Sara Ginzberg, MD, MSHP[4]; Elias Mimouni, BA[5]; Matthew Nazarian, MD[6]; Hanna M Zafar, MD[7]; Lisa P Jones, MD[8]; Tessa Cook, MD[9]; Heather Wachtel, MD[10]

[1]University of Pennsylanvia, Philadelphia, PA, US; [2]University of Pennsylvania, Philadelphia, PA, US; [3]University of Pennsylvania, Philadelphia, PA, US; [4]University of Pennsylvania, Philadelphia, PA, US; [5]University of Pennsylvania, Philadelphia, PA, US; [6]University of Pennsylvania, Philadelphia, PA, US; [7]University of Pennsylvania, Philadelphia, PA, US; [8]University of Pennsylvania, Philadelphia, PA, US; [9]University of Pennsylvania, Philadelphia, PA, US; [10]University of Pennsylvania, Philadelphia, PA, US

INTRODUCTION: Incidental adrenal nodules are commonly detected on CT and MRI. Historical rates of guideline-concordant evaluation are low. We aimed to assess rates of evaluation and follow-up of these nodules at our institution and to identify potential areas for improvement. **METHODS:** This retrospective cohort study included all patients with adrenal nodules on index CT or MRI performed for non-adrenal indications at our quaternary-care health system (2016-2020). Patients with a known adrenal nodule were excluded (n=7). Patient demographic and clinical data were abstracted from the electronic health record, and unweighted Elixhauser score was derived. The primary outcome was the receipt of follow-up testing: imaging (i.e. cross-sectional CT or MRI imaging performed ≤2 years after the index study) or biochemical evaluation (i.e. androgen, catecholamine/metanephrine, glucocorticoid, or mineralocorticoid testing). Logistic regression was used to assess the association between patient demographic and clinical characteristics and primary outcomes. **RESULTS:** Of 2756 patients included, the median age was 68.0±18 years. The median Elixhauser score was 8.0 (IQR=8.0). Index scans were primarily performed in the emergency department (ED) (39%); inpatient (23%) and outpatient (37%) settings. Among patients who received follow-up (1454/2756, 52%) most received follow-up imaging (1289/1454, 89%) and less than a third received biochemical testing (457/1454, 31%). Those with follow up were significantly younger (68 vs. 69 yo, p=0.004), had higher median Elixhauser comorbidity scores (10 vs 7, p<0.001), were less likely to be identified on CT (84% vs. 90%, and were least likely to be imaged in the ED setting (33% vs 47%, p<0.001). Patients with a primary care physician (PCP) affiliated with the health system were less likely to have additional imaging (83% vs. 91%, p<0.001) and more likely to complete biochemical evaluation testing (42% vs. 27%, (Table 1). On multivariable logistic regression, younger age (OR: 4.504, higher Elixhauser score (OR: 1.076, receipt of index MRI compared to CT (OR: 1.583, outpatient imaging compared to ED or inpatient (OR: 2.196, non-benign categorization of the nodule (OR: 1.515, p=0.001), and in-system PCP (OR: 1.802, p<0.001) were all significantly associated with follow-up. **CONCLUSIONS:** Rates of biochemical evaluation are lowest in patients who undergo imaging in the ED. Improving follow-up of incidental adrenal masses identified during ED visits represents an important opportunity to optimize patient care.

Table 1. Biochemical and imaging evaluation of patients with incidental adrenal masses, by primary care physician (PCP) affiliation.

	Total Cohort (n=1454)	Patients with Penn PCP (n=459)	Patients without Penn PCP (n=995)	P-value
Imaging evaluation (%)	1,289 (89.0%)	383 (83.0%)	906 (91.0%)	<0.001
Biochemical evaluation (%)				
Any	457 (31.0%)	192 (42.0%)	265 (27.0%)	<0.001
Androgens	75	41	34	0.015
Catecholamines/ Metanephrines	196	97	99	0.005
Glucocorticoids	358	145	213	0.200
Mineralocorticoids	216	101	115	0.052

P342. A window-of-opportunity trial using neoadjuvant hepatic artery chemotherapy for patients with localized pancreas cancer: Interim safety, feasibility, and oncologic outcomes

Ethan S Agritelley[1]; Elishama N Kanu, MD[2]; Jiayin Bao[3]; Ashley A Fletcher[4]; Julia L Button, MD[5]; Holly Skinner[6]; Adi Molvin[7]; Stacy Murray[8]; Charles Y Kim, MD[9]; Brendan Cline, MD[10]; Eric Mastria, MD, PhD[11]; David Johnson, MD[12]; Nicholas C DeVito, MD[13]; Gerard C Blobe, MD[14]; James L Abbruzzese, MD[15]; Erika J Crosby, PhD[16]; Allison N Martin, MD, MPH[17]; Sabino Zani, MD[18]; Niharika B Mettu, MD, PhD[19]; Peter J Allen, MD[20]; Daniel P Nussbaum, MD[21]

[1]Duke University School of Medicine, Durham, NC, US; [2]Duke University Medical Center, Durham, NC, US; [3]Duke University Medical Center, Durham, NC, US; [4]Duke University Medical Center, Durham, NC, US; [5]Duke University Medical Center, Durham, NC, US; [6]Duke University Medical Center, Durham, NC, US; [7]Duke University Medical Center, Durham, NC, US; [8]Duke University Medical Center, Durham, NC, US; [9]Duke University Medical Center, Durham, NC, US; [10]Duke University Medical Center, Durham, NC, US; [11]Duke University Medical Center, Durham, NC, US; [12]Duke University Medical Center, Durham, NC, US; [13]Duke University Medical Center, Durham, NC, US; [14]Duke University Medical Center, Durham, NC, US; [15]Duke University Medical Center, Durham, NC, US; [16]Duke University Medical Center, Durham, NC, US; [17]Duke University Medical Center, Durham, NC, US; [18]Duke University Medical Center, Durham, NC, US; [19]Duke University Medical Center, Durham, NC, US; [20]Duke University Medical Center, Durham, NC, US; [21]Duke University Medical Center, Durham, NC, US

INTRODUCTION: Among patients who undergo curative-intent therapy for pancreatic ductal adenocarcinoma (PDAC), actual 10-year survival is approximately 5%. The liver is the most common site of recurrent disease and is associated with the worst survival outcomes. Randomized trials in patients with localized colorectal cancer have shown the addition of single-dose, neoadjuvant hepatic artery (HA) chemotherapy via catheter-based interventional radiology techniques improve liver metastasis-free and overall survival. Because PDAC and colorectal cancer have similar recurrence patterns and are treated with similar systemic therapy, we hypothesized this strategy would be safe and feasible in patients with PDAC and might improve recurrence rates and overall survival. **METHODS:** This is a prospective, non-randomized window-of-opportunity trial testing single-dose neoadjuvant HA chemotherapy in patients with resectable or borderline resectable PDAC. Target enrollment is 20 patients treated in two arms: 1) upfront surgery followed by six months of adjuvant mFOLFIRINOX, or 2) three months of neoadjuvant mFOLFIRINOX followed by surgery and completion of therapy postoperatively. In both arms, patients undergo diagnostic laparoscopy and percutaneous delivery of the experimental HA therapy (floxuridine 325 mg/m2 and oxaliplatin 37.5 mg/m2) one week before surgery. Patients then undergo resection of their primary tumor, followed by short-term follow-up, where safety evaluations are performed for 30 days. Patients then enter long-term follow-up, where efficacy will be assessed every three months for up to three years. The primary endpoint is safety and feasibility. Secondary endpoints include three-year disease-free, liver metastasis-free, and overall survival. This trial also involves several correlative scientific aims focused on the mechanisms underlying hepatic metastases. Funding is provided by the Lustgarten Foundation for Pancreatic Research. **RESULTS:** To date, sixteen patients have been screened and eleven enrolled: six in the neoadjuvant therapy arm and five in the upfront resection arm. Nine patients have completed the treatment and short-term follow-up periods. Mean age was 64±9 years and 64% were female. Mean CA 19-9 prior to resection was 46.6±45 U/mL. Conventional hepatic artery anatomy was present in 45%

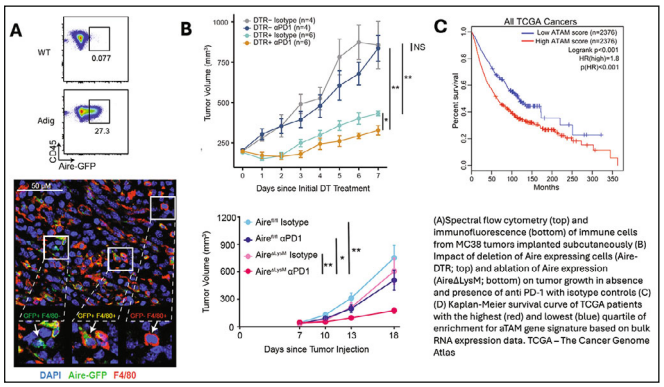
of patients. HA chemotherapy was delivered through the proper hepatic artery in 64% of patients, and via the left and right hepatic arteries in 36%. Concomitant ligation or embolization of accessory hepatic arteries was required in 45%. Pathologic assessment of resected specimens demonstrated a mean tumor size of 2.1±1.1 cm, lymph node metastases in 67%, perineural invasion in 89%, and lymphovascular invasion in 56%; three patients had a microscopically positive resection margin. Four of the eleven patients experienced adverse events, including one grade 1 event, two grade 2 events, three grade 3 events, and one grade 4 event. However, none were attributed to the experimental therapy. At a medium follow up of 6.5 months, two patients have evidence of recurrent disease, though only one patient has disease in the liver. **CONCLUSIONS:** At this interim analysis, single-dose neoadjuvant HA chemotherapy appears to be safe and feasible in patients undergoing resection of localized pancreatic cancer. We anticipate enrollment to be completed by March 2025. Continued long-term follow-up will be required to resolve survival outcomes and correlative endpoints.

P343. Aire-Expressing Tumor-Associated Macrophages Promote Cancer Immune Evasion

Han Yin[1]; Matthew Arvedson[2]; Sophia Guldberg[3]; Alexander Gupta, MD[4]; Simon Chu, MD[5]; Sophia Hernandez, MD[6]; Ajay Maker, MD[7]; Matthew Spitzer, PhD[8]; James Gardner, MD, PhD[9]

[1]University of California, San Francisco, San Francisco, CA, US; [2]University of California, San Francisco, San Francisco, CA, US; [3]University of California, San Francisco, San Francisco, CA, US; [4]University of California, San Francisco, San Francisco, CA, US; [5]University of California, San Francisco, San Francisco, CA, US; [6]University of California, San Francisco, San Francisco, CA, US; [7]University of California San Francisco, San Francisco, CA, US; [8]University of California, San Francisco, San Francisco, CA, US; [9]University of California, San Francisco, San Francisco, CA, US

INTRODUCTION: Peripheral immune populations expressing the Autoimmune Regulator (Aire) gene have been suggested to play critical roles in immune self-education, but their roles have not been defined in the tumor microenvironment (TME). Here we elucidate the role of Aire-expressing immune populations in immunosuppressive programs that promote tumor tolerance to uncover potential new avenues for therapeutic targeting. **METHODS:** To find Aire expressing cells in the TME, Aire-GFP reporter mice were implanted with tumors from multiple cancer cell lines (MC38, B16, Hep53.4). The resulting GFP+ cells were extensively phenotyped using spectral flow cytometry, immunofluorescence, CyTof and scRNA-seq. Mice without Aire-expressing cells or cell-type specific loss of Aire were used to determine the role of Aire-expressing cells in promoting tumor growth alone and in conjuction with immune checkpoint inhibition therapy. Publicly available human cancer transcriptional and outcome data was analyzed to identify and assess analogous Aire expressing immune populations in humans. **RESULTS:** We demonstrate the presence of Aire-expressing macrophages (aTAMs) across multiple mouse tumor models (A). These aTAMs display a unique transcriptional and metabolic profile characterized by increased immunosuppressive and proliferative features. The Aire gene is central to the formation of these aTAMs, as Aire-deficient mice exhibit a decrease in the aTAM population and in the gene signature that characterizes this cell population**.** Ablation of aTAMs (LysM-Cre x LSL-Aire-DTR) improves tumor control across multiple immunotherapy-resistant tumor models in a CD8 T cell-dependent manner resulting in increased CD8 T cell activation and inflammatory remodeling of the myeloid compartment. Notably, both macrophage-specific loss of Aire (LysM-Cre x Airefl/fl) or aTAM ablation (Aire-DTR) synergizes with anti-PD-1 to improve anti-tumor immunity (B) demonstrating a previously undiscovered role of extrathymic Aire. Finally, cells transcriptionally similar to aTAMs can be found in human scRNA-seq tumor datasets across multiple tumor types and the aTAM gene signature is associated with poor prognosis(C). **CONCLUSIONS:** Our data identify a novel macrophage population and demonstrate that extrathymic Aire in this phenotypically and functionally distinct population plays a critical role in inhibiting anti-tumor immunity.



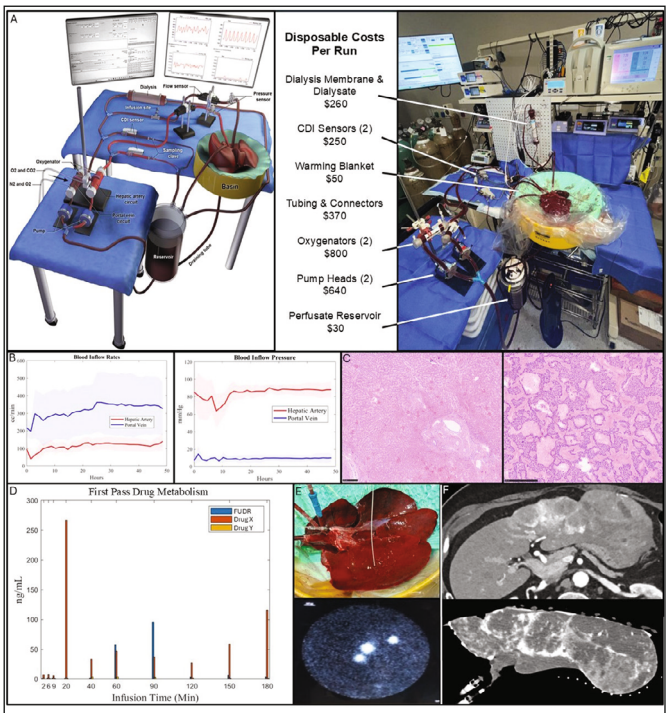
P344. An open-source normothermic perfusion system for the research scientist

Lindsay R Friedman[1]; Hannah Stepp[2]; Kenneth Luberice[3]; Jacob Lambdin[4]; Allen Luna[5]; Stephanie Lux[6]; Alyssa Eade[7]; Carolina Larrain[8]; Ashley Rainey[9]; Alexander Rossi[10]; Michael Wach[11]; Samantha Ruff[12]; Jeremy L. Davis, MD[13]; Andrew M Blakely[14]; David Kleiner[15]; Taylor Noel[16]; Randy Pursely[17]; Tom Pohida[18]; John Kakareka[19]; Jonathan M Hernandez[20]

[1]National Institutes of Health, National Cancer Institute, Surgical Oncology Program, Bethesda, MD, US; [2]National Institutes of Health, Bethesda, MD, US; [3]National Institutes of Health, Bethesda, MD, US; [4]National Institutes of Health, Bethesda, MD, US; [5]National Institutes of Health, Bethesda, MD, US; [6]National Institutes of Health, Bethesda, MD, US; [7]National Institutes of Health, Bethesda, MD, US; [8]National Institutes of Health, Bethesda, MD, US; [9]National Institutes of Health, Bethesda, MD, US; [10]National Institutes of Health, Bethesda, MD, US; [11]National Institutes of Health, Bethesda, MD, US; [12]National Institutes of Health, Bethesda, MD, US; [13]National Cancer Institute, Bethesda, MD, US; [14]National Institutes of Health, Bethesda, MD, US; [15]National Institutes of Health, Bethesda, MD, US; [16]National Institutes of Health, Bethesda, MD, US; [17]National Institutes of Health, Bethesda, MD, US; [18]National Institutes of Health, Bethesda, MD, US; [19]National Institutes of Health, Bethesda, MD, US; [20]National Institutes of Health, Bethesda, MD, US

INTRODUCTION: The integration of organ perfusion machines prior to transplantation has improved outcomes for recipients while revealing novel avenues of investigation for translational medicine. However, commercially available machines present a significant upfront cost investment and prohibitive per- use cost to the research scientist. **METHODS:** We constructed a cost-effective modular perfusion machine from readily sourced parts (Fig). Circuit creation begins with a cell saver reservoir, from which perfusate is pumped through parallel circuits using magnetic centrifugal pumps. Oxygenators are integrated immediately following pumps. Side circuits allow for hemodialysis and real-time monitoring of biochemical values. The organ is housed in a cushioned polyethylene drum funnel with an oscillating diaphragm for pressure offloading. Normothermia is ensured by heated water jackets. Organ inflow is monitored by in-line pressure and flow sensors. Medications to support organ function, antibiotics, and anticoagulation are infused continuously. Hardware components are controlled by Python code augmented by a custom user interface. **RESULTS:** 21 blood-only and 35 porcine liver perfusions were performed during system optimization. 14 tumor-bearing hepatic segments were perfused during the validation and application phases. Mean perfusion duration for human liver segments was 72 hours. Mean hepatic arterial pressure was 84 ± 11 mmHg and mean portal venous pressure was 9 ± 4 mmHg, with flows of 113 ± 66 ml/min and 317 ± 302 ml/min, respectively. Mean SO_2 in the hepatic artery, portal vein, and hepatic vein was 98 ± 3%, 92 ± 7%, and 86 ± 9%, respectively. Mean pH measurement was 7.3 ± 0.09. Mean bile synthesis rate was 1.4 mL/hour. Histologic analysis demonstrated preservation of normal hepatic parenchyma and tumor microenvironment after perfusion (Fig). To demonstrate the translational applicability, we conducted a series of experiments (Fig). To help identify new agents for hepatic artery infusion therapy, we simulated in vivo pump conditions and compared timed drug concentrations in the artery and vena cava. Next, we injected fluorescently labeled lymphocytes (simulating cell therapy) and used a probe detector to evaluate cell recruitment over time. Finally, we modified the system for transport and performed a contrast-enhanced CT scan of the ex-vivo liver for patho-radiomic evaluation. **CONCLUSIONS:** The results presented serve as a blueprint that can be modified, adapted, and repurposed in an open-source

manner to fit any number of experimental needs and to foster collaboration, creative discovery, and innovative research.



A. 3D Schematic of hepatic perfusion circuit (left) and with per-use costs demonstrated on the system during perfusion experiment (right). **B.** Mean perfusion portal venous and arterial inflow rates (left) and pressures (right). **C.** Post-perfusion H&E normal liver parenchyma (left) and neuroendocrine tumor (right). **D.** Analysis of pre- and post-hepatic drug concentrations of FUDR, and Experimental Drug X and Y. **E.** Probe detector (left) and immunofluorescent labeled lymphocytes circulating within specimen (right) **F.** Post-experiment contrast CT of ex-vivo partial hepatectomy specimen (bottom) compared to preoperative scan (top)

Figure 1. The Open-Source Perfusion System.

P345. Assessing response and outcomes to modern multiagent neoadjuvant chemotherapy for pancreatic ductal adenocarcinoma

Paul H McClelland, MD[1]; Megan A Satyadi, MD[2]; Ryan P Johnson, MD[3]; Rosetta Jacob, MPH[4]; Jianmin Pan, PhD[5]; Jayesh Rai, MS[6]; Shesh Rai, PhD[7]; Gregory C Wilson, MD[8]; Sameer H Patel, MD[9]; Syed A Ahmad, MD[10]
[1]University of Cincinnati College of Medicine, Cincinnati, OH, US; [2]University of Cincinnati College of Medicine, Cincinnati, OH, US; [3]University of Cincinnati College of Medicine, Cincinnati, OH, US; [4]University of Cincinnati College of Medicine, 513-558-4748, OH, US; [5]Biostatistics and Informatics Shared Resource, University of Cincinnati Cancer Center, Cincinnati, OH, US; [6]Biostatistics and Informatics Shared Resource, University of Cincinnati Cancer Center, Cincinnati, OH, US; [7]Biostatistics and Informatics Shared Resource, University of Cincinnati Cancer Center, Cincinnati, OH, US; [8]University of Cincinnati College of Medicine, Cincinnati, OH, US; [9]University of Cincinnati College of Medicine, Cincinnati, OH, US; [10]University of Cincinnati College of Medicine, Cincinnati, OH, US

INTRODUCTION: Neoadjuvant chemotherapy (NAC) is utilized for resectable and borderline-resectable pancreatic ductal adenocarcinoma (PDAC). Imaging, biochemical, and histopathological response rates are not well-documented and require clarification for modern multiagent chemotherapy. **METHODS:** We queried our prospectively managed, single-center database for patients with PDAC undergoing either FOLFIRINOX- or gemcitabine-based NAC (2008-2024). Response rates were based on radiologic (RECIST v1.1, NCCN resectability criteria), biochemical (≥ 45% CA 19-9 decrease), and histopathologic criteria (CAP score 0-2). Regression models were used to determine factors affecting progression-free survival (PFS) or overall survival (OS). **RESULTS:** Among 183 included patients, the median age was 66 [Q1-Q3 60-73] years, with male (53%) and White/Caucasian (86%) preponderance. Patients received either FOLFIRINOX- (51%) or gemcitabine-based therapy (49%) over a median duration of 4 [3-5] months, and 64% of patients received radiation. Overall imaging response after NAC was 27% (23% PR, 4% CR), with 17% downstaged by resectability criteria. Similarly, biochemical response to NAC was 82%, with 35% of patients achieving optimal ≥ 85% CA 19-9 reduction. Following NAC, 71% of patients underwent resection, whereas 7% had local progression on imaging; of the latter, 73% still had resectable disease. Among resected patients, histopathologic response was seen in 76%; for those with stable disease on imaging (60%), 56% had partial response (CAP 2), and 14% had complete or near-complete response (CAP 0-1). Patients with imaging response (PR + CR) had no significant difference in PFS or OS (median OS 30 vs. 35 months, p = 0.41); likewise, imaging response was not predictive of survival in regression models. By contrast, optimal biochemical (HR 0.58, 95% CI 0.33-0.99; = 0.047) and histopathological response (HR 0.55, 95% CI 0.35-0.89; $p = 0.014$)were both predictive of increased OS, whereas pathologic lymph node positivity was independently predictive of worse PFS (aHR 2.38, 95% CI 1.47-3.85; p < 0.001)andOS (aHR 1.93, 95% CI 1.02-3.65; = 0.044). **CONCLUSIONS:** These results establish a baseline for PDAC response markers in the era of modern systemic therapy. Our results demonstrate: (1) response and downstaging can occur with NAC; (2) radiologic response does not correlate with histopathologic response and should not preclude surgical decision-making; (3) imaging response does not necessarily predict survival; and (4) NAC is rarely associated with a lost opportunity to operate.

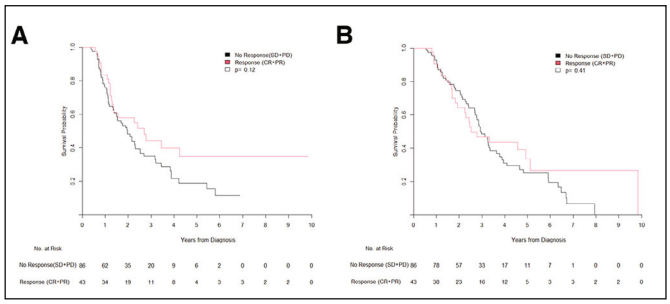


Figure 1. (A) Progression-free survival and (B) overall survival of patients undergoing curative-intent resection for pancreatic ductal adenocarcinoma (PDAC), stratified by objective imaging response after neoadjuvant therapy.

P346. Association of Patient Travel with Receipt of Chemotherapy and Clinical Outcomes for Patients Undergoing Pancreatic Surgery at High-Volume Hospitals

Alexa Hughes, MD, MEd[1]; Kristen N Kaiser[2]; Brian Ruedinger, PhD[3]; Anthony Yang, MD, MS[4]; Anita A Turk, MD[5]; Thomas K Maatman, MD[6]; Michael G House, MD[7]; Karl Y Bilimoria, MD, MS[8]; Ryan J Ellis, MD, MS[9]
[1]Indiana University, Indianapolis, IN, US; [2]Indiana University, Indianapolis, IN, US; [3]Surgical Outcomes and Quality Improvement Center (SOQIC), Department of Surgery, Indiana University, Indianapolis, IN, US; [4]Surgical Outcomes and Quality Improvement Center (SOQIC), Department of Surgery, Indiana School of M, Indianapolis, IN, IN, US; [5]Division of Hematology/Oncology, Department of Medicine, Indiana University, indianapolis, IN, US; [6]Division of Surgical Oncology, Department of Surgery, Indiana University, Indianapolis, IN, US; [7]Division of Surgical Oncology, Department of Surgery, Indiana University, Indianapolis, IN, US; [8]Surgical Outcomes and Quality Improvement Center (SOQIC), Department of Surgery, Indiana University, Indianapolis, IN, US; [9]Surgical Outcomes and Quality Improvement Center (SOQIC), Department of Surgery, Indiana University, Indianapolis, IN, US

INTRODUCTION: Surgical outcomes for patients undergoing resection for pancreatic ductal adenocarcinoma (PDAC) are known to be better at high-volume hospitals (HVHs). However, the relationship between travel distance and receipt of guideline-concordant adjuvant therapy is poorly characterized for those patients traveling to HVHs for care. The objectives of this study were to (1) evaluate associations between travel distance and receipt of adjuvant chemotherapy in patients undergoing upfront resection for PDAC at HVHs and (2) characterize the interplay between travel distance, adjuvant chemotherapy, and survival of patients treated at HVHs. **METHODS:** Patients who underwent upfront PDAC resection at a HVH (≥20 cases/year) between 2007-2021 were identified in the National Cancer Database. Travel distance was calculated based on the linear distance to the reporting facility as either the upper tertile (>45 miles) or the lower two tertiles (≤45 miles). Factors associated with adjuvant chemotherapy were assessed using multivariate logistic regression. Survival was assessed using Kaplan Meier analyses and Cox proportional hazard models. Cox models were performed both with and without adjustment for receipt of

adjuvant chemotherapy. **RESULTS:** Overall, 17,807 patients from 97 HVHs were included. Most patients had stage II disease (77.2%) and tumors in the head of the pancreas (71.5%). The overall rate of adjuvant chemotherapy was 57.3%, which increased from 54.7% in 2007 to 71.6% in 2021 (p<0.001). In analyses adjusted for patient, tumor, and sociodemographic factors, patients traveling >45 miles were less likely to receive adjuvant chemotherapy (48.9% vs 61.5%; aOR 0.46, 95%CI 0.34-0.58; P<0.001). Median overall survival (OS) was significantly shorter in patients traveling >45 miles (23.9 vs 26.6 months if ≤45 miles, P<0.001; Figure 1). Patients traveling >45 miles also had worse 5-year OS (23%) compared to those traveling ≤45 miles (27%, P<0.001). In adjusted survival models that did not account for receipt of adjuvant chemotherapy, traveling >45 miles was associated with worse OS (HR 1.08, 95% CI 1.01-1.16; P=0.03). In models adjusting for receipt of adjuvant chemotherapy, distance traveled was no longer associated with survival (HR 1.05, 95% CI 0.97-1.12; P=0.22). **CONCLUSIONS:** Patients undergoing resection for PDAC at a HVH were less likely to receive adjuvant chemotherapy if they traveled further for care, with this disparity potentially driving the observed differential survival based on travel distance. As surgical care becomes increasingly centralized to HVHs, multidisciplinary systems both within and across health systems may improve multimodal care delivery and outcomes for patients traveling for complex surgical care.

P347. Automated Radiomics Model for Preoperative Pancreatic Neuroendocrine Tumor Grade Prediction

Pratik Chandra, MD[1]; Naaz Nasar, MD[2]; Hadi Ghahremannezhad, PhD[3]; Kevin Soares, MD[4]; Vinod Balachandran, MD[5]; Jeffrey Drebin, MD PhD[6]; Michael D'Angelica, MD[7]; T. Peter Kingham, MD[8]; William R Jarnagin, MD[9]; Jayasree Chakraborty, PhD[10]; Alice C Wei, MD MSc[11]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US; [11]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: The clinical behavior of pancreatic neuroendocrine tumors (PNETs) is primarily determined by tumor grade, which is often available only after resection or a core biopsy. By contrast, imaging analysis with radiomics may reveal biological data, such as tumor grade, without tissue sampling. This study aimed to create an automatic pipeline from segmentation to radiomics-signature building to preoperatively predict tumor grade. **METHODS:** Patients who underwent resection between 2003-2021 with adequate preoperative arterial phase CT scans were divided into training and validation cohorts. In the training cohort, the pancreas and tumor regions were manually segmented and used to train an auto-segmentation model, which was used for the validation cohort. A total of 255 radiomics features were extracted from the tumor region. Correlated features were removed, and the minimum redundancy maximum relevance (mRMR) method was used to select the final feature set. These features were used to train a Support Vector Machine (SVM)-based classifier through the training cohort to predict grade, dichotomized into grade I versus II/III. The radiomic-based prediction model was then evaluated in the automatically segmented validation cohort. **RESULTS:** 186 patients were identified and divided into training (n = 140) and validation (n = 46) cohorts. Median age was 57 (27, 85) and 52% were male. 113 (62%) and 70 (38%) patients were grades I and II/III, respectively. Median tumor size was 24 mm (6, 200), and 43 (26%) patients had positive nodal disease. The auto-segmentation model was able to accurately segment the tumor region in 33 (72%) patients of the validation cohort. In the training cohort (n = 140), the radiomics-signature produced an area under the curve (AUC) of 0.87 (0.81, 0.93). Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 0.94 (0.9, 0.98), 0.74 (0.66, 0.81), 0.72 (0.65, 0.80), and 0.97 (0.94, 1.00) respectively. In the auto-segmented validation cohort (n = 33), the radiomics model produced an AUC of 0.75 (0.61, 0.90). Sensitivity, PPV, and NPV were 0.88 (0.77, 0.99), 0.62 (0.46, 0.79), 0.71 (0.56, 0.87), and 0.83 (0.71, 0.96), respectively. **CONCLUSIONS:** The proposed auto-segmentation model accurately identified tumor regions within the pancreas, and the radiomic signature correlated closely with tumor grade. This automatic pipeline bypasses manual segmentation and could help incorporate a radiomics signature into preoperative clinical decision-making for PNETs.

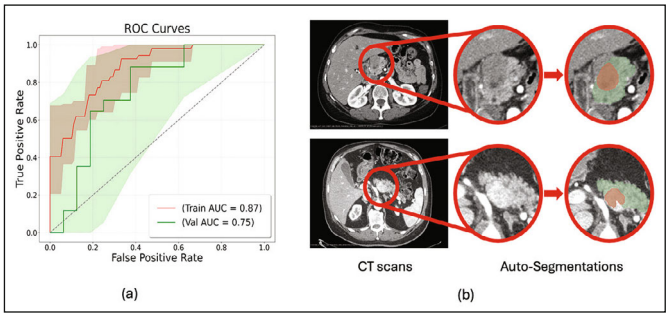


Figure. {a) Receiver Operating Characteristic Curve of the SVM Model. {b) Sample AutoSegmentations of Pancreas {green) and Tumor {red).

P348. Challenging Paradigms: Utilizing Pancreatic Cancer Organoids To Advance Personalized Medicine

Nicholas Jette[1]

[1]University of Saskatchewan, Saskatoon, SK, CA

INTRODUCTION: When asked if he could cure cancer, the renowned surgeon-scientist Judah Folkman famously responded, "Yes, in mice." For decades, cancer research has relied heavily on 2D cell cultures and murine xenograft models, which, while informative, often fail to predict how human tumors respond to treatment due to their unnatural cell interactions and tumor microenvironments. Recently, 3D patient-derived tumor models known as "organoids" have emerged. These organoids, which closely replicate the architecture of the original tumor, represent a promising model for studying human cancer. The application of organoids to pancreatic cancer holds potential for advancing cancer therapy and improving survival outcomes. **METHODS:** Pancreatic organoids were derived from primary and metastatic tumor samples obtained from patients. The average time from sample collection to organoid testing was four weeks. Gene essentiality analysis was processed using scores from DepMap, shRNA/CRISPR screens were utilized and genes with significant (p<0.01) differences with a Mann-Whitney U test were prioritized for validation studies. **RESULTS:** Of 30 patients who provided surgical samples, 16 organoids were successfully developed. These organoids were tested against a library of chemotherapy and targeted therapies. Drug sensitivities and resistances were distributed to medical oncologists to guide treatment decisions. To account for resistance mechanisms that arise during ongoing in-vivo treatment, a subset of organoids were treated with the same chemotherapeutic regimen as patients. The updated resistance profiles were then used to inform second- and third-line therapies. Furthermore, using the organoid system and synthetic lethal screens, we identify important genes related to telomerase activity and resultant replicate immortality. **CONCLUSIONS:** The application of organoids to the treatment of pancreatic cancer offers immense opportunity to impact care and patient survival. Here we show the potential impact patient derived organoid tissue could have to guide treatment decisions in 2nd and third line therapies and identify potential druggable targets utilizing synthetic lethal screens.

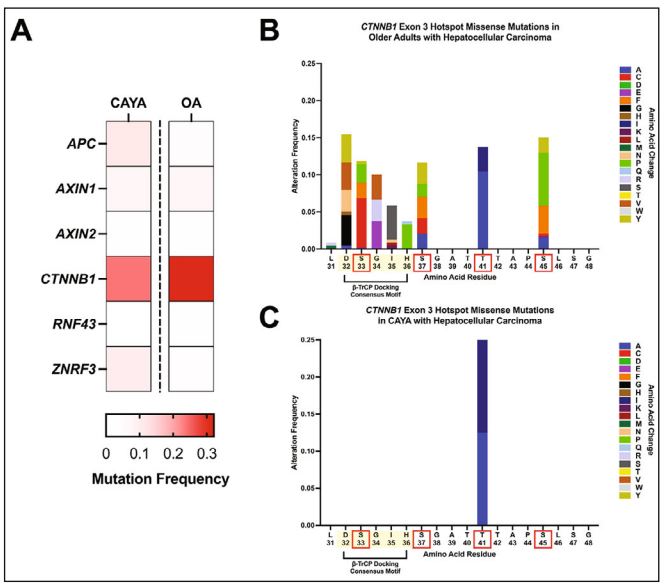
P349. CTNNB1 exon 3 hotspot mutations in early-onset hepatocellular carcinoma

Andrew M Fleming, MD[1]; Jenna Davis, MD, MPH[2]; Daniel B Gehle, MD[3]; Harold N Lovvorn, MD[4]; Evan S Glazer, MD, PhD[5]; Max R Langham, MD[6]; David Shibata, MD[7]; Chandrasekhar Padmanabhan, MD[8]; Andrew J Murphy, MD[9]

[1]The University of Tennessee Health Science Center/St. Jude Children's Research Hospital, Memphis, TN, US; [2]The University of Tennessee Health Science Center, Memphis, TN, US; [3]The University of Tennessee Health Science Center/St. Jude Children's Research Hospital, Memphis, TN, US; [4]Vanderbilt University Medical Center, Nashville, TN, US; [5]The University of Tennessee Health Science Center/St. Jude Children's Research Hospital, Memphis, TN, US; [6]The University of Tennessee Health Science Center/St. Jude Children's Research Hospital, Memphis, TN, US; [7]The University of Tennessee Health Science Center/St. Jude Children's Research Hospital, Memphis, TN, US; [8]Vanderbilt University Medical Center, Nashville, TN, US; [9]The University of Tennessee Health Science Center/St. Jude Children's Research Hospital, Memphis, TN, US

INTRODUCTION: Hepatocellular carcinoma (HCC) frequently exhibits overactivation of WNT–β-catenin signaling. Children, adolescents, and young adults (CAYA) (NCI definition: age ≤ 39 years) with HCC demonstrate distinct

clinicopathologic features despite similar rates of *CTNNB1* alterations. The current analysis interrogated hallmark *CTNNB1* exon 3 hotspot mutations in CAYA and older adults with HCC using the largest publicly available cancer clinicogenomic dataset to assess for distinct mechanisms of β-catenin signaling dysregulation. **METHODS:** The American Association for Cancer Research (AACR) Project Genomics Evidence Neoplasia Information Exchange (GENIE) dataset "GENIE Cohort v16.0-public," released June 2024, was queried for HCC samples with complete sequencing data and known patient age via cBioPortal for Cancer Genomics. Sample-level genomic alterations in known regulators of WNT–β-catenin signaling were analyzed. Multiple hypothesis testing-corrected q-values <.01 denoted statistical significance. Individual frequencies of *CTNNB1* exon 3 hotspot mutations were quantified and visualized using annotated stacked bar charts. **RESULTS:** In total, 835 HCC samples met inclusion criteria. Of these, 55/831 were from patients age ≤ 39 years (6.6%), and 776/831 were age > 39 years (93.4%). Compared to older adults, CAYA with HCC were more often female sex (54.6% vs. 25.0%, q<.0001) and had lower median mutation counts (3.0 vs. 6.0, q=.01). Rates of *CTNNB1* mutations were similar between groups (23.6% vs. 32.1%, q=1.0), as were rates of other known regulators of WNT–β-catenin signaling, including *APC* (11.1% vs. 4.8%, *AXIN1* (7.7% vs. 7.8%, *AXIN2*(2.6% vs. 2.6%, *RNF43* (0.0% vs. 1.7%, and *ZNRF3* (10.0% vs. 4.2%, q=1.0) (Figure 1A). All *CTNNB1* mutations were somatic in both groups. Only older adult patients demonstrated hotspot mutations in the β-catenin destruction complex / β-TrCF binding site along *CTNNB1* exon 3 (121 / 240 *CTNNB1* mutations profiled, 50.4%) (Figure 1B, 1C). Similar rates of T41I (12.5% vs. 3.3%, q=1.0) and T41A (12.5% vs. 10.4%, q=1.0) missense mutations at GSK3B phosphorylation sites were identified between the groups (Figure 1B, 1C). **CONCLUSIONS:** Hallmark *CTNNB1* exon 3 hotspot mutations are notably absent in this large cohort of young patients with HCC, suggesting distinct mechanisms of β-catenin signaling dysregulation among CAYA and older adults. Further validation and transcriptomic analysis are warranted given the biological plausibility of these findings and potential relevance to investigational targeted therapies.



P350. Chromosome 9p deletions are associated with higher rates of R1 resection across GI cancers

Madeline M Silva, MD[1]; Candice Vieira, MD[2]; Sukeshi P Arora, MD[3]; Neil B Newman, MD[4]; Caitlin A McIntyre, MD[5]; Mio Kitano, MD, MPH[6]; Alexander A. Parikh, MD, MPH[7]; Chun-Liang Chen, PhD[8]; Colin M Court, MD, PhD[9]
[1]University of Texas Health San Antonio, San Antonio, TX, US; [2]University of Texas Health San Antonio, San Antonio, TX, US; [3]UT Health San Antonio, MD Anderson- Mays Cancer Center, San Antonio, TX, US; [4]University of Texas Health Science Center San Antonio, San Antonio, TX, US; [5]University of Texas Health San Antonio MD Anderson- Mays Cancer Center, San Antonio, TX, US; [6]University of Texas Health San Antonio, San Antonio, TX, US; [7]University of Texas Health San Antonio MD Anderson - Mays Cancer Center, San Antonio, TX, US; [8]University of Texas Health San Antonio, San Antonio, TX, US; [9]UT Health San Antonio MD Anderson- Mays Cancer Center, San Antonio, TX, US

INTRODUCTION: Determining adequate surgical margins in gastrointestinal (GI) cancers remains imprecise due to the limitations of frozen section accuracy and the infiltrative nature of certain tumors. Chromosome 9p deletions, particularly involving the CDKN2A gene, are implicated in the dysregulation of cell cycle and tumor progression across multiple cancer types. These alterations are associated with worse prognoses and more aggressive tumor characteristics in both renal and gastrointestinal (GI) cancers. We investigated if the more aggressive and infiltrative biology of chromosome 9p deletions was associated with rates of microscopic margin positivity (R1 resection) across GI cancers. **METHODS:** The Cancer Genome Atlas (TCGA) was used to identify GI cancer patients who underwent primary tumor resection and had genomic information from the primary tumor available for analysis. Chromosome 9p deletions were identified from the arm_level copy number variation dataset and correlated with residual microscopic disease (R0 vs R1 resection) at primary tumor resection. **RESULTS:** A total of 1417 patients with 5 different GI cancers had clinical and genomic data available: hepatocellular carcinoma (n = 362), cholangiocarcinoma (n = 42), pancreas (n = 171), gastric (n = 368), colorectal (n = 477). Microscopically positive resection (R1 resection) occurred in 102 (7.2%) patients. Chromosome 9p deletions were associated with R1 resections for all GI cancers ($\chi 2 = 21.25$, $p = 0.000004$). R1 resection rates were higher in patients with chromosome 9p deletions for all GI cancers individually with the exception of cholangiocarcinoma in which the rate of R0 and R1 resections was the same for patients with and without chromosome 9p deletions (Fig. 1). **CONCLUSIONS:** This exploratory study revealed that the rate of R1 positivity in gastrointestinal cancers was higher in patients with chromosome 9p deletion. This suggests that 9p deletion may be associated with a more infiltrative cancer subtype, potentially impacting surgical management. Patients with known chromosome 9p deletions could benefit from resections with wider margins to reduce the risk of residual disease. This study has implications for pursuing a more precision medicine approach to surgical resection margins.



Figure 1. Correlation of Chr9p deletion with RO vs R1 resection across GI cancers

P351. Comparison of prediction models for postoperative pancreatic fistula formation after pancreaticoduodenectomy

Pathik Aravind[1]; Leanne M Brown[2]; Wendy Feng[3]; Lauren M Raymond-King, MD[4]; Nicholas V Peters[5]; Sajid Khan, MD, FACS[6]; Kevin Billingsley[7]; Ronald A Salem[8]; John W Kunstman[9]
[1]Yale School of Medicine, New Haven, CT, US; [2]Yale School of Medicine, New Haven, CT, US; [3]Yale School of Medicine, New Haven, CT, US; [4]Yale School of Medicine, New Haven, CT, US; [5]Yale School of Medicine, New Haven, CT, US; [6]Yale University School of Medicine, New Haven, CT, US; [7]Yale School fo Medicine, New Haven, CT, US; [8]Yale School of Medicine, New Haven, CT, US; [9]Yale School of Medicine, New Haven, CT, US

INTRODUCTION: Pancreaticoduodenectomy (PD) is an effective approach to periampullary malignancy, but morbidity, driven by pancreatic fistula (PF) formation, hinders optimal perioperative and oncologic outcomes. Identification of PF risk can favorably inform care; approaches include the fistula risk score (FRS – derived during surgery) and surgical drain amylase (SDA) measurement. We have shown that serum C-reactive protein (CRP) strongly predicts real time PF risk and sought to assess the relative predictive ability of CRP, FRS, and

SDA both singly and in combination. **METHODS:** A prospectively maintained database of patients undergoing PD from 2016-2023 was queried. The primary outcome was occurrence of either PF as defined by international consensus (any grade) or organ/space abscess defined as postoperative drainage with positive cultures (PF/A). Clinically-relevant (grade B/C) PF or organ/space abscess (CR-PF/A) was assessed as a second primary outcome. We previously defined CRP ≥ 270 mg/dL during postoperative days (POD) 2-4 as being most predictive of PF/A; based on prior literature, SDA on POD 1 ≥ 5000 U/L (SDA-D1), SDA on POD 3 ≥ 600 U/L (SDA-D3), and calculated FRS of moderate/high risk (FRS ≥ 3) were assessed as comparators singly and in aggregate via logistic regression modelling. **RESULTS:** 401 patients were evaluated; the aggregate incidence of PF/A was 31.2% (n=125) and CR-PF/A was 20% (n=80). The individual incidence of biochemical leak (grade A PF), CR-PF, and abscess was 12% (n=48), 12.7% (n=51), and 12.7% (n=51). Table 1 displays the relative accuracy and predictive value for both PF/A and CR-PF/A outcomes for CRP ≥ 270, SDA-D1 ≥ 5000, SDA-D3 ≥ 600, and FRS ≥ 3. For both outcomes, CRP was the most predictive (PF/A OR = 3.72 p<0.01; CR-PF/A OR = 4.41, p<0.01) metric and was highly specific (PF/A - 81.2%, NPV = 76.9%; CR-PF/A - 100%, NPV = 80.5%). Conversely, SDA-D1 was least predictive (PF/A OR = 1.33, p=0.26; CR-PF/A OR = 1.77, p=0.07). As CRP, SDA-D3, FRS all demonstrated a significant correlation with PF/A and CR-PF/A, an aggregate prediction model was constructed which was highly specific for PF/A development (87.4%, NPV = 74.4%). **CONCLUSIONS:** Maximum CRP, SDA-D3, and FRS are all significantly associated with PF/A and CR-PF/A following PD, with CRP being most independently predictive. Early identification of patients at high risk can facilitate more timely PF/A intervention. Equally significant, the ability to recognize patients at negligible PF/A risk could enable earlier discharge and initiation of adjuvant systemic therapy, ideally improving both operative and oncologic outcomes.

Table 1. Comparison of prediction metrics for pancreatic fistula (all grades) + abscess (PF/A) and clinically-relevant pancreatic fistula (grade B/C) + abscess (CR-PF/A). OR, odds ratio; POD, postoperative day; PPV, positive predictive value; NPV, negative predictive value.

Prediction Models - PF/A	OR (p-value)	Sensitivity	Specificity	PPV	NPV
Maximum CRP, POD 2-4 ≥ 270	3.72 (<0.01)	46.4%	81.2%	52.7%	76.9%
Drain amylase, POD 1 ≥ 5000	1.33 (0.26)	28.6%	76.8%	32.8%	73.1%
Drain amylase, POD 3 ≥ 600	1.93 (0.02)	25.7%	84.8%	34.1%	78.9%
Fistula risk score ≥ 3	2.34 (<0.01)	79.2%	38%	57.9%	80.2%
Prediction Models - CR-PF/A	OR (p-value)	Sensitivity	Specificity	PPV	NPV
Maximum CRP, POD 2-4 ≥ 270	4.41 (<0.01)	53.8%	79.1%	39.1%	87.1%
Drain amylase, POD 1 ≥ 5000	1.77 (0.07)	81.3%	28.9%	22.2%	86.1%
Drain amylase, POD 3 ≥ 600	3.64 (<0.01)	91.3%	25.9%	23.5%	92.2%
Fistula risk score ≥ 3	2.23 (<0.01)	80%	23.7%	23.7%	87.8%

P352. Degree of Dedifferentiation of Hepatocellular Carcinoma is Not Associated with Decrease Expression of Sphingosine 1-Phosphate Receptor 2

Elizabeth Josephine Olecki, MD[1]; Rongrong Wu[2]; Takashi Ishikawa[3]; Kazuaki Takabe, MD, PhD[4]

[1]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [2]Tokyo Medical University, Tokyo, JP; [3]Tokyo Medical University, Tokyo, JP; [4]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US

INTRODUCTION: Sphingosine 1-phosphate receptor 2 (S1PR2), a S1P specific receptor, has previously been shown to play an essential role in lipid and glucose metabolism in hepatocytes by binding to bile acids. Given that S1PR2 signaling is involved in vital function of hepatocytes, we hypothesize that as hepatocellular carcinoma (HCC) cells dedifferentiate during malignant transformation, S1PR2 will be expressed at lower levels and therefore S1PR2 has potential to serve as marker of biologically less aggressive HCC in patients. Additionally, this study examines the relationship between S1PR2 and sphingosine kinase 1 (SphK1), a known promotor of malignant progression and metastasis in HCC. **METHODS:** Using The Cancer Genome Atlas (TCGA) Liver Hepatocellular Carcinoma cohort (TCGA_LIHC, n=358) the relationship between S1PR2 expression and HCC patient's clinico-pathological characteristics and survival outcomes were examined. The cytolytic activity score (CYT) was calculated using gene expression of S1PR2. Statistically significant for comparison analysis between groups utilized by Kruskal-Wallis and Mann-Whitney U test. Overall survival (OS) was determined using Kaplan-Meier method. **RESULTS:** Despite median S1PR2 expression being higher in HCC, there was no statistical difference in expression between HCC and normal liver tissue (p>0.05). When comparing S1PR2 expression and expression of SphK1 that is known to be related with extracellular S1P, there was a moderate association in HCC (r=0.41, p<0.01), whereas no correlation was seen with SphK2 that is related with intracellular S1P. There was no significant difference in S1PR2 expression by the cause of HCC, although median was the lowest in non-alcoholic fatty liver disease. Unexpectedly, S1PR2 expression showed correlation with HCC tumor grade (G1-4) that there was high expression in grade 4 (undifferentiated) HCC compared to grade 1 (well differentiated) (p=0.01). There was no difference in S1PR2 expression by the tumor size (T1-4), lymph node metastasis, or distant metastasis. Although there was no significant difference in S1PR2 expression by Stage (I-IV), the median of expression was highest in Stage IV tumor. There was no significant difference in disease-free, disease-specific, or overall survival (OS) by the expression of S1PR2. **CONCLUSIONS:** In the current study, S1PR2 expression did not show correlation with less aggressive HCC in patients. Given the correlation with SphK1 and not with SphK2 expression, future work is warranted to determine S1PR2 expression in HCC is related more with S1P production than bile acid signaling.

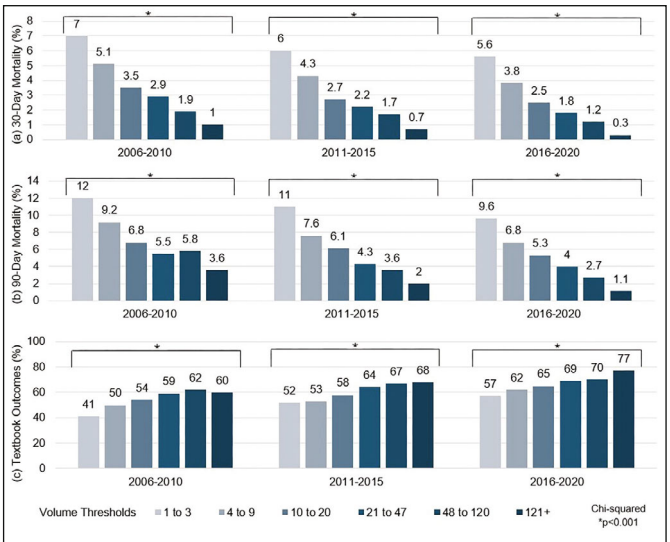
P353. Developing Reproducible Volume Thresholds for Pancreatectomy using Stratum Specific Likelihood Ratios

Kristen N Kaiser, MD[1]; Alexa J Hughes, MD, MEd[2]; Brian Ruedinger, PhD[3]; Jeanette W Chung, PhD[4]; Katie H Ross-Driscoll, PhD[5]; Karl Y Bilimoria, MD,MS[6]; Ryan J Ellis, MD,MS[7]

[1]Surgical Outcomes and Quality Improvement Center (SOQIC), Indiana University, Indianapolis, IN, US; [2]Surgical Outcomes and Quality Improvement Center (SOQIC), Indiana University, Indianapolis, IN, US; [3]Surgical Outcomes and Quality Improvement Center (SOQIC), Department of Surgery, Indiana University, Indianapolis, IN, US; [4]Surgical Outcomes and Quality Improvement Center (SOQIC), Indiana University, Indianapolis, IN, US; [5]Surgical Outcomes and Quality Improvement Center (SOQIC), Indiana University, Indianapolis, IN, US; [6]Surgical Outcomes and Quality Improvement Center (SOQIC), Department of Surgery, Indiana University, Indianapolis, IN, US; [7]Surgical Outcomes and Quality Improvement Center (SOQIC), Department of Surgery, Indiana University, Indianapolis, IN, US

INTRODUCTION: Despite associations between procedural volume and outcomes, empirically derived volume thresholds have been elusive, and most volume-based thresholds are based on expert consensus. Stratum specific likelihood ratios (SSLR) may yield reproducible, empiric volume thresholds. The objectives of this study were to (1) define hospital-level volume thresholds for pancreatectomy using SSLR, (2) determine outcome variation between volume strata, and (3) characterize temporal outcome changes by volume strata. **METHODS:** Patients undergoing pancreatectomy from 2004-2021 were identified using the National Cancer Database. Hospital volume was calculated as the average annual number of pancreatectomies. Volume strata were defined by sequentially collapsing overlapping confidence intervals for likelihood ratios based on facility-level 90-day postoperative mortality. Outcomes included 30- and 90-day mortality as well as textbook outcome (length of stay ≤14 days, negative margin, survival >90 days, no 30-day readmission) and were compared across volume strata by Chi-squared. The optimal volume threshold was identified by maximizing the area under the curve (AUC) of risk adjusted logistic regression models. Temporal threshold stability was assessed by stratified outcome analysis. **RESULTS:** Overall, 61,920 patients underwent pancreatectomy at 982 facilities with a 90-day mortality rate of 5.4%. SSLR analysis yielded six volume strata: ≤3, 4-9, 10-20, 21-47, 48-120, and ≥121. Mortality decreased across strata for 30-day mortality (≤3: 6.2%, 4-9: 3.8%, 10-20: 3.0%, 21-47: 2.1%, 48-120: 1.3%, and ≥121: 0.7%; p<0.001) and 90-day mortality (≤3: 11%, 4-9: 7.3%, 10-20: 6.1%, 21-47: 4.2%, 48-120: 3.3%, and ≥121: 2.3%;0.001). Textbook outcome also improved across each threshold (≤3: 50%, 4-9: 56%, 10-20: 59%, 21-47: 64%, 48-120: 66%, and ≥121: 69%;0.001). An optimal threshold of 21 procedures/year was identified by maximizing AUC in adjusted models (0.70, 95%CI 0.69-0.71). Temporal stratification into five-year periods (2006-2010, 2011-2015, 2016-2020) demonstrated persistent volume-outcome associations across volume strata (Figure 1; all p<0.001).

CONCLUSIONS: Use of SSLR can yield empirically derived, procedure-specific volume thresholds that are associated with multiple outcome measures and robust to temporal changes in procedural outcomes. Such reproducible strata may be superior to values derived by expert consensus or other methods for future quality reporting and policy development.



Variation in (a) 30-day mortality, (b) 90-day mortality, and (c) textbook outcome across SSLR-derived volume thresholds stratified by time. Volume thresholds are mean annual volume thresholds defined as number of procedures per year .

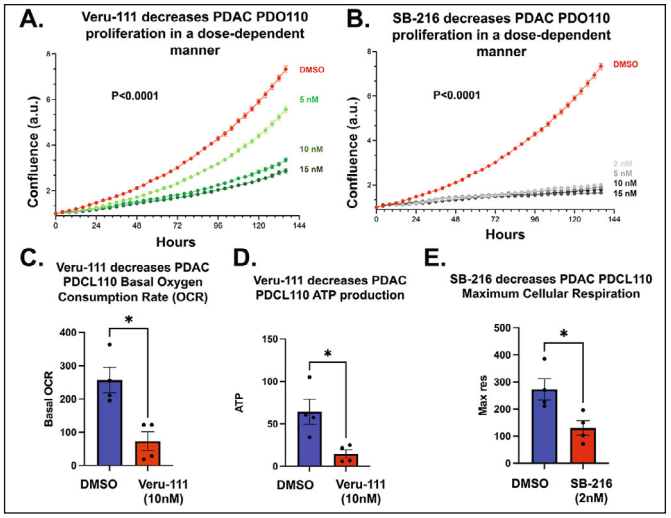
Figure 1. Temporal Trends for Outcomes Over Time using SSLR Derived Thresholds

P354. Dual Inhibition of Mitochondrial and Microtubular Function Disrupts Bioenergetics and Cellular Growth in Pancreatic Ductal Adenocarcinoma

Michael Spinrad[1]; Chun Cai[2]; Lauren Gattie[3]; David Shibata, MD[4]; Evan S Glazer, MD, PhD[5]

[1]The University of Tennessee Health Science Center, Memphis, TN, US; [2]The University of Tennessee Health Science Center, Memphis, TN, US; [3]The University of Tennessee Health Science Center, Memphis, TN, US; [4]The University of Tennessee Health Science Center, Memphis, TN, US; [5]The University of Tennessee Health Science Center, Memphis, TN, US

INTRODUCTION: Pancreatic Ductal Adenocarcinoma (PDAC) is one of deadliest cancers with a five-year survival rate of only 12%. Development of PDAC metastases is dependent on increased bioenergetics and oncogenic microtubule isotypes and is associated with epithelial mesenchymal transformation (EMT). We have previously demonstrated that BRD4, a targetable transcription factor and member of the bromo- and extra-terminal domain (BET) protein family, regulates mitochondrial complex gene expression and increases bioenergetics. We hypothesized that novel dual-function inhibitors (Veru-111 and a more potent derivative, SB-216), which block both BRD4-mediated mitochondrial activation and β-tubulin polymerization, decrease PDAC cell progression. **METHODS:** To examine circulating tumoral DNA levels, DNA sequencing followed by gene set enrichment analysis (GSEA) was performed on plasma cell-free DNA (cfDNA) from patients with PDAC, comparing samples from patients with high- and low- tumor burden. Commercial- and patient-derived PDAC cell lines (PDCL) and organoids (PDO) were treated with variable doses of Veru-111 and SB-216. Proliferation was measured with the IncuCyte Live-cell system, protein expression was evaluated by Western Blot, and mitochondrial function was assessed with the Seahorse XF mitochondrial respiration assay. **RESULTS:** GSEA revealed cfDNA is enriched for the Mitochondrial Inheritance gene set in the plasma of patients with high-tumor burden PDAC (NES 2.1, P<0.0001) as well as other mitochondrial-related gene sets. Genes enriched within these sets encode core subunits for the mitochondrial complexes of the electron transport chain and are a requisite for ATP production. SB-216 and Veru-111 reduced BRD4 expression and inhibited cell proliferation in PDCL and PDO (each P <0.0001). SB-216 and Veru-111 inhibited mitochondrial function with decreased ATP production (P<0.05) and cellular respiration (P<0.05) in PDCL and PDO. SB-216 induced cPARP (a marker for apoptosis) and BCL-xL (a marker for mitochondrial outer membrane loss) in PDCL, indicating apoptosis following mitochondrial injury. SB-216 and Veru-111 decreased oncogenic β-tubulin subtypes (P<0.05). **CONCLUSIONS:** GSEA suggests that patients with higher PDAC tumor burden have increased mitochondrial demand. Use of dual function inhibitors simultaneously targeting mitochondria-associated proteins and microtubules successfully reduced bioenergetics and inhibited cell growth in PDAC cells. Our novel strategy targeting multiple hallmarks of cancer represent an innovative strategy for future PDAC therapy.



P355. Early signs of cardiac impairment in pre-metastatic pancreatic ductal adenocarcinoma

Vignesh Vudatha[1]; Leslie Ogilvie[2]; Arunima Punjala, MD[3]; Vashti Bandy[4]; Jeremy Simpson[5]; Jose Trevino[6]

[1]VCU Health, Richmond, VA, US; [2]University of Guelph, Guelph, ON, CA; [3]VCU Health, Richmod, VA, US; [4]Virginia Commonwealth University, Richmond, VA, US; [5]University of Guelph, Guelph, ON, CA; [6]VCU Health, Richmond, VA, US

INTRODUCTION: Patiens with pancreatic ductal adenocarcinoma (PDAC) tend to develop skeletal muscle cachexia, leading to physical debilitation and increased mortality. However, there is minimal data regarding cardiac dysfunction in the setting of PDAC. In this study, we utilized preclinical in-vivo models of PDAC to evaluate the early impact of PDAC on cardiac structure and function. **METHODS:** Patient-derived xenograft (PDX) models of PDAC were generated by orthotopically implanting human PDAC tissue from a single patient into NSG mice. Tumor bearing mice and matched controls were generated. After tumor engraftment, left heart catheterization was performed to fully evaluate cardiac function. **RESULTS:** The NSG mice underwent catheterization in the pre-metastatic phase, when tumor volumes were low. At this point, there were no differences in body, heart, or ventricular weights between control and tumor bearing mice. Similarly, there was no significant difference in typical structural and function metrics including ejection fraction, cardiac output, systemic pressures, or cardiac dimensions. However, the tumor-bearing mice had decreased contractility with a significantly reduced maximum rate of contractility (p<0.01) and rate (p<0.01) at left ventricular pressure of 40 mmHg. The tumor-bearing mice also demonstrated impairments in diastolic function with a significantly increased ventricular relaxation time (p<0.05) and elevated filling pressures (p<0.05). **CONCLUSIONS:** PDAC is an aggressive malignancy that can leads to changes in cardiac function, even in early stages of disease. Further investigation is needed to determine the spectrum of cardiac changes as the tumor progresses and metastasizes.

P356. Enhancing Survival in Pancreatic Ductal Adenocarcinoma: A Multi-Center Analysis of Adherence to Operative Standards and Guideline-Recommended Therapy

Abdullah Khalid[1]; Lyudmyla Demyan[2]; Daniel Alexander King[3]; Elliot Newman[4]; Danielle DePeralta, MD[5]; Sepideh Gholami, MD[6]; Matthew John Weiss[7]; Marcovalerio Melis[8]

[1]Northwell Health, Manhasset, NY, US; [2]Northwell Health, Manhasset, NY, US; [3]Northwell Health, Manhasset, NY, US; [4]Northwell Health, Manhasset, NY, US; [5]Northwell Health, Manhasset, NY, US; [6]Northwell Health, Manhasset, NY, US; [7]Northwell Health, Manhasset, NY, US; [8]Northwell Health, Manhasset, NY, US

INTRODUCTION: Optimal outcomes in pancreatic adenocarcinoma (PDAC) rely on a multidisciplinary approach consisting of curative-intent resection with oncological standards and neoadjuvant or adjuvant therapy. This study aimed to investigate the factors influencing adherence to standard-adherent surgery (SAS) and guideline-recommended therapy (GRT) and to assess their impact on patient survival. **METHODS:** This study retrospectively analyzed a multicenter database of patients who underwent resection for PDAC between 2014-2023 at Northwell Health. SAS was defined as pancreatic resection with negative margins and examination of ≥ 15 lymph nodes. Stage-specific GRT was performed per the National Comprehensive Cancer Network (NCCN) guidelines (v 1.2022), including various strategies based on resection margins and neoadjuvant or adjuvant therapies. Survival analysis was performed using the Kaplan-Meier technique with log-rank tests, while the Mann-Whitney U test and Chi-square tests were used to compare factors between patients receiving both SAS and GRT and others. **RESULTS:** Among the 343 PDAC patients who underwent resection, 182 (53.1%) achieved SAS, 242 (70.5%) achieved GRT, and 133 (38.7%) achieved both. Factors associated with attainment of both SAS and GRT included lower age (p=0.044) Charlson comorbidity index < 2 (p=0.047), and administration of adjuvant chemotherapy (p<0.001). These patients also had a shorter stay in the ICU (p=0.049), decreased incidence of delayed gastric emptying (p=0.022), postoperative pancreatic fistula (p=0.047), postoperative bleeding (p=0.010), Clavien-Dindo classification ≥III (p=0.013), and 30- and 90-day mortality rates (p = 0.012 and 0.017) (Table 1). Patients achieving only GRT had a median overall survival (mOS) of 17.38 months (95% CI: 13.75-21.02), surpassing the SAS-only group's 14.80 months (95% CI: 10.82-18.78). Patients who met both SAS and GRT criteria had a mOS of 15.17 months (95% CI: 10.65-19.69). When neither SAS nor GRT criteria were met, mOS was only 5.17 months (95% CI: -2.16-12.50). Statistically significant survival advantages were observed for the GRT-only group versus neither (p= 0.001), the SAS-only group versus neither (p=0.017), and the combined GRT and SAS group versus neither (p=0.003). **CONCLUSIONS:** Our analysis showed that patients who met both SAS and GRT criteria after resection of PDAC experienced significantly fewer post-operative complications and longer survival. This study confirms that compliance with NCCN guidelines and personalized patient care enhances the quality of life and survival rates in patients undergoing resection for PDAC.

Table 1. Impact of Standard -Adherent Surgery and Guideline-Recommended Therapy on Survival in PDAC Patients: A Comparative Analysis.

Variable	Patients with SAS, GRT, or neither (n=210, 61.3%)	Patients with both SAS and GRT (n=133, 38.7%)	p-value
Age (mean ± S.D.)	73.43 ± 11.39	71.39 ± 9.49	0.044
Gender			0.430
Males	105 (50.20%)	61 (45.90%)	
Females	104 (49.80%)	72 (54.10%)	
BMI (mean ± S.D.)	25.97 ± 5.46	26.36 ± 5.37	0.265
Race			0.632
White	122 (58.10%)	82 (61.70%)	
Black or African American	31 (14.80%)	17 (12.80%)	
Asian	20 (9.50%)	12 (9.00%)	
American Indian/Alaska Native	3 (1.40%)	2 (1.50%)	
More Than One Race	29 (13.80%)	13 (9.80%)	
Unknown / Not Reported	5 (2.40%)	7 (5.30%)	
CCI (Charlson comorbidity index)			0.047
<2	113 (53.80%)	86 (64.70%)	
≥2	97 (46.20%)	47 (35.30%)	
Neoadjuvant chemotherapy	46 (22.01 %)	41 (31.06%)	0.062
Adjuvant chemotherapy	84 (41.38%)	110 (83.33%)	<0.001
Tumor Size			0.496
<3cm	175 (83.3%)	107 (80.5%)	
≥3cm	35 (16.7%)	26 (19.5%)	
Grade			0.237
Well differentiated	13 (6.3%)	15 (11.3%)	
Moderately differentiated	115 (55.6%)	74 (55.6%)	
Poor/Undifferentiated/anaplastic	65 (31.4%)	38 (28.6%)	
No invasive cancer	0 (0.0%)	1 (0.8%)	
Other	14 (6.8%)	5 (3.8%)	
ICU stay (days, mean ± S.D.)	3.39 ± 7.04	2.19 ± 5.89	0.049
AJCC T stage			0.003
Tx	6 (2.9%)	0 (0.0%)	
T0	0 (0.0%)	3 (2.3%)	
T1	30 (14.4%)	28 (21.1%)	
T2	85 (40.9%)	67 (50.4%)	
T3	86 (41.3%)	35 (26.3%)	
T4	1 (0.5%)	0 (0.0%)	
AJCC N Stage			0.240
Nx	5 (2.4%)	0 (0.0%)	
N0	84 (40.4%)	49 (36.8%)	
N1	82 (39.4%)	55 (41.4%)	
N2	37 (17.8%)	29 (21.8%)	
Unknown	2 (1.0%)	1 (0.8%)	
Complications			
Delayed Gastric Emptying (DGE) (Grades B/C)	73 (34.8%)	38 (28.6%)	0.022
Postoperative pancreatic fistula (POPF) (Grades B/C)	49 (23.3%)	25 (18.8%)	0.047
Postoperative bleeding	14 (6.7%)	4 (3.0%)	0.010
Clavien-Dindo classification (≥III)	53 (25.2%)	18 (13.5%)	0.013
30-day mortality	10 (4.90%)	0	0.012
90-day mortality	16 (7.6%)	2 (1.5%)	0.017

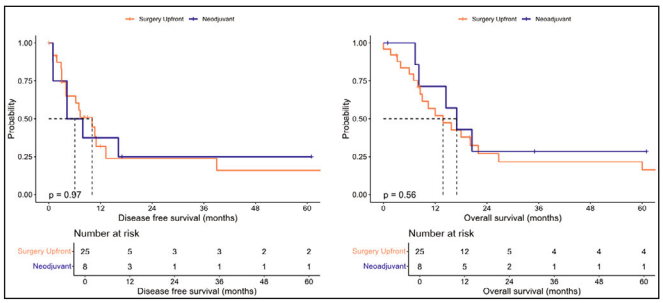
P357. Evaluating Outcomes of Patients with Resectable and Borderline-resectable Pancreatic Adenosquamous Carcinoma in a Contemporary Neoadjuvant Cohort

Marco Ventin[1]; Shahrzad Arya[2]; Alexandra Gangi, MD, FSSO[3]; Nicholas Nissen, MD[4]; Motaz Qadan, MD, PhD[5]; Carlos Fernandez-del Castillo, MD[6]; Vikram Deshpande, MD[7]; Brent K. Larson, DO[8]; Arsen K. Osipov, MD[9]; Keith D. Lillemoe, MD[10]; Cristina R. Ferrone, MD, MS, FSSO[11]

[1]Cedars-Sinai Medical Center, Los Angeles, CA, US; [2]Cedars-Sinai Medical Center, Los Angeles, CA, US; [3]Cedars-Sinai Medical Center, Los Angeles, CA, US; [4]Cedars-Sinai Medical Center, Los Angeles, CA, US; [5]Massachusetts General Hospital, Harvard Medical School, Boston, MA, US; [6]Massachusetts General Hospital, Harvard Medical School, Boston, MA, US; [7]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, US; [8]Cedars-Sinai Medical Center, Los Angeles, CA, US; [9]Cedars-Sinai Medical Center, Los Angeles, CA, US; [10]Massachusetts General Hospital, Harvard Medical School, Boston, MA, US; [11]Cedars-Sinai Medical Center, Los Angeles, CA, US

INTRODUCTION: Pancreatic adenosquamous carcinoma (PASC) has a worse prognosis than pancreatic ductal adenocarcinoma (PDAC). Introduction of modern neoadjuvant therapy regimens has led to improved survival outcomes in patient with borderline and locally advanced PDAC. However, the impact of contemporary neoadjuvant therapies in patients with PASC are lacking. **METHODS:** Retrospective analysis of patients undergoing pancreatectomy for PASC at the Massachusetts General Hospital (2007-2021) and Cedars-Sinai Medical Center (2013-2023) between 2007 and 2023. Patient demographics, tumor characteristics, treatment modalities, and median disease free (DFS) and overall (OS) survival were evaluated. **RESULTS:** A total of 35 patients with PASC were identified during the study period. The majority of patients were diagnosed as resectable (n=26, 75.0%), followed by borderline resectable (n=7, 19.4%) and locally advanced (n=2, 5.5%) disease. The median radiologic tumor size at diagnosis was 29.5 (IQR, 10.0) mm, and median CA 19-9 was 109.0 (IQR, 182.0) U/mL. Among patients with resectable/BR disease (n=33), the majority (n=25, 75.7%) underwent an upfront operation, and only 8 patients (24.3%) received neoadjuvant therapy with FOLFIRINOX or gemcitabine/abraxane followed by chemoradiation (n=5, 62.5%) and surgery. Two patients (25.0%) received gemcitabine/abraxane only, and one patient (12.5%) received capecitabine/XRT. The median number of neoadjuvant chemotherapy cycles was 8. Among patients treated with neoadjuvant therapy, only 3 patients (37.5%) demonstrated a biochemical response with CA 19-9 normalization, while the remaining 5 patients (62.5%) had a persistently elevated CA19-9 level or interval tumor size increase on imaging. A negative margin (R0) resection was achieved in 84.8% of patients. The median pathologic tumor size was 36.0 (IQR 20.0) mm, and the median number of collected lymph nodes was 22.0 (IQR, 16.0). Despite a smaller median pathological tumor size in neoadjuvant patients (38.0mm vs. 29.0mm, P=0.23), the rate of lymph node metastasis did not differ between upfront resection and neoadjuvant groups (64.0% vs. 62.5%, P=0.93). There were no significant differences in high-risk features including lymphovascular invasion (64.5% vs. 50.0%, P=0.63) or perineural invasion (88.0% vs. 71.4%, P=0.28). After a median follow-up period of 61 months, 24 patients (68.6%) developed tumor recurrence with a median DFS and OS of 7.9 (95% CI, 3.2 – 12.6) and 14.5 (95% CI, 8.1 – 20.9) months, respectively. Neoadjuvant therapy was not associated with significantly improved DFS or OS (Figure 1). The 5-year OS rate of surgery upfront and neoadjuvant groups was 16.2% and 29.6% (P=0.56), respectively. **CONCLUSIONS:** Pancreatic adenosquamous carcinoma is an aggressive malignancy with a poor prognosis. In our cohort standard neoadjuvant therapy was not associated with significant histopathologic

effects or an improved survival. Our findings warrant further investigation whether current neoadjuvant therapy should be considered in patients with potentially resectable PASC.



P358. Evaluating Synthetic Data Quality: Gaussian and CT-GAN Models in Replicating Clinical Outcomes in Pancreas Cancer Research

Adriana C Gamboa, MD[1]; Cong Pan, [2]; Laura R Prakash, [3]; Reed I Ayabe, [4]; Naruhiko Ikoma, MD[5]; Michael P. Kim, MD[6]; Jessica E. Maxwell, MD MBA[7]; Rebecca A. Snyder, MD, MPH[8]; Ching-Wei D. Tzeng, MD[9]; Matthew H.G. Katz, MD[10]; Heather G. Lyu, MD[11]

[1]MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas Health Science Center at Houston, Houston, TX, US; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [4]University of California Irvine, Irvine, CA, US; [5]UT MD Anderson Cancer Center, Houston, TX, US; [6]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [7]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [8]MD Anderson Cancer Center, Houston, TX, US; [9]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [10]MD Anderson Cancer Center, Houston, TX, US; [11]MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Synthetic data generation (SDG) plays an important role in clinical and translational research as it allows development of privacy-preserving datasets, ensures safe data sharing, and augments small datasets to accelerate model development. Synthetic data can potentially be used to simulate clinical scenarios and explore the impact of different interventions or treatments without the practical constraints of clinical trials. Using two different models, we aimed to generate synthetic data from an existing pancreas data set and assess its utility. **METHODS:** We synthesized synthetic datasets from an existing prospectively maintained database of patients who underwent pancreaticoduodenectomy for any diagnosis managed on a risk-stratified pancreatectomy care pathway at a single institution from October 2016 to December 2021. Two types of generative models were used: a Gaussian Model and a Conditional Tabular – Generative Adversarial Network (CT-GAN) Model. Various metrics were used to evaluate the utility of the generated data sets including data validity, data structure, column shape, and column pair trends. Overall quality score was assigned as a composite measure indicating excellent quality (>90%), good quality (80-90%), moderate quality (70-80%), and poor quality (<70%). **RESULTS:** A synthetic population of 500 patients was generated. Compared to the original dataset, Gaussian and CT-GAN models had 100% data validity and data structure scores, 97% and 88% column shape scores, 83% and 81% column pair trends score, and 90% and 85% overall scores, respectively. Correlation matrices are shown in *Figure 1*. Since the data were relatively parametric with a normal distribution and linear relationships, the Gaussian model was able to replicate the data with fewer complexities and lower risk of overfitting. However, both models produced good to excellent quality synthetic data. **CONCLUSIONS:** Synthetic data generated using a Gaussian and CT-GAN models mimic clinicopathologic and postoperative outcome data while anonymizing patient information. SDG can be used to augment existing data and future studies should be performed to assess the possibility of producing synthetic control arms or synthetic cohorts for in-silico trials.

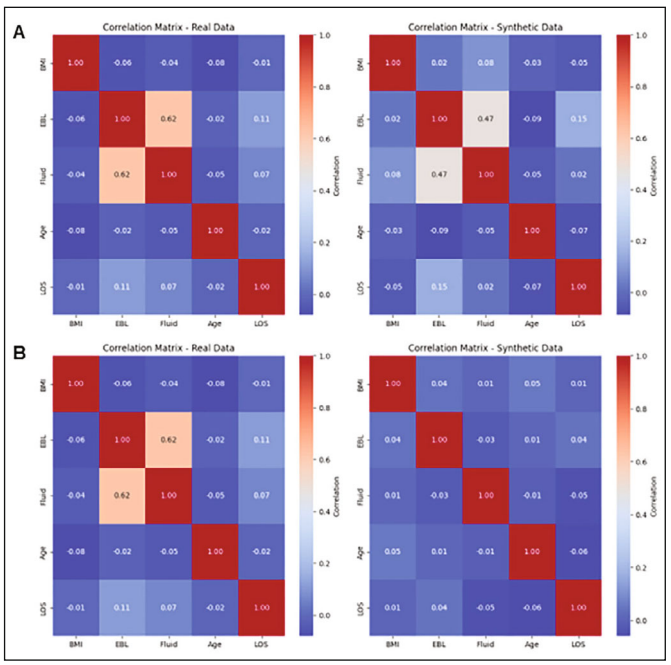


Figure 1. Correlation matrices for Gaussian model (A) and CT-GAN model (B)

P359. Extracellular vesicles as therapeutic nanoparticles for pancreatic cancer

Matan Shimron[1]; Saeed Sirhan[2]; Shelly Loewenstein[3]; Guy Lahat[4]

[1]Tel Aviv Sourasky Medical Center, Tel Aviv, IL; [2]Tel Aviv Sourasky Medical Center, Tel Aviv, IL; [3]Tel Aviv Sourasky Medical Center, Tel Aviv, IL; [4]Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel, IL

INTRODUCTION: Pancreatic ductal adenocarcinoma (PDAC) is a leading cause of cancer-related mortality and often presenting as a systemic, metastatic disease with poor prognosis and limited therapeutic options. Novel therapies are urgently needed to improve patient survival. Extracellular vesicles (EVs) are spherical nanovesicles that have gained attention as therapeutic agents due to their their ability to deliver therapeutic cargos to tumor sites. MiR-141, a known tumor suppressor, is downregulated in pancreatic cancer and plays a key role in epithelial to mesenchymal transition (EMT). This study explores the therapeutic potential of EVs enriched with miR-141 (EV-miR-141) using an innovative 3D PDAC spheroid model. **METHODS:** EVs enriched with miR-141 were generated from human embryonic kidney (HEK293) cells engineered to stably express miR-141 via lentiviral shMIMIC-miR-141. Mir-141 levels in both engineered cells and their EVs were quantified by qRT-PCR. The effects of EV-miR-141 on the proliferation, migration, and invasion of pancreatic cancer cells were assessed through various in vitro assays. EMT-related gene expression in treated pancreatic cancer cells was analyzed using qRT-PCR. Additionally, 3D PDAC spheroids derived from both human cell lines and patient-derived tumors were treated with EV-miR-141, and tumor cell viability was monitored over time using live-cell imaging. **RESULTS:** HEK293 cells stably expressing miR-141 showed a 150-fold increase in miR-141 levels compared to non-targeting controls. EVs isolated from these cells demonstrated a 300-fold enrichment of miR-141 compared to control EVs. Treatment of human PANC1 pancreatic cancer cells with EV-miR-141 resulted in significantly reduced proliferation, migration and invasion compared to cells treated with control-EVs. In addition, EV-miR-141 reduced the expression levels of the EMT related genes ZEB1, TWIST, Snail and Vimentin, while increasing the expression level of the epithelial marker E-cadherin. Finally, we engineered two 3D PDAC spheroids models: one consisting of PANC1 cell line and the other formed from patient-derived pancreatic tumors. The EV-miR-141 reduced effectively the spheroid size in both models. **CONCLUSIONS:** Our findings indicate that EVs enriched with tumor-suppressor miR-141 effectively inhibit PDAC cell growth and EMT, demonstrating their potential as a targeted treatment for PDAC. Moreover, the use of patient-derived 3D spheroid models presents a valuable platform for assessing treatment efficacy and advancing novel therapeutic strategies for pancreatic cancer.

P360. Factors associated with refusal of surgery in Stage I-III Pancreatic Ductal Adenocarcinoma and their effect on survival

Malek Moumne[1]; Imad Radi[2]; Raag Patel[3]; Alicia Arnold[4]; Steven Colquhoun[5]; Daniel Milgrom[6]; Danny Yakoub[7]
[1]Medical College of Georgia, Augusta, GA, US; [2]Medical College of Georgia, Augusta, GA, US; [3]Medical College of Georgia, Augusta, GA, US; [4]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US; [5]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US; [6]Wellstar Medical College of Georgia at Augusta University, Augusta, GA, US; [7]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US

INTRODUCTION: Pancreatic ductal adenocarcinoma (PDAC) is an aggressive cancer, and for stages I-III, surgery is the only potentially curative treatment. However, some patients still refuse surgery. We examined factors associated with refusal and its effect on median overall survival (OS). **METHODS:** The NCDB (2004-2019) was queried for stage I-III PDAC patients recommended for surgery. Patients who underwent surgery were compared to those who refused. Logistic regression identified predictors of refusal. Propensity score matching (PSM) produced comparable groups. Kaplan Meir, Log Rank, and Cox models analyzed the effect of refusal on OS. **RESULTS:** Out of 82,684 patients with stage I-III PDAC recommended for surgery, 3,915(4.5%) patients refused it. Multivariate logistic regression showed that age 50+ (OR=2.95), female sex (OR=1.31), non-Hispanic Black race (OR=1.17), urban residence (OR=1.13), tumor size 2-4 cm (OR=1.42), and 4+ cm (OR=1.21), treatment in non-academic centers (OR=1.43), opting for palliative care (OR=5.82), refusal of radiation (OR=3.36) and chemotherapy (OR=31.5) were associated with an increased probability of refusal. Patients with a Charleson comorbidity index (CCI) 1 (OR=0.91), private insurance (OR=0.44), median income (MI) $50,354-$63,332 (OR=0.76) and $63,332+ (OR=0.72), residence in southern states (OR=0.71), distance from care center 50-200 (OR=0.56) and 200+ miles (0.55), tumor location in the body (OR=0.76) and tail (OR=0.34), and stages 2 (OR=0.17) and 3 (OR=0.36) were associated with a decreased probability of refusal. Kaplan Meir and Log Rank analysis of PSM groups showed a decrease in OS in those refusing surgery across all stages (Figure 1): Stage 1 [29.7 vs 8.19 mos. HR=3.57], Stage 2 [16.4 vs 7.00 mos. HR=2.33], and Stage 3 [11.8 vs 5.93 mos. HR=1.84]. Multivariate survival analysis in patients refusing surgery indicated that CCI 2+ (HR=1.18), residence in Southern (HR=1.17) and Midwestern states (HR=1.16), MI <$40,227 (HR=1.15), treatment in non-academic centers (HR=1.19), stage 2 (HR=1.13) and 3 (HR=1.19) disease, tumor size 2-4 cm (HR=1.24) and 4+ cm (HR=1.49), opting for palliative care (HR = 1.18), refusal of radiation (HR=1.51) and chemotherapy (HR = 1.74) were associated with decreased survival. Tumor location in the body (HR=0.82) or tail (HR=0.81) were associated with increased survival. All variables met statistical significance (P<0.01). **CONCLUSIONS:** Surgery is associated with improved survival in stage I-III PDAC. Targeted counseling can mitigate the factors associated with surgery refusal to improve outcomes.

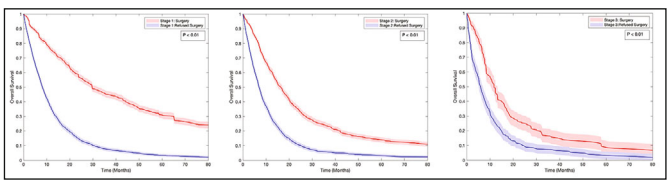


Figure 1. Kaplan-Meier Survival Curves for patients with Stage 1-111 Pancreatic Ductal Adenocarcinoma who underwent and refused surgery

P361. Genome-Derived Classification Signature of Pancreatic Acinar Cell Carcinoma Reveals Association with KRAS Wildtype Pancreatic Ductal Adenocarcinoma

Gregory A Wasserman, DO, PhD[1]; Mengyuan Liu, MD[2]; Kenneth Seier[3]; Mithat Gonen, PhD[4]; Carlie Sigel, MD[5]; Joslyn Jung[6]; Alex B Blair[7]; Thomas C Howell[8]; Diane L Reidy-Lagunes, MD[9]; Michael E Lidsky, MD[10]; Peter J Allen, MD[11]; Dan G Blazer, MD[12]; Sabino Zani, MD[13]; Alice C Wei, MD MSc[14]; Jeffrey Drebin, MD PhD[15]; Vinod P Balachandran, MD[16]; Michael D'Angelica, MD[17]; Kevin Soares, MD[18]; T Peter Kingham[19]; William R Jarnagin, MD[20]
[1]Northwell/Lenox Hill Hospital, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, NEW YORK, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, NEW YORK, NY, US; [6]Memorial Sloan Kettering Cancer Center, NEW YORK, NY, US; [7]Memorial Sloan Kettering Cancer Center, NEW YORK, NY, US; [8]Duke University, Durham, NC, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Duke University Medical Center, DURHAM, NC, US; [11]Duke University Medical Center, DURHAM, NC, US; [12]Duke University Medical Center, Durham, NC, US; [13]Duke University Medical Center, DURHAM, NC, US; [14]Memorial Sloan Kettering Cancer Center, New York, NY, US; [15]Memorial Sloan Kettering Cancer Center, New York, NY, US; [16]Memorial Sloan Kettering Cancer Center, New, NY, US; [17]Memorial Sloan Kettering Cancer Center, New York, NY, US; [18]Memorial Sloan Kettering Cancer Center, New-York, NY, US; [19]Memorial Sloan Kettering Cancer Center, New York, NY, US; [20]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Acinar cell carcinoma (ACC) is a rare form of pancreatic cancer characterized by heterogeneous histological subtypes. However, its specific genetic signature remains inadequately explored. To address this, we employed the hidden genome classifier (HGC), a machine learning algorithm designed to characterize tumor genomic alterations, to identify genetic features of pancreatic ACC. **METHODS:** The HGC was trained on genomic data from KRAS-mutated pancreatic ductal adenocarcinoma (PDAC) (n=1,872), KRAS wildtype (WT) PDAC (n=251), and well-differentiated pancreatic neuroendocrine tumors (G1/G2 PNET, n=127). HGC was then applied to assess primary and metastatic ACC across various histological subtypes. **RESULTS:** The *KRAS* WT PDAC classification was primarily associated with increased chromosomal copy number variations on chromosomes 1, 2 and 11, the KRAS class was predicted based on mutations in KRAS, and the PNET category showed a predominance of *ATRX* and *VHL* mutations. Among the sequenced ACC samples, the majority were classified as *KRAS* WT PDAC (49/62, 72%), followed by *KRAS* mutant (3/62, 4.8%), PNET (5/62, 8%), and indeterminate (5/62, 8%). Histologically, the tumors were classified as ACC (n=47), mixed ACC-ductal (n=4), and mixed ACC-neuroendocrine (n=11), with no significant correlation between HGC genomic classification and histological subtype observed. Notably, paired analyses of a set of primary and metastatic ACC indicated a change in copy number alteration, rather than an enrichment in specific gene mutations. **CONCLUSIONS:** Despite the histological heterogeneity of pancreatic ACC, our analysis using the hidden genome classifier indicates significant genomic similarities with KRAS wildtype PDAC. This classification was primarily driven by copy number alteration, rather than single gene mutations. Additionally, paired assessments of ACC samples reveal an accumulation of chromosomal copy changes as they evolve and metastasize.

P362. Hepatic recurrence rate based on extent of adjuvant floxuridine exposure after resection of colorectal liver metastases

Omar A Zaki, MD[1]; Raja R Narayan[2]; Rami Srouji[3]; Thomas Boerner[4]; Kenneth Seier[5]; Mithat Gonen, PhD[6]; Vinod Balachandran[7]; Kevin Soares, MD[8]; Jeffrey Drebin, MD PhD[9]; T. Peter Kingham, MD[10]; Alice C Wei, MD MSc[11]; William R Jarnagin, MD[12]; Louise Connell[13]; Andrea Cercek[14]; Nancy Kemeny[15]; Michael D'Angelica, MD[16]
[1]Memorial Sloan Kettering, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New-York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US; [11]Memorial Sloan Kettering Cancer Center, New York, NY, US; [12]Memorial Sloan Kettering Cancer Center, New York, NY, US; [13]Memorial Sloan Kettering Cancer Center, New York, NY, US; [14]Memorial Sloan Kettering Cancer Center, New York, NY, US; [15]Memorial Sloan Kettering Cancer Center, New York, NY, US; [16]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Hepatic arterial infusion (HAI) chemotherapy is an effective liver-directed therapy for patients with colorectal liver metastases (CRLM) and improves hepatic recurrence rates and survival in the adjuvant setting. Dose reductions/holds of HAI floxuridine (FUDR) are very common as a result of hepatotoxicity. The impact of these dose adjustments on patient outcomes is unclear. **METHODS:** We retrospectively analyzed patients who underwent adjuvant HAI pump placement for CRLM between 1/2000 and 10/2017. Only patients intended to receive 6 cycles of HAI FUDR were included. The number of FUDR cycles received and FUDR dose density were correlated with hepatic recurrence and overall survival (OS). Dose density was defined as the actual dose of FUDR received divided by the expected

total dose over 6 cycles. **RESULTS:** During the study period, 344 patients were identified who met inclusion criteria – 173 received 4 or fewer cycles of FUDR and 171 received greater than 4 cycles. The median dose density for all patients was 0.42 (range, 0.17-1.15) and the median total dose of FUDR received was 543.5mg (range, 146-1962). The ≤4 cycles group was more likely to have received neoadjuvant bevacizumab, adjuvant fluorouracil, bevacizumab, or fluorouracil + leucovorin + oxaliplatin. The cumulative incidence of hepatic recurrence at 5 years was 0.33. A competing risk analysis of the two groups found no significant difference in risk for liver recurrence (p=0.36). Cycles of FUDR received (hazard ratio (HR) 0.93, p= 0.24) and FUDR dose density (HR 1.26, p=0.63) were not associated with an increased risk of hepatic recurrence. On multivariable analysis, age at CRLM diagnosis (HR 0.98, p=0.02), positive lymph node status (HR 1.57, number of CRLM (HR 1.08, p=.02), and concurrent ablation with hepatectomy (HR 2.30, p=<0.001) were associated with increased risk of hepatic recurrence. Recurrence free survival did not differ between the ≤4 cycles and >4 cycles groups (p=0.43). There was no significant difference in median OS between the ≤4 cycles and the >4 cycles groups (7.8 vs 14.0 years, p=0.07). **CONCLUSIONS:** Neither the number of FUDR cycles received nor the dose density of FUDR were associated with hepatic recurrence in patients undergoing adjuvant HAI pump therapy for CRLM. As most patients do not receive their full intended dose of FUDR, dosing regimens should be re-evaluated.

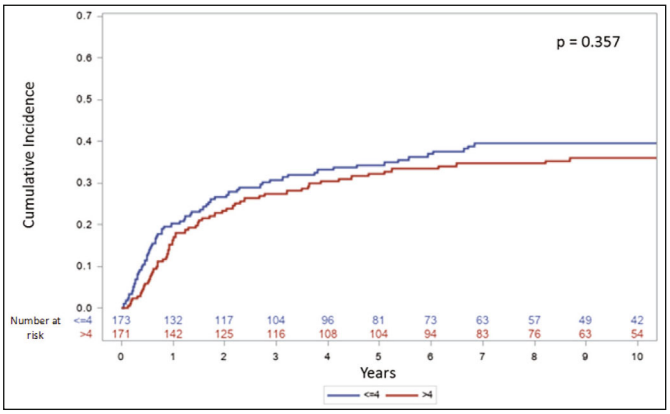


Figure 1. Competing risk analysis of ≤4 cycles and >4 cycles of FUDR on the cumulative incidence of hepatic recurrence

P363. Histotripsy for Treatment of Liver Tumors: A Novel Transthoracic Approach

Chloe E. Hanson, MD[1]; Kristen Kolberg, MD[2]; Dominique Pataroque, MD[3]; Clayton Tsang, MD[4]; Susan Vetto, A.R.N.P.[5]; Marc Horton, MD[6]; Mohamed Alassas, MD[7]; Evan Ong, MD[8]

[1]Swedish Medical Center, Seattle, WA, US; [2]Division of Surgical Oncology, Swedish Medical Center, Seattle, WA, US; [3]Division of Surgical Oncology, Swedish Medical Center, Seattle, WA, US; [4]Division of Surgical Oncology, Swedish Medical Center, Seattle, WA, US; [5]Division of Surgical Oncology, Swedish Medical Center, Seattle, WA, US; [6]Division of Surgical Oncology, Swedish Medical Center, Seattle, WA, US; [7]Swedish Medical Center, Seattle, WA, US; [8]Swedish Medical Center, Seattle, WA, US

INTRODUCTION: Histotripsy, a novel therapy to treat liver tumors, has previously been described using a transabdominal targeting approach. Anatomic constraints, however, are a common cause for inability to target a lesion. We describe lesion targeting with histotripsy using a novel transthoracic/intercostal approach, highlighting its technical considerations, safety, and efficacy. **METHODS:** We conducted a retrospective review of patients treated with histotripsy at our institution between November 2023 through September 2024. Length of follow up was one month. Charts were queried for details regarding demographics, treatment, postoperative course, and treatment success. **RESULTS:** We identified 55 patients who underwent histotripsy. Of these, we utilized a transthoracic only approach for 13 and both subcostal (SC) and TT for 6. The most common liver segments targeted via a TT approach were segments 6, 7 and 8. Average voltage and treatment time per TT lesion was 37.35% and 27.2 minutes compared to 31.39% and 21.0 minutes for SC-only treatments. Average total treatment time was 58 minutes for the TT group, 48 minutes for the combined group, and 40 minutes for the SC only group. Comparing the voltage and treatment time required between the 6 patients who had both a TT and SC approach, we found that the TT approach required more voltage (42.3% vs 36.5%) and took longer (18.3 vs 12.9 minutes). The average number of liver metastasis treated was 2 for TT treatments, 3 for the combined group, and 2 for the SC group. Postoperatively, 5 patients who underwent TT approach developed complications including fatigue, abdominal pain, UTI and GI bleed. Most patients who underwent TT treatment were discharged home on the same day (14/19, 74%). As opposed to the SC approach, TT targeting required specific positioning and maneuvers for optimal visualization including reverse Trendelenburg, angling, increasing PEEP, bump under the right side with arm overhead, footboard, and bed flexion. **CONCLUSIONS:** Anatomic constraints are a common cause of inability to target a lesion when using histotripsy. We trialed implementing a transthoracic approach to target difficult lesions. When comparing length of treatment and voltage required, we demonstrate that transthoracic targeting required higher voltage and longer treatment times. We found that the transthoracic approach is helpful for targeting high, anterior, and superficial lesions in segment 7 and 8. We describe a novel transthoracic/intercostal approach that allows for the safe, feasible, and effective targeting of a broader array of lesions.

Table 1. Patient and tumor characteristics

Characteristics	Value (n=19)
Median age, (IQR) years	67 (52-78)
Sex, *n* (%)	
Male	11 (57.9)
Female	8 (42.1)
ECOG performance status, *n* (%)	
0	10 (52.6)
1	6 (31.6)
2	2 (10.1)
3	1 (5.3)
Treated tumor type, *n* (%)	
Breast	1 (5.3)
Colorectal	6 (100)
Endometrial	1 (5.3)
Gastric	1 (5.3)
Hepatocellular	2 (10.1)
Liposarcoma	1 (5.3)
Neuroendocrine	4
Pancreas	1 (5.3)
Prostate	2 (10.1)
Prior catheter-directed therapy, *n* (%)	7 (36.8)
Prior surgical liver resection, *n* (%)	3 (15.8)
Prior chemotherapy, *n* (%)	17 (89.5)
Metastasis location, *n* (%)	
Liver-only metastases	7 (36.8)
Extra-hepatic disease	12 (63.1)
Treatment intent, *n* (%)	
Debulking	8 (42.1)
Palliative	2 (10.1)
Abscopal	6 (31.6)
Curative	3 (15.8)
Number of metastases treated, *n*	46
Transthoracic	33
Liver segment targeted, *n*	
3	2
4a	2
5	5
6	6
7	7
8	5

IQR: Interquartile range; ECOG PS: Eastern Cooperative Oncology Group.

P364. Histotripsy for the Treatment of Liver Tumors: A review of patients treated at a single institution

Chloe E. Hanson, MD[1]; Dominique Pataroque, MD[2]; Kristen Kolberg, MD[3]; Clayton Tsang, MD[4]; Susan Vetto, A.R.N.P.[5]; Marc Horton, MD[6]; Mohamed Alassas, MD[7]; Evan Ong, MD[8]

[1]Swedish Medical Center, Seattle, WA, US; [2]Division of Surgical Oncology, Swedish Medical Center, Seattle, WA, US; [3]Division of Surgical Oncology, Swedish Medical Center, Seattle, WA, US; [4]Division of Surgical Oncology, Swedish Medical Center, Seattle, WA, US; [5]Division of Surgical Oncology, Swedish Medical Center, Seattle, WA, US; [6]Division of Surgical Oncology, Swedish Medical Center, Seattle, WA, US; [7]Swedish Medical Center, Seattle, WA, US; [8]Swedish Medical Center, Seattle, WA, US

INTRODUCTION: Histotripsy utilizes real-time focused ultrasound and is the first noninvasive, non-ionizing and non-thermal ablation technology approved for the treatment of liver tumors. It is a novel therapy and little published literature exists on clinical outcomes. We describe our experience using histotripsy to treat liver tumors with primary outcomes of acute technical success and safety. **METHODS:** We conducted a retrospective review of all patients treated with histotripsy for liver tumors between November 2023 to September 2024. We excluded patients with lack of 30-day follow up. Charts were queried for details regarding demographics, treatment, perioperative complications, postoperative course, and technical treatment success. Acute technical success was defined as our ability to see an adequate zone of ablation in real-time and on immediate postoperative imaging. **RESULTS:** A total of 55 patients were analyzed. We observed acute technical success in 50/55 (90.1) of patients, with 4 instances of device complication. Median total treatment time was 45 minutes (IQR 15-70). We targeted all liver segments. Most treatments were completed via a transabdominal approach (36/55, 65%) however we pioneered a transthoracic approach on 19 patients (35%). The median longest tumor diameter was 2.5 cm (IQR 2-6) and the median ablation zone volume was 9 cm3 (IQR 6.5-18.7). We observed 10 CTCAE grade 1 and 2 complications (18.1%), the most common of these being pain (4/55, 7.3%). Other grade 1 and 2 complications included nausea/vomiting (2/55), UTI (1/55), thrombosis (2/55), and bleeding (1/55). We observed 7 CTCAE major complications (12.7%), including acute renal failure (1/55), biliary tract infection (1/55), ascites (2/55), UGIB (1/55), failure to thrive (1/55) and acute liver failure resulting in death (1/55). Most patients had an outpatient procedure (32/55, 58%). Since histotripsy, 33/55 patients (60%) have initiated chemotherapy, 3/55 have received liver-directed therapy (5.4%), 2/55 have received surgical resection (3.6%), and 3/55 have received a second histotripsy treatment (5.4%). **CONCLUSIONS:** Histotripsy is a new and noninvasive treatment modality in the locoregional management of liver tumors. We treated a broad range of tumor types with treatment intents of abscopal, conversion, debulking, palliative, and curative and were able to transition to an outpatient procedure. Our complications resemble those of previously published literature. Immediate data demonstrates that histotripsy is both technically feasible and safe.

Table 1. Patient and tumor characteristics

Characteristics	Value (n=55)
Median age, (IQR) years	66 (55-74)
Sex, *n* (%)	
Male	27 (49.1)
Female	28 (50.9)
ECOG performance status, *n* (%)	
0	24 (43.6)
1	19 (16.4)
2	8 (14.5)
3	3 (5.5)
4	1 (1.8)
Primary tumor location, *n* (%)	
Breast	4 (7.3)
Colorectal	20 (36.4)
Cholangiocarcinoma	10 (18.2)
Hilar	4
Intrahepatic	6
Endometrial	1 (1.8)
Gastric	2 (3.6)
Hepatocellular	5 (9.1)
Liposarcoma	2 (3.6)
Neuroendocrine	5 (9.1)
Pancreatic	4 (7.3)
Prostate	2 (3.6)
Prior catheter-directed therapy, *n* (%)	18 (32.7)
Prior surgical liver resection, *n* (%)	11 (20.0)
Prior chemotherapy, *n* (%)	49 (89.1)
Metastasis location, *n* (%)	
Liver-only metastases	21 (38.2)
Extra-hepatic disease	29 (52.7)
Treatment intent, *n* (%)	
Abscopal	14 (25.5)
Conversion	4 (7.3)
Curative	9 (16.4)
Debulking	24 (43.6)
Palliative	4 (7.3)

IQR: Interquartile range; ECOG PS: Eastern Cooperative Oncology Group.

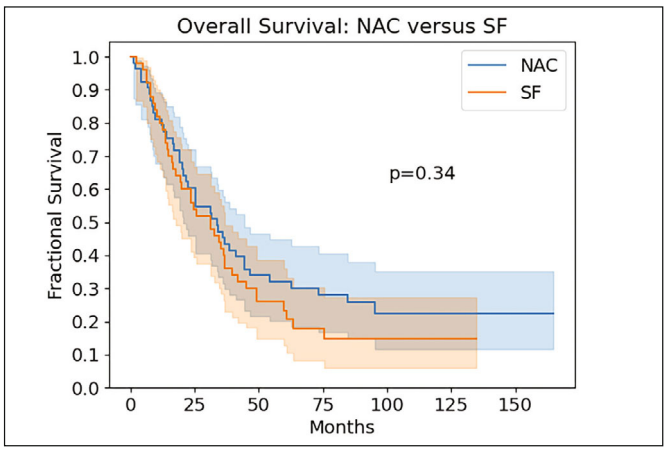
P365. Impact of Neoadjuvant Chemotherapy on Operative Outcomes Following Pancreaticoduodenectomy for Pancreatic Adenocarcinoma

Leanne M Brown[1]; Pathik Aravind[2]; Lauren M Raymond-King, MD[3]; Marla Fortoul[4]; Wendy Feng[5]; Sara Abou Azar[6]; Sajid Khan, MD, FACS[7]; Kevin Billingsley[8]; Jill Lacy[9]; Ronald A Salem[10]; John W Kunstman[11]

[1]Yale New Haven Health, New Haven, CT, US; [2]Yale New Haven Health, New Haven, CT, US; [3]Yale New Haven Hospital, Yale University, New Haven, CT, US; [4]Yale New Haven Hospital, New Haven, CT, US; [5]Yale New Haven Health, New Haven, CT, US; [6]University of Chicago, Chicago, IL, US; [7]Yale University School of Medicine, New Haven, CT, US; [8]Yale New Haven Health, New Haven, CT, US; [9]Yale New Haven Health, New Haven, CT, US; [10]Yale New Haven Health, New Haven, CT, US; [11]Yale New Haven Health, New Haven, CT, US

INTRODUCTION: Neoadjuvant chemotherapy (NAC) followed by surgery is an accepted curative approach to pancreatic ductal adenocarcinoma (PDAC), but its impact on surgical morbidity is unclear. Patients undergoing pancreaticoduodenectomy (PD) via a NAC or surgery-first (SF) approach were matched for surgical risk and outcomes were compared. **METHODS:** A prospectively collected dataset of patients undergoing PD for PDAC at a

high-volume institution between April, 2012 and March, 2020 was queried. Receipt of ≥2 cycles of chemotherapy prior to surgery defined the NAC cohort. Morbidity risk was quantified by "Serious Complication" risk using the ACS-NSQIP Surgical Risk Calculator and the validated Fistula Risk Score quantified clinically-relevant pancreatic fistula risk (CR-PF). Patients were stratified by NAC or SF and propensity matched 1:1 by both risk metrics. Primary outcomes were 90-day major morbidity (Clavien-Dindo Grade ≥3) and CR-PF rate. Secondary outcomes included overall survival (OS), tumor pathology, and perioperative outcomes. Categorical and continuous variables were assessed via Chi-squared and two-tailed t-tests, respectively; survival analysis was via the Kaplan-Meier method. **RESULTS:** 259 patients underwent curative-intent PD and were assessed for matching; of these,106 patients comprised the study cohort. The mean ACS-NSQIP risk was 27.5±3.8% and 28.0±4.8% in the NAC and SF cohorts, respectively (p=0.61). Of the NAC patients, the median number of preoperative cycles was 8 (IQR 6-9); 88.7% received FOLFIRNOX. 22.6% of NAC patients required non-index biliary procedures prior to surgery compared to 1.9% of SF patients (p<0.01). There was no difference between the matched NAC and SF cohorts in major morbidity (17.0% vs 15.1%, p=1.0), CR-PF incidence (0% vs 5.7%, p=0.07), or operative mortality (1.9%, both). Index length of stay (5.9±3.9d [NAC] vs 5.8±3.1d [SF], p=0.80) and readmission rates (15.1% [NAC] vs 28.3% [SF], p=0.12) were similar. Operative blood loss was higher in NAC compared to SF patients (544.7±576.7 mL vs 305.1±190.4 mL; p=0.01). Contrasting SF to NAC patients, 13.2% compared to 3.8% had a positive (R1) margin (p=0.16) whereas 79.3% compared to 49.1% had regional (N1/2) disease (p=0.01), respectively. Median OS was 39.4 months following NAC versus 25.7 compared to SF (p=0.34). **CONCLUSIONS:** Patients undergoing PD for PDAC following NAC compared to SF when matched by surgical risk experienced increased operative blood loss but had no detrimental effect on overall postoperative major morbidity, CR-PF rate, or related operative outcomes.



P366. Inflammatory differences in the tumor microenvironment of diabetic patients with pancreatic ductal adenocarcinoma

Kelly Herremans[1]; Andrea Riner[2]; Patrick Underwood[3]; Steven Hughes[4]
[1]University of Florida College of Medicine, Gainesville, FL, US; [2]Ohio State University School of Medicine, Columbus, OH, US; [3]Ohio State University School of Medicine, Columbus, OH, US; [4]University of Florida College of Medicine, Department of Surgery, Gainesville, FL, US

INTRODUCTION: A history of long-standing diabetes mellitus as well as new-onset diabetes mellitus have been associated with increased risk of the development of pancreatic ductal adenocarcinoma (PDAC). Prior studies have shown differences in the systemic inflammatory response of diabetic patients diagnosed with PDAC. The purpose of this study was to identify differences within tumor inflammatory markers in patients diagnosed with diabetes mellitus. **METHODS:** Fifty-nine PDAC tumor specimens from patients naïve to treatment and 37 benign pancreatic controls were homogenized and probed for 41 unique inflammatory proteins using a multiplex assay. Diabetes status was determined preoperatively based on patients' reported past medical history and preoperative laboratory values. Comparative analysis was performed using Wilcoxon rank sum test. **RESULTS:** Compared to non-diabetic patients with pancreatic ductal adenocarcinoma, the tumor microenvironment of diabetic patients had significantly higher levels of FGF-2 (p=0.018), MCP-3 (p=0.029), TNF-β (p=0.011) and most notably, IL-1Ra (p<0.01). When benign pancreatic controls of diabetic patients were compared to tumor samples of diabetic patients, IL-1Ra was significantly increased (p<0.01). **CONCLUSIONS:** The tumor microenvironment is altered in patients with diabetes. Furthermore, IL-1Ra may differentiate tumor vs. benign controls in diabetic patients. Additional work is needed to evaluate the temporal changes in the tumor microenvironment and their relationship poor glycemic control.

P367. Intratumoral lymphangiogenesis does not correlate with outcomes in Hepatocellular Carcinoma

Aeryn N Kangas-Dick, MD[1]; Rongrong Wu[2]; Takashi Ishikawa[3]; Kazuaki Takabe, MD, PhD[4]
[1]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [2]Tokyo Medical University, Tokyo, JP; [3]Tokyo Medical University, Tokyo, JP; [4]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US

INTRODUCTION: High density of peritumoral lymphatic vessels is negatively associated with disease-free (DFS), disease-specific (DSS), and overall survival (OS) in many types of cancer including hepatocellular carcinoma (HCC), presumably due to increase in conduits for lymph node metastasis. Lymphangiogenesis (LA) is the generation of new lymphatic vessels, thus we hypothesized that HCC with enhanced LA is associated with aggressive disease biology and worse OS. **METHODS:** Transcriptome linked with clinical parameters of HCC from the Cancer Genome Atlas (TCGA) was analyzed (n=358). All samples were deemed intratumoral based on collection criteria by TCGA. LA was quantified by gene set variation & expression analysis of KEGG LA gene set. The cohort was divided by median cut off to LA high and low groups. **RESULTS:** LA score correlated with expressions of known LA associated genes; VEGF-C, FLT4, KDR, Angiopoietin-1, TIE1, TEK, CDH5, and with infiltrations of lymphatic endothelial cells (all p<0.01). LA high HCC were not associated with a statistically significant difference in DFS, DSS, or OS. LA was elevated in T4, N1, M1 and stage IV disease; however, these trends were not statistically significant, likely due to low overall numbers. LA was higher in HCC due to NAFLD compared with HBV, HCV or alcohol abuse and LA high HCC was not associated with mutation rates or neoantigens. Immune cells such as CD4+ naïve cells, CD8 TCM, regulatory T cells, megakaryocytes, conventional Dendritic Cells, and macrophages were associated with LA high HCC, whereas CD4 TEM cell, CD8 naïve cell, natural killer T cell, plasma cells, pro B cells, and Th1 cell were associated with LA low HCC. LA high HCC was associated with higher TGF- β response and macrophage regulation, BCR evenness, TCR Shannon, TCR Richness, suggesting activated T cell response. Gene set enrichment analysis of HALLMARK collection showed that LA high HCC enriched not only LA associated sets like; Angiogenesis, Apical Junction, Apical Surface pathway, but also immune response related sets like; TGF-β signaling, IL2 signaling, IL6 signaling, TNF-α signaling, and Inflammatory response, as well as cancer stem cell phenotype related sets like; Epithelial Mesenchymal Transition, NOTCH signaling, Hedgehog signaling, and WNT signaling. **CONCLUSIONS:** Intratumoral LA quantified by computational algorithm was not associated with worse survival. However high LA was associated with immune activation and response as well as stem cell phenotype and epithelial mesenchymal transition suggesting the mechanism of aggravating and alleviating cancer counterbalance when LA is activated in HCC.

P368. Lipid Rafts Modulate c-Myc Phosphorylation in Pancreatic Cancer In Vitro

Jakob S Hamilton, MS, BS, BA[1]; Ryan M Thomas, MD, BS[2]
[1]University of Florida College of Medicine, Gainesville, FL, US; [2]University of Florida College of Medicine Department of Surgery, Gainesville, FL, US

INTRODUCTION: Overexpression of c-Myc is associated with increased mortality and chemoresistance in pancreatic ductal adenocarcinoma (PDAC), the 3rd leading cause of cancer-related deaths in the United States. Recent studies indicate lipid raft proteins, specifically Flotillin-2 (FLOT-2), stabilize c-Myc in human cancers, promoting uncontrolled cell proliferation. This mechanism is poorly characterized, as c-Myc stability is classically regulated by the phosphorylation of serine-62 (phos-S62-c-Myc), which prevents its degradation. Our prior work has shown that lipid raft inhibition reduces PDAC cell proliferation, leading us to hypothesize this effect is driven by changes in c-Myc phosphorylation states. **METHODS:** Lipid raft and whole cell lysate proteins were separately extracted from three human PDAC cell lines (BxPC-3, L3.6pl, and MIA-PaCa-2) using the Minute Plasma Membrane-Derived Lipid Raft Isolation Kit and visualized by immunoblot. After overnight serum starvation, cells were incubated with Dynasore (10 μM) for 24-72 hours, disrupting lipid rafts through changes in cholesterol trafficking. Using ImageJ

software, raft inhibition was confirmed by a reduction in FLOT-2 expression standardized to transferrin receptor 2, while changes in c-Myc and phos-S62-c-Myc expression were assessed by normalizing to GAPDH and total c-Myc, respectively. **RESULTS:** Phos-S62-c-Myc expression varies between human PDAC cell lines, with BxPC-3 exhibiting the highest, and L3.6pl the lowest, levels despite similar baseline c-Myc expression. While lipid raft inhibition did not change total c-Myc expression in any experimental condition, phos-S62-c-Myc decreased by up to 48%, 73%, and 16% ($p<0.01$) in MIA PaCa-2, as well as 75% ($p=0.04$), 44%, and 34% in BxPC-3 when compared to the DMSO vehicle control at 24, 48, and 72 hours, respectively. L3.6pl phos-S62-c-Myc expression also decreased by 69% ($p=0.014$) at 24 hours, but returned to baseline levels at 48 hours ($p=0.014$) and further increased by 240% ($p<0.001$) at 72 hours. **CONCLUSIONS:** Lipid rafts modulate phosphorylation of c-Myc at its S62 site without altering expression, suggesting their inhibition could reduce c-Myc stability in PDAC. These findings align with our previous data demonstrating lipid raft disruption decreases PDAC cell proliferation, where lower levels of phos-S62-c-Myc may contribute to this effect. Considering the differential phosphorylation patterns observed, further exploration of this mechanism could inform the utility of lipid rafts as novel therapeutic targets in the treatment of PDAC.

P369. Liver Metastasectomy in Ovarian Cancer: Is There a Survival Benefit?

Lauren Springsteen[1]; Cameron Jackson[2]; Malek Moumne[3]; Christina H Bae, Medical Student[4]; Christy Daniel[5]; Jack Mcgarty[6]; Steven Colquhoun[7]; Daniel Milgrom[8]; Bunja Rungruang[9]; Danny Yakoub[10]

[1]Medical College of Georgia, Augusta University, Augusta, GA, US; [2]Medical College of Georgia, Augusta University, Augusta, GA, US; [3]Medical College of Georgia, Augusta, GA, US; [4]Medical College of Georgia, Augusta, GA, US; [5]Medical College of Georgia, Augusta, GA, US; [6]Medical College of Georgia, Augusta, GA, US; [7]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US; [8]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US; [9]Division of Gynecologic Oncology, Medical College of Georgia, Augusta, GA, US; [10]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US

INTRODUCTION: The role of resection of hepatic metastases during ovarian cancer cytoreductive surgery (OCRS) in Stage IV Ovarian Cancer (OC) remains controversial due to the high chemosensitivity of OC. We aim to compare the overall survival (OS) in patients who had OCRS with and without liver metastasectomy (LM). **METHODS:** The National Cancer Database (NCDB 2010-2019) was queried for Stage IV epithelial OC with liver metastasis. Demographics, tumor characteristics, and treatment factors specifically, neoadjuvant chemotherapy (NACT), were compared. OS was compared between groups using Kaplan-Meier, Log-Rank, and Cox proportional hazard model analysis. **RESULTS:** A total of 874 Stage IV OC patients with metastasis to the liver who underwent OCRS followed by chemotherapy were identified. OCRS+LM was done in 105 patients, while 482 patients only received OCRS. The two groups were similar in age and Charleson Comorbidity Index (CCI). LM patients did not have increased 30 or 90-day mortality, nor was LM associated with a significant difference in OS (46.62 vs. 39.85 months for OCRS+LM and OCRS respectively, $p=0.475$, Fig 1A). To assess the effect of NACT, patients who had OCRS+LM (n=105), were compared to 287 patients who had NACT+OCRS without LM. There was no significant difference in age or CCI between these two groups. Again, there were no significant difference in 30 or 90-day mortality; nor in OS for OCRS+LM vs. NACT+OCRS (46.62 vs. 39.85 months, respectively, $p=0.357$, Fig. 1B). On multivariate analysis of the OCRS+LM group, variables associated with decreased survival were distance >50 miles from treatment center (HR=3.97), and positive lymph-vascular invasion (LVSI) (HR=3.70). On the other hand, in the NACT+OCRS group, variables associated with decreased survival were non-Hispanic black race (HR=2.83), positive LVSI (HR=1.77), and clear cell histology (HR=3.97); median income $74,063+ was associated with improved survival (HR=0.85). In the OCRS only group, CCI score of 1 (HR=1.48) or 2 (HR=2.24), mucinous histology (HR=3.66), and clear cell histology (2.74) were associated with worse survival, while Hispanic white race (HR=0.55) was associated with improved survival. All variables met statistical significance ($p<0.05$). **CONCLUSIONS:** There was no significant overall survival benefit of LM in Stage IV OC. Further studies may evaluate the role of LM with OCRS on progression free survival in OC with systemic as well as intraperitoneal chemotherapy regimens.

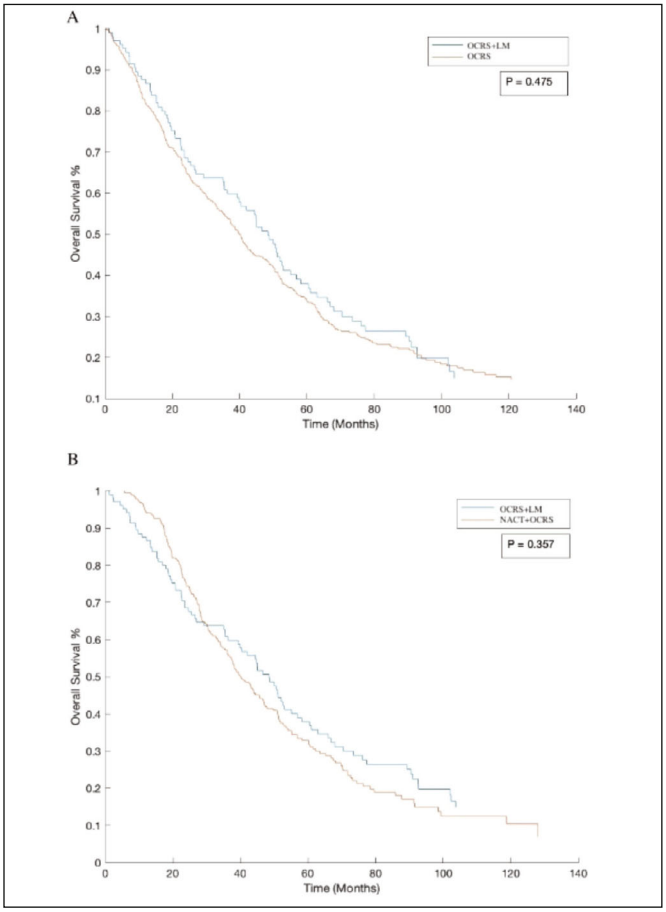


Figure 1. Kaplan-Meier survival curves for overall survival of OCRS with and without LM (Fig. IA) and OCRS with LM vs OCRS preceded by NACT (Fig. IB)

P370. Liver resection versus transarterial chemoembolization for huge hepatocellular carcinoma (>10cm): a nationwide propensity score adjusted analysis

Jai Young Cho[1]; Boram Lee[2]

[1]Seoul National University, Seoul, KR; [2]Seoul National University, Seoul, KR

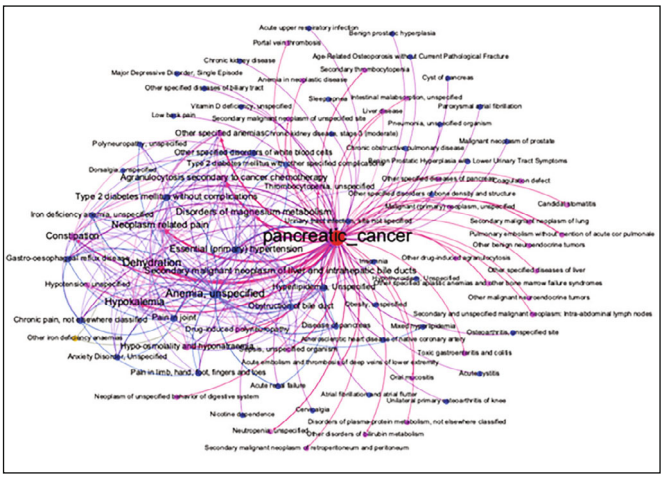
INTRODUCTION: The treatment of hepatocellular carcinoma (HCC) larger than 10 cm remains controversial, with varying recommendations across different guidelines. This study aims to address the important controversy regarding the management of large HCC, focusing on providing insights into the comparative effectiveness of liver resection (LR) and Ttransarterial chemoembolization (TACE). **METHODS:** Patients registered in the Korean Primary Liver Cancer Registry (KPLCR) were selected. The KPLCR is a random sample consisting of approximately 15% of patients newly diagnosed with primary liver cancer registered in the Korean Central Cancer Registry (KCCR), which is a nationwide cancer registry and includes more than 95% of all cancer cases in Korea. The patients in the KPLCR were selected from the KCCR using a probability proportional to size method and stratification by region in a given year. Therefore, the KPLCR is a representative group of patients with newly diagnosed HCC in Korea. The study design utilizes data from the KPLCR covering the years 2008 to 2017 to investigate the treatment outcomes for HCC larger than 10 cm. Starting with 15,307 cases, the study identified 9,310 HCC patients with follow-up data, excluding those with missing initial treatment data (n=5,863) and follow-up loss (n=132). From these, 7,662 patients with single HCC were selected, further excluding cases with multiple HCC (n=1,394) and distant metastasis (n=254). This refined the cohort to 504 patients with HCC tumors larger than 10 cm, who were then divided into two treatment groups: 122 patients underwent liver resection (LR), and 382 patients received TACE. **RESULTS:** After PSM, the baseline characteristics showed no significant differences between the LR group (n=99) and the TACE group (n=99). Key indicators of hepatic function, including serum albumin, bilirubin, INR,

creatinine, sodium, ALT, and platelet levels, were also well-matched, with no significant differences observed. Before PSM, the hazard ratio (HR) for LR was 3.41 (95% CI: 2.62-4.43, p<0.001), indicating a significantly better survival probability for the LR group compared to the TACE group. After PSM, the HR for LR was slightly reduced to 3.06 (95% CI: 2.18-4.29, but the survival advantage of LR over TACE remained highly significant. The analysis of recurrence-free survival (RFS) for patients with HCC larger than 10 cm also shows significant differences between two groups. Before PSM, the HR for LR was 3.29 (95% CI: 2.59-4.17, indicating a markedly better RFS for the LR group compared to the TACE group. After PSM, the HR for LR increased slightly to 3.37 (95% CI: 2.43-4.68, maintaining the significant survival advantage of LR over TACE. **CONCLUSIONS:** This study provides a comprehensive analysis of treatment outcomes for HCC larger than 10 cm, comparing LR and TACE using data from the KPLCR. The results indicate that LR is associated with significantly OS and RFS compared to TACE, both before and after PSM.

P371. Mapping Multimorbidity Trajectories for Pancreas Cancer from Real World Data

Adriana C Gamboa, MD[1]; Rui Li[2]; Hongfang Liu[3]; Andrew Wen[4]; Qiuhao Lu[5]; Jinlian Wang[6]; Matthew H.G. Katz, MD[7]; Liwei Wang[8]; Heather G. Lyu, MD[9]
[1]MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas Health Science Center at Houston, Houston, TX, US; [3]The University of Texas Health Science Center at Houston, Houston, TX, US; [4]The University of Texas Health Science Center at Houston, Houston, TX, US; [5]The University of Texas Health Science Center at Houston, Houston, TX, US; [6]The University of Texas Health Science Center at Houston, Houston, TX, US; [7]MD Anderson Cancer Center, Houston, TX, US; [8]The University of Texas Health Science Center at Houston, Houston, TX, US; [9]MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: In the years leading up to diagnosis of pancreatic cancer, patients develop symptoms that serve as potential predictors of disease onset. Disease trajectories were recently proposed as a novel way of studying causal and temporal relationships between diagnoses and potentially guiding the development of screening programs. We aimed to discover signature disease trajectories for pancreatic cancer leveraging large-scale electronic health record (EHR) data. **METHODS:** The IQVIA Oncology Electronic Medical Record database is an expansive database containing anonymized, patient-level oncology data from 2015-2023. Significant diagnosis pairs were identified through a series of computations starting with the extraction of the first instance of a pancreas cancer diagnosis using ICD-10 codes. Statistically significant diagnosis pairs were identified as those more likely in patients with pancreas cancer than in a comparison cohort of patients. Directionality within the diagnosis pairs was established through a right-tailed binomial hypothesis test and disease trajectories were plotted using Gephi, an open-source platform for visualizing large networks. Significant disease pairs were then validated using real world data from UT Houston mapped to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM). **RESULTS:** In the IQVIA database, there were 13,606 patients with pancreatic cancer. Average age at diagnosis was 68. A total of 580 diagnosis pairs were identified. After determining the directionality, 15 diagnosis pairs were identified as comorbidities, and 232 diagnosis pairs were found to have a sequential relation. There were 31 pairs starting from pancreas cancer and 41 pairs leading to pancreas cancer (*Figure 1*). All diagnosis pairs occurred within 2 years. The strongest associations for temporal progression to pancreas cancer included type 2 diabetes mellitus, essential (primary) hypertension, and disorders of lipoprotein metabolism. Strongest associations for temporal progression from pancreas cancer included anemias, dehydration, and secondary malignant neoplasm of respiratory and digestive organs. In the validation cohort, there were 2,555 patients with pancreatic cancer. All the significant diagnosis pairs were identified while 33% of undirected trajectories and 9% of directed trajectories were detected in the validation cohort. **CONCLUSIONS:** In this study, we utilized large-scale EHR data to extract signature disease trajectories for pancreatic cancer. Our methodology offers both causal and temporal relationships between these diagnoses with the intent of facilitating the design of screening programs for early detection of pancreatic cancer in high-risk patients.



P372. Modulation of RBP-1 Phosphorylation is a Novel Therapeutic Vulnerability in Fibrolamellar Carcinoma

Patrick Carney[1]; Manabu Nukaya[2]; Sean M Ronnekleiv-Kelly, MD[3]
[1]University of Wisconsin-Madison, Madison, WI, US; [2]University of Wisconsin-Madison, Madison, WI, US; [3]University of Wisconsin-Madison, Madison, WI, US

INTRODUCTION: Fibrolamellar carcinoma (FLC) is a rare cancer that is highly lethal and disproportionately affects young individuals without known genetic or environmental predisposition. Unfortunately, 5-year survival for this disease is approximately 30-45% and the lack of robust systemic therapy options is a major barrier to long-term survival. A unique gene fusion between heat shock protein 40 (*DNAJB1*) and the catalytic subunit alpha of protein kinase A (*PRKACA*) is present in FLC and results in the production of an oncoprotein (DNAJ-PKAc). DNAJ-PKAc causes epigenetic remodeling and emergence of FLC specific super enhancers that results in FLC-specific gene expression, leading to an aggressive cancer phenotype. We have identified aberrant RNA polymerase II (RBP-1) activity in DNAJ-PKAc expressing cells, and this is likely driven by cyclin dependent kinase 7 (CDK7). **METHODS:** Human FLC, HCC, CCA and matched normal liver samples were evaluated for presence of the DNAJ-PKAc oncoprotein and for phosphorylated RBP-1 protein at serine-2, -5 and -7 residues (Western Blot). Phosphorylation of RBP-1 serine residues is regulated by CDK7 (preferential target serine-5) and CDK9 (serine-2). A CDK7 specific inhibitor (SY-5609) and a CDK9 specific inhibitor (VIP-152) were evaluated in our engineered cell line expressing DNAJ-PKAc and in FLC organoids to assess FLC specific gene expression and synergy of these compounds. **RESULTS:** Human FLC tumor tissue samples show increased phosphorylation of RBP-1 serine-5 residue as compared to human HCC, CCA and normal liver samples. Treatment of DNAJ-PKAc expressing cells and FLC patient derived organoids with SY-5609 and VIP-152 showed suppression of FLC specific super enhancer driven genes in a dose dependent manner (Figure 1). **CONCLUSIONS:** Testing of patient FLC tumor samples harboring the DNAJ-PKAc oncoprotein shows heightened phosphorylation of RBP-1; aberrant activation of RBP-1 has been shown to cause emergence of cancer-specific super enhancers. Treatment of both *DNAJB1-PRKACA* expressing human hepatoblastoma cells and patient derived FLC organoids with a CDK7 specific inhibitor (SY-5609) and CDK9 specific inhibitor (VIP-152) demonstrate suppressed RBP-1 phosphorylation and downregulation of FLC specific genes. This combination is more potent than either drug in isolation. Our daya shows that RBP-1 phosphorylation is a clinically relevant target in FLC and that dual CDK7 and CDK9 inhibition effectively suppresses expression of FLC specific genes.

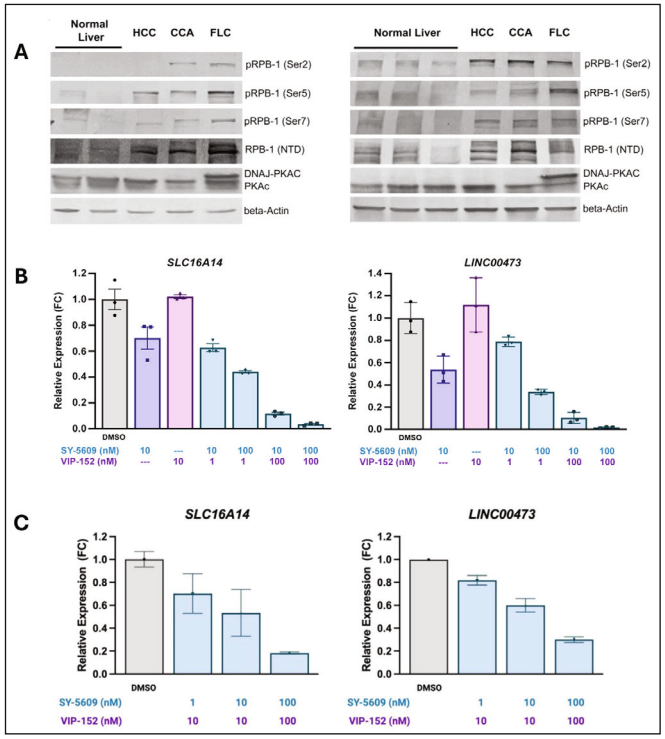


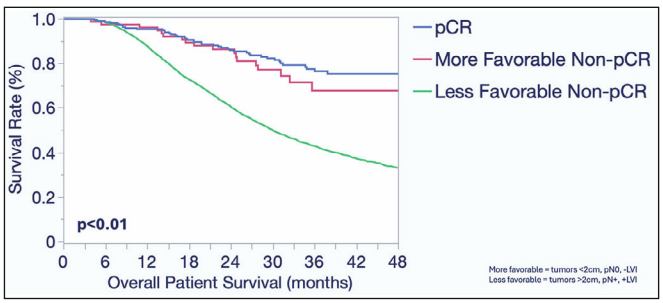
Figure 1. (A) Individual patient normal liver, HCC, CCA and FLC samples (NC1, NC2, NC3, HCC3, CCA2, FLC109 and NC4, NC5, HCC6, CCA6, FLC55) were evaluated for phosphorylated RPB-1 (Ser-2, -5, -7). The presence of the DNAJ-PKAc oncoprotein was confirmed in FLC samples but not in normal liver, HCC or CCA. (B) Expression of the FLC specific genes SLC16A14 and LINC00473 were decreased in a dose dependent manner in response to dual CDK7 and CDK9 inhibitor treatment in DNAJB1-PRKACA expressing human HCC cells and (C) FLC patient derived organoids.

P373. National Assessment of Pathologic Complete Response to Modern Neoadjuvant Therapy Regimens in Pancreatic Ductal Adenocarcinoma

Szu-Aun Long, MD[1]; Catherine G Pratt, MD[2]; Gregory C Wilson, MD[3]; Syed A Ahmad, MD[4]; Sameer H Patel, MD[5]

[1]University of Cincinnati Medical Center, Cincinnati, OH, US; [2]University of Cincinnati College of Medicine, Cincinnati, OH, US; [3]University of Cincinnati College of Medicine, Cincinnati, OH, US; [4]University of Cincinnati College of Medicine, Cincinnati, OH, US; [5]University of Cincinnati College of Medicine, Cincinnati, OH, US

INTRODUCTION: The treatment of localized pancreatic ductal adenocarcinoma (PDAC) has evolved in the past decade with the increasing use of preoperative multiagent therapeutic regimens. This has led to a small subset of patients achieving a pathologic complete response (pCR), which has been associated with better survival outcomes. However, the factors and outcomes associated with pCR remain unclear in the modern era. The aim of this study was to provide a national assessment of pCR in an era of effective *modern* multimodal neoadjuvant therapy. **METHODS:** The National Cancer Database (NCDB) was queried from 2018-2021 for non-metastatic PDAC patients who received either neoadjuvant chemotherapy or chemoradiation. Rates of pCR were assessed, and overall survival (OS) was evaluated with Kaplan-Meier modeling and compared between pCR and non-pCR groups. Cox proportional hazard regression modeling was used to assess the association between clinical parameters and OS in both pCR and non-pCR groups. **RESULTS:** 7,159 patients were included in this study, of whom 287 (4.0%) achieved pCR. Patients who achieved pCR were more likely to be younger, male, have private insurance, have clinical T1 (cT1) disease, and have *clinically* positive nodal disease. Median OS for non-pCR group was 30.1 months; the median OS for the pCR group was not reached. Treatment at an academic facility (HR, 0.40; 95% CI, 0.22-0.74) was associated with better OS in the pCR group. In the non-pCR group, having tumors >2cm (HR, 1.35; 95% CI 1.11-1.64), positive lymph nodes (HR, 1.82; 95% CI, 1.35-2.45), lymphovascular invasion (LVI) (HR, 1.22; 95% CI, 1.12-1.34) or Charlson-Deyo (CD) scores > 1 (HR, 1.19; 95% CI, 1.10-1.29) were associated with poorer OS. When stratified by clinicopathologic factors, patients with a CD score of 0 with <2cm primary tumors, negative lymph nodes, and no LVI (favorable features) had equivalent OS to the pCR group (FIGURE). Finally, in the pCR group, 62.1% of patients achieved a complete response with neoadjuvant chemotherapy alone, without radiation. **CONCLUSIONS:** Even with the use of modern neoadjuvant therapy, pCR rates remain low but are still associated with significantly improved OS compared to non-pCR patients. However, there are a subset of non-pCR patients that have equivalent survival outcomes to pCR patients. These patients have low comorbidities (CD score of 0), have smaller tumors (<2cm), are node negative, and have no LVI. Identifying factors associated with pCR and a "more favorable" non-pCR status can improve prognostication for PDAC patients and help risk-stratify their postoperative care.



P374. National Assessment of Systemic Therapy Approaches for Intrahepatic Cholangiocarcinoma

Catherine G Pratt, MD, MS[1]; Szu-Aun Long, MD[2]; Ralph C Quillin, MD[3]; Shimul A Shah, MD, MHCM[4]; Gregory C Wilson, MD[5]; Syed A Ahmad, MD[6]; Sameer H Patel, MD[7]

[1]University of Cincinnati College of Medicine, Cincinnati, OH, US; [2]University of Cincinnati, Cincinnati, OH, US; [3]University of Cincinnati College of Medicine, Cincinnati, OH, US; [4]University of Cincinnati College of Medicine, Cincinnati, OH, US; [5]University of Cincinnati College of Medicine, Cincinnati, OH, US; [6]University of Cincinnati College of Medicine, Cincinnati, OH, US; [7]University of Cincinnati College of Medicine, Cincinnati, OH, US

INTRODUCTION: In the past decade, the success of trials evaluating systemic therapy for biliary malignancies such as intrahepatic cholangiocarcinoma (iCCA) have increased potential treatment approaches. While most non-metastatic patients undergo surgery first followed by an adjuvant regimen, some patients undergo a neoadjuvant (NAT) or perioperative approach. This study aimed to evaluated treatment approaches to non-metastatic iCCA at the national level in the present era of multimodal therapy. **METHODS:** The National Cancer Database (NCDB) was queried from 2019-2021 for all patients with non-metastatic iCCA who completed surgical treatment. Patients were grouped based upon approach to systemic therapy: NAT, perioperative, or adjuvant. Perioperative systemic therapy was defined as having received chemotherapy both before and after definitive surgical treatment. Baseline characteristics, cancer-specific factors, and overall survival (OS) were evaluated. **RESULTS:** A total of 1,566 patients fit study inclusion criteria, of these 311 (19.9%) underwent NAT therapy, 180 (11.5%) had perioperative therapy, and 1,075 (68.6%) received adjuvant therapy. A NAT approach was more likely employed at academic programs and less likely utilized at comprehensive community cancer programs compared to community and integrated cancer programs. Patients with cT1 and cN0 disease were more likely to receive a surgery-first approach with adjuvant therapy whereas cT2 and cT3 (regardless of clinical nodal stage) underwent perioperative or NAT. An adjuvant approach was less likely to include multiagent chemotherapy or radiation than NAT or perioperative regimens. Among NAT patients, pathologic complete response (pCR) was achieved in only 14 (4.5%) patients. Median OS for the NAT cohort was 37.1 months (3-year 60.7%) but was not met in the group that had pCR (3-year 81.8%). Similarly, median OS for the perioperative and adjuvant treatment cohorts were not reached (3-year 68.5% and 68.3%, respectively) (**Figure**). On sensitivity analysis of survival for pCR compared to systemic therapy approaches, OS was significantly worse than the pCR, perioperative, and adjuvant groups. **CONCLUSIONS:** There remain a variety of treatment approaches for non-metastatic iCCA. The outcomes for patients using an adjuvant or perioperative therapy approach are associated with significantly improved OS. Amongst all patients that received NAT, the minority that achieved a pCR had OS comparable to the other treatment sequences. This

national analysis emphasizes the importance of an individualized treatment approach for iCCA and the need to identify patient-specific factors that increase likelihood of pCR following NAT.

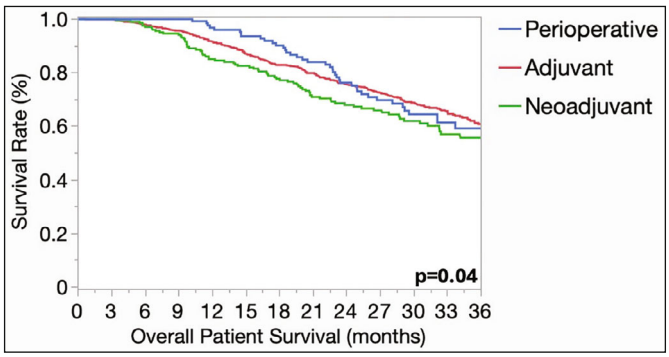


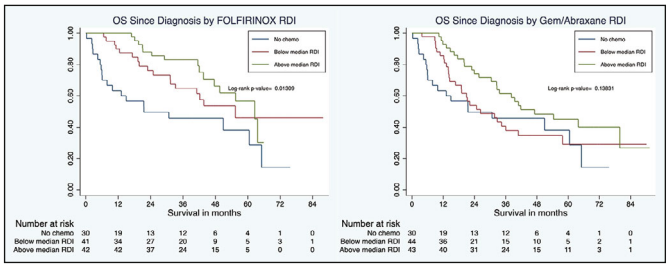
Figure. Kaplan-Meier survival analysis by systemic therapy approach.

P375. Optimizing Perioperative Management of Pancreatic Ductal Adenocarcinoma: Interplay Between Chemotherapy Relative Dose Intensity and CA 19-9

Jiage Qian, MSPH[1]; Nikhil V Tirukkovalur, MD[2]; Janie Y Zhang, MD[3]; Anwaar Saeed, MD[4]; Sebastiaan Ceuppens, MD[5]; Aatur D Singhi, MD, PhD[6]; Kenneth K Lee, MD[7]; Amer H. Zureikat, MD[8]; Alessandro Paniccia, MD[9]

[1]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [2]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [3]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [4]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [5]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [6]UPMC Medical Center, Pittsburgh, PA, US; [7]UPMC Medical Center, Pittsburgh, PA, US; [8]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [9]UPMC Medical Center, Pittsburgh, PA, US

INTRODUCTION: Chemotherapy is a key element in the multimodal treatment strategy of pancreatic ductal adenocarcinoma (PDAC). However, the optimal balance between neoadjuvant and adjuvant therapy, the ideal chemotherapy relative dose intensity (RDI) for survival, and RDI's correlation with clinical markers such as CA 19-9 remain uncertain. This study aims to evaluate the impact of RDI on survival and its relationship with CA 19-9 dynamics during treatment. **METHODS:** Retrospective analysis of 200 PDAC patients who underwent pancreatectomy between 2017 and 2021 at a single institution. Patients either received no chemotherapy or a single regimen (FOLFIRINOX or gemcitabine/nab-paclitaxel [GEM-NabP]). RDI was calculated by dividing the delivered dose intensity by the intended dose intensity, as established by randomized controlled trials, over 6 months. The total intended doses were Fluorouracil 28800 mg/m², Irinotecan 1800 mg/m², Oxaliplatin 1020 mg/m², GEM 18000 mg/m², and NabP 2250 mg/m². The median RDI was used as a threshold for survival analysis. **RESULTS:** Of the 200 patients, 30 received no chemotherapy; 83 received FOLFIRINOX; 87 received GEM-NabP. The median perioperative RDI was 72.5% for FOLFIRINOX (Fluorouracil: 68.1%; Irinotecan: 72.9%; Oxaliplatin: 70.2%) and 46.5% for GEM-NabP (GEM: 66.8%; NabP: 23.9%). Among CA 19-9 secretors, 33.1% achieved pre-operative normalization: 21.8% in patients with <median RDI, and 53.0% with >median RDI (p<0.001). The median time to normalization was 12 weeks, with no significant difference between treatment regimens (p=0.38). In the FOLFIRINOX cohort, the median RDI was 58.3% for those achieving normalization and 45.6% for those not normalizing (p=0.30). In the GEM-NabP group, the median RDI was 46.0% for those who normalized and 30.2% for those who did not (p=0.027). Patients who received ≥72.5% FOLFIRINOX had significantly better OS than those without chemotherapy (median OS: 62.6 vs. 21.5 months; HR: 0.38; 95% CI: 0.19–0.76). Those receiving <72.5% FOLFIRINOX still showed improved survival, though to a lesser extent (HR: 0.53; median OS: 55.4 months; 95% CI: 0.27–1.01). In the GEM-NabP group, patients receiving ≥46.5% RDI had a HR of 0.57 (median OS: 47.1 months; 95% CI: 0.31–1.04), compared to a HR of 0.88 for those receiving <46.5% (median OS: 26.3 months; 95% CI: 0.49–1.59). **CONCLUSIONS:** Receiving higher RDI of chemotherapy was associated with increased CA 19-9 normalization and improved OS. Our results encourage a shift toward using RDI as a more precise metric for optimizing treatment and survival outcomes.



P376. Outcomes of Incidental Gallbladder Cancer – results from a high-volume tertiary care centre in North India

Puneet Prakash, MBBS, MS, MCh[1]

[1]King George's Medical University, Lucknow, Uttar Pradesh, IN

INTRODUCTION: Gallbladder cancer (GBC) is a lethal and challenging disease. Incidentally detected gallbladder cancer (IGBC) presents a unique opportunity for early management and better outcomes. We present the institutional experience of a high-volume tertiary care center in northern India. **METHODS:** Retrospective analysis of a prospectively maintained database was performed and data of all IGBC patients between January 2014 to December 2021 was analyzed. **RESULTS:** There were 125 patients of IGBC among the 750 patients of GBC seen during the study period. Of these 125 patients, 72 (57.6%) patients were not eligible for surgery. Successful completion radical cholecystectomy (CRC) was possible in 37 (69.8%) of the 53 patients who underwent surgery. On univariate analysis, thickness of gallbladder wall 10 mm or more (p<0.001, OR 19.0, 95% CI 4.58-78.76), pathological stage (p < 0.001, OR 5.8, 95% CI 2.45-14.98) and median delay of 16 weeks or more (p<0.001, OR 17.0, 95% CI = 4.08–70.76), were associated with inoperability. However, on multivariate analysis only gallbladder wall thickness of 10 mm or more (p<0.001, AOR 17.9, 95% CI 3.24-98.78) and median delay of 16 weeks or more (p<0.001, AOR 32.33, 95% CI 6.05-172.66) remained significant. Median time to recurrence (TTR) and overall survival (OS) was not reached after a median follow up of 30 months in patients undergoing successful CRC. **CONCLUSIONS:** Successful outcomes of IGBC are dependent on several factors. Diligent workup of suspicious thickening before simple cholecystectomy for gallstone disease and timely referral of IGBC to tertiary care are the keystones for good outcomes.

Table. Multivariate analysis of determinants of operability in IGBC (N = 125).

	Parameter	P value	Adjusted Odds Ratio (AOR)	95 % confidence interval (AOR)	
				Lower	Upper
1	**Pre index surgery GB wall thickness on USG**				
a	Less than or equal to 3 mm	Ref	-	-	-
b	more than 3 mm but less than or equal to 10 mm	0.65	0.79	0.28	2.23
c	More than 10 mm	**0.001**	17.90	3.24	98.78
2	**Stage after index surgery**				
a	pT1	Ref	-	-	-
b	pT2	0.34	1.45	0.47	8.23
c	pT3	0.53	1.55	0.39	6.09
3	**Delay in CRC**				
a	Less than or equal to 8 weeks	Ref	-	-	-
b	More than 8 weeks but less than or equal to 16 weeks	**0.001**	4.53	1.60	12.80
c	More than 16 weeks	**0.001**	32.33	6.05	172.66

P377. Pancreatic fistula after distal pancreatectomy: an updated global evaluation of rates and risk factors

Liti Zhang, MD[1]; Dimitri Raptis, MD, MSc, PhD[2]; Martina Nebbia[3]; Giuseppe K Fusai, MS FRCS[4]; Cristina R. Ferrone, MD, MS, FSSO[5]
[1]Cedars-Sinai Medical Center, Los Angeles, CA, US; [2]Royal Free Hospital, London, GB; [3]Karolinska Institutet, Stockholm, SE; [4]Royal Free Hospital, London, GB; [5]Cedars-Sinai Medical Center, Los Angeles, CA, US

INTRODUCTION: Postoperative pancreatic fistula (POPF) remains the most common complication after distal pancreatectomy (DP) with rates between 15-40%. Most retrospective studies reflect on data that is 5-10 years old, without a clear consensus on risk factors. The global snapshot (PancreasGroup.org) reports modern rates and risk factors, including the effect of the global human development index (HDI). **METHODS:** Data from the snapshot of distal pancreatectomies from the International Pancreatic Surgery Outcomes Study (PancreasGroup.org) between January 2021-22 was analyzed. Only patients with data on clinically relevant POPF were included. Patients were grouped into "low/medium" or "high/very high" HDI countries. Multivariable logistic regression was performed to identify patient-specific and operative risk factors. **RESULTS:** Of 1033 patients, 963 from 52 countries were identified. Median age was 62 years (IQR 51-72) and 54% of patients were female. A majority underwent DP for malignancy (67.3%) with pancreatic ductal adenocarcinoma (PDAC) (34.8%) and neuroendocrine tumor (20.9%) being most common. Cystic lesions were the most common benign pathology (15.7%). POPF rate was 14.7%. Patients in low/medium HDI countries were younger, had lower ASA class, lower BMI, more benign pathology, and more open surgery and ICU stays compared to patients in high/very high HDI countries. However, POPF rates in the low/medium and high/very high groups were similar (12.8% vs 14.8%, p = 0.86). There was no significant difference in POPF rate when comparing stump closure techniques (10%-18.5%, p = 0.35) or pathology (16.9% benign vs 15.5% PDAC vs 19.7% other malignancy, p = 0.54). On multivariable regression analysis (n=898), BMI > 35 (OR 2.2, p = 0.02), chronic renal failure (OR 2.3, p = 0.04), spleen preserving procedure (OR 1.6, and intra- or postoperative octreotide (OR 2.0, p <0.01) were significantly associated with increased POPF. Age, sex, ASA class, cardiac disease, diabetes, preoperative chemoradiotherapy, HDI, approach (open vs minimally invasive), stump closure technique, and pathology were not significantly associated with POPF. **CONCLUSIONS:** The rate of POPF after DP remains substantial at 14.7%. BMI > 35, chronic renal failure, spleen preserving procedure, and octreotide are associated with higher incidence of POPF. Despite differences in patient-specific and operative factors, POPF rates are similar globally by HDI. Although HDI sample sizes were disproportional, knowledge of these factors can still contribute to surgical planning and developing strategies for mitigating POPF.

Table 1. Patient demographics and POPF risk factors

		Human Development Index (HDI)		
	All Patients (n=963)	**Low/Medium (n = 39)**	**High/Very High (n = 924)**	
Female, %	54.4	51.3	54.5	
Age, median (IQR)	62 (51-72)	49 (41-56)	62 (52-72)	p < 0.0001
ASA > 2, %	30.7	10.3	31.6	p = 0.004
BMI > 35, %	4.3	0.0	4.4	
Splenectomy, %	81.4	71.8	81.8	p = 0.1385
Spleen Preserving, %	18.6	28.2	18.2	
Robotic, %	9.9	0.0	10.3	p = 0.0007
Laparoscopic, %	27.2	10.3	27.9	
Open, %	62.9	89.7	61.8	
Malignancy, %	67.3	59.0	68.0	p = 0.2940
ICU Stay, %	40.5	61.5	39.6	p = 0.0075
Intermediate Unit Stay, %	28.5	38.5	28.0	p = 0.2032
Pathology, %				p = 0.0296
PDAC	34.8	20.5	35.4	
NET	20.9	15.4	21.1	
Metastatic Disease	3.5	2.6	3.6	
Other Malignancy	8.4	20.5	7.9	
Benign Cystic Lesion	15.7	20.5	15.5	
Chronic Pancreatitis	5.4	12.8	5.1	
IPMN	9.2	5.1	9.4	
Other Benign	2.1	2.6	2.1	
Stump Closure Technique, %				p = 0.0003
Hand Sewn	22.4	48.7	21.3	
Hand Sewn + Staple	2.8	2.6	2.8	
Ligament Patch	0.7	0.0	0.8	
Pancreaticoenteric Anastomosis	0.8	2.6	0.8	
Reinforced Staple	13.5	10.3	13.6	
Separate Ligation of Pancreatic Duct	2.4	7.7	2.2	
Staple	49.8	20.5	51.1	
Other	2.3	0.0	2.4	
Not reported	5.2	7.7	5.1	
POPF, %	14.7	12.8	14.8	p = 0.8630
Hand Sewn	15.3			
Hand Sewn + Staple	18.5			
Reinforced Staple	10.0			
Separate Ligation of Pancreatic Duct	17.4			
Staple	16.9			
90-Day Mortality, %	2.2	3.3	2.3	

P378. Perceived Challenges and Strategies in Managing Biliary Sclerosis: A Qualitative Study of Hepatic Arterial Infusion Pump Chemotherapy Providers

Lauren M Janczewski, MD, MS[1]; Sarah B Hays, MD[2]; Nancy Kemeny[3]; Andrea Cercek[4]; Louise Connell[5]; Michael D'Angelica, MD[6]; Michael E Lidsky, MD[7]; Ryan P Merkow, MD, MS[8]
[1]Northwestern Medicine, Chicago, IL, US; [2]University of Chicago, Chicago, IL, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Duke University Medical Center, DURHAM, NC, US; [8]University of Chicago, Chicago, IL, US

INTRODUCTION: Hepatic arterial infusion pump (HAIP) chemotherapy has shown improved outcomes for highly selected patients with colorectal liver metastases, however, biliary sclerosis is one of the most enigmatic and feared complications. With the exponential expansion of new HAIP programs there are concerns regarding increased rates of biliary sclerosis, yet little is known about its risk factors and current management strategies. The objective of this study was to identify perceptions of common challenges and strategies in managing biliary sclerosis among experienced HAIP providers. **METHODS:** Semi-structured interviews were conducted with HAIP providers through this qualitative study, including surgical and medical oncologists, who described their experiences managing biliary sclerosis. Research team dyads independently coded transcripts using an inductively developed codebook and the constant comparative approach with differences reconciled by consensus. **RESULTS:** Overall, 15 surgeons and 5 medical oncologists from 20 programs participated. Five overarching themes were identified: risk factors, patient counseling, multidisciplinary teamwork, impact on outcomes, and mitigation strategies. Common perceived risk factors identified included extensive pretreatment with chemotherapy, extensive resection and/or ablation, and the presence of hepatic steatosis (Table). For patient counseling, providers described extensive patient education and consent processes yet feel that patients remain inadequately prepared when biliary sclerosis occurs. All providers stated that establishing an experienced multidisciplinary team was critical. For impact on outcomes, providers felt that biliary sclerosis does not directly influence survival but

significantly effects future treatment options. Many providers also expressed concern regarding patient outcomes because of the rapid expansion of HAIP programs. However, several perceived mitigation strategies which could be implemented across HAIP programs to possibly improve outcomes including conservative dose reductions, liberal steroid and ursodiol use, modified dosing protocols, and performing a multidisciplinary team site visit at a high-volume institution. **CONCLUSIONS:** Although HAIP providers discussed challenges in managing biliary sclerosis, common risk factors, patient counseling approaches, and mitigation strategies were identified. These data may inform the implementation of interventions across HAIP programs through shared strategies and potentially reduce biliary sclerosis risk.

Table. Illustrative Quotes for Themes Described by HAIP Providers.

Theme	Illustrative Quotes
Risk Factors	"It's a combination of host factors that I think contribute to [biliary sclerosis]. I haven't been able to pinpoint it, but I've noticed that patients who have inhospitable livers, who have treatment issues related to steatohepatitis, who have some baseline, fatty liver disease tend to have a higher risk of having biliary sclerosis." **Surgeon #6, High-Volume Program** "My preconceived hypothesis is that it's the people that have had more extensive pre-treatment are more likely to get [biliary sclerosis], although that is yet to be proven...Extensive dissection on the bile ducts can probably predispose people to [biliary sclerosis] and extensive liver surgery probably also brings increases risk, but these are all sort of anecdotes." **Surgeon #7, High-Volume Program**
Patient Counseling	"No, I don't [think patients are prepared]. Just like anybody with biliary disease they're never prepared for what the extent of involvement there is in trying to go through multiple stent placements and things like that. Thankfully it is rare, but the people that I've had to put through it, it was just very hard on them, emotionally and physically. But even if they knew it was coming, no words would have prepared them for it, nor would any words talk them out of having [HAIP] done." **Surgeon #1, Low-Volume Program** "Patients are desperate for hope when they come in that situation, especially for the cancers that we deal with as hepatobiliary surgical oncologists. So, a lot of times, my sense is that patients are just trying to think of the positive, the hope, the option for surgery that they're potentially candidates. They're grateful for that. They don't really think about the potential life-threatening issues so there's a psychosocial element to it, and there's also a patient counseling element to it. You can never be too busy to see a patient twice before surgery and that's something that has stuck with me through practice." **Surgeon #6, High-Volume Program**
Multidisciplinary Teamwork	"You really do need a medical oncologist who's going to be a champion and advocate, and I will tell you, my own personal experience here has been maybe not so much the oncologists, but the APP's in med onc, the infusion nurses, and the pharmacists, they kind of viewed this as a surg-onc program, i.e. my program. And they were like, we have to do this program now because the surgeons want it. I kept trying to show them the data. I gave multiple PowerPoint presentations. I said, guys, this is not my program. I'm not doing this for me, this doesn't do anything for me to put pumps in. But we think that, based on the data this is good for patients. I tried to explain that to them multiple times, I still to this day do not feel like the infusion nurses and or the APPs have fully embraced the program and that's something I think we really need to work on." **Surgeon #4, Low-Volume Program** "I think that's the key, the multidisciplinary approach. Fortunately, in our program, we have a great well-functioning multidisciplinary team. We have special dedicated coordinator for HAI pumps that work with the medical oncologists for the evaluation in addition to what we do as surgeons in clinic when we first meet the patients and that would be a recommendation that I can make to any center that is thinking about embarking into this program. And then the rest is like everything else, it's a learning curve. I think this whole effort of putting together a national consortium with routine meetings with HAIP centers presenting cases sort of as a tumor board is very helpful." **Surgeon #11, Low-Volume Program**
Impact on Outcomes	"I think [biliary sclerosis] can definitely affect long-term outcomes. Whether or not it affects their cancer specific survival, I'm not totally aware of that, but it definitely affects their ability to receive systemic and pump chemotherapy. I think most patients should be made aware that managing biliary sclerosis can come in many different flavors. Some are easily managed with occasional dilations, some are more fulminant and multifocal, and require procedure after procedure and indwelling stents, and readmissions for cholangitis, and it's a long roller coaster that they're on." **Surgeon #5, Low-Volume Program** "I think that it's been an interesting experiment. We'll see if this backfires This is such a rapid expansion from the couple centers that were doing [HAIP] to now diffusing it out to the world. And it's like, okay, are we moving really fast? And that's a good thing, or are we moving really fast? And then we're going to realize we moved a little too fast. We didn't set minimum standards that everybody can agree on. We'll find out." **Surgeon #3, High-Volume Program**
Mitigation Strategies	"I'm very, very quick to dose reduce the floxuridine for even a hint of toxicity. Even if it doesn't meet the 1.2 times reference value range. I am just very, very cautious about damaging their livers, especially in the adjuvant setting, but I'm cautious in general. And anytime someone does have the 1.2 times the reference value, I'm always dose reducing their floxuridine and I don't ever return to full dose after that." **Medical Oncologist #2, High-Volume Program** "We've been very liberal with usage of steroids. So, on the off-cycle refills with heparin we often will re-dose with steroids, or even give systemic steroids following the dose reductions that are recommended, and the holding of doses as needed have mostly been our best mitigation strategies." **Surgeon #1, Low-Volume Program** "I think we have been a little bit more nimble in terms of attenuating the dose while giving steroids through the pump, for example, or prophylactically putting patients on Actigall a lot sooner. I suspect that those practice patterns will reflect in reduced biliary sclerosis rates maybe, 6 months to a year down the road. We're just starting to adopt those things." **Surgeon #6, High-Volume Program** "One thing that Dr. [X] and others did before they started their [HAIP] programs was do a site visit at [our institution] so that everyone at their program could get training before actually treating patients with HAIP. People haven't really been doing that as much anymore prior to opening their programs and I do have concerns that it'll affect the patients." **Medical Oncologist #1, High-Volume Program** "We looked over our data and we saw that a majority of our patients were having significant dose reductions and/or holds after the 1st couple of cycles, so people are often getting down to a 50% reduction. I mean the numbers and dosing for this is fairly arbitrary. It's not super well established, and that really hasn't been evaluated with the advent of modern systemic therapeutics and other targeted biologics. So, we said, 'Hey, we can always give more so why don't we just start at 50%, and if they're responding after 2 months, then why would we give more?' And so with that, we've shown that we're able to give many more consecutive, uninterrupted doses. No significant dose reductions. We thought it was important to report this strategy, because we were converting more patients with a higher burden of disease from unresectable to resectable." **Surgeon #15, High-Volume Program**

*High- vs Low-Volume Programs defined as those which place more or less than 10 HAI pumps annually, respectively.

P379. Pharmacodynamics of intra-arterial vs. intravenous gemcitabine in locally advanced pancreatic cancer: results of a phase III randomized clinical trial

Emmanuel Zervos, MD[1]; Paula Novelli, MD[2]; Amer H. Zureikat, MD[3]; Michael Pishvaian, MD, PhD[4]; Kenneth Meredith, MD[5]; Hassan Hatoum, MD[6]; Reza Nazemzadeh, MD[7]; Sandeep Laroia, MD[8]; Ramtin Agah, MD[9]

[1]East Carolina University, Greenville, NC, US; [2]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [3]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [4]Johns Hopkins University School of Medicine, Washington D.C., DC, US; [5]Sarasota Memorial Health Care System, Sarasota, FL, US; [6]University of Oklahoma College of Medicine, Oklahoma City, OK, US; [7]Levine Cancer Institute, Charlotte, NC, US; [8]University of Iowa Medical Center, Iowa City, IA, US; [9]RenovoRx, Los Altos, CA, US

INTRODUCTION: Localized double balloon catheter-mediated, intra-arterial delivery of gemcitabine (IAG) has been shown to effect superior perivascular concentration of chemotherapy compared to other delivery systems in animal models. In patients with locally advanced pancreatic cancer (LAPC) receiving IAG as part of a Phase III prospective randomized trial (TIGeR-PaC), we sought to validate these findings in human subjects. **METHODS:** PK analyses were performed on 19 subjects from 6 sites in the TIGeR-PaC study: 11 receiving IAG with the RenovoCath® dual balloon catheter at 1000 mg/m2 over 20 minutes and 8 receiving intravenous gemcitabine (IVG) (5 at 1000 mg/m2, 2 at 800 mg/m2, 1 at 500 mg/m2) over 30 minutes. IAG target treatment arteries were either the superior mesenteric artery (SMA) (n=5) or branches of the celiac axis (n=6). At T = -5, 10, 15, 20, 30, 40, 60, and 90 minutes from the onset of infusion, 2 mL of blood was collected in heparinized tubing containing 25 mcg/mL of tetrahydrouridine. Plasma from each sample was frozen and assayed in a single reference lab. Maximum plasma drug concentration (C_{max}) and the area under the drug plasma concentration curve (AUC) based on the terminal phase were compared between the two groups; for these dose-dependent parameters, only participants who received 1000 mg/m2 gemcitabine (IAG, N=11; IVG, N=5) were included in the comparison analysis. **RESULTS:** AUC was significantly lower with IAG compared to IVG (4.99 vs 9.97 mcg/ml, P = 0.019). Peak plasma gemcitabine concentration was also lower with IAG vs IVG (12.9 vs 14.6 mcg/mL, respectively) despite a 50% higher drug concentration during IAG vs IVG (1000 mg/m2 infused over 20 minutes vs. 30 minutes, respectively) (Table). There was no difference in plasma levels between IAG treatment sites (SMA vs celiac axis). **CONCLUSIONS:** In this analysis, localized, dual-balloon catheter-mediated IAG resulted in lower systemic levels compared to IVG while providing increased local potency. As such, IAG may be beneficial in decreasing chemotherapy-related systemic side effects. Correlative patient reported outcomes in patients receiving IAG supports this approach as an alternative for LAPC patients who are having difficulty tolerating more traditional systemic regimens. Clinical trial information: NCT03257033.

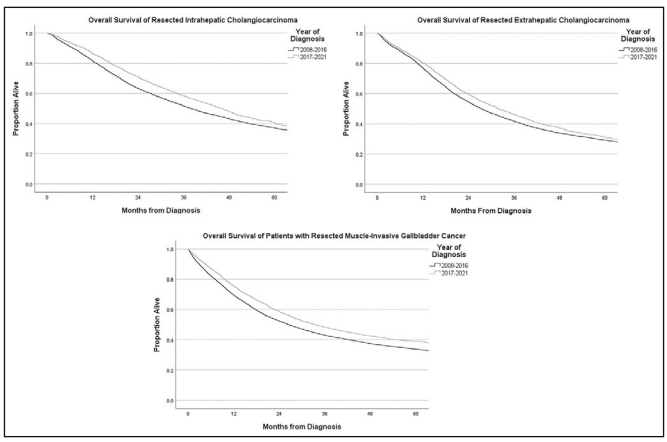
P380. Practice Patterns and Outcomes for Perioperative Systemic Therapy for Biliary Tract Malignancies in the Post-BILCAP Era: A National Cancer Database Analysis

Thomas L Sutton, MD, MCR[1]; Teodora Dumitra[2]; Timothy DiPeri, MD[3]; Rayne Peerenboom[4]; Alexandra Gangi, MD, FSSO[5]

[1]Cedars-Sinai Medical Center, Los Angeles, CA, US; [2]Cedars-Sinai Medical Center, Los Angeles, CA, US; [3]Cedars-Sinai Medical Center, Los Angeles, CA, US; [4]Cedars-Sinai Medical Center, Los Angeles, CA, US; [5]Cedars-Sinai Medical Center, Los Angeles, CA, US

INTRODUCTION: In 2017, the results of the BILCAP trial for resected biliary tract cancers (BTCs) were released, demonstrating improved overall survival (OS) for patients treated with adjuvant capecitabine compared to placebo. The extent to which practice patterns have changed in the post-BILCAP era is unstudied, as are the downstream effects on OS. **METHODS:** The National Cancer Database was queried for patients with nonmetastatic intra/extrahepatic cholangiocarcinoma and muscle-invasive gallbladder cancer undergoing surgical resection from 2008-2021. Receipt of adjuvant systemic chemotherapy was evaluated, and multivariable logistic regression was performed to identify factors associated with receipt of adjuvant systemic therapy in the post-BILCAP era. OS was evaluated with Kaplan-Meier analysis and multivariable Cox proportional hazards modeling. **RESULTS:** 38221 patients were identified (n=21501 pre-2017 and n=16720 post-2017; n=17676 gallbladder adenocarcinoma, n=11177 extrahepatic cholangiocarcinoma, n=9368 intrahepatic cholangiocarcinoma). Adjuvant systemic therapy use increased from 37.5% pre-2017 to 48.1% post-2017 (P<0.001). Of patients receiving adjuvant chemotherapy with identifiable regimens (n=17543), 50.5% were single-agent regimens pre-2017, with a decrease to 49.0% post-2017 (P<0.001). Median follow-up was 100.5 months for the pre-2017 cohort and 38.5 months for the post-2017 cohort. Median OS increased across disease sites for the post-2017 era, including for gallbladder (33.4 vs. 26.4 months, *P<0.001),* intrahepatic cholangiocarcinoma (45.9 vs. 37.9 months, *P<0.001)*, and extrahepatic cholangiocarcinoma (31.7 vs. 27.3 months, *P<0.001).* On multivariable analysis adjusting for age, comorbidities, margins, stage, and primary site, both receipt of adjuvant chemotherapy (HR 0.75, P<0.001) and diagnosis in 2017 or later (HR 0.85, P<0.001) were independently associated with improved OS. On multivariable logistic regression, factors independently

associated with receiving adjuvant systemic therapy in the post-BILCAP era were later year of diagnosis (OR 1.08/year), R1 surgical margins (OR 1.36), nodal metastases (OR 2.83), and highest income quartile (OR 1.22), while a gallbladder primary (OR 0.77), nonprivate insurance (OR 0.63), Charlson-Deyo comorbidity score ≥3 (OR 0.58) were independently associated with lower odds (all P<0.001). **CONCLUSIONS:** The use of adjuvant therapy for BTCs has measurably increased, with concordant improvements in OS across all disease sites. However, a persistent gap between treatment realities and guideline-concordant care exists.



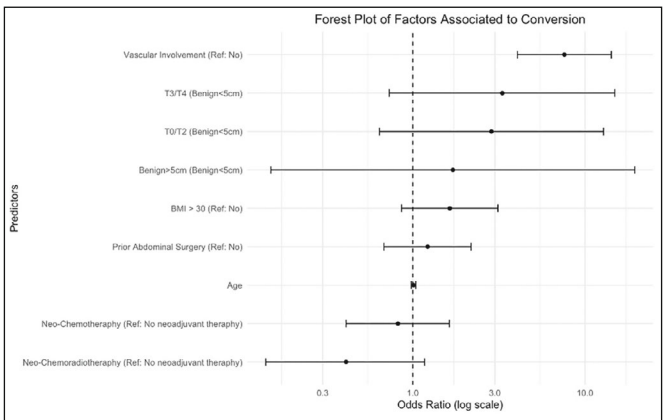
P381. Predictors and Outcomes of Conversion from Robotic to Open Pancreatoduodenectomy: A Large Multicenter Analysis

Ricardo E. Nunez-Rocha, MD[1]; Samy Castillo-Flores, MD[2]; Amr I. Al Abbas, MD[3]; Amudhan Kannan, MD[4]; Sarah Hays, MD[5]; Cristal Espinosa, MS[6]; Syed Mehdi, MBBS[7]; Kristen Ranson, MS[8]; Aram Rojas, MD[9]; Adam Tcharni, BS[10]; Brian A. Boone, MD[11]; Alessandro Paniccia, MD[12]; Carl Schmidt, MD[13]; Mark Talamonti[14]; Herbert J Zeh, MD[15]; Amer H. Zureikat, MD[16]; Melissa Hogg, MD, FSSO[17]; Patricio M. Polanco, MD[18]

[1]University of Texas Southwestern Medical Center, DALLAS, TX, US; [2]University of Texas Southwestern, Dallas, TX, US; [3]UT Southwestern Medical Center, Dallas, TX, US; [4]University of Texas Southwestern Medical Center, DALLAS, TX, US; [5]NorthShore University HealthSystem, Evanston, IL, United States, Evanston, IL, US; [6]West Virginia University, Morgantown, WV, US; [7]NorthShore University HealthSystem, Evanston, IL, US; [8]West Virginia University, Morgantown, WV, US; [9]NorthShore University HealthSystem, Evanston, IL, US; [10]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [11]West Virginia University, Morgantown, WV, US; [12]UPMC Medical Center, Pittsburgh, PA, US; [13]West Virginia University, Morgantown, WV, US; [14]NorthShore University HealthSystem, Evanston, IL, US; [15]UT Southwestern Medical Center, Dallas, TX, US; [16]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [17]Northshore University Health System, Evanston, IL, US; [18]University of Texas Southwestern Medical Center, Dallas, TX, US

INTRODUCTION: Minimally invasive pancreatoduodenectomies (PD) aim to reduce postoperative complications while improving long-term outcomes. However, conversion rates remain a challenge. This study evaluates factors associated with conversion in pancreatoduodenectomy and its impact on perioperative and long-term outcomes. **METHODS:** This was a retrospective review of a prospectively collected database of patients who underwent PD at 4 high-volume centers. Patients were divided into three groups by surgical approach. Demographics, preoperative characteristics, intraoperative, and postoperative outcomes, overall survival (OS), and disease-free survival (DFS) were collected. Statistical tests included chi-square, Mann-Whitney U, and Kruskal-Wallis. Multivariable logistic regression identified predictors of conversion. Cox hazard models were used for survival analysis in patients with malignant histology. **RESULTS:** A total of 2,175 patients were included: 845 (38.9%) robotic, 55 (2.5%) conversion, and 1275 (58.6%) open. Converted cases had higher BMI (p=0.002), tumor size (p=0.001), R1 margins (p=0.001), and vascular involvement (p<0.001). Major complications (p<0.001) and reoperations (p=0.02) were also higher. Converted cases had a higher 30- (p=0.004) and 90-day mortality (p=0.03). DFS was shorter in converted cases (9 months) vs. robotic (12.8) and open (15) (p<0.001), while OS was worse in converted (17.0 months), with robotic yielding the best OS (35.8; p<0.001).

Cox model showed vascular involvement increased conversion risk (OR: 7.59; 95% CI: 4.05–14.2;0.001). Neoadjuvant chemo- (HR: 1.49; p=0.04) and chemoradiotherapy (CRT) (HR: 1.71; p=0.04) reduced DFS. Adjuvant therapy did not affect DFS, while R1 resection decreased it (HR: 1.93;0.001). Conversion (HR: 1.48; 95% CI: 0.97–2.26; p=0.06) and T3/T4 category (HR: 1.18; p=0.07) showed a slight association with worse OS. Local/distal recurrence increased mortality risk by 46% (HR: 1.46;0.001), and R1 by 69% (HR: 1.69; 95% CI: 1.38-2.06;0.001). Adjuvant chemo- and CRT lowered mortality risk by 27% (HR: 0.73; 95% CI: 0.60-0.89; p=0.002) and 41% (HR: 0.59; 95% CI: 0.45-0.77;0.001), respectively. **CONCLUSIONS:** Tumor vascular involvement significantly increased the likelihood of conversion. Conversion is associated with higher morbidity, mortality, and decreased DFS and OS, likely due to higher rates of R1 resections. Despite this, the robotic approach yielded the best OS. These findings underscore the importance of careful patient selection and preoperative planning to improve postoperative and long-term outcomes.



Factors associated with conversion

Factors	OR (95% CI)	p-value
Age	1.01 (0.98–1.03)	0.54
Prior abdominal surgery (Ref: No)	1.22 (0.68–2.18)	0.50
BMI >30 (Ref: ≤30)	1.64 (0.86–3.11)	0.13
Neoadjuvant chemotherapy (Ref: No neoadjuvant therapy)	0.82 (0.41–1.62)	0.57
Neoadjuvant chemoradiotherpy (Ref: No neoadjuvant therapy)	0.40 (0.14–1.16)	0.09
Histology group		
Benign (<5cm)	Reference	
Benign (>5cm)	1.71 (0.15-19.45)	0.6
Malignant T0/T2	2.86 (0.63-12.8)	0.16
Malignant T3/T4	3.31 (0.73-14.89)	0.11
Vascular involvement (Ref: No)	7.59 (4.05-14.22)	**<0.001***

Figure 1. Forest plot of factors associated with conversion from robotic to open pancreatoduodenectomy.

P382. Preoperative nomogram based on DUPAN-2, tumor size, and neutrophil/lymphocyte ratio (DIZNEY score) for deciding the appropriate time of radical resection for pancreatic cancer

Hiromitsu Maehira[1]; Nobuhito Nitta[2]; Hajime Ishikawa[3]; Takeru Maekawa[4]; Takeshi Sonoda[5]; Reiko Otake[6]; Soichiro Tani[7]; Katsushi Takebayashi[8]; Masatsugu Kojima[9]; Sachiko Kaida[10]; Toru Miyake[11]; Masaji Tani[12]

[1]Department of Surgery, Shiga University of Medical Science, Otsu, Shiga, JP; [2]Department of Surgery, Shiga University of Medical Science, Otsu, Shiga, JP; [3]Department of Surgery, Shiga University of Medical Science, Otsu, Shiga, JP; [4]Department of Surgery, Shiga University of Medical Science, Otsu, JP; [5]Department of Surgery, Shiga University of Medical Science, Otsu, Shiga, JP; [6]Department of Surgery, Shiga University of Medical Science, Otsu, Shiga, JP; [7]Department of Surgery, Shiga University of Medical Science, Otsu, Shiga, JP; [8]Department of Surgery, Shiga University of Medical Science, Otsu, Shiga, JP; [9]Department of Surgery, Shiga University of Medical Science, Otsu, Shiga, JP; [10]Department of Surgery, Shiga University of Medical Science, Otsu, Shiga, JP; [11]Department of Surgery, Shiga University of Medical Science, Otsu, Shiga, JP; [12]Department of Surgery, Shiga University of Medical Science, Otsu, Shiga, JP

INTRODUCTION: Survival outcome after radical resection for pancreatic cancer (PC) became improved owing to the advanced technique and chemotherapy. However, we sometimes encountered the patients with early recurrence, subsequently poor survival than who received only chemotherapy.

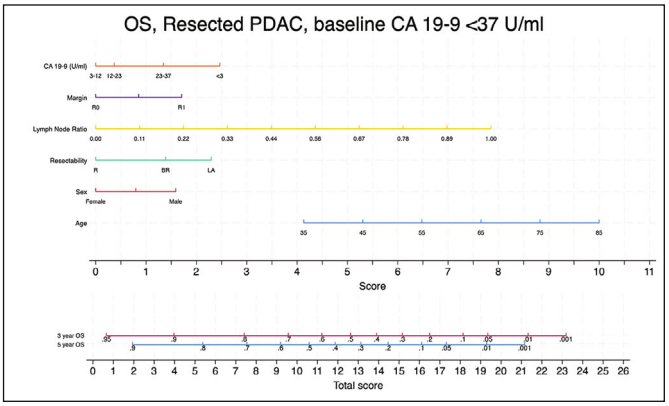
This study conducted the identification of risk factor of early recurrence after radical resection for PC including patients with neoadjuvant therapy. **METHODS:** The medical records of patients who underwent radical resection for PC from 2011 to 2022 were retrospectively reviewed. Early recurrence (ER) was defined as tumor recurrence within 6 months after surgery. The variables which can evaluate preoperatively were compared between ER and non-ER groups. **RESULTS:** A total of 146 patients were enrolled in this study. Thirty-six patients (24.7%) had early recurrence. The prevalence of abnormal value of DUPAN-2 (p=0.019) and prevalence of neutrophil/lymphocyte ratio ≥4 (p=0.007) were higher, and tumor size (TS) was larger (p<0.001) in the ER group. Multivariate analysis showed that abnormal value of **D**UPAN-2 (HR, 2.002; p=0.041), tumor s**iz**e (HR, 1.035; p=0.003), and **ne**utrophil/l**y**mphocyte ratio 4 (HR, 2.546; p=0.016) were independent risk factors of the early recurrence. A nomogram (DIZNEY score) was constructed using these three factors. The incidence of early recurrence was significantly associated with DIZNEY score (Cochran-Armitage test, p < 0.001). The median survival time was significantly shorter in the patients with DIZNEY score <,serif">60 (15 months vs 39 months; p<0.001). Similar result was observed in the patients with neoadjuvant therapy (17 months vs 60 months; p=0.006). **CONCLUSIONS:** DIZNEY score may predict early recurrence and poor survival outcome after radical resection for PC. It may be better to reconsider whether the radical resection brings about a good outcome or not for the patients with DIZNEY score <60.

P383. Prognostic Nomogram for CA19-9 Non-Secretors with Resected Pancreatic Ductal Adenocarcinoma

Jurgis Alvikas[1]; Ahmed Hamed[2]; Nikhil Tirukkovalur[3]; William Bachman[4]; Sebastiaan Ceuppens, MD[5]; Adam Tcharni[6]; Ellie Qian[7]; Asmita Chopra[8]; Genia Dubrovsky[9]; Amer H. Zureikat, MD[10]; Alessandro Paniccia[11]

[1]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [2]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [3]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [4]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [5]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [6]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [7]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [8]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [9]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [10]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [11]UPMC Medical Center, Pittsburgh, PA, US

INTRODUCTION: CA19-9 is the most commonly utilized biomarker for patients with pancreatic ductal adenocarcinoma (PDAC). Its level at diagnosis and its dynamic changes during systemic treatment serve as strong prognostic indicators and influence therapeutic decisions. However, a subset of patients with PDAC show no elevation of serum CA19-9 (<37 U/ml) at the time of diagnosis, complicating both accurate biological classification and assessment of their response to treatment. This study aims to investigate survival differences within a cohort of CA19.9 non-secretors (diagnostic level <37 U/mL) and to develop a prognostic nomogram for patients undergoing perioperative chemotherapy and surgical resection. **METHODS:** Retrospective review of patients with PDAC who had pre-treatment CA19-9 <37 U/ml who underwent curative-intent resection at a single institution between 2009 to 2022. Patients with metastatic disease were excluded. Demographic, comorbidities, neoadjuvant therapy, operative variables, pathological findings and postoperative outcomes were collected and analyzed. Primary outcome of interest was overall survival (OS) from the time of diagnosis. CA 19-9 level at diagnosis was categorized into quartile (<3U/mL, 3-12 U/mL, 12-23U/mL and 23-37 U/mL) A multivariable-adjusted Cox proportional hazard model was developed and used to construct a prognostic nomogram. **RESULTS:** A total of 274 patients were included in the analysis. Baseline characteristics were compared across the four CA19-9 quartiles, revealing comparable groups in terms of age, gender, tumor size, performance status, neoadjuvant and adjuvant treatments, and pathologic factors (including T and N stage, lymphovascular invasion, perineural invasion, SMAD4, and KRAS mutation status). The final multivariable-adjusted model identified significant predictors of outcomes: age (HR 1.02, p=0.002), sex (female, HR 0.71, p=0.04), resectability (borderline resectable, HR 1.35, p=0.087; locally advanced, HR 1.65, p=0.065), lymph node ratio (HR 5.52, p=0.001), surgical margin status (R1, HR 1.45, p=0.028), and CA19-9 levels (3-12 U/ml, HR 0.58, p=0.017; 12-23 U/ml, HR 0.63, p=0.04; 23-37 U/ml, HR 0.78, p=0.24). Importantly, patients with CA19-9 levels <3 U/ml had the poorest survival (median OS 23.9 months, log-rank p=0.01). **CONCLUSIONS:** This study identifies age, sex, resectability, lymph node ratio, surgical margin status, and pre-treatment CA19-9 levels as the most significant predictors of overall survival in patients with resected PDAC and low serum CA19-9 levels (<37 U/mL). Notably, patients with CA19-9 levels below 3 U/mL demonstrated the poorest survival outcomes, highlighting a subgroup that may require distinct therapeutic considerations.



P384. Prognostic Value of Preoperative CA19-9 in Patients with Pancreatic Cancer

Pratik Chandra, MD[1]; Robert J. Torphy, MD[2]; Joanne F Chou, MPH[3]; Mithat Gonen, PhD[4]; Kevin Soares, MD[5]; Vinod Balachandran, MD[6]; Jeffrey Drebin, MD PhD[7]; Michael D'Angelica, MD[8]; T. Peter Kingham, MD[9]; Alice C Wei, MD MSc[10]; William R Jarnagin, MD[11]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan Kettering Cancer Center, New-York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US; [11]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Patient selection for upfront resection of pancreatic ductal adenocarcinoma (PDAC) relies heavily on imaging-based anatomical factors, while biological determinants of resectability are ill-defined. This study aimed to assess preoperative CA19-9 levels as a marker of 'biological' resectability and to define the optimal CA19-9 threshold for recurrence in anatomically resectable PDAC. **METHODS:** Patients who underwent upfront resection for PDAC between 2011-2022 with preoperative CA19-9 were included. Patients with elevated preoperative bilirubin (> 2 mg/dL) and CA19-9 non-producers (< 5 U/mL) were included. Recurrence-free survival (RFS) and overall survival (OS) were calculated from the time of resection and estimated using Kaplan-Meier methods. Preoperative CA19-9 inflection points optimized for RFS were determined using the decision tree approach in 3 separate groups: unobstructed head tumors (bilirubin < 2 mg/dL), obstructed head tumors (bilirubin ≥ 2 mg/dL), and body/tail tumors. The model assessed CA19-9 as a continuous variable, CA19-9 producer vs. non-producer, and demographics. **RESULTS:** 765 patients met inclusion criteria, of which 508 were included in our training cohort - 204 (40%) had unobstructed head tumors, 167 (33%) had obstructed head tumors, and 136 (27%) had body/tail tumors. The median age was 70, and 54% were male. 375 (74%) underwent pancreaticoduodenectomy. Median preoperative CA19-9 was 104 U/mL (IQR: 29, 318), and 58 (11%) were CA19-9 non-producers. Overall median RFS and OS were 14 (95% CI: 12, 15) and 31 (95% CI: 28, 34) months, respectively. The decision tree approach identified inflection points for preoperative CA19-9 and RFS of < 30 U/mL, 30-431 U/mL, and > 431 U/mL in unobstructed head tumors. Median RFS for low (< 30 U/mL), medium (30-431 U/mL), and elevated CA19-9 (> 431 U/mL) were 21 (95% CI: 13, 58), 14 (95% CI: 12, 21), and 11 (95% CI: 7, 19) months, respectively. For body/tail tumors, the cutoff was 117 U/mL, and median RFS for those with a low (< 117 U/mL) or elevated (> 117 U/mL) CA19-9 were 16 (95% CI: 13, 28) and 9 (95% CI: 6, 11) months, respectively. In patients with biliary obstruction (bilirubin > 2 mg/dL), we found no significant association of CA19-9 with RFS (HR 1 [0.95, 1.04], p = 0.83) and OS (HR 0.99 [0.95, 1.03], p = 0.71). **CONCLUSIONS:** In this cohort, preoperative CA19-9 levels were significantly associated with RFS

in unobstructed pancreatic head and body/tail tumors, although the optimal cutoff values differed between the two. The prognostic value of CA19-9 was lost in the presence of jaundice. Validation in a larger cohort is needed.

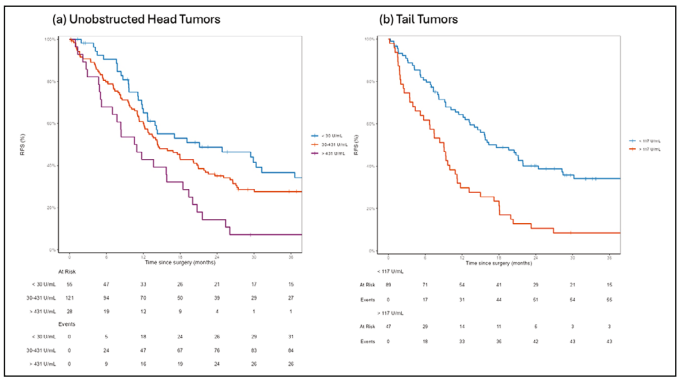


Figure. Kaplan-Meier Curves for RFS in Unobstructed Head Tumors (a) and Tail Tumors (b)

P385. Recurrence Patterns for Pancreatic Adenocarcinoma Treated with Upfront Surgical Resection Versus a Neoadjuvant Approach: A Systematic Review and Meta-analysis

Akie Watanabe[1]; Lucas Streith[2]; Peter Kim[3]; Bassam Sonbol[4]; Christina Wu[5]; Tanios Bekaii-Saab[6]; Jonathan Ashman[7]; William Rule[8]; Terence T Sio[9]; Nabil Wasif, MD, MPH[10]; Chee-Chee H. Stucky, MD[11]; Zhi Ven Fong, MD, MPH, DrPH[12]

[1]University of British Columbia, Vancouver, BC, CA; [2]University of British Columbia, Vancouver, BC, CA; [3]University of British Columbia, Vancouver, BC, CA; [4]Mayo Clinic, Phoenix, AZ, US; [5]Mayo Clinic, Phoenix, AZ, US; [6]Mayo Clinic, Phoenix, AZ, US; [7]Mayo Clinic, Phoenix, AZ, US; [8]Mayo Clinic, Phoenix, AZ, US; [9]Mayo Clinic, Phoenix, AZ, US; [10]Mayo Clinic, Phoenix, AZ, US; [11]Mayo Clinic Arizona, Phoenix, AZ, US; [12]Mayo Clinic Arizona, Phoenix, AZ, US

INTRODUCTION: Neoadjuvant therapy (NAT) has been increasingly used in the treatment of pancreatic adenocarcinoma (PDAC) to select for favorable biology and optimize survival after surgical resection. However, it is unclear if NAT reduces postoperative distant recurrence (DR), which could necessitate better locoregional control with radiation therapy (RT). This meta-analysis aims to investigate the impact of NAT on rates of locoregional recurrence (LR) and DR compared to upfront surgical resection (UFS) in PDAC patients. **METHODS:** We identified randomized controlled trials (RCTs) and observational studies reporting pancreatic recurrence patterns from 2013-2023 (PROSPERO CRD 42023397000). Random-effects models were used to measure the impact of UFS versus NAT on the relative risk (RR) of LR and DR. A sensitivity analysis was performed after stratifying for resectability criteria and separately for NAT with and without RT. **RESULTS:** Fourteen studies met inclusion criteria, yielding a total of 3,577 resectable or borderline resectable PDAC patients. One RCT and 13 cohort studies were included. On meta-analysis, NAT significantly reduced LR (RR 0.73, 95% CI 0.60-0.89, p=0.002, $I2$= 41%) but was not associated with reduced DR (RR 0.98, 95% CI 0.92-1.06, p=0.67, $I2$=7%) when compared to UFS. More specifically, there were no differences in liver (RR 0.85, 95% CI 0.66-1.08, p=0.18, $I2$=47%) or lung recurrence (RR 1.03, 95% CI 0.79-1.34, p=0.84, $I2$=0%) for patients who had NAT versus UFS. Sensitivity analyses stratifying by upfront versus borderline resectable disease showed similar results. Compared to UFS, NAT with RT significantly reduced the risk of LR (RR 0.79, 95% CI 0.63-0.98, p=0.04, $I2$=48%), whereas NAT without RT did not (RR 0.71, 95% CI 0.41-1.24, p=0.24, $I2$=0%). In contrast, both NAT with RT (RR 0.98, 95% CI 0.90-1.06, p=0.58, $I2$=0%) or without RT (RR 0.85, 95% CI 0.54-1.33, p=0.47, $I2$=48%) were not associated with reduced DR. There was no significant publication bias amongst all meta-analysis models (Egger's tests p>0.05). **CONCLUSIONS:** The use of NAT to better select patients with PDAC for surgical resection was not associated with reduced DR compared to UFS. NAT with RT improved locoregional control but had no impact on DR when compared to UFS. Future efforts need to focus on developing better systemic treatments to combat PDAC's poor prognosis.

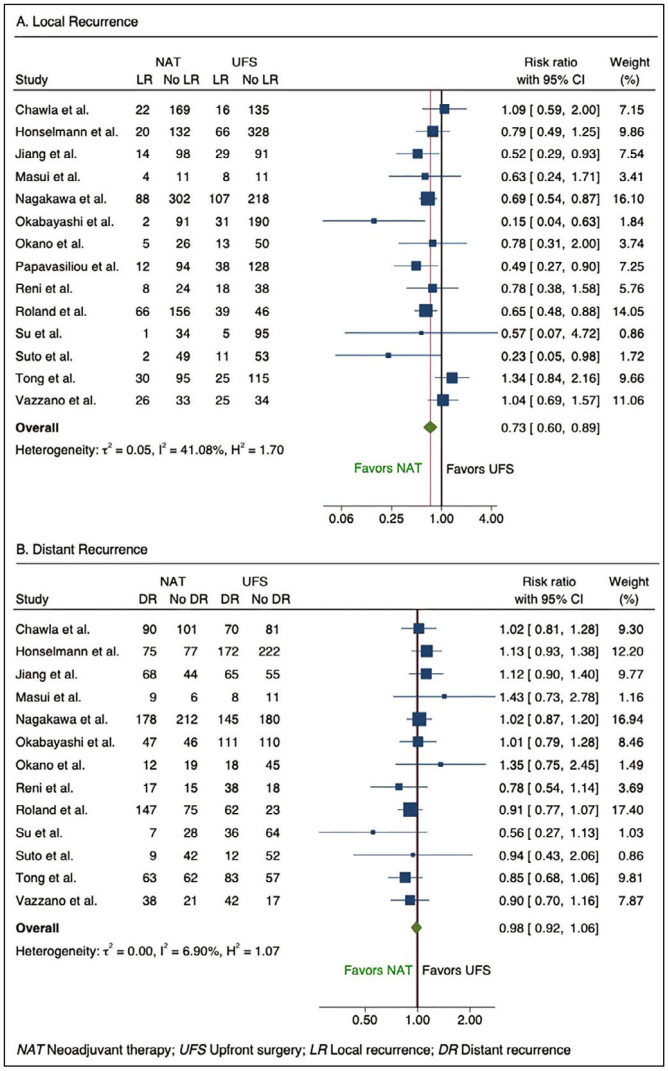


Figure 1. Impact of NAT versus UFS on A) local recurrence and B) distant recurrence in patients with upfront and borderline resectable pancreatic cancer

P386. Response After Neoadjuvant Therapy for Pancreatic Neuroendocrine Tumors

Makayla Slaby, BS[1]; Kaitlyn Nimmer, BA[2]; Naveen M Kulkarni[3]; Brian Di Giacinto, DO[4]; Tamara Giorgadze[5]; Kathleen Christians[6]; Michael I Holt[7]; Douglas B Evans, MD[8]; Alexandria I Phan, MD[9]; Callisia N. Clarke, MD, MS, FSSO[10]

[1]Medical College of Wisconsin, Milwaukee, WI, US; [2]Medical College of Wisconsin, Milwaukee, WI, US; [3]Medical College of Wisconsin, Milwaukee, WI, US; [4]Medical College of Wisconsin, Milwaukee, WI, US; [5]Medical College of Wisconsin, Milwaukee, WI, US; [6]Medical College of Wisconsin, Milwaukee, WI, US; [7]Medical College of Wisconsin, Milwaukee, WI, US; [8]Medical College of Wisconsin, Milwaukee, WI, US; [9]Medical College of Wisconsin, Milwaukee, WI, US; [10]Medical College of Wisconsin, Milwaukee, WI, US

INTRODUCTION: Surgical resection is critical to optimize survival outcomes in advanced PNET. The use of neoadjuvant therapy (NAT) has been widely employed in pancreatic adenocarcinoma to facilitate multimodality therapy and optimize survival duration, however data to support the routine use of NAT in advanced PNET is lacking. This study aims to investigate the overall response rate in patients with advanced PNET undergoing NAT. **METHODS:** We performed a retrospective review of patients with PNET who underwent NAT followed by surgery at a single tertiary cancer center from 1/2009 to 8/2023. Demographic and clinicopathologic characteristics were evaluated. The primary endpoint was overall response which was defined by either serologic, radiologic, or pathologic response. Serologic response was defined as a ≥ 30% reduction of Chromogranin A (CgA) or functional serum hormone level (e.g.

serum insulin in patient with insulinoma). Radiographic response was defined per RESIST v1.1 criteria. Pathologic response was defined by tumor downgrading after neoadjuvant therapy (e.g. G2 tumor on initial biopsy to G1 tumor after NAT). Secondary endpoints were progression-free survival (PFS) and overall survival (OS). **RESULTS:** 34 patients met inclusion criteria (Table 1) with a median follow-up of 42 months (IQR 18-99). 25 (74%) patients had metastatic disease at presentation. 26 (76%) patients received neoadjuvant Capecitabine + Temozolomide (CAPTEM), 2 (6%) received Everolimus, 2 (6%) received Etoposide + Cisplatin, 2 (6%) received Streptozotocin + 5-FU + Leucovorin, 1 (3%) received Sunitinib, and 1 (3%) received Bevacizumab. 23 (68%) underwent resection of all visible lesions, while 11 (32%) patients underwent cytoreductive surgery with >70% debulking. 18 (53%) patients had progression of disease after resection with a median PFS of 33 months (IQR 5-43). Median OS of the cohort was not reached. 3 (9%) patients died due to disease (median time from resection to death was 58 months). Disease control rate was 88% (30 of 34 patients); 8 (23%) showed partial response, 22 (65%) had stable disease, and 3 (9%) had disease progression by radiologic RECIST 1.1. Serologic response was seen in 20 (59%), and 10 (29%) had pathologic response. Overall response rate (radiologic, serologic or pathologic) after NAT for the entire cohort was 74% (25 of 34 patients). 4 (12%) patients showed response by all 3 criteria; they all received CAPTEM. **CONCLUSIONS:** NAT was associated with an overall response rate of 74% and an objective disease control rate of 88% in a cohort of advanced PNET. NAT was associated with favorable response and durable PFS and OS. Further investigation of this approach is warranted.

Table 1. Demographic and Clinicopathological Characteristics of Study Cohort

Cohort Characteristics	N = 34 (%)
Median Age, yrs (IQR)	56 (45-63)
Sex	
Male	15 (44%)
Female	19 (56%)
Race	
White	31 (91%)
Black	2 (6%)
Other	1 (3%)
Ethnicity	
Non-Hispanic	32 (94%)
Hispanic	2 (6%)
Tumor Grade	
Grade 1	8 (23%)
Grade 2	21 (62%)
Grade 3	5 (15%)
Surgical Procedure to address primary tumor	
Distal Pancreatectomy	21 (62%)
Pancreatoduodenectomy	9 (26%)
Total Pancreatectomy	4 (12%)
Median largest primary tumor Size, cm (IQR)	5.0 (3.4-8.0)
Primary Tumor Margin Status	
R0	23 (68%)
R1	11 (32%)
Nodal Metastasis	
N0	11 (32%)
N1	23 (68%)
Distant Metastasis	
M0	9 (26%)
M1	25 (74%)
Liver	20 (59%)
Multiple sites	5 (15%)
Neoadjuvant Cytotoxic Regimen	
CAPTEM	26 (76%)
Streptozotocin, 5-FU, and Leucovorin	2 (6%)
Everolimus	2 (6%)
Bevacizumab	1 (3%)
Sunitinib	1 (3%)
Etoposide and Cisplatin	2 (6%)

P387. Surgical referrals for colorectal liver metastases: Assessing patterns and outcomes at a high-volume, safety-net hospital

Morgan F Pettigrew, MD[1]; Munir H Buhaya, MD[2]; Victoria F Peters, BS[3]; Nafeesah Fatimah, MD[4]; Christine F. Johansen, BS[5]; Radhika Kainthla, MD[6]; Matthew R. Porembka, MD[7]; Sam C. Wang, MD[8]; Alex C. Kim, MD PhD[9]; Patricio M. Polanco, MD[10]; John C Mansour, MD[11]; Herbert J Zeh, MD[12]; Adam C. Yopp, MD[13]; Cecilia G Ethun, MD MS[14]

[1]UT Southwestern Medical Center, Dallas, TX, US; [2]UT Southwestern Medical Center, Dallas, TX, US; [3]UT Southwestern Medical Center, Dallas, TX, US; [4]UT Southwestern Medical Center, Dallas, TX, US; [5]UT Southwestern Medical Center, Dallas, TX, US; [6]UT Southwestern Medical Center, Dallas, TX, US; [7]UT Southwestern Medical Center, Dallas, TX, US; [8]UT Southwestern Medical Center, Dallas, TX, US; [9]UT Southwestern Medical Center, Dallas, TX, US; [10]UT Southwestern Medical Center, Dallas, TX, US; [11]UT Southwestern Medical Center, Dallas, TX, US; [12]UT Southwestern Medical Center, Dallas, TX, US; [13]UT Southwestern Medical Center, Dallas, TX, US; [14]UT Southwestern Medical Center, Dallas, TX, US

INTRODUCTION: Surgical resection is the only potential curative treatment for patients with colorectal liver metastases (CRLM). However, many patients are never evaluated by a oncology-trained liver surgeon, leading to undertreatment and inferior outcomes. We sought to determine factors predictive of surgical referral and the association of surgical referral and multimodal management with survival in patients with CRLM. **METHODS:** All patients diagnosed with CRLM at Parkland Memorial Hospital from 2016-2023 were included. Parkland is a safety-net hospital where most patients receive care solely within the Parkland system, minimizing external referral bias. Patients were case-matched by referral status according to age, performance status, and adverse clinicopathologic factors. Liver-directed therapy (LDT) was defined as resection, ablation, arterial-based therapies, and/or radiation. Primary outcome was overall survival (OS). Secondary outcome was surgical referral. **RESULTS:** Of 427 patients with CRLM, most were male (62%), Hispanic (42%) or Black (35%), and uninsured (61%). Surgical referral was placed for 199 (47%). Factors associated with surgical referral were better performance status, lower carcinoembryonic antigen (CEA) levels, unilobar disease, ≤3 liver lesions, and absence of extrahepatic disease (all p<0.001). Of 124 patients (29%) who received LDT, 95% were referred to a liver surgeon prior to liver intervention. Among the case matched cohort (total n=212), there were no differences in receipt of surgical referral based on age, sex, race/ethnicity, insurance, performance status, CEA, bilobar disease, number of liver lesions, or extrahepatic disease. On univariable analysis, poor performance status, higher CEA, and bilobar disease were associated with worse OS (all p<0.05). Surgical referral and receipt of LDT were associated with improved survival (both p<0.001). On multivariable analysis, poor performance status and bilobar disease were associated with worse OS. Surgical referral (p=0.008) and receipt of liver-directed therapy (p<0.001) were associated with improved OS. **CONCLUSIONS:** Patients with CRLM referred for surgical evaluation are more likely to receive LDT. Both surgical referral and receipt of LDT are associated with improved OS, even when accounting for extent of disease and other clinicopathologic factors. All patients with CRLM, regardless of tumor burden, should be referred for surgical evaluation as part of a multidisciplinary treatment approach.

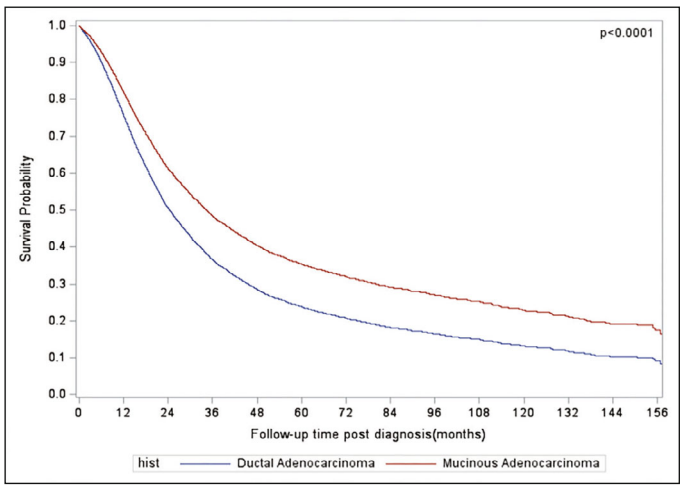
Table 1. Univariable and multivariable analysis of factors associated with survival in patients with colorectal liver metastases

	Hazard Ratio	95% Confidence Interval	P value	Hazard Ratio	95% Confidence Interval	P value
Age						
	1.02	0.99 - 1.04	0.08			
Sex						
Male	ref					
Female	1.25	0.90 - 1.75	0.19			
Race/Ethnicity						
White	ref					
Hispanic	0.77	0.48 - 1.22	0.26			
Black	1.23	0.77 - 1.95	0.39			
Asian	0.83	0.32 - 2.18	0.71			
Native American	0.98	0.13 - 7.22	0.98			
Primary payor						
Private	ref					
Public	0.91	0.40 - 2.03	0.81			
None	0.54	0.25 - 1.17	0.12			
ECOG Performance Status						
0/1	ref			ref		
2	1.16	0.70 - 1.90	0.57	1.10	0.67 - 1.84	0.69
3/4	2.19	1.26 - 3.81	**0.006**	2.30	1.30 - 4.06	**0.004**
CEA						
	1.00	1.00 - 1.00	**0.01**	1.00	1.00 - 1.00	0.05
Lobar involvement						
Unilobar	ref			ref		
Bilobar	1.84	1.20 - 2.81	**0.005**	2.08	1.34 - 3.25	**0.001**
	ref					
Number of Liver Lesions						
≤ 3	ref					
> 3	1.45	0.98 - 2.16	0.06			
Size of Largest Lesion (cm)						
< 5	ref					
≥ 5	1.12	0.78 - 1.61	0.55			
Extrahepatic disease						
Absent	ref					
Present	1.23	0.85 - 1.79	0.28			
Referral to Surgical Oncology						
No	ref			ref		
Yes	0.38	0.27 - 0.55	**<0.001**	0.58	0.39 - 0.87	**0.008**
Liver Directed Therapy						
No	ref			ref		
Yes	0.19	0.11 - 0.30	**<0.001**	0.30	0.17 - 0.51	**<0.001**

P388. Survival of pancreatic mucinous adenocarcinoma versus pancreatic ductal adenocarcinoma: A 10-year propensity score-matched analysis

Hadley D. Freeman, MD[1]; Anup Y Parikh[2]; Naveenraj L. Solomon, MD[3]; David Caba Molina, MD, MS, MPH[4]; Nephtali Gomez, MD[5]; Mark E. Reeves, MD, PhD[6]; Liang Ji, DrPH[7]; Oliver S Eng[8]; Michael O'Leary[9]
[1]Loma Linda University Health, Loma Linda, CA, US; [2]Loma Linda University, Loma Linda, CA, US; [3]Loma Linda University Health, Loma Linda, CA, US; [4]Loma Linda University Health, Riverside University Health System/UC Riverside, Loma Linda, CA, US; [5]Loma Linda University Health, Loma Linda, CA, US; [6]Loma Linda University Health, Loma Linda, CA, US; [7]Loma Linda University Health, Loma Linda, CA, US; [8]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [9]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US

INTRODUCTION: Pancreatic mucinous adenocarcinoma (PMAC) is a rare histologic subtype of pancreatic carcinoma, accounting for approximately 1-3% of all pancreatic adenocarcinoma cases. While survival outcomes for the most common subtype, pancreatic ductal adenocarcinoma (PDAC), have been established, survival for PMAC is not well defined. The aim of this study was to compare overall survival (OS) of PDAC vs. PMAC, stratified by clinical stage. **METHODS:** The National Cancer Database was used to identify all patients with PMAC and PDAC undergoing surgery from 2008-2018. Chemotherapy recipients were excluded. Clinicopathologic variables were matched for age, race and ethnicity, clinical stage, and margin status. Survival analysis was performed using the Kaplan-Meier method and a multivariate Cox proportional hazards model. **RESULTS:** A total of 10,767 patients were included in the study. Of these, 814 (7.6%) had PMAC and 9,953 (92.4%) had PDAC. Compared to PMAC, PDAC had higher number of regional lymph nodes examined (16 vs 14, p<0.001) and longer median interval time to surgery (22 days (IQR 47) vs 10 days (IQR 38), p<0.001). After matching, PDAC had higher risk of mortality among those with stage I (HR 2.00, 95% CI 1.64-2.44) and stage II (HR 1.32, 95% CI 1.18-1.48) disease, whereas survival among stage III (HR 1.10, 95% CI 0.73-1.64) and stage IV disease (HR 1.23, 95% CI 0.91-1.65) was similar. Estimated 5-year OS for PMAC was 35.4%, compared to 23.8% for PDAC (p<0.001). **CONCLUSIONS:** Among patients undergoing surgery, PMAC appears to have a more favorable prognosis among patients with stage I or stage II disease compared to PDAC. For patients with locally advanced or metastatic disease, however, survival remains equally poor. OS for PDAC is worse than for PMAC.



P389. TNIK Inhibition Increases Invasiveness in Classical Subtype Pancreatic Adenocarcinoma

Hannah Trembath, MD, MS[1]; Ian McCabe, BS[2]; Sandra Zarmer, BS[3]; Michelle LaBella, MD[4]; Mariaelena Nabors, BS[5]; Joseph Kearney, MD[6]; Yi Xu, PhD[7]; Jen Jen Yeh, MD[8]
[1]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [2]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [3]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [4]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [5]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [6]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [7]University of North Carolina at Chapel Hill, Chapel Hill, NC, US; [8]University of North Carolina at Chapel Hill, Chapel Hill, NC, US

INTRODUCTION: There are two main molecular subtypes of pancreatic adenocarcinoma (PDAC), basal and classical, that are predictive of survival and treatment response, with basal having worse outcomes and resistance to FOLFIRINOX. Basal and classical PDAC have unique kinase profiles and represent potential for subtype targeted therapies. TNIK is a top classical kinase and is under evaluation as a therapeutic target in other cancers; the objective of this study is to evaluate the impact of TNIK inhibition in classical subtype PDAC. **METHODS:** Classical subtype PDAC patient derived xenograft (PDX) organoids CRISPR-Cas9 non-targeting (NT) and TNIK knockouts (KO) were generated. Downstream signaling was evaluated via western blots and immunofluorescence imaging (IF). Invasiveness was evaluated using collagen assays and orthotopic pancreatic injections. **RESULTS:** Loss of TNIK resulted in disorganized and less differentiated architecture and increased expression of basal-like subtype genes. TNIK KO organoids exhibited increased invasive branching formation when plated in collagen (Figure 1) and increased local invasion in vivo. 6/6 mice with TNIK KO tumors showed local invasion on necropsy compared to 1/4 NT KO mice, p=0.033. Two of the main pathways TNIK is involved in is as an essential activator of Wnt pathway, leading to nuclear translocation of β-catenin, as well as regulation of actin cytoskeleton through its interaction with Rap2. There was no difference in β-catenin localization on IF. Active Rap2 levels were significantly decreased between TNIK compared to NT KO on pathway evaluation. **CONCLUSIONS:** TNIK is required to maintain a more differentiated phenotype. Decreases in active Rap2 between TNIK KO and NT KO imply an important role between TNIK and Rap2 and cytoskeleton regulation/dynamics. Our findings suggest that TNIK may be a gatekeeper to increased tumor invasiveness. TNIK inhibition is being evaluated as a promising therapeutic approach in preclinical studies across multiple cancers, however, our data suggests that targeted TNIK may be harmful in PDAC.

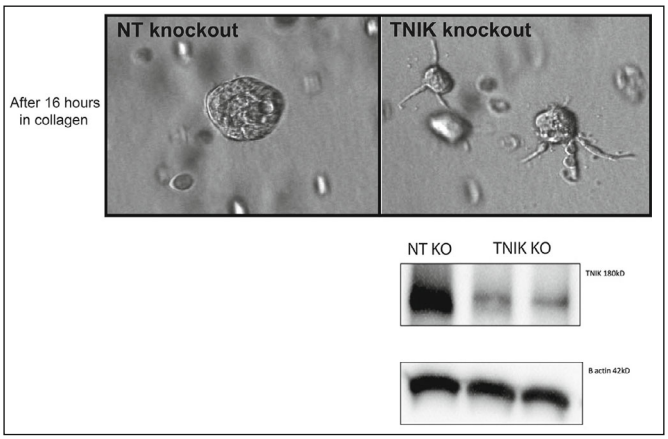


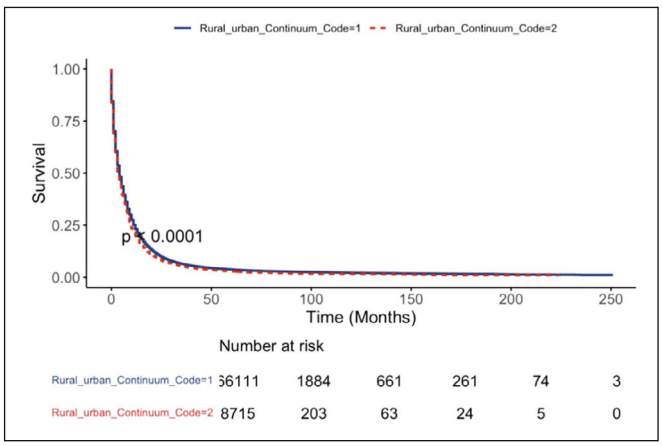
Figure 1. Left, A classical organoid line nontargeting (NT) sgRNA knockout (KO) plated in collagen. Right, a TNIK KO exhibiting development of invasive tendrils. Below, blot confirming knockdown.

P390. The Effect of Rurality Status on Radiation Outcomes for Pancreatic Adenocarcinoma. A Retrospective Study of the Surveillance, Epidemiology, and End Results Database

Saad Khan[1]; Robert Zhang[2]; Samuel J Kim[3]; Praneet Khanna[4]; Bianca Ituarte[5]; Steven Nyugen[6]; Patrick Weldon[7]; Sara Trompeter[8]; An-Lin Cheng[9]; Xiang Ping Chu[10]
[1]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [2]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [3]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [4]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [5]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [6]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [7]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [8]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [9]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [10]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US

INTRODUCTION: Pancreatic adenocarcinoma (PA) is the third leading

cause of cancer-related death in the United States. Previous investigations have demonstrated the impact of socioeconomic status (SES) on PA survival outcomes including the effects of rurality on poorer PA survival. Despite this, studies on rurality and PA outcomes have yet to establish a relationship between therapy access and survival outcomes. The purpose of this investigation is to describe the association between radiation therapy and rurality on PA survival. **METHODS:** This investigation queried the Surveillance, Epidemiology, and End Results (SEER) for pancreatic adenocarcinoma cases. The SEER registries included in our study include 17 cancer registries between the years 2000-2020. Cases were identified using the International Classification of Diseases (ICD) for Oncology, Third Revision morphology codes (8140/3), localized to the pancreas. Chi-square analysis, Kaplan Meier (KM) curves, cox proportional hazards models, paired t-tests, and analysis of variance (ANOVA) were used to describe differences in survival. P-values less than 0.05 were considered significant. **RESULTS:** 74, 921 patients were included in this study. The majority were male (n=39107), >60 years (n=58,831), in a metropolitan area (n=66,111), and did not receive radiation (n=65,529). Differences between rural and metropolitan areas in overall survival (OS) were significant in paired t-tests (p<0.001). Radiotherapy resulted in improved survival outcomes on ANOVA (p<0.001). Rurality was associated with poor radiation usage while metropolitan status was associated with beam radiation on bivariate analysis (p<0.001). Rurality was associated with poorer OS on KM curves (p<0.0001) as seen on Figure 1. Patients living in rural areas have a 10% greater risk of death due to PA than those living in metropolitan areas (HR=1.10; 95% CI: 1.07-1.12; p<0.001). **CONCLUSIONS:** This investigation found that rurality was associated with decreased radiation therapy access (p<0.001) and that radiotherapy was associated with improved OS (p<0.001). Recent studies suggest the efficacy of neoadjuvant radiotherapy for improving PA outcomes. Future research must be dedicated to advancing equitable disbursement of developing sequences of treatment for PA.

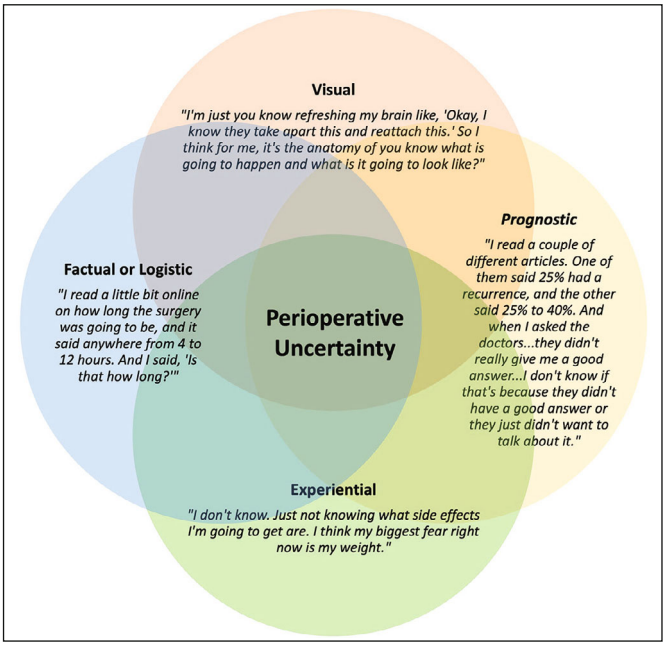


P391. The Experience and Perception of Uncertainty in Patients with Pancreatic Cancer Undergoing Neoadjuvant Therapy

Orly N Farber, MD[1]; Amanda J Reich, MD, MPH[2]; George Molina, MD, MPH[3]; Elizabeth J. Lilley, MD, MPH[4]

[1]Brigham and Women's Hospital, Boston, MA, US; [2]Center for Surgery and Public Health, Boston, MA, US; [3]Brigham and Women's Hospital, Boston, MA, US; [4]Brigham and Women's Hospital, Boston, MA, US

INTRODUCTION: Patients with cancer awaiting surgical plans face heightened medical uncertainty. Yet, little work has addressed how these patients experience or perceive uncertainty. This study sought to explore the phenomenon of medical uncertainty in patients with pancreatic cancer in the window between neoadjuvant therapy and potential surgery. **METHODS:** This qualitative study involved both in-clinic observations and interviews across two institutions. We observed visits between surgical oncologists and patients with non-metastatic pancreatic cancer being considered for or undergoing neoadjuvant therapy, followed by semi-structured interviews with patients. Field notes from clinic observations and transcripts from interviews were thematically analyzed using a combination of deductive and inductive coding strategies. Deductive coding relied on a three-dimensional taxonomy for medical uncertainty, which includes: locus (who experiences the uncertainty?), source (what are its origins?), and issue (what is the substance or topic?). **RESULTS:** We observed 15 unique patient-surgeon dyads in clinic. Of the enrolled patients, 11 completed interviews. We identified four major themes: 1) Visual uncertainties, 2) Factual or logistic uncertainties, 3) Experiential uncertainties, and 4) Prognostic uncertainties. Visual uncertainties refer to patients' inability to imagine aspects of their care (e.g., picturing operative anatomy). Factual or logistic uncertainties can reside with either surgeons or patients and pertain to the absence of concrete information (e.g., operating room availability, next steps in treatment). Experiential uncertainties reside with patients and relate to the unpredictability of an experience (e.g., potential side effects of therapy, ability to return to work). Last, prognostic uncertainties exist for both patients and surgeons and derive from the unknowability of outcomes (e.g., likelihood of recurrence, anticipated change in tumor size). These four themes are not mutually exclusive but constitute the major domains of perioperative uncertainty in our observations and interviews. **CONCLUSIONS:** Our study is one of the first efforts to explore medical uncertainty in patients with pancreatic cancer awaiting surgical decisions. These findings offer a framework for clinicians to understand the types of uncertainty experienced and perceived by patients and help lay the groundwork for developing strategies to manage perioperative uncertainty.



P392. The Oncopig cancer model, an innovative large animal platform for evaluating novel endoscopic and surgical applications

Ajay V Maker, MD[1]; Andreas Autlitzky[2]; F Edward Boas[3]; Jonathan Coleman[4]; Mark Carlson[5]; Lobna Elkhadragy[6]; Ron Gaba[7]; Kevin Haas[8]; Natalia Kudinova[9]; Matthew Niemeyer[10]; Hooman Yarmohammadi[11]; Lawrence B Schook[12]; Kyle M Schachtschneider[13]

[1]University of California San Francisco, San Francisco, CA, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]City of Hope, Duarte, CA, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]University of Nebraska Medical Center, Omaha, NE, US; [6]University of Illinois at Chicago, Chicago, IL, US; [7]University of Illinois at Chicago, Chicago, IL, US; [8]University of Illinois at Chicago, Chicago, IL, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]University of Illinois at Chicago, Chicago, IL, US; [11]Memorial Sloan Kettering Cancer Center, New York, NY, US; [12]Sus Clinicals Inc., Chicago, IL, US; [13]Sus Clinicals Inc, Chicago, IL, US

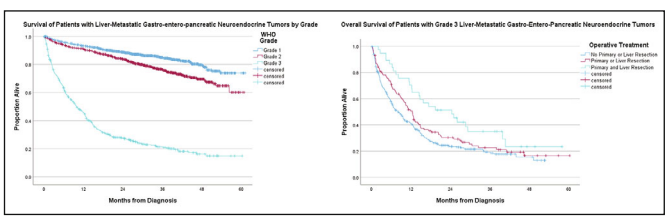
INTRODUCTION: Pigs serve as a promising preclinical model for surgical applications given their similar physiology, size, genetics, immunity, and metabolism compared to humans. While pigs are frequently utilized in surgical studies, the inclusion of tumor-bearing pigs would enhance the translatability and clinical significance of these investigations. Here, we propose the Oncopig cancer model as a valuable option for preclinical assessment of innovative surgical and cancer treatment approaches. **METHODS:** The Oncopig cancer model is capable of modeling a range of tumor types through induced expression of KRASG12D and TP53R167H driver mutations utilizing an adenoviral vector encoding Cre recombinase (AdCre). Several tumor models were generated through AdCre injection into target organs, including pancreatic, bladder,

liver, lung, and colorectal tumors. Tumor progression was monitored using clinically relevant imaging modalities, including CT scan (pancreatic, and lung tumors) and endoscopy (bladder and colorectal tumors). Tumors were assessed histologically (H&E and KRASG12D). **RESULTS:** Oncopig tumor formation was successfully achieved across all models within two weeks, demonstrating the efficacy of the established protocols. Tumor sizes varied by organ type, with notable dimensions as follows: pancreatic tumors ranged from 0.5 to 5.1 cm, bladder tumors from 0.2 to 3 cm, liver tumors from 0.5 to 4 cm, lung tumors from 0.5 to 4 cm, and colorectal tumors from 2 to 10.9 cm. Notably, targeted AdCre injection consistently resulted in poorly differentiated carcinomas characterized by significant immune infiltration. Further characterization of pertinent tumor markers in each model is being performed. **CONCLUSIONS:** The establishment of these organ-specific Oncopig tumor models represents an advancement in the preclinical evaluation landscape for surgical oncology. By mimicking human anatomy and physiology, these models provide a robust platform for assessing novel surgical techniques and multimodal cancer treatment strategies, and have the potential to enhance translational research in our field.

P393. The Role of Primary and Liver Resection for Liver-Metastatic Gastro-Entero-Pancreatic Neuroendocrine Tumors: Grade Matters

Thomas L Sutton, MD MCR[1]; Teodora Dumitra[2]; Timothy DiPeri, MD[3]; Alexandra Gangi, MD, FSSO[4]
[1]Cedars-Sinai Medical Center, Los Angeles, CA, US; [2]Cedars-Sinai Medical Center, Los Angeles, CA, US; [3]Cedars-Sinai Medical Center, Los Angeles, CA, US; [4]Cedars-Sinai Medical Center, Los Angeles, CA, US

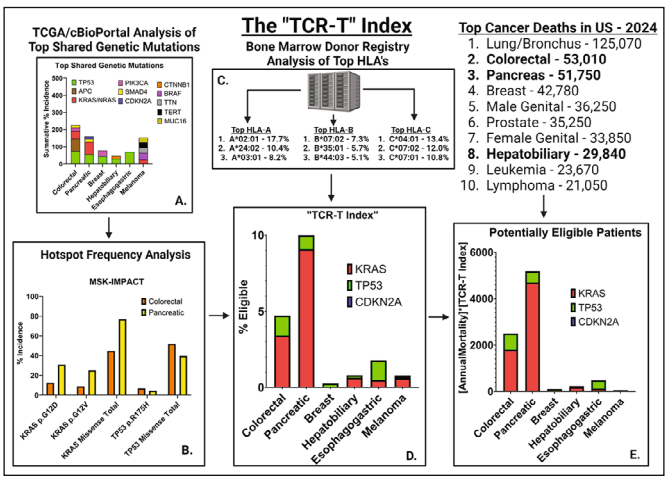
INTRODUCTION: In patients with synchronous liver-metastatic gastro-entero-pancreatic neuroendocrine tumors (GEPNETs), resection of primary and liver disease has been associated with improved overall survival (OS). Well-differentiated grade 3 GEPNETs are a newly recognized entity under 2017 WHO classifications, with a markedly worse prognosis than grade 1/2 disease. The oncologic benefit of primary and liver resection in grade 3 metastatic GEPNETs has not been previously studied. **METHODS:** The National Cancer Database was queried for patients with GEPNETs and synchronous liver-only metastatic disease from 2018-2021, using updated WHO grading classifications to identify tumor grade. Kaplan-Meier and multivariable Cox proportional hazards modeling were utilized to evaluate the association of primary tumor and liver resection on OS. **RESULTS:** 3198 patients were identified (grade 1: n=1434, grade 2: n=1113, grade 3: n=651). Receipt of either primary or distant-site surgery varied significantly by grade; grade 1: 67.3% (n=966), grade 2: 62.4% (n=695), grade 3: 31.3% (n=204), $P<0.001$ for grade 3 versus grade 1/2. Median follow-up was 35.5 months, and 3-year OS varied significantly by tumor grade (grade 1: 84.9%, grade 2: 76.2%, grade 3: 21.3%, $P<0.001$ for all comparisons). In patients with grade 3 disease, 447 received no primary or distant-site surgery (median OS 8.1 months), 153 received primary-only or liver-only surgery (median OS 11.8 months), and 51 received both (median OS 24.4 months). Receipt of either primary resection or liver debulking was associated with a 4.7-month improvement in median OS in patients with grade 3 GEPNETs (12.8 vs. 8.1 months, $P=0.005$), though with similar survival at 3 years (25.7% vs. 19.3%). Conversely, in grade 1/2 GEPNETs, receipt of primary or distant site surgery was associated with a dramatic improvement in 3-year OS (88.2% vs. 67.1%, $P<0.001$) On multivariable analysis adjusting for age, Charlson-Deyo comorbidity index, and site of origin, the receipt of primary or liver-only resection (HR 0.70, 95% CI 0.54-0.91, $P=0.008$) and combined primary/liver resection (HR 0.54, 95% CI 0.37-0.82, $P=0.004$) were associated with a lower hazard of death compared to no surgery. **CONCLUSIONS:** Primary and liver resection are associated with meaningfully improved OS in patients with grade 1/2 liver-metastatic GEPNETs. Prognosis in grade 3 metastatic disease is grim, regardless of primary or liver-directed surgical intervention. Surgical intervention should therefore be carefully considered and patients counselled appropriately.



P394. The T Cell Receptor T Cell (TCR-T) Index: The potential of targeting gastrointestinal cancer with off-the-shelf TCR-T cells

Aaron Dinerman[1]; Noam Levin[2]; Sanghyun P Kim[3]; James Yang[4]; Steven A. Rosenberg[5]; Nicholas Klemen[6]
[1]NCI, Bethesda, MD, US; [2]Surgery Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, US; [3]Surgery Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, US; [4]NCI, Bethesda, MD, US; [5]NCI, Bethesda, MD, US; [6]NCI, Bethesda, MD, US

INTRODUCTION: Solid epithelial malignancies are the top cause of cancer-related mortality. T Cell Receptor (TCR)-T cell therapy (TCR-T) targeting immunogenic hotspot mutations is an emerging investigative treatment for patients with solid tumors. This off-the-shelf treatment depends on three factors: (1) a hotspot mutation, (2) Human Leukocyte Antigen (HLA)-matched presentation, and (3) T cell specificity for the hotspot neoantigen-HLA combination. The "TCR-T Cell Index" is an evolving metric that quantifies the frequency of immunogenic HLA-hotspot combinations in GI cancers that can be potentially targeted by off-the-shelf TCR-T. **METHODS:** First, we identified the most lethal GI cancers using the 2024 ACS report. We then identified the top 5 mutations within these cancer types and their respective hotspot frequencies using TCGA datasets and queried top HLA haplotype frequencies from the National Marrow Donor Program (NMDP, Figure 1A, C). Finally, we cross-referenced these combinations with reactive TCRs discovered at a single institution to calculate the TCR-T cell index (Figure 1D). **RESULTS:** Several GI cancers were among the most lethal malignancies: colorectal cancer (CRC, #2), pancreas ductal adenocarcinoma (PDAC, #3), and hepatobiliary cancers (#8). KRAS and TP53 were their most frequently altered genes; the hotspots KRASG12D, KRASG12V, and TP53R175H were seen in 30.8%, 25.1%, and 4.5% of patients with PDAC and 12.4%, 8.9%, and 6.8% with CRC (Figure 1A and B). In contrast, APC is the most common altered gene in CRC (74.8%), but it lacks recurrent missense hotspots (99% truncating, 590 different mutations) and so negligibly contributes to the TCR-T index. Multiple TCRs recognize KRAS and TP53 hotspots in the context of several common class I HLAs (A*02:01, A*11:01, C*01:02, and C*08:02) and class II HLAs (DRB1*07:01, DRB1*13:01). TCRs specific for less common hotspot-HLA combinations have also been identified (e.g., TP53Y220C restricted by HLA-DRB1*04:01), but contribute minimally to the index. Top hotspots in other cancer types BRAFV600E (melanoma) and EGFRL858R (lung cancer) have no confirmed T cell reactivities to date and thus also do not contribute. Merging hotspot (TCGA) and HLA frequencies (NMDP) with annual mortality estimates (ACS), the latter as a surrogate for patients with stage IV disease in need of novel systemic treatment options, we estimate potentially eight thousand patients with GI cancers per year could be candidates for clinical trials evaluating neoantigen-directed TCR-T (Figure 1E). **CONCLUSIONS:** Investigational TCR-T cell therapy for solid tumors is an ongoing area of translational research with promising, but unproven efficacy. A significant proportion of patients with pancreatic and colorectal cancers harbor mutations at immunogenic hotspots that can be potentially targeted with off-the-shelf TCR-T cells in clinical trials.



P395. The practice of pancreatic neck margin testing and outcomes after pancreatoduodenectomy for pancreatic cancer

Kimberly P Woo, MD[1]; William C Bennett, MD[2]; Jenny H Chang, MD[3]; Chase J Wehrle, MD[4]; Robert Naples, MD[5]; Daniel Joyce, MBBCh[6]; Robert Simon, MD[7]; Toms Augustin, MD[8]; R. Matthew Walsh, MD[9]; Samer A Naffouje, MD[10]
[1]Cleveland Clinic, Cleveland, OH, US; [2]Cleveland Clinic, Cleveland, OH, US; [3]Cleveland Clinic - Cleveland, OH, Cleveland, OH, US; [4]Cleveland Clinic, Cleveland, OH, US; [5]Cleveland Clinic, Cleveland, OH, US; [6]Cleveland Clinic, Cleveland, OH, US; [7]Cleveland Clinic, Cleveland, OH, US; [8]Cleveland Clinic, Cleveland, OH, US; [9]Cleveland Clinic, Cleveland, OH, US; [10]Cleveland Clinic - Cleveland, OH, Cleveland, OH, US

INTRODUCTION: Checking the pancreatic neck margin during pancreatoduodenectomy (PD) for pancreatic ductal adenocarcinoma (PDAC) is a subject of ongoing debate. The primary goal of this practice is to achieve an R0 resection. We aim to study the practices of checking and revising the pancreatic neck margin (PNM) and their impact on long-term surgical outcomes. **METHODS:** Patients who underwent PD for PDAC or other malignant subtypes at our institution from 2018-2023 were identified. The electronic medical record was reviewed for intraoperative pancreatic neck margin frozen section (PNM-FS) testing practices. The primary outcome was pancreatic neck recurrence free survival (PN-RFS). Secondary outcomes were distant recurrence free survival (D-RFS) and overall survival (OS). Kaplan-Meier method was used to analyze survival outcomes. **RESULTS:** A total of 416 patients were included; median follow-up and surveillance were 19 and 16 months, respectively. PNM-FS was checked in 371 patients (89.2%) and was negative at first attempt in 293 patients (79.0%). Of the 78 patients with positive PNM-FS, the margin was revised in 65. The margin was converted to negative in 51 patients (78.5%), nine patients completed their PD with a positive PNM, and five underwent a completion total pancreatectomy (TP). 12 out of the 78 patients with positive PNM-FS at first attempt did not receive a margin revision and one patient directly underwent a TP. All six of the patients who underwent completion TP progressed and died of disease within 12 months. One had total neoadjuvant therapy, one completed adjuvant therapy, and four were not able to complete adjuvant therapy as intended. Among patients who had PNM-FS checked, 47 (12.7%) developed pancreatic neck recurrence during surveillance. Median PN-RFS for those who had negative PNM-FS at first attempt, PNM-FS cleared with revision, PNM-FS cleared with TP, and positive PNM-FS was 22.0±2.2 vs. 16.0±3.0 vs. 11.0±4.2 vs. 16.0±.2.8 months, respectively (p=0.017) (Figure 1). Median D-RFS for these groups was 16.0±1.2 vs. 14.0±2.3 vs. 8.0±1.1 vs. 11.0±3.1 months (p=0.010). Median OS was 25.0±2.8 vs. 22.0±5.3 vs. 11.0±4.3 vs. 16.0±2.8 (p=0.016). **CONCLUSIONS:** Our data suggests that PNM-FS is a prognostic marker. Pursuing pancreatic neck clearance with margin revision is not associated with improved PN-RFS, D-RFS, or OS. Furthermore, pursuing a completion TP to clear the margin may be associated with shorter OS either from the infiltrative nature of the tumor or from the surgical morbidity associated with TP.

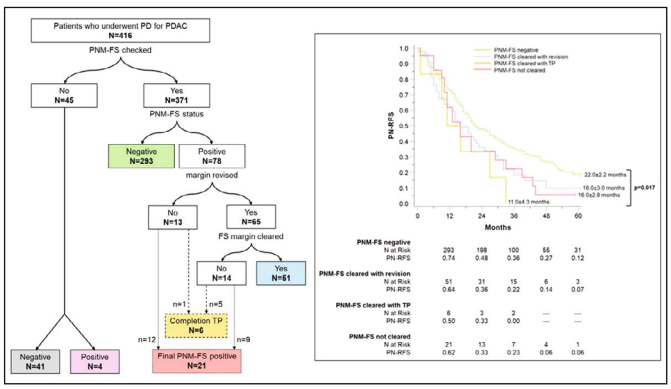


Figure 1. Study population and pancreatic neck recurrence free survival (PN-RFS)

P396. Well-moderately differentiated 1-2cm non-functional pancreatic neuroendocrine tumors: what factors impact management?

Omid Salehi[1]; Abdul Saied Calvino[2]; Ponnandai Somasundar[3]; N Joseph Espat[4]; Mohammad Ali[5]; Sasha L Lightfoot, DO[6]; Sung Kwon, MD MPH[7]
[1]Roger Williams Medical Center, Providence, RI, US; [2]Roger Williams Medical Center, Providence, RI, US; [3]Roger Williams Medical Center, Providence, RI, US; [4]Roger Williams Medical Center, Providence, RI, US; [5]Roger Williams Medical Center, Providence, RI, US; [6]Roger Williams Medical Center, Providence, RI, US; [7]Roger Williams Medical Center, Providence, RI, US

INTRODUCTION: Current National Comprehensive Cancer Network guidelines for well to moderately differentiated non-functional pancreatic neuroendocrine tumors (NF-PNET) for tumors 1-2cm are unclear, with observation (OB) vs enucleation (EN) vs pancreatic resection (PR) all as viable options. The objective of this study is to analyze factors that are impactful in predicting survival differences for each approach. **METHODS:** A retrospective analysis of the National Cancer Database from 2004 to 2021 for patients with 1-2cm well-moderately differentiated NF-PNET with known management strategy was performed stratified by OB, EN, and PR. Main outcomes were factors predicting survival stratified by management strategy using multivariable Cox proportional hazards models. **RESULTS:** 5600 patients met the inclusion criteria with average age of 61.3 ± 13 years and 53.5% being males; 1431 (25.5%) OB, 414 (7.4%) underwent EN, and 3755 (67.1%) had PR. Patients across the 3 treatment domains differed in several characteristics: larger tumor size in PR patients (15.6mm vs 14.9mm in OB), tail location predominance in OB and PR (31.1% & 46.6% vs 19.8% EN), lower ki-67 index in OB (88.3% G1 vs 57.9% EN & 73.7% PR), and having government-based insurance in OB (65.3% vs 42% EN & 46.7% PR). On multivariable analysis, factors predicting worse survival for the entire cohort included age (HR 1.05, 95% CI 1.04-1.06), Black race (HR 1.62, 95% CI 1.26-2.08), and Charleson-Deyo Score >1 (HR 1.61, 95% CI 1.34-1.92), whereas female sex (HR 0.76, 95% CI 0.63-0.91) and private insurance (HR 0.65, 95% CI 0.51-0.83) were associated with improved survival. When evaluating three different treatment strategies separately, age and comorbidity were associated with worse survival across the treatment strategies. Black race were associated with worse survival in EN and PR patients while government-based insurance groups and male sex were associated with worse survival in PR patients but these three variables were not associated with worse survival in OB patients. **CONCLUSIONS:** For 1-2cm well to moderately differentiated NF-PNET, we found male sex, Black race and government-based insurance to be important factors in predicting worse survival outcomes among those undergoing invasive interventions (EN and PR) but not in OB group indicating elevated risks of operations without significant long-term survival benefit in these group of patients. It may be useful to incorporate sex, race, and insurance types when determining the management strategy for 1-2cm well to moderately differentiated NF-PNET.

P397. Who Are the Long-Term Survivors in Pancreatic Ductal Adenocarcinoma (PDAC)?: An Analysis of the National Cancer Database

Julien Hohenleitner, MD[1]; Oliver Standring, MD[2]; Emma Gazzara, MD[3]; Shruti Koti, MD[4]; Alex Liu[5]; Gerardo Vitiello, MD[6]; Sepideh Gholami, MD[7]; Matthew John Weiss[8]; Danielle DePeralta, MD[9]
[1]Northwell Health, Manhasset, NY, US; [2]Northwell Health, Manhasset, NY, US; [3]Northwell Health, New Hyde Park, NY, US; [4]Northwell Health, Manhasset, NY, US; [5]Downstate Medical Center, Brooklyn, NY, US; [6]Northwell Health, New Hyde Park, NY, US; [7]Northwell Health, New Hyde Park, NY, US; [8]Northwell Health, Manhasset, NY, US; [9]Northwell Health, New Hyde Park, NY, US

INTRODUCTION: Long term survival (LTS) of PDAC (10+ years) is a rare outcome. Previous reports identify adjuvant chemotherapy, pathologic T-stage, and lymph node ratio as key indicators; however, the impact of more recent advances in diagnosis and management is unknown. In this study we present the largest analysis of LTS in resected PDAC patients to date using the National Cancer Database (NCDB). **METHODS:** A retrospective review of the NCDB from 2004-2019 was performed in which all patients diagnosed with non-metastatic, PDAC who underwent curative-intent surgical resection were included. Patients eligible for LTS analysis were defined as those who underwent surgical resection between 2006-2009 and survived 10 years or more with adequate follow up. A multivariable logistic regression model was deployed to identify factors with significant correlation with 10+ year survival. Statistical significance was set at $p < 0.05$. **RESULTS:** A total of 15,598 patients who underwent resection in 2006-2009 were included in the LTS analysis. Of those, 1,068 (6.84%) survived 10 years with adequate follow up. This cohort consisted of 537 (50.3%) males and 531 (49.7%) female patients. Patient race was reported as white 932 (88.4%), black 86 (8.2%) Asian 22 (2.1), and Other 14 (1.3%). The mean age was 62.9 with a standard deviation (SD) of 9.8. The most common tumor location was the head of the pancreas

744 (78.1%), with tail 121 (12.7%) and body 88 (9.2%) in the minority. Mean tumor size was 2.94cm (SD 2.49). The most common resection performed was In terms of non-surgical treatment, the most common chemotherapy strategy was adjuvant therapy 699 (65.9%), followed by no chemotherapy 258 (24.2%), neoadjuvant (NAT) only 79 (7.4%), and NAT + adjuvant 32 (3.0%). Radiation was not administered in most patients (516, 50%). Adjuvant radiation was given in 446 (43.2%) cases, and neoadjuvant radiation was administered in 70 (6.8%) cases. After univariate and multivariate analysis factors associated with 10-year survival included: pathologic T1 staging (OR 3.38), negative lymph nodes (OR 3.34), R0 resection (OR 2.56), Private/Medicare Insurance (OR 2.31/1.816), Charlson-Deyo Score of 0 or 1 (OR 2.18/1.67), and well-differentiated pathology (OR 1.751). **CONCLUSIONS:** Long term survival in patients after surgical resection is a rare occurrence. In this analysis, 6.84% of patients survived 10+ years after resection of their PDAC tumor. The strongest factors associated with long term survival included pathologic T staging, lymph node status, and R0 resection.

P398. A 10-Year review of Merkel Cell Carcinoma evaluating surgical margin width and other predictors of disease recurrence

Jack W. Sample, MD[1]; Amy Glasgow[2]; Clark Otley, MD[3]; Tina J. Hieken, MD[4]; Mara A. Piltin, DO, FACS[5]
[1]Mayo Clinic, Rochester, MN, US; [2]Mayo Clinic, Rochester, MN, US; [3]Mayo Clinic, Rochester, MN, US; [4]Mayo Clinic, Rochester, MN, US; [5]Mayo Clinic, Rochester, MN, US

INTRODUCTION: Merkel Cell Carcinoma (MCC) is a primary cutaneous carcinoma of neuroendocrine origin, characterized by high recurrence and poor survival, especially in cases with distant metastasis. Although rare, the incidence of MCC has increased significantly over the past decade and is projected to rise further due to aging of the population. This study aims to evaluate surgical margin width and other factors in association with oncologic outcomes among patients operated on over a recent 10-year period. **METHODS:** With institutional review board approval, we retrospectively identified patients treated surgically for MCC at our institution from January 2013 through January 2023 and followed for a minimum of 18 months. Data regarding oncologic diagnosis, treatment, and surveillance were abstracted from the medical record. Statistical analysis was performed using IBM SPSS Statistics (Version 28, Armonk, NY, USA: IBM Corp). **RESULTS:** Of 144 patients who underwent surgery for MCC,136 were evaluable after exclusion of patients with de novo metastatic disease and insufficient follow-up. Median patient age was 72.0 years and mean patient body mass index (BMI) was 31.5 kg/m2. 54 patients (39.7%) experienced disease recurrence (30.4% local, 44.6% regional, 41.1% distant). Head and neck was the most common primary tumor location (n=62, 44.9%) and male sex was associated with higher risk of recurrence (p=0.018). After exclusion of cT0 patients, 115 were evaluable for *in vivo* surgical margin width. This was ≤1 cm in 53 (46.1%), 1.01-2 cm in 45 (39.1%) and >2 cm in 17 (14.8%) patients. Margins of ≤1 cm were more frequent for head/neck tumors than for tumors at other body sites, (p<0.001). Adjuvant radiation was delivered most frequently to patients treated with margins of ≤1 cm and 1.01-2 cm compared to >2 cm (38.9%, 48.6%, 12.5%, respectively). Among these 115 patients, 44 recurred (38.2%), with first recurrence including an isolated local recurrence in 10 (8.7%). There were no significant differences observed in disease recurrence or overall survival by surgical margin width. **CONCLUSIONS:** Our study found that that male sex was a predictor of disease recurrence. Importantly, *in vivo* surgical margin width was not associated with recurrence nor overall survival. These data raise the possibility that narrow margin excision for MCC, often combined with radiation therapy, may not be associated with increased local recurrence rates.

Table 1. Patient demographics and disease characteristics by in vivo surgical margin width

	Surgical Margin *in vivo* (cm)				
	≤1	1.01-2.0	>2.0	Total	
Baseline Patient Characteristic	**N (%)**				***p*-value**
Subjects, n (%)	53 (46.1)	45 (39.1)	17 (14.8)	115 (100)	
Median Age, years (range)	73.0 (41-95)	73.0 (27-95)	72.0 (60-94)	73.0 (27-94)	0.934
Percent male sex	50.9	57.8	70.6	56.5	0.355
Body mass index, kg/m2 (range)	30.8 (19-50)	31.6 (19-49)	33.3 (21-44)	31.5 (19-50)	0.455
Oncologic variables, N (%)					
Location of primary					**<0.001**
Head/neck	41 (69.5)	17 (28.8)	1 (1.7)	59 (100)	
Trunk	0 (0.0)	6 (85.7)	1 (14.3)	7 (100)	
Extremities	12 (24.5)	22 (44.9)	15 (30.6)	49 (100)	
Disease Recurrence					0.075
Yes	16 (36.4)	23 (52.3)	5 (11.3)	44 (100)	
Locoregional	12 (37.5)	17 (53.1)	3 (9.4)	32 (100)	
Distant	4 (23.5)	10 (58.8)	3 (17.7)	17 (100)	
Both	1 (12.5)	6 (75.0)	1 (12.5)	8 (100)	
Clinical Tumor (cT) category					0.664
T1	43 (47.8)	36 (40.0)	11 (12.2)	90 (100)	
T2	7 (35.0)	8 (40.0)	5 (25.0)	20 (100)	
T3	2 (50.0)	1 (25.0)	1 (25.0)	4 (100)	
T4	1 (100)	0 (0.0)	0 (0.0)	1 (100)	
Clinical Nodal (cN) category					0.653
N0	46 (45.5)	40 (39.6)	15 (14.9)	101 (100)	
N1	5 (41.7)	5 (41.7)	2 (16.6)	12 (100)	
N2	2 (100)	0 (0.0)	0 (0.0)	2 (100)	
N3	0 (0.0)	0 (0.0)	0 (0.0)	0 (100)	
Pathologic Tumor (pT) category					0.518
T1	41 (46.6)	37 (42.0)	10 (11.4)	88 (100)	
T2	8 (40.0)	7 (35.0)	5 (25.0)	20 (100)	
T3	2 (50.0)	1 (25.0)	1 (25.0)	4 (100)	
T4	2 (66.7)	0 (0.0)	1 (33.3)	3 (100)	
Pathologic Nodal (pN) category					0.683
N0	32 (44.4)	29 (40.3)	12 (16.7)	72 (100)	
N1	16 (48.5)	13 (39.4)	4 (12.1)	33 (100)	
N2	1 (50)	0 (0.0)	1 (50)	2 (100)	
N3	1 (100)	0 (0.0)	0 (0.0)	1 (100)	
NX	3 (42.9)	4 (57.1)	0 (0.0)	7 (100)	
Adjuvant Radiation					**0.026**
Yes	28 (38.9)	35 (48.6)	9 (12.5)	72 (100)	
No	25 (58.1)	10 (23.3)	8 (18.6)	43 (100)	

P399. An Exploration of Rural Access Disparities for Patients with Stage III-IV Melanoma

Brailyn Weber, BS[1]; Connor Sheridan, MS4[2]; Hilla I. Sang, PhD[3]; Bharghav Mistry, MD[4]; Sabha Ganai, MD, PhD, MPH, FACS, FSSO[5]
[1]University of North Dakota School of Medicine, Grand Forks, ND, US; [2]University of North Dakota School of Medicine, Grand Forks, ND, US; [3]Sanford Fargo Medical Center, Fargo, ND, US; [4]Sanford Fargo Medical Center, Fargo, ND, US; [5]University of North Dakota School of Medicine, Fargo, ND, US

INTRODUCTION: In this study, we compare treatment and prognosis outcomes of rural and urban dwelling patients diagnosed with stage III-IV melanoma and hypothesize that patients from rural areas experience longer duration to guideline concordant care, higher stage at diagnosis, and decreased overall survival rates. **METHODS:** We conducted a retrospective chart review of patients diagnosed with stage III-IV melanoma from 2011-2022 at 4 hospital locations spanning across 3 states in the Upper Midwest. For each patient, rural versus urban residence was assigned by using zip code data to generate rural-urban commuting area (RUCA) codes. Population density quartiles (PDQs) were also calculated with PDQ-1 and PDQ-4 representing the least and most populous areas, respectively. The primary endpoints of the study included the number of days from melanoma diagnosis to immunotherapy and surgery start dates, stage at diagnosis, and time-to-event survival analysis. **RESULTS:** Our study population was comprised of 344 patients, of which 197 were rural and 147 were urban. Stage III melanoma diagnoses accounted for 246 patients, while stage IV melanoma diagnoses accounted for 98 patients. Approximately 31% of urban patients were diagnosed with stage 4 melanoma at disease presentation, compared to 26% of rural patients. The mean age of patients was 62.2 years. Significant differences in gender were observed between the two categories, with 70% of patients from rural areas being male compared to 59% in urban locations (p=.04). Race was relatively

homogenous across both rural and urban patients and PDQs. Patients in PDQ-3 had the highest mean BMI (48.37), followed by patients in PDQ-1 (41.44) (p=.025). No statistically significant differences were observed in the number of days between melanoma diagnosis and start of immunotherapy or surgery. However, trends of longer duration to immunotherapy and surgery for patients in rural areas was observed, with patients in PDQ-1 experiencing 82 and 31 day wait periods, compared to patients in PDQ-4 who experienced 68 and 29 day wait periods, respectively. Pertaining to specific immunotherapy received, rural patients were significantly more likely to receive pembrolizumab than urban patients (p=.006). No statistically significant differences were observed in stage at diagnosis across both rural and urban patients and PDQs. **CONCLUSIONS:** No statistically significant results were observed to support our hypothesis. However, both rural and urban patients diagnosed with stage III-IV melanoma experienced a period 1–2-months between diagnosis and receipt of guideline concordant care, likely a result of specialized provider scarcity in the Upper Midwest.

P400. Assessing the 10% Rule in Sentinel Lymph Node Biopsy in Merkel Cell Cancer

Neha Malik, MD, MS[1]; Amblessed Onuma[2]; Brandon M Cope[3]; Phyu Aung[4]; Rohini Morey[5]; Davis Ingram[6]; Varshini Arunkumar[7]; Yi-Ju Chiang[8]; Devarati Mitra[9]; Russell G. Witt[10]; Emily Z Keung[11]

[1]MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [3]MD Anderson Cancer Center, Houston, TX, US; [4]MD Anderson Cancer Center, Houston, TX, US; [5]MD Anderson Cancer Center, Houston, TX, US; [6]MD Anderson Cancer Center, Houston, TX, US; [7]MD Anderson Cancer Center, Houston, TX, US; [8]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [9]MD Anderson Cancer Center, Houston, TX, US; [10]University of Virginia, Charlottesville, VA, US; [11]MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Merkel cell carcinoma (MCC) is a rare cutaneous malignancy with a predisposition to spread to regional lymph nodes. Sentinel lymph node biopsy (SLNB) is recommended to assess for locoregional spread, to facilitate staging, and to inform prognosis. Many surgeons who use dual tracer of technetium labelled sulfur colloid (Tc99) and blue dye use the "10% + blue" rule adopted from the SLNB technique in breast cancer and melanoma surgery, where all nodes with a count ≥10% of the hottest node ex vivo or blue dye staining are removed. The goal of this study was to assess the rate of SLN positivity among nodes removed harboring ≥10% of the highest count in our cohort of patients with MCC. **METHODS:** We performed a retrospective review of patients with MCC treated at our institution between 2005-2023 who underwent SLNB (N=184). Operative notes and pathology reports were reviewed for each patient. The number of SLNs removed per patient, the ex vivo count of each SLN, and the presence of nodal metastasis were recorded. **RESULTS:** Most patients were male (N=119, 65%), white (N=170, 92%), and immunocompetent (N=158, 86%) with a mean age of 69 years (range 28-83) (Table 1). MCC most commonly arose in the upper extremities (36%), head/neck region (34%), and lower extremities (23%) and drained to the axillary (38%), inguinal (24%) and cervical (18%) nodal basins. The mean number of SLNs identified was 2 (range 1-7) with a mean number of positive SLNs of 0.7 (range 1-5). A total of 428 SLNs were identified of which 400 (93%) harbored counts of at least 10% of the highest count. In total, 126 (29%) SLNs were positive, of which 7 SLNs (6% of 126) harbored less than 10% of the highest count. 302 (71%) SLNs were negative, of which 196 (65%) harbored ≥ 10% of the highest count. Among 125 patients who had ≥ 2 SLNs identified, there were 55 positive SLNs found and 48 SLNs (87%) had ≥ 10% of the highest count. **CONCLUSIONS:** The observed rate of SLN positivity in this cohort is consistent with that reported in the literature. While the true predictive value of SLNB in breast cancer and melanoma with the 10% cutoff is known and exceeds 94%, this practice has not been fully evaluated for MCC. Alternative cutoffs could be explored to optimize the yield of positive SLNs identified while minimizing the number of negative lymph nodes removed in patients with MCC.

	Number	%
Age (mean, SD)	69.3 (11.5)	
SEX		
Female	65	35
Male	119	65
Race/Ethnicity		
White	170	92
Black	1	1
Hispanic	8	4
Asian	2	1
Other	2	1
Immunocompetent		
No	26	14
Yes	158	86
History of Prior Cancer		
No	93	51
Yes	91	49
Median Overall Survival	195	
1-Year Overall Survival	92%	
5-Year Overall Survival	61%	
1-Year Nodal Recurrence Free Survival	92%	
5-Year Nodal Recurrence Free Survival	82%	

P401. CD45RO-Based Digital Spatial Proteomic Signatures Predict Immunotherapy Response in Melanoma

David G Su, MD[1]; Thazin N Aung[2]; Jonathan H Warrell[3]; David Schoenfeld[4]; Sandra Martinez-Morilla[5]; Noam S Gaiger[6]; Nay NN Chan[7]; Dijana Djureinovic[8]; Kelly Olino, MD[9]; Lucia Jilaveanu[10]; David L Rimm[11]; Harriet M. Kluger[12]

[1]Yale New Haven Hospital, New Haven, CT, US; [2]Yale University School of Medicine , US; [3]Yale University School of Medicine, US; [4]Yale School of Medicine, New Haven, CT, US; [5]Yale University School of Medicine , US; [6]Yale School of Medicine, New Haven, CT, US; [7]Yale University School of Medicine , US; [8]Yale School of Medicine, New Haven, CT, US; [9]Yale University School of Medicine, Department of Surgery, New Haven, CT, US; [10]Yale School of Medicine, New Haven, CT, US; [11]Yale University School of Medicine , US; [12]Yale School of Medicine, New Haven, CT, US

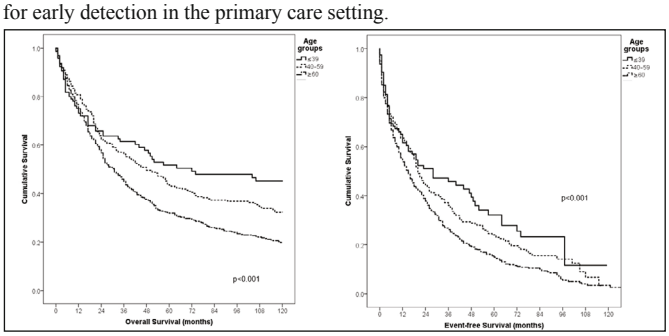
INTRODUCTION: Melanoma, an aggressive and immunogenic form of skin cancer, presents significant treatment challenges due to the varied responses patients exhibit to immune checkpoint inhibitors (ICIs). Our work aims to identify predictive biomarkers for ICI response in advanced melanoma by using digital spatial profiling (DSP) of protein expression within the tumor immune microenvironment (TIME). **METHODS:** We investigated spatial protein expression in two independent cohorts of melanoma patients (A: 69; B: 51) treated with PD-1-based monotherapy or dual PD-1/CTLA-4 therapy. Tumors were stained with fluorescent antibodies against S100/PMEL (tumor), CD45 (immune), and SYTO (nuclear dye) to define compartments and captured with an oligo-based 68 plex protein panel for proteomic analysis. For analysis, we employed univariable and multivariable analyses, as well as LASSO Cox regression models to assess response and resistance to therapy. **RESULTS:** In the tumor compartment, CD45RO expression was significantly associated with better progression-free survival (PFS), with an HR of 0.37 (95% CI: 0.198–0.699) and an adjusted p-value of 0.014. In the CD45+ immune cell compartment, CD45RO, CD95/Fas, and Ki67 emerged as predictive features of treatment resistance in the training cohort (HR = 1.8, 95% CI: 1-3.4, p = 0.05). However, this signature did not achieve validate in the independent cohort (HR = 1.4, 95% CI: 0.77-2.5, p = 0.13). In the CD68+ macrophage compartment, CD44, and Ki67 were identified as predictive features of treatment resistance in the training cohort (HR = 1.9, 95% CI: 1-3.5, p = 0.04). This signature was successfully validated in the validation cohort (HR = 1.8, 95% CI: 0.96-3.2, p = 0.03). **CONCLUSIONS:** Our proteomic analysis revealed CD45RO as a potential marker for treatment resistance. The identification of compartment-based biomarkers has implications for providing predictive power in the response to immunotherapy.

P402. Clinical Characteristics and Outcomes of Melanoma Among Latin American Adolescents and Young Adults Compared to Middle-Aged and Elder population: A Cohort Analysis Over 10 years

Gonzalo Ziegler Rodriguez[1]; Gabriel A De la Cruz Ku[2]; Jiddu A Guart[3]; Jessica J Farzan[4]; Anshumi Desai[5]; Kabir A Torres[6]; Marcelo Chávez-Diaz[7]; Camila Franco[8]; Jessica Mroueh[9]; Vanessa Mroueh[10]; Nichita Kulkarni, MD[11]; Hamed Sarikhani[12]

[1]Instituto Nacional de Enfermedades Neoplasicas, Lima, PE; [2]University of Massachusetts Medical School, Worcester, MA, US; [3]University of Massachusetts Medical School, Worcester, Worcester, MA, US; [4]University of Massachusetts Medical School, Worcester, MA, US; [5]University of Miami Miller School of Medicine, Miami, FL, US; [6]University of Massachusetts Medical School, Worcester, MA, US; [7]Guillermo Almenara Irigoyen National Hospital, Lima, PE; [8]University of Texas Medical Branch at Galveston, Texas, Galveston, TX, US; [9]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, US; [10]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [11]University of Massachusetts Medical School, Worcester, MA, US; [12]Montefiore Medical Center, Bronx, NY, US

INTRODUCTION: Melanoma has shown to have unique characteristics in Hispanic population, outcomes among this population are rarely explored in adolescents and young adults (AYAs). Our aim was to compare sociodemographic, clinical, and survival outcomes of Latin American AYAs (≤39y) with middle-aged (40–59y) and older (≥60y) patients with melanoma. **METHODS:** A single-center retrospective cohort study among patients with melanoma stages I–IV was conducted in Lima, Peru, 2010-2019. We evaluated overall survival (OS) and event-free survival (EFS) rates. Cox regression analysis was used to assess the prognostic factors. **RESULTS:** Of 1121 patients with melanoma, 118 (10.5%) were AYAs, 357 (31.9%) were middle-aged, and 645 (57.6%) were elderly. Less frequency of lower extremity as primary site (56.8%, 68.9%, 82.3%, p<0.01), ulceration (46.8%, 58.8%, 72.5%, and acral histology (22.6%, 32.8%, 44.3%, p<0.01) were present in AYAs. Moreover, AYAs had higher frequency of AJCC stage I (16.1%, 10.1%, 7.9%) and IV (25.4%, 24.6%, 21.9%, p<0.01). AYAs had more frequent amputation of fingers, toes, and extremities (30.6%, 20.6%, 33.0%, p=0.01), as well as adjuvant chemotherapy (10.3%, 18.4%, 11.2%, p=0.03). There were no differences in sex, Breslow depth, and number of mitosis per mm2, and lymph node surgery. With a median follow-up of 9.8 years, the 5-year OS and EFS rates for AYAs (52%, 32) were better than middle-aged (43%, 23%) and older population (32%, 15%) (p<0.01). When analysis was performed by stage, AYAs had better 5-year OS rates in stages I (100% vs. 90% vs. 73%,p=0.03), II (68% vs. 68% vs. 44%, and III (37% vs. 28% vs.20%, while no differences in stage IV. In regards to EFS, similar differences were found in stages I, II, and III (p<0.01). Multivariate analyses showed that AYAs had better prognosis than elderly population (≥60y, HR=1.93), while subgroup analysis according to stage showed elderly population was a prognostic factor of worse OS for stages II (HR=3.32) and III (HR=1.85); and worse EFS for stage III (HR=1.32). **CONCLUSIONS:** Latin American AYAs with melanoma have different characteristics than other populations with better outcomes than middle-aged and older populations, therefore younger age is a protector factor for better OS and EFS when treatment is optimal and according to the stage. Due to the high frequency of Stage IV in AYAs, it is crucial to develop strategies for early detection in the primary care setting.



P403. Defining Real-World Treatment Failure of First-line Immunotherapy in Locally Advanced and Metastatic Melanoma

Walter Donica[1]; Tyler Jones[2]; Maiying Kong, PhD[3]; Michael Goldsby, PhD[4]; Jason Chesney, MD PHD[5]; Kelly McMasters, MD, PhD[6]; Michael E. Egger, MD, MPH[7]

[1]University of Louisville, Louisville, KY, US; [2]University of Louisville, Louisville, KY, US; [3]University of Louisville, Louisville, KY, US; [4]University of Louisville, Louisville, KY, US; [5]University of Louisville, Louisville, KY, US; [6]University of Louisville, Louisville, KY, US; [7]University of Louisville Department of Surgery, Louisville, KY, US

INTRODUCTION: As many as 69% of patients with cutaneous melanoma progress while on immune checkpoint inhibitors (ICI). Little is known about risk factors for progression. Here we seek to define progression rates based on ICI regimens and characterize factors associated with progression. **METHODS:** A real-world, retrospective cohort of patients with locally advanced or metastatic melanoma treated with ICI in community oncology practices was identified from the Flatiron Health database. Progression-free survival, defined as clinical, radiographic, or pathologically confirmed progression or death, was evaluated using the Kaplan-Meier method stratified by the first-line ICI and extent of disease (locoregional vs. metastatic). Cox-proportional hazards models were used to evaluate risk factors for progression. **RESULTS:** A total of 6,128 patients with locoregional (N=1,015, 17%) or distant metastatic (N = 5,113, 83%) melanoma were treated with ICIs. Median age was 67 [IQR 57-76] and 68% were male. The greatest proportion of patients were treated with PD-1 monotherapy (59%) followed by combination PD-1/CTLA-4 inhibition (21%), with the remainder on single-agent CTLA-4 (16%) or combination PD-l/LAG-3 (4%). Patients on PD-1 monotherapy tended to be older, while patients on CTLA-4 monotherapy had fewer comorbidities (Table). First-line ICI in metastatic disease was predominately PD-1 monotherapy (45%) and combination PD-1/CTLA-4 (38%) with a minority receiving single-agent CTLA-4 (14%) or dual-agent PD-1/LAG-3 (3%). PD-1 monotherapy was more likely to be used in locoregional disease (OR 2.57 [95% CI 2.22-2.96]) and M1a/b compared to M1c/d disease (OR 1.84 [1.62-2.09]). Combination PD-1/CTLA-4 was used more often in metastatic disease (OR 2.26 [1.92-2.65]) and specifically M1c/d compared to M1a/b (OR 1.71 [1.49-1.96]). At 6 months, 34% [95% CI 32-36%] of patients on PD-1, 45% [43-47%] on PD-1/CTLA-4, and 53% [50-57%] on CTLA-4 progressed on 1st-line therapy for stage IV disease. Rates of progression at 6 months in locoregional disease were similar between groups (PD-1 18% [15-21%] vs. PD-1/CTLA-4 23% [17-28%] vs. CTLA-4 17% [8-26%]). Increasing M-classification (M1c 1.94 [1.48-2.53], M1d 2.94 [2.26-3.82]) was a risk factor for disease progression controlling for additional factors. **CONCLUSIONS:** Real-world data demonstrate ICI regimen selection is tailored to disease severity and progression rates are similar in those with locally advanced melanoma at 6 months. After adjusting for ICI, only increasing M-classification significantly predicted time to progression in stage IV disease.

Table. Demographic and clinical characteristics.

Characteristic	Overall N = 5,892[1]	PD-1 N = 2,965	PD-1/CTLA-4 N = 2,131	CTLA-4 N = 796	p-value
Median Age (IQR)	67 (57-76)	70 (61-78)	63 (53-71)	65 (55-74)	<0.001
Male	4,033 (68%)	2,003 (68%)	1,489 (70%)	541 (68%)	0.20
CCI[2]					<0.001
0	1,726 (29%)	856 (29%)	562 (26%)	308 (39%)	
1	291 (4.9%)	168 (5.7%)	99 (4.6%)	24 (3.0%)	
≥2	3,875 (66%)	1,941 (65%)	1,470 (69%)	464 (58%)	
Ulceration Status					<0.001
No	1,296 (22%)	726 (24%)	418 (20%)	152 (19%)	
Yes	1,545 (26%)	831 (28%)	523 (25%)	191 (24%)	
Unknown	3,051 (52%)	1,408 (47%)	1,190 (56%)	453 (57%)	
T-Stage at Initial Diagnosis					<0.001
T0	65 (1.1%)	33 (1.1%)	23 (1.1%)	9 (1.1%)	
T1	380 (6.4%)	180 (6.1%)	151 (7.1%)	49 (6.2%)	
T2	736 (12%)	371 (13%)	262 (12%)	103 (13%)	
T3	915 (16%)	508 (17%)	284 (13%)	123 (15%)	
T4	1,009 (17%)	581 (20%)	306 (14%)	122 (15%)	
Unknown	2,787 (47%)	1,292 (44%)	1,105 (52%)	390 (49%)	
Stage at Initial Diagnosis					<0.001
0	27 (0.5%)	9 (0.3%)	11 (0.5%)	7 (0.9%)	
I	527 (8.9%)	240 (8.1%)	230 (11%)	57 (7.2%)	
II	1,047 (18%)	562 (19%)	351 (16%)	134 (17%)	
III	1,451 (25%)	850 (29%)	418 (20%)	183 (23%)	
IV	1,853 (31%)	832 (28%)	786 (37%)	235 (30%)	
Unknown	987 (17%)	472 (16%)	335 (16%)	180 (23%)	
ICI Treatment Setting					<0.001
Locally Advanced	980 (17%)	684 (23%)	216 (10%)	80 (10%)	
Metastatic	4,912 (83%)	2,281 (77%)	1,915 (90%)	716 (90%)	
M-classification[3]					<0.001
M1a	400 (8.1%)	232 (10%)	121 (6.3%)	47 (6.6%)	
M1b	822 (17%)	475 (21%)	252 (13%)	95 (13%)	
M1c	1,692 (34%)	734 (32%)	699 (37%)	259 (36%)	
M1d	1,862 (38%)	749 (33%)	808 (42%)	305 (43%)	
Unknown	136 (2.8%)	91 (4.0%)	35 (1.8%)	10 (1.4%)	
BRAF Mutation Detected	1,712 (29%)	781 (26%)	751 (35%)	180 (23%)	<0.001

[1]Excludes patients on PD-1/LAG-3 therapy due to small sample size and limited follow-up (N = 190), patients without follow-up (N = 44), and patients with other ICI regimens (N = 2)

[2]Charleson Comorbidity Index

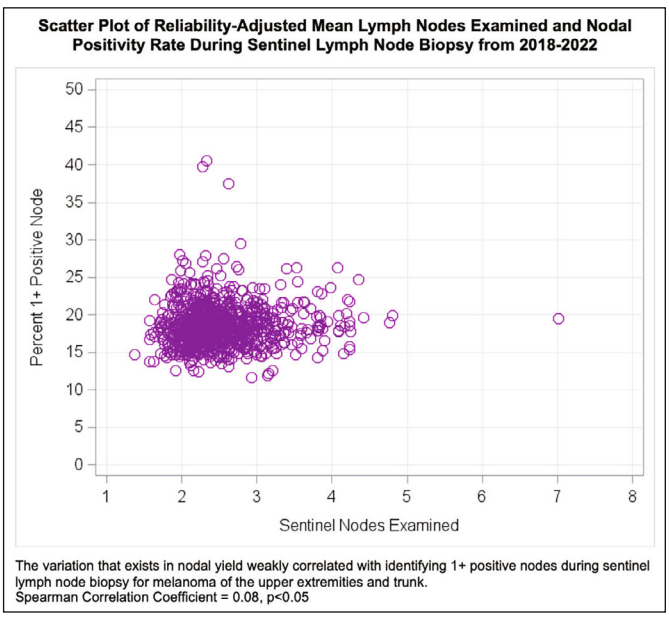
[3]M-classification at start of immunotherapy

P404. Evaluating Variation in Lymph Node Sampling During Sentinel Lymph Node Biopsy for Melanoma of the Trunk and Upper Extremities

Crystal D Taylor, MD, MPH, MS[1]; Vanessa S Niba, MD, MS[2]; Alison S Baskin, MD[3]; Nicole Mott, MD, MSCR[4]; Abigail Kappelman[5]; Erin Kim[6]; Brandy R Sinco, MA, MS[7]; Ton Wang, MD, MS[8]; Tasha Hughes, MD, MPH[9]; Lesly A Dossett, MD, MPH[10]

[1]University of Michigan, Ann Arbor, MI, US; [2]University of Michigan, Ann Arbor, MI, US; [3]University of California, San Francisco, San Francisco, CA, US; [4]University of colorado, Aurora, CO, US; [5]University of Michigan, Ann Arbor, MI, US; [6]University of Michigan, Ann Arbor, MI, US; [7]University of Michigan, Ann Arbor, MI, US; [8]Duke University Medical Center, Durham, NC, US; [9]University of Michigan, Ann Arbor, MI, US; [10]University of Michigan, Ann Arbor, MI, US

INTRODUCTION: The American College of Surgeons operative standards for melanoma does not address the quality or quantity of lymph node sampling. Nodal sampling, performed through techniques such as sentinel lymph node biopsy (SLNB), is important in melanoma as it directly affects staging, prognostication, and adjuvant therapy decisions. We sought to characterize the current facility-level variation in lymph node yield and nodal positivity performed during SLNB in melanoma to assess if there is opportunity for improvement through standardization. **METHODS:** We performed a cohort study using the National Cancer Database of men and women who underwent SLNB for T1b-T4 cutaneous melanoma of the upper extremities and trunk from 2018-2022. Melanoma of the upper extremities and trunk were chosen to limit the variation observed related to the location where SLNB is performed by restricting it only to the axilla. Reliability-adjusted estimates for nodal yield were generated from generalized linear mixed models (GLMM) by using Poisson regression with random intercepts for hospitals, while reliability-adjusted estimates for lymph node positivity were computed from GLMM using logistic regression with random intercepts for hospitals. The correlation between mean nodal yield and nodal positivity was calculated by using the Spearman correlation coefficient. **RESULTS:** 48,653 patients who underwent SLNB for cutaneous melanoma of the upper extremities and trunk across 1,167 facilities were evaluated. Median age of our cohort was 65 (IQR 54-73) years. SLNB median facility-level nodal yield was 2.4 (IQR 1.4-2.7) for melanoma with nodal yields ranging from 1.4 to 7.0 across facilities. The median nodal positivity rate for SLNB in melanoma was 18.0% (IQR 11.6%-19.5%), with facility rates of nodal positivity ranging from 11.6% to 40.5% (Figure 1). A weak correlation between nodal yield and nodal positivity rate was observed (Spearman correlation coefficient = 0.08, p<0.05). **CONCLUSIONS:** Facility-level variation in nodal yield was present for SLNB. However, this variation was minimal and weakly correlated with nodal positivity. The data suggests that SLNB performed for melanoma of the trunk and upper extremities is well standardized. Future efforts to improve technical quality for this procedure may be considered by examining SLNB performed for sites other than the axilla or other axillary surgery procedures such as axillary lymph node dissection.



P405. Factors Influencing Sentinel Lymph Node Biopsy Utilization in Non-Ulcerated Melanomas 1mm or Greater

Mackenzie M Mayhew, MD[1]; Chengli Shen[2]; Nidhi Kuchimanchi[3]; Jacob Sellers[4]; Lynn Dengel, MD[5]; Craig Slingluff, MD[6]; Russell G. Witt, MD[7]

[1]University of Virginia, Charlottesville, VA, US; [2]University of Virginia, Charlottesville, VA, US; [3]University of Virginia, Charlottesville, VA, US; [4]University of Virginia, Charlottesville, VA, US; [5]University of Virginia, Charlottesville, VA, US; [6]University of Virginia, Charlottesville, VA, US; [7]University of Virginia, Charlottesville, VA, US

INTRODUCTION: The National Comprehensive Cancer Network (NCCN) guidelines recommend against sentinel lymph node biopsy (SLNB) in patients with a sentinel node metastasis risk below 5% and in favor of SLNB for those with a risk of 10% or greater. In 2020, the Melanoma Institute of Australia (MIA) introduced a validated nomogram to predict individual sentinel node metastasis risk. We analyzed data collected prior to the nomogram's implementation and applied the MIA risk calculator to stratify patients with non-ulcerated melanomas ≥1mm into risk groups of <5% and >10%, with the goal of identifying factors linked to performing SLNB in low-risk patients (<5%) and omitting SLNB in high-risk patients (>10%). **METHODS:** Patients diagnosed with cutaneous melanoma between 2018 and 2020 with a Breslow thickness of ≥1mm and no ulceration were identified from the National Cancer Database (NCDB). Ulcerated melanomas were excluded, as ulceration is a well-established risk factor for sentinel lymph node metastasis and SLNB use is less ambiguous. Using the MIA risk calculator, patients were stratified into <5% and >10% risk groups. Patient and tumor characteristics associated with receiving SLNB in both risk groups were analyzed using univariate and multivariable logistic regression models. **RESULTS:** Of the 7116 patients included, 935 had an estimated <5% risk of sentinel node metastasis and 6181 had an estimated >10% risk. In the <5% risk group, 29.8% (n=279) received SLNB while in the >10% risk group, 79.4% (n= 4901) received SLNB. Younger age was the only factor significantly associated with receipt of SLNB in the <5% risk group (Table 1). In the >10% group, the factors associated with being less likely to receive SLNB included older age and increasing Charlson-Deyo scores. Increasing mitotic rate was associated with an increased likelihood of receiving SLNB in the >10% group. Facility type was not associated with performance of SLNB. **CONCLUSIONS:** Among patients with non-ulcerated melanomas ≥1mm, 29.8% of those with an estimated sentinel lymph node metastasis risk <5% underwent SLNB, while 20.6% of those with a risk >10% did not. Age and comorbidities significantly impacted SLNB decisions, with younger patients more likely to undergo SLNB despite a metastasis risk <5%, while older patients and those with more comorbidities were less likely to receive SLNB even when their risk exceeded 10%. This study was conducted with data that predates the implementation of the MIA risk calculator and provides a baseline for future assessments of the calculator's influence on SLNB practice patterns.

Table 1. Independent predictors of undergoing sentinel lymph node biopsy for patients with less than 5% and greater than 10% sentinel lymph node metastasis risk.

	<5% Risk Group		>10% Risk Group	
Variable	**Odds Ratios [95% CI]**	**P-value**	**Odds Ratios [95% CI]**	**P-value**
Sex (ref: female)				
Male	0.79 [0.57, 1.10]	0.2	1.09 [0.94, 1.25]	0.2
Ethnicity (ref: Hispanic)				
Non-Hispanic	1.01 [0.11, 7.77]	>0.9	1.02 [0.63, 1.62]	>0.9
Facility type (ref: community program)				
Comprehensive Community Cancer Program	0.58 [0.20, 1.44]	0.3	1.10 [0.78, 1.54]	0.6
Academic/Research Program	0.44 [0.16, 1.04]	0.082	1.02 [0.73, 1.42]	0.9
Integrate Network Cancer Program	0.71 [0.24, 1.83]	0.5	1.35 [0.94, 1.91]	0.10
Age	0.92 [0.90, 0.94]	<0.001	0.95 [0.94, 0.95]	<0.001
Charlson-Deyo Score (ref: 0)				
1	1.46 [0.93, 2.34]	0.11	0.78 [0.64, 0.94]	0.009
2	0.67 [0.37, 1.26]	0.2	0.72 [0.53, 0.98]	0.032
3	1.19 [0.58, 2.55]	0.6	0.64 [0.49, 0.85]	0.002
Insurance Status (ref: uninsured)				
Private	-	-	1.28 [0.76, 2.08]	0.3
Medicaid	-	-	0.69 [0.38, 1.21]	0.2
Medicare	-	-	1.58 [0.93, 2.60]	0.08
Lymphovascular Invasion (ref: absent)	-	-	0.85 [0.71, 1.03]	0.09
Mitotic rate (ref: 0)				
1	0.93 [0.63, 1.37]	0.7	3.63 [2.36, 5.58]	<0.001
2	1.36 [0.87, 2.16]	0.2	3.69 [2.49, 5.43]	<0.001
3	1.13 [0.69, 1.85]	0.6	3.24 [2.24, 4.68]	<0.001

P406. Gender stratified by age does not impact survival in patients with advanced melanoma receiving immunotherapy

Hilary R Keller, MD[1]; Douglas A Hanes, PhD[2]; Danny Lascano, MD[3]; Jillian McCabe, MD[4]; Paul J Shin, MD/PhD[5]; Melanie Goldbarb, MD[6]; Richard Essner, MD[7]

[1]Providence Saint John's Cancer Institute, Santa Monica, CA, US; [2]Center for Cardiovascular Analytics, Research and Data Science, Providence Research Network, Portland, OR, US; [3]Providence Saint John's Cancer Institute, Santa Monica, CA, US; [4]Saint John's Cancer Institute, Santa Monica, CA, US; [5]Saint John's Cancer Institute, Santa Monica, CA, US; [6]Saint John's Cancer Institute at Providence Saint John's Health Center, Santa Monica, CA, US; [7]Providence Saint John's Cancer Institute, Santa Monica, CA, US

INTRODUCTION: It remains unclear whether the therapeutic effect of immunotherapy varies by gender in patients with advanced melanoma, according to menopausal hormonal status in females. We evaluated outcomes in stage IV melanoma patients who received immunotherapy, stratified by gender and age to estimate pre-, peri- and post-menopausal status. **METHODS:** The National Cancer Database (NCDB) was queried to identify patients with stage IV melanoma who did or did not receive first course immunotherapy from 2012 to 2019. Demographics including age and gender were summarized for the cohort and subgroups. Other demographics included race, insurance status, geographic location, facility type, and Charlson-deyo score. Multivariable Cox regression and Kaplan-Meier analyses of overall survival were performed. **RESULTS:** Of 20023 patients with stage IV melanoma, 67.7% were male (n=13552), 32.3% female (n=6471), and 44.2% received immunotherapy (n=8854). On multivariable analysis, among those patients who did not receive first course immunotherapy, female gender was associated with improved overall survival compared to males (HR 0.90, 95% CI 0.86-0.94, p<0.001), but there was no difference in survival between males and females among those who received immunotherapy (HR 0.95, 95% CI 0.9-1.01, p=0.106). The benefit of immunotherapy was smaller in females compared to males overall (HR 1.08, 95% CI 1.00-1.17, p=0.039), and greater in those aged 45-60 years (HR 0.82, 95% CI 0.72-0.95, p=0.006) and age >60 (HR 0.84, 95% CI 0.74-0.96, p=0.008), relative to 18-44-year-old patients, regardless of gender. The association of age with benefit of immunotherapy did not differ between males and females (p=0.50 for the three-way interaction between age group, gender, and immunotherapy). **CONCLUSIONS:** Among stage IV melanoma patients who received first course immunotherapy, there was no difference in survival outcomes between male and female patients, even when stratified by age groups to estimate hormonal status in female patients. The benefit of immunotherapy was greatest in those aged >45 years, regardless of gender. Female patients showed superior survival without immunotherapy but less benefit from immunotherapy treatment, which eliminated the disparity in OS between males and females. Further studies assessing the age disparities in patients receiving immunotherapy and increasing access to immunotherapy should be advocated.

P407. Impact of Time to Surgery on Outcomes Following Surgery for Melanoma

Rainya N Heath[1]; Tamara Damrel[2]; Gabriel Ologun[3]; Christopher J Gannon[4]; Omar H Llaguna[5]

[1]Memorial Healthcare System, Hollywood, FL, US; [2]Memorial Healthcare System, Hollywood, FL, US; [3]Memorial Healthcare System, Hollywood, FL, US; [4]Memorial Healthcare System, Hollywood, FL, US; [5]Memorial Healthcare System, Hollywood, FL, US

INTRODUCTION: The National Comprehensive Cancer Network (NCCN) indicates that, similar to other malignancies, the stage at presentation in melanoma significantly influences patient outcomes, with 84% of patients presenting with localized disease and over 90% achieving 5-year survival. However, there are no official guidelines regarding the timing of surgical intervention for melanoma or studies assessing its impact on outcomes. **METHODS:** This study examines the effect of time to surgical intervention on survival outcomes in patients with non-metastatic melanoma, using the NCDB (2004-2021). We identified 732,219 patients who underwent surgery and categorized them by time to surgery: within 1 month, 2-3 months, and 4 or more months post-diagnosis. Statistical analyses included Pearson's chi-square tests for categorical variables and Kaplan-Meier methods for overall survival (OS) estimates. **RESULTS:** Within one month, 77.9% of patients had surgery, while only 2.4% waited 4 or more months. Patients in the ≥4 months cohort were older, more likely to be male, non-White, and treated at academic/research facilities (58.5%) (p < 0.001). This cohort also displayed advanced disease characteristics, including a higher incidence of pathologic T4 (12.7%), N2 (3.3%) and M1 (0.5%) disease (p < 0.001). Additionally, compared to other cohorts, the ≥4 months cohort had a higher likelihood of regional lymph node examination (65.4%) and having 4 or more positive lymph nodes (4.8%) (P < 0.001). Survival analysis revealed that patients who had surgery after ≥4 months were the least likely to be alive at the last contact (71.6%) and the least likely to achieve long-term survival, defined as surviving five or more years, (45.3%) (P < 0.001). **CONCLUSIONS:** Survival analyses demonstrated significantly shorter mean OS times for the ≥4 months cohort across clinical and pathologic stages. These findings highlight the importance of timely surgical intervention in enhancing outcomes for melanoma patients, emphasizing that timeliness should be a priority in treatment strategies for non-metastatic melanoma.

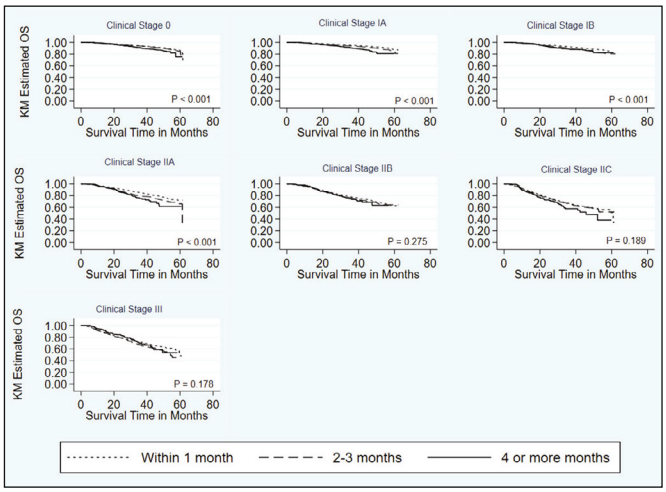


Figure 1. Kaplan-Meier survival functions, by clinical stage and time to surgery cohorts

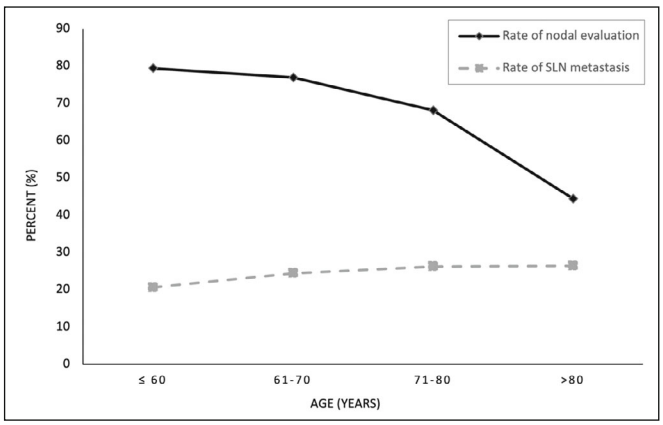
P408. Is Patient Age Associated with Sentinel Lymph Node Metastasis in Merkel Cell Carcinoma?

Neha Shafique[1]; Emily Ertmann, BS[2]; Gracia M Vargas, MD[3]; Mohammad S. Farooq, MD, MS[4]; Phyllis Gimotty, PhD[5]; Giorgos C Karakousis, MD[6]; John T Miura, MD[7]

[1]Hospital of University of Pennsylvania, Philadelphia, PA, US; [2]University of Pennsylvania Perelman School of Medicien, Philadelphia, PA, US; [3]Hospital of University of Pennsylvania, Philadelphia, PA, US; [4]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [5]University of Pennsylvania Perelman School of Medicine, Department of Biostatistics, Epidemiology, a, Philadelphia, PA, US; [6]University of Pennsylvania, Philadelphia, PA, US; [7]University of Pennsylvania, Philadelphia, PA, US

INTRODUCTION: Merkel cell carcinoma (MCC) is an aggressive, cutaneous malignancy and its management often parallels guidelines for melanoma due to the rarity of MCC. Multiple studies in melanoma have highlighted a significant inverse relationship between increasing age and sentinel lymph node (SLN) metastasis. Since MCC predominantly affects patients in their mid-seventies and older, identifying a similar relationship in MCC could aid in clinical decision making. We examined the association of age and SLN positivity in MCC in a national cohort and assessed if a low-risk group could be identified in which SLN biopsy could be safely deferred. **METHODS:** The National Cancer Database was used to identify patients diagnosed with clinically localized (cN0M0) MCC between 2004 and 2020. The primary outcome was SLN metastasis. Univariable and multivariable logistic regression analyses were used to investigate the association with patient age and SLN metastasis with a subgroup analysis for tumors with size <0.5cm. **RESULTS:** We identified 13,500 patients, of which 8,503 (63%) patients underwent nodal evaluation. Rates of nodal evaluation decreased with increasing age, with 79.4% of patients aged <60 years and 44.4% patients aged >80 years undergoing nodal evaluation (Figure 1). Of patients that underwent nodal evaluation (n=8,503), the median age was 73 years (IQR: 66-80), 63% patients were male, and 94.4% patients were White. 2,133 patients (25%) had SLN metastasis with rates ranging from 20.6% for patients aged <60 years to 26.4% for patients aged >80 years (Figure 1). Older age was not associated with SLN positivity on either univariate analysis nor in a multivariable logistic regression model including other patient demographic and tumor factors. With the reference group of 61-

70 years old, the adjusted odds ratios [OR] with 95% confidence interval [CI] for the other age groups were: <60 years: 0.85 (0.70-1.02); 71-80 years: 1.09 (0.96-1.24); and >80 years: 1.08 (0.93-1.25). In a subgroup analysis of patients with tumors <0.5cm (n=1,042), SLN positivity ranged from 9.7% for patients aged <60 years to 9.4% for patients aged > 80 years. There was again no age group that had significantly different odds of SLN positivity on multivariable analysis compared to the reference group of patients aged 61-70 years old (OR (95% CI) for <60 years: 1.17 (0.57-2.42); 71-80 years: 1.57 (0.95-2.60); >80 years: 1.03 (0.56-1.91). **CONCLUSIONS:** Unlike in melanoma, there was no significant association observed between age and SLN metastasis controlling for other variables including tumor size in patients with MCC. Moreover, even among the oldest patient group (>80 years), the rate of SLN metastasis for the smallest tumors (<0.5 cm) was still appreciable (9.4%). There does not appear to be a subgroup of MCC patients whereby SLNB can be omitted based on age. While MCC and melanoma are both cutaneous malignancies often treated similarly, this study supports previous research indicating these neoplasms can have varied clinical behaviors.



P409. National Utilization of Completion Lymph Node Dissection for Melanoma in Patients with Multiple Positive Sentinel Lymph Nodes

Tyler P Robinson, MD, MS[1]; Kristen N Kaiser, MD[2]; Brian Ruedinger, PhD[3]; Theodore F Logan, MD[4]; John R. Hyngstrom, MD[5]; William A Wooden, MD[6]; Ryan J Ellis, MD, MS[7]; Karl Y Bilimoria, MD, MS[8]

[1]Surgical Outcomes and Quality Improvement Center (SOQIC), Department of Surgery, Indiana University, Indianapolis, IN, US; [2]Indiana University, Indianapolis, IN, US; [3]Surgical Outcomes and Quality Improvement Center (SOQIC), Department of Surgery, Indiana University, Indianapolis, IN, US; [4]Indiana University School of Medicine and IU Simon Cancer Center, Indianapolis, IN, US; [5]Rush, Chicago, IL, US; [6]Division of Plastic and Reconstructive Surgery, Department of Surgery, Indiana University, Indianapolis, IN, US; [7]Surgical Outcomes and Quality Improvement Center (SOQIC), Department of Surgery, Indiana University, Indianapolis, IN, US; [8]Surgical Outcomes and Quality Improvement Center (SOQIC), Department of Surgery, Indiana University, Indianapolis, IN, US

INTRODUCTION: Clinical trials for patients with melanoma have demonstrated the safety of observation in lieu of completion lymph node dissection (CLND) following a positive sentinel lymph node (SLN) biopsy. Patients with ≥2 positive SLNs were included in small number in these trials, but no data exist on outcomes in this subpopulation. Immunotherapy's increasing role recently may have also impacted practice patterns and outcomes. The objectives of this study were to (1) assess national trends of CLND use in patients with ≥2 positive SLN, (2) examine factors associated with CLND use with ≥, >2 positive SLN, and (3) examine survival among these patients. **METHODS:** Patients with stage I-III melanoma who underwent SLN biopsy between 2012 and 2021 were identified from the National Cancer Database. Patients were stratified as having ≥2 positive SLNs vs. 1 positive SLN. Proportions of patients who were treated with CLND and immunotherapy were determined. Factors associated with undergoing CLND were assessed by hierarchical logistic regression. Overall survival for patients with ≥2 positive SLN who underwent observation vs CLND was estimated with Kaplan Meier curves and Cox proportional hazards models. **RESULTS:** Among 151,442 patients (median age 61; 41.3% female) who underwent SLN biopsy for melanoma, 21,980 (14.5%) had a positive SLN, and 5,440 of those (25.2%) had ≥2 positive SLNs. Use of CLND for patients with 2 positive SLNs decreased from 73% in 2012 to 14% in 2021 while immunotherapy increased from 38% in 2012 to 76% in 2021 (Figure 1). During 2018-2021, patients with 2 positive SLNs were more likely to undergo CLND if they had melanoma located in the head/neck region (27.9% vs 17.3% for other locations; OR=1.80 95%CI 1.12-2.89) or ulcerated lesions (18.5% vs 15.4% for non-ulcerated lesions; OR=1.47 95%CI 1.06-2.05); however, there was no difference in receipt/recommendation of immunotherapy by number of SLN positive (83.0% in 1 positive SLN vs 82.3% for 2 positive SLNs for receiving/recommending immunotherapy; OR 0.92 95%CI 0.65-1.31). For patients with ≥2 positive SLN who underwent observation vs CLND between 2018-2020, there was no difference in 3-year overall survival (70.5% for 1+ SLN vs 70.8% for 2 positive SLNs, p-value 0.563) which persisted on adjusted analysis (HR 1.09, 95%CI 0.78-1.50). **CONCLUSIONS:** CLND utilization declined from 2012 to 2021 for melanoma patients with ≥2 positive SLNs in concordance with results from major clinical trials. There was no difference in survival for observation vs CLND in patients with melanoma with ≥, >2 positive SLNs on SLN biopsy. Rapidly evolving treatment recommendations have largely been incorporated into practice in the U.S.

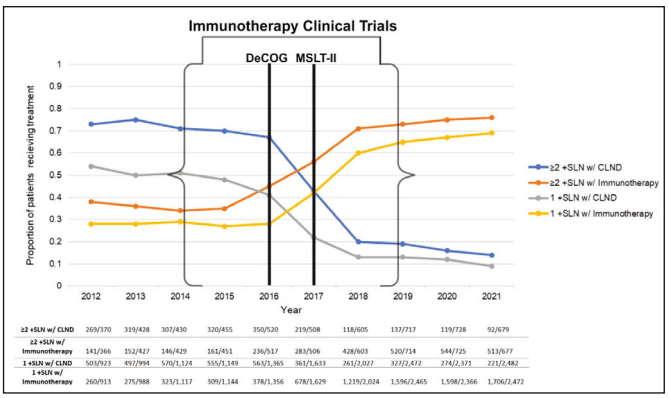


Figure 1. CLND and immunotherapy utilization in patients with positive SLN biopsy

P410. Obesity Associates with Poorer Recurrence-Free Survival Outcomes in Stage III Melanoma Patients Treated with Adjuvant Immunotherapy

Hailey Seibert[1]; Natalie N Chakraborty, MD[2]; Maira A Bhatty[3]; Kevin G. Zablonski, MD[4]; Adam Wade[5]; Jarred M. Boone, MD[6]; Trisha Lal[7]; Richard Hoehn, MD[8]; Iris Y. Sheng[9]; Luke D. Rothermel, MD, MPH[10]

[1]Case Western Reserve University School of Medicine, Cleveland, OH, US; [2]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [3]Case Western Reserve University School of Medicine, Cleveland, OH, US; [4]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [5]Case Western Reserve University School of Medicine, Cleveland, OH, US; [6]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [7]Case Western Reserve/University Hospitals, Cleveland, OH, US; [8]University Hospitals, Cleveland Medical Center, Cleveland, OH, US; [9]University Hospitals Cleveland Medical Center/Case Western Reserve University, Cleveland, OH, US; [10]University Hosptials Cleveland, Cleveland, OH, US

INTRODUCTION: The "obesity paradox" is a phenomenon whereby obesity is associated with increased incidence of cancer but may also confer a survival advantage in certain patients treated with immune checkpoint inhibitors (ICIs). Prior studies have demonstrated an association between obesity and improved overall survival in patients with unresectable melanoma treated with ICIs. However, the implications of obesity for patients with stage III melanoma receiving adjuvant immunotherapy remain unexplored. **METHODS**: Patients with stage III melanoma diagnosed between 2015 and 2022 who were treated with adjuvant immunotherapy at our institution were included. Patients were excluded if adjuvant therapy was started more than 90 days after surgery. Obesity was defined as having a body mass index (BMI) ≥ 30. A Cox proportional hazards model assessed factors independently associated with recurrence-free survival (RFS). Multivariable logistic regression was then used to assess factors associated with adverse events from first-line adjuvant immunotherapy. **RESULTS:** We abstracted 124 patients who received adjuvant immunotherapy for stage III melanoma, of whom 120 (97%) received anti-PD-1

monotherapy. 73 patients (59%) were obese, while 51 patients (41%) were not obese, with BMIs ranging from 16-29.9. Obese patients were more likely to be male (59% vs 45%), have higher Charlson Comorbidity Indices (CCI > 0 in 52% vs 37%), and have lower N stage (N1 disease in 69% vs 58%) compared with non-obese patients, although none of these differences reached statistical significance. Obese patients who received adjuvant immunotherapy experienced decreased RFS (HR 2.31; 95% CI: 1.04-5.13) compared to non-obese patients. Additionally, we observed no difference in the rates of adverse events between obese and non-obese patients. **CONCLUSIONS:** Whereas prior studies suggest improved survival outcomes in obese patients with metastatic melanoma treated with ICIs, our study shows an association of obesity with poorer RFS in stage III melanoma patients undergoing adjuvant ICI therapies. Future studies are needed to elucidate the underlying mechanisms by which obesity influences melanoma progression and treatment efficacy.

Table 1. Adjusted Hazard Ratios for Recurrence-Free Survival among Patients with Stage III Melanoma Who Received Adjuvant Immunotherapy

Covariate	No. *(%)*	Adjusted HR (95% CI)	p-value
Body Mass Index			
<30	73 *(59%)*	*Ref.*	
≥30	51 *(41%)*	2.31 (1.04-5.13)	0.04
Age at Diagnosis			
18-59	54 *(44%)*	*Ref.*	
60-79	63 *(50%)*	1.64 (0.73-3.68)	0.229
80+	7 *(6%)*	0.85 (0.22-3.33)	0.819
Sex			
Male	66 *(53%)*	*Ref.*	
Female	58 *(47%)*	0.74 (0.36-1.52)	0.406
Area Deprivation Index			
1-75 Percentile	93 *(75%)*	*Ref.*	
76-100 Percentile	30 *(24%)*	2.87 (1.39-5.96)	0.005
Unknown	1 *(1%)*	5.98 (0.67-53.37)	0.11
Charlson Comorbidity Index			
0	67 *(54%)*	*Ref.*	
1-2	41 *(33%)*	1.06 (0.44-2.58)	0.893
3	16 *(13%)*	2.40 (0.94-6.13)	0.066
T Stage			
T1-T2	38 *(32%)*	*Ref.*	
T3	48 *(40%)*	0.73 (0.26-2.02)	0.542
T4	34 *(28%)*	4.06 (1.61-10.25)	0.003
N Stage			
N1	79 *(64%)*	*Ref.*	
N2	37 *(30%)*	1.66 (0.79-3.50)	0.181
N3	8 *(6%)*	10.91 (3.13-38.04)	<0.001
Type of Therapy			
Pembrolizumab or Nivolumab Monotherapy	120 *(97%)*	*Ref.*	
Other Immunotherapy, Including Trial Drug	4 *(3%)*	1.73 (0.21-14.15)	0.61

P411. Outcomes of Clinically Detected Stage III Melanoma Through Individualized Neoadjuvant (PRADO) Approach At a Single Institution

Drew Erali, MD, MPH[1]; Elizabeth Josephine Olecki, MD[2]; Alicia Goldenberg, MD[3]; Doru A Andea, MD[4]; Shalana B.L. O'brien, MD[5]; John Kane, MD[6]; Igor Puzanov, MD[7]; Benjamin Switzer, DO, MHSA, MS[8]; Joseph Skitzki, MD[9]

[1]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [2]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [3]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [4]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [5]Roswell Park, Buffalo, NY, US; [6]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [7]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [8]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [9]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US

INTRODUCTION: Therapeutic lymph node dissection (TLND) and one year of adjuvant systemic therapy have historically been utilized for patients with clinically positive stage III melanoma. Recently, the PRADO trial demonstrated the safety and efficacy of de-escalating surgery and omitting adjuvant therapy in patients who achieve a major pathologic response (mPR) following neoadjuvant ipilimumab (ipi) and nivolumab (nivo). We provide outcomes of patients treated with a PRADO-style protocol at a single institution. **METHODS:** A prospectively maintained database of stage III melanoma patients treated with a PRADO-style protocol at a single institution from 2023-2024 was reviewed. Patients included received two doses of neoadjuvant ipi (1mg/kg) and nivo (3mg/kg) followed by index lymph node (ILN) resection per PRADO protocol with at least one surveillance follow-up visit. Chi-squared and Wilcoxon analysis was performed for categorical and continuous variables, respectively. **RESULTS:** Twenty-five patients were included in the final analysis, including 13 (52%) patients who did not meet original PRADO inclusion criteria or follow the formal protocol. There were no differences in sex, site of ILN, pathologic class, and *BRAF* mutation status between patients who did and did not meet original PRADO inclusion criteria (p>0.05). Average age was 63 years, 9 (36%) patients were female, 8 (32%) with unknown primaries, and 11 (44%) with recurrent disease. Grade ≥3 toxicities were observed in 3 (12%) patients and one (4%) death secondary to a treatment-related adverse event prior to ILN resection. Three (12%) patients did not undergo surgery (disease progression or death). Of the 22 patients who underwent ILN resection, 16 (72.7%) demonstrated mPR (≤ 10% viable tumor), 2 (9.1%) partial responses (pPR, > 10 and ≤ 50%) and 4 (18.2%) non-responders (pNR, > 50% viable tumor). Of the 6 patients who did not exhibit a mPR, 3 underwent subsequent TLND (1 with mPR on final pathology), 1 declined TLND, and 2 patients underwent lymph node dissection instead of ILN resection due to bulky/progressive disease. Two (9.1%) patients developed post-operative complications (grade 1 and 3). 5/6 (83.3%) patients without mPR received adjuvant nivo and 1/6 (16.7%) stopped treatment due to side effects. At a median follow-up of 6.2 months (1.2 – 18.2), all patients who underwent surgery have no evidence of recurrent disease. **CONCLUSIONS:** A personalized approach based on pathologic assessment of the ILN following neoadjuvant ipi/nivo to guide stage III melanoma treatment is feasible and possible applications exist beyond the original PRADO study inclusion criteria. Longer-term follow-up is needed.

P412. Practice Patterns for Performing Sentinel Lymph Node Biopsy for T1b Melanoma Patients

Claire Baptiste, MPH[1]; Peter Callas[2]; Conor H. O'Neill[3]; Jessica A. Cintolo-Gonzalez, MD[4]

[1]Larner College of Medicine, University of Vermont, Burlington, VT, US; [2]Department of Mathematics and Biostatistics, University of Vermont, Burlington, VT, US; [3]Division of Surgical Oncology, University of Vermont Medical Center, Burlington, VT, US; [4]Division of Surgical Oncology, University of Vermont Medical Center, Burlington, VT, US

INTRODUCTION: Sentinel lymph node biopsy (SLNB) has established prognostic benefit in melanoma and results can direct further management. National Comprehensive Cancer Network (NCCN) guidelines recommend discussion of SLNB for patients with pT1b lesions acknowledging that age, comorbidities, and other pathologic features may influence decision for SLNB whereas gene expression profiling (GEP) testing requires further evidence for incorporation into clinical decision making. We aimed to assess rate of SLNB for patients with cT1b melanoma presenting to our institution and factors associated with SLNB. **METHODS:** Single-institution retrospective review was conducted of patients presenting with cT1b malignant melanoma between 2010 and 2024. Patients were defined as T1b according to current AJCC guidelines: For patients diagnosed before 2018, T1b was defined as a Breslow thickness ≤ 1.0mm with either ulceration or mitotic rate ≥1mm2 whereas post 2018, T1b lesions were Breslow thickness 0.8-1.0mm or any thickness ≤ 1.0mm with ulceration. Demographic, clinical, and pathologic data along with treatment details were collected. Initial bivariate analysis was performed using two-sample t-test for continuous variables and Fisher's exact test for categorical variables. Next, logistic regression was used to identify independent predictors of performing SLNB. Variables with a p-value <0.20 were included in the initial model with subsequent backward removal of nonsignificant variables. **RESULTS:** Of 218 patients identified who met exclusion and inclusion criteria, 133 (61%) underwent SLNB. On bivariate analysis, younger age (p=0.008), Breslow thickness ≥0.8mm (p<0.001) and higher risk histologic subtype (p<0.001) was associated with SLNB whereas presence of cardiac disease (p=0.04) and having GEP testing (p=0.003) was inversely associated with SLNB performed. (Table-1). Logistic regression found advanced age inversely associated with SLNB (OR for 10 year increase 0.64 (0.50-0.82), p<0.001) whereas Breslow thickness 0.8-1.0mm was associated with SLNB (OR=11.60 (5.63-23.88), p<0.001). While only 9 patients underwent GEP testing, only 1 had SLNB indicating that GEP testing was associated with lower rate of SLNB (OR=0.05 (0.01-0.42), p=0.006). **CONCLUSIONS:** Despite SLNB being recommended for cT1b melanoma by NCCN guidelines, only 61% of patients with T1b melanoma underwent SLNB. Younger patients and those with thicker melanomas were more likely to undergo SLNB. The small percent who had GEP testing were less likely to have SLNB warranting further understanding into decisions for using GEP testing and its clinical implications.

Table 1. Characteristics of study population and Association with SLNB Procedure (n=218)

			Mean (SD)	P value*
Age	SLNB Performed	Yes	59 (14)	0.008
		No	65 (16)	
		Total N	N (%) SLNB	P value*
N		218	133 (61%)	
Sex	Female	98	55 (56%)	0.21
	Male	120	78 (65%)	
Race	White	212	131 (62%)	0.21
	Unknown / Not Reported	6	2 (33%)	
Cardiac disease	Yes	30	13 (43%)	0.04
	No	188	120 (64%)	
Morbid obesity	Yes	8	4 (50%)	0.71
	No	210	129 (61%)	
COPD	Yes	7	4 (57%)	1.00
	No	211	129 (61%)	
Diabetes	Yes	25	17 (68%)	0.52
	No	193	116 (60%)	
Prior history: melanoma	Yes	23	14 (61%)	1.00
	No	195	119 (61%)	
Prior history: nonmelanoma	Yes	42	25 (60%)	0.86
skin cancer	No	176	108 (61%)	
Prior history: other cancer	Yes	8	7 (88%)	0.15
	No	210	126 (60%)	
Deep margin positive on Biopsy	Yes	61	37 (61%)	1.00
	No	157	96 (61%)	
Histology subtype	acral / dm / nm	4	3 (75%)	<0.001
	lentigo	33	11 (33%)	
	nodular	8	7 (88%)	
	nos	12	12 (100%)	
	ss	161	100 (62%)	
Breslow thickness (mm)	<0.8	74	23 (31%)	<0.001
	0.8-1.0	144	110 (76%)	
Ulceration	Yes	17	13 (76%)	0.20
	No	201	120 (60%)	
Mitotic rate ≥1mm^2	Yes	147	88 (60%)	0.66
	No	71	45 (63%)	
Decision Dx performed	Yes	9	1 (11%)	0.003
	No	209	132 (63%)	
Decision Dx score	Class 1a	7	1 (14%)	1.00
	Class 1b	2	0 (0%)	

* two-sample t test for age, Fisher's exact test for categorical variables

P413. Prospective Standardized Surveillance of Early-Stage Cutaneous Melanoma Based on Anatomic Staging and Molecular Profiling

Jason M. Aubrey, MD[1]; Jesse Kelley, MD[2]; Mariam Khan[3]; Hordur M Kolbeinsson, MD[4]; Hannah Liefeld[5]; Randa Preihs, NP[6]; Alexandra Bengel, PA-C[7]; Chantelle Koch, PA-C[8]; Lisa Martin, PA-C[9]; Jennifer Charchan, PA-C[10]; Kimberly Texley-Quigg, PA-C[11]; Marianne Melnik, MD[12]; G. Paul Wright, MD[13]

[1]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [2]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [3]Corewell Health West, Grand Rapids, MI, US; [4]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [5]Corewell Health West/Michigan State University, Grand Rapids, MI, US; [6]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [7]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [8]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [9]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [10]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [11]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [12]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [13]Corewell Health West - Michigan State University, Grand Rapids, MI, US

INTRODUCTION: Gene expression profiling (GEP) of cutaneous melanoma has become pervasive in clinical practice with minimal independent, non-industry-sponsored, data to guide implementation and influence practice patterns. We developed a scoring system based on anatomic staging and molecular profiling to risk stratify patients into four categories for prospective surveillance. **METHODS:** Patients with cutaneous melanoma were recruited from 2019-2023 for enrollment into the study. Inclusion criteria included pathologic stage IA-IIC and performance of a commercialized 31-GEP. Patients were stratified into one of four surveillance groups: A1 (stage IA-IIA/GEP Class 1), A2 (stage IA-IIA/GEP Class 2), B1 (stage IIB-IIC/GEP Class 1), and B2 (stage IIB-IIC/GEP Class 2). Surveillance schedules are listed in Figure 1. The primary outcome measure is rate of asymptomatic imaging-detected recurrence. Interim analysis has been performed at median follow-up of 24 months. **RESULTS:** A total of 200 patients were enrolled. Mean age is 61.0 years (SD=14.6) and 55.5% of the population was male. Primary lesions were distributed between the head & neck (n=40, 20%), trunk (n=76, 38%), and extremity (n=84, 42%). Median depth was 1.1 mm (range 0.3-8.8 mm) and 14% had ulceration present. Stage distribution was: IA (n=82, 41.0%), IB (n=71, 35.5%), IIA (n=27, 13.5%), IIB (n=16, 8.0%), IIC (n=4, 2.0%). GEP classification was Class 1 (n=145, 72.5%) and Class 2 (n=55, 27.5%). This provided a distribution of 71.0% in A1, 19.5% in A2, 2.0% in B1, and 7.5% in B2. Recurrences have been detected in 16 patients (8.0%) including 12 local/regional (6.0%) and 4 distant (2.0%) recurrences. Recurrence rates by surveillance group are: A1=4.9%, A2=10.3%, B1=0%, and B2=33.3%. Recurrences were detected by surveillance imaging in 5 (2.5%), H&P in 10 (5.0%), and symptoms in 1 patient (0.5%), respectively. **CONCLUSIONS**: Pragmatic implementation of a risk-stratified surveillance strategy has resulted in few instances of asymptomatic, imaging-detected recurrences among early-stage cutaneous melanoma patients at short-term follow-up benchmarks. Further follow-up is necessary to determine the validity of this approach.

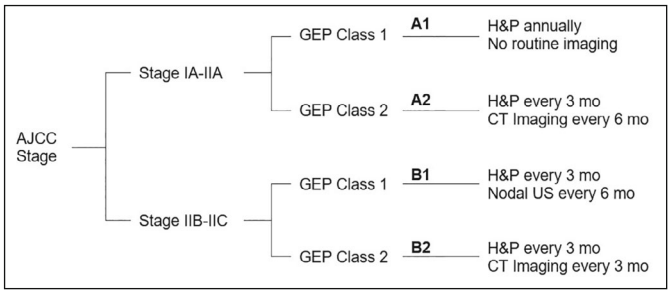


Figure 1. Risk stratification schema

P414. Provider credentials influence type of biopsy performed but not deep margin status in melanoma

Amelia Grace Stapleton Van Doren, BA[1]; Hemali Shah, MD[2]; Dia Shah, BS[3]; Ruthia Chen, MD[4]; Lucie Joerg, BS[5]; Ekaterina Sazon, BS[6]; Francisco Alicandri, BS[7]; Aasim Jaffri, BS[8]; Paytra Klein, MBA[9]; Lindy Davis, MD, FACS, FSSO[10]

[1]Albany Medical College, Albany, NY, US; [2]University of Pittsburgh Medical Center, Department of Dermatology, Pittsburgh, NY, US; [3]Albany Medical College, Albany, NY, US; [4]Albany Medical Center, Department of Surgery, Albany, NY, US; [5]Albany Medical College, Albany, NY, US; [6]Albany Medical College, Albany, NY, US; [7]Albany Medical College, Albany, NY, US; [8]Albany Medical College, Albany, NY, US; [9]Albany Medical College, Albany, NY, US; [10]Albany Medical Center, Department of Surgery, Albany, NY, US

INTRODUCTION: Diagnostic biopsy procedures for primary melanoma vary with examples including shave, punch, and excisional biopsy. A proper biopsy allows for an accurate pathology report, which becomes the basis for initial melanoma management. We aimed to assess the quality of initial melanoma biopsy in our region, question whether a provider's credentials influenced biopsy type, and whether biopsy type influenced deep margin status. **METHODS:** Retrospective review from 9/2017-2/2023 identified 523 pathology reports from melanoma patients referred to our academic center. Statistical analysis was performed using Chi-square analyses. **RESULTS:** Of 523 biopsies, 308 were performed by a physician (58.9%) and 215 by an advanced practice provider (APP, 41.1%) (Table 1). Shave biopsy was the most common type of biopsy (58.6%). APPs and physicians performed shave biopsies at similar rates (p = 0.14). Significantly more excisional biopsies were performed by physicians (15.6% vs. 3.7%, p = 0.00016), while significantly more punch biopsies were performed by APPs (20.0% vs. 13.0%, p = 0.03). Deep margin status was only reported in 360 pathology reports, with 240 of these reporting a positive deep margin (66.7%). Of the total positive deep margins, there were 175 shave biopsies (72.9%), 18 punch (7.5%), and 13 excisional biopsies (5.4%). Shave biopsies were significantly more likely to have a positive deep margin compared to all other biopsy types combined (p = < 0.00001). Physicians and APPs performed biopsies with similar deep margin positivity rates (p =

0.29). Seventeen of the 26 melanomas upstaged after oncologic resection had a positive deep margin on biopsy. Of the melanomas upstaged, 10 were shave biopsies, 10 were punch biopsies, 5 were biopsies not specified, and 1 was an incisional biopsy. **CONCLUSIONS:** In conclusion, we identified significant differences in the biopsy type performed by physicians and APPs. In addition, more than half of biopsies reporting deep margin findings had a positive deep margin (66.7%), with shave biopsies being the most likely to have a positive deep margin. Physicians and APPs had similar high deep margin positivity rates. The type of biopsy did not impact upstaging upon oncologic excision; however, our dataset is too small to draw a definitive conclusion. Future directions include education in our community to lower the deep margin positivity rate for melanoma biopsy as well as investigation into whether other regions have similar shave biopsy implementation and positive deep margin rates.

Table 1. Characteristics of biopsy type and biopsy providers

Biopsy type	**N of biopsies (% of total)**
Shave	306 (58.6)
Punch	83 (15.9)
Excisional	56 (10.7)
Incisional	14 (2.7)
Biopsy providers	
Physician	308 (58.9)
MD	280 (52.5)
Dermatology	208 (39.8)
Plastic surgery	44 (8.4)
Primary care	16 (3.1)
Surgical oncology	9 (1.7)
Otorhinolaryngology	2 (0.38)
General surgery	1 (0.19)
DO	26 (5.0)
Dermatology	24 (4.6)
Doctor of Podiatric Medicine (DPM)	2 (0.38)
Advanced practice provider	215 (41.1)
PA	172 (32.9)
NP	43 (8.2)
Biopsy type: Physician vs. APP	**N (% of provider specific total)**
Physician	308 (58.9)
Shave	172 (55.8)
Punch	40 (13.0)
Excisional	48 (15.6)
Advanced practice provider	215 (41.1)
Shave	134 (62.3)
Punch	43 (20.0)
Excisional	8 (3.7)

P415. Relationship of Mitochondrial Complex I Activity and Response to Immunotherapy Treatment in Melanoma Patients

Annmarie F Butare, DO[1]; Kelsey Fisher-Wellman, PhD[2]; Raphael Aruleba, PhD[3]; Debjani Ghosh, PhD[4]; Nasreen A. Vohra, MD[5]
[1]East Carolina University/Brody School of Medicine, Greenville, NC, US; [2]Wake Forest University School of Medicine, Winston-Salem, NC, US; [3]Wake Forest University School of Medicine, Winston-Salen, NC, US; [4]East Carolina University, Brody School of Medicine, Greenville, NC, US; [5]East Carolina University, Brody School of Medicine, Greenville, NC, US

INTRODUCTION: Despite the success of immunotherapy (IT) in melanoma, up to 50% of patients do not respond. While this poor response rate is likely multifactorial, a growing body of evidence is emerging, which causally links effector T-cell failure to disruptions in mitochondrial bioenergetics. The aim of this study is to evaluate the mitochondrial bioenergetic pathway in melanoma T-cells and correlate this with clinical response to immunotherapy and patient outcomes. **METHODS:** Previously treated and treatment-naive melanoma patients undergoing surgery were enrolled in an ongoing translational study starting in December 2022. CD8+ T-cells were isolated from freshly procured primary or metastatic tumor, or lymph node. Patients were divided into three groups: no prior IT (NoIT), prior IT with complete or near-complete response (CR), and prior IT with no response (NR). Bioenergetic mitochondrial phenotyping was performed with quantitative flux measurements of total respiratory capacity and oxidative phosphorylation efficiency. Ratio of Complex I (CI) and Complex II (CII) activity was analyzed. Bioenergetic flux and CI:CII ratio were then compared across the three groups **RESULTS:** To date, 21 patients have been enrolled; of those, 10 patients had sufficient fresh CD8+ T-cells isolated for analysis. The average age was 71 years, with equal distribution of males and females. 2 patients did not receive prior IT. Of the 8 patients that received IT, 2 achieved CR and 4 had NR. Most patients received combination Nivolumab and Ipilimumab; one patient received Pembrolizumab only. There was no significant difference between groups for the following variables: Breslow thickness, mitotic rate, ulceration, Clark level, lymphovascular invasion, T-stage, and BRAF status. There was a statistically significant difference in CI:CII activity ratio across all three groups (NoIT 0.0556, CR 0.5014, NR 0.2429; p=0.033). Comparison of NR vs. CR did not reach statistical significance, however, may be clinically significant, with CI activity in CR more than double that of NR (p=0.092). **CONCLUSIONS:** Mitochondrial bioenergetic analysis from melanoma CD8+ T-cells demonstrates a deficiency in a specific component of the respiratory pathway. Patients who have had a complete response with IT show higher CI activity. Identification of specific deficiencies in the bioenergetic pathway of T-cells may open avenues for enhancing efficacy of immunotherapy in melanoma.

P416. Sentinel Lymph Node Biopsy for Cutaneous Squamous Cell Carcinoma

Mary Martos[1]; Lucy Min[2]; Susan B. Kesmodel, MD[3]; Alexandra Lopez-Aguiar[4]; Julie Grossman[5]; Wei Zhao[6]; Tulay Koru-Sengul[7]; Jennifer Tang[8]; Keyvan Nouri[9]; Leonel Hernandez-Aya[10]; Jose Lutzky[11]; Jessica S. Crystal, MD[12]
[1]University of Miami, Miami, FL, US; [2]University of Miami, Miami, FL, US; [3]University of Miami Health System, Miami, FL, US; [4]University of Miami, Miami, FL, US; [5]University of Miami, Miami, FL, US; [6]University of Miami, Miami, FL, US; [7]University of Miami, Miami, FL, US; [8]University of Miami, Miami, FL, US; [9]University of Miami, Miami, FL, US; [10]University of Miami, Miami, FL, US; [11]University of Miami, Miami, FL, US; [12]University of Miami School of Medicine, Miami, FL, US

INTRODUCTION: The majority of cutaneous squamous cell carcinomas (cSCC) present localized to the skin. When cSCC metastasizes to the regional lymph nodes (RLN) the prognosis declines. Knowledge of RLN status may be relevant for treatment and surveillance; however, the role of sentinel lymph node biopsy (SLNB) in clinically localized cSCC is not well defined. This study evaluates the prognostic significance of SLNB in cSCC and attempts to identify the optimal patient population for this procedure. **METHODS:** Patients with cSCC who underwent wide local excision (WLE) alone or WLE+SLNB were selected from the National Cancer Database (NCDB) from 2010-2020. Overall survival (OS) of patients who underwent WLE alone vs. WLE+SLNB were compared. Subgroup analyses were performed for patients based on SLNB positivity and the addition of completion lymph node dissection (CLND) after SLNB. Adjusted hazard ratios (HR) and 95% confidence intervals (95%CI) were calculated. **RESULTS:** Analysis of 2680 patients (n=1530 (57%) WLE alone, n=1150 (43%) WLE+SLNB) showed no difference in OS in patients who underwent WLE alone vs. WLE+SLNB (HR 1.15, 95%CI 1.00-1.32, p=0.053). Characteristics of WLE+SLNB patients are shown in Table 1. In an adjusted survival model, worse OS was associated with presence of a positive SLNB (HR 2.52, 95%CI 1.33-4.75 , p=.004), male sex (HR 1.40, 95%CI 1.10-1.79, p=.007), and Charlson-Deyo Score (CDS)≥1 (CDS=1: HR 1.43, 95%CI 1.08-1.89, p=.012; CDS=2-3: HR 2.45, 95%CI 1.74-3.44, p<.001). Better OS was associated with receipt of radiation therapy to the primary site (HR 0.56, 95%CI 0.41-0.75, p <.001), but not to the lymph node basin (HR 1.42, 0.95% CI 0.82-2.49, p =0.213). On subgroup analysis of SLNB positive patients, worse OS was associated with larger tumor size 2.1-4.0 cm (HR 3.91, 95%CI 1.24-12.45, p=.022). There was no difference in OS in patients who underwent CLND. **CONCLUSIONS:** This study of cSCC patients showed no OS difference whether a SLNB or CLND was performed or not; yet it did demonstrate a worse prognosis in patients with a positive SLNB. Further studies are needed to better define the role of SLNB and the optimal management of SLNB positive patients.

P417. Sentinel lymph node biopsy remains valuable in the management of presumed high-risk stage II cutaneous melanoma

Hesham S Mohamed[1]; Michael Fadel[2]; Michelle Wilkinson[3]; Justin Weir[4]; Kieran Power[5]; Andrew Hayes[6]; Myles J.F. Smith, MD, PhD[7]
[1]Royal Marsden Hospital, London, GB; [2]Imperial College, London, GB; [3]Royal Marsden Hospital, London, GB; [4]Royal Marsden Hospital, London, GB; [5]Royal Marsden Hospital, London, GB; [6]Royal Marsden Hospital, London, GB; [7]Royal Marsden Hospital, London, GB

INTRODUCTION: Sentinel lymph node biopsy (SLNB) has utility in melanoma staging, regional control, prognosis, and identifying patients benefitting from adjuvant therapy. Some suggest omitting SLNB for high-risk (pT3b-pT4b)

melanoma. We aimed to determine the incidence of sentinel lymph node metastasis in this population and assess the predictive value of clinical models. **METHODS:** We retrospectively analyzed 300 patients with cutaneous melanoma who underwent SLNB from April 2018 to 2023. Patients were divided into low-risk (T1-T3a, n=211 [Group A]) and high-risk (T3b-T4b, n=89 [Group B]). We recorded age, gender, ASA grade, Breslow thickness, mitotic index, ulceration, satellite lesions, tumor type, anatomical location, and Melanoma Institute of Australia predictive tool (MIA) score. Intraoperative findings included SLN localization, SLN metastasis (SLNM), and oncological outcomes. **RESULTS:** The median age was 60.7 years, with 51% female patients. No significant differences were found between groups, except for sex. Mean follow-up was 524 days. At last follow-up, 81% of Group A (171 patients) were alive without recurrence, while only 65% of Group B (58 patients) were alive recurrence-free. SLNM was identified in 66 patients (22.0%), and recurrence occurred in 48 (16.0%) of the cohort. SLNM was significantly higher in the presumed "high-risk" Group B (31.5%, 28/89) vs. Group A (18%, 38/211) (p = 0.009). Median disease-free survival (DFS) for Group A and B were 1481 days and 1141 days, respectively (P value < 0.001). MIA score was calculated for each patient in group B with a mean risk prediction of 28.5%, however, it was not statistically significant in correlation with the actual SLNB positivity (P value = 0.130). **CONCLUSIONS:** Thirty percent of "high-risk" melanoma were ultimately diagnosed with sentinel lymph node metastasis. Clinical prediction tools may underestimate the risk of SLN metastasis in some populations. Complete pathological response to single-agent immunotherapy (IO) occurs in a minority of patients, therefore omitting SLNB in our series, while administering single-agent IO, may have compromised prognosis, prediction of response to therapy, and nodal basin control.

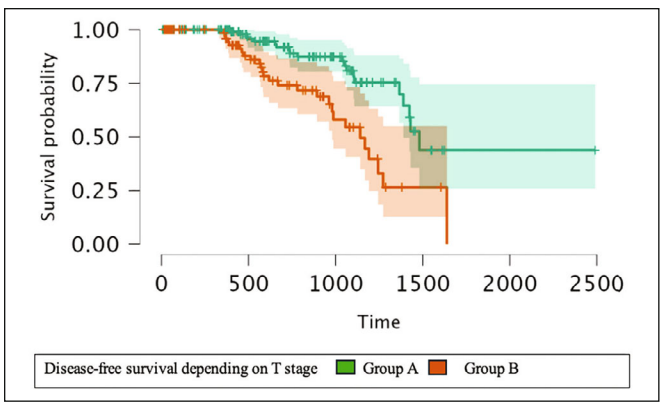


Figure 1. The disease-free smvival (days) of)ow risk melanoma (Group A) versus high risk melanoma (Group B).

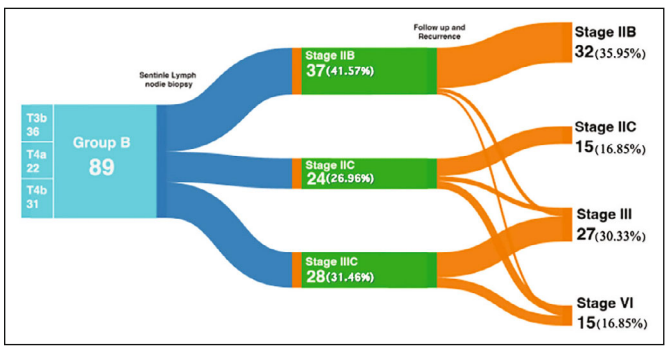


Figure 2. Clinical stage recording and migration for the high-risk melanoma group.

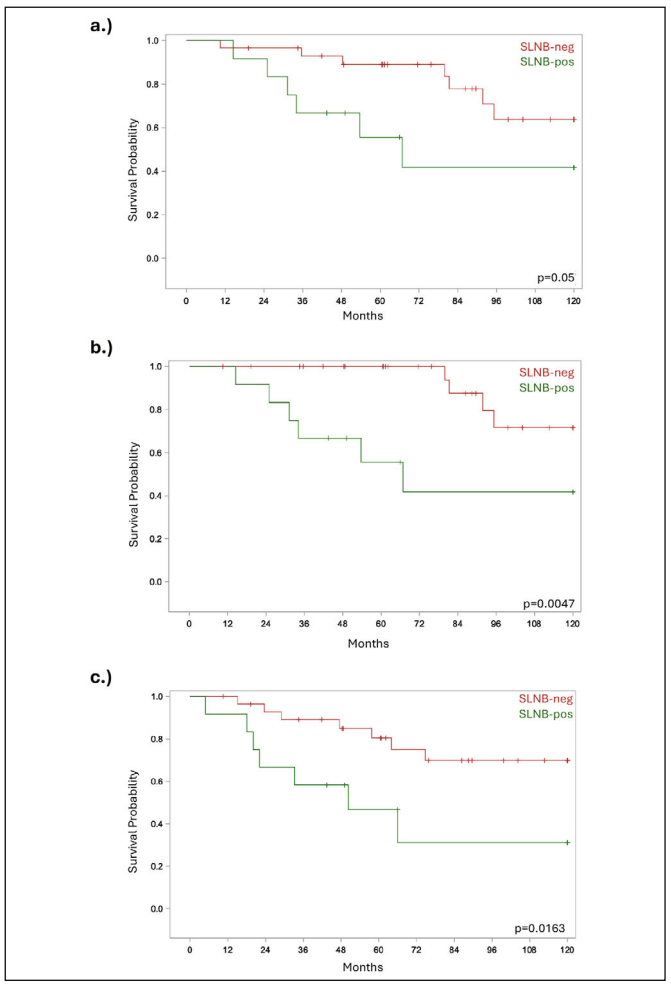
P418. Subungual Melanoma: A Half-Century Experience Demonstrating the Prognostic Value of Nodal Staging

Brian E Diskin, MD[1]; Jillian McCabe, MD[2]; Leland Foshag, MD[3]; Trevan Fischer, MD[4]

[1]Saint John's Cancer Institute, Santa Monica, CA, US; [2]Saint John's Cancer Institute, Santa Monica, CA, US; [3]Saint John's Cancer Institute, Santa Monica, CA, US; [4]Saint John's Cancer Institute, Santa Monica, CA, US

INTRODUCTION: Subungual melanoma is a rare subtype of cutaneous melanoma arising from the nail unit. Surgical management has traditionally been amputation with lymphadenectomy, but there is a paucity of data regarding the prognostic value of nodal staging in subungual melanoma. Here we report our high-volume center experience managing subungual melanoma, including clinicopathologic characteristics and treatment factors associated with disease-free survival (DFS), melanoma-specific survival (MSS), and overall survival (OS). **METHODS:** We analyzed all patients diagnosed with subungual melanoma from our institutional database. Descriptive statistics were performed, including univariable and multivariable analyses, Kaplan-Meier curves, and survival analyses. **RESULTS:** Our institution treated 114 patients from 1971 to 2022 with a median follow-up of 62.5 months. The cohort had a median age of 57.1 years and was largely male (60.5%) and White (67.5%). Upper extremity digits were the most common tumor location (57.9%), median Breslow thickness was 2.2 mm, and ulceration was present in 37.7% of cases. 44.7% of patients underwent amputation compared to 51.8% who underwent wide local excision (WLE). 46.4% underwent no nodal staging, 9.6% had either therapeutic or elective lymph node dissections (LND), and 41 patients (36%) had sentinel lymph node biopsies (SLNB). Overall, 12/41 (29.2%) patients had a positive SLNB and 11/12 (91.6%) had a completion lymph node dissection. 72 (63.1%) patients developed recurrences (1 in-transit, 39 regional, and 32 distant). Median OS for all patients was 74.9 months. LND was associated with an improved DFS (HR 0.47, 95% CI 0.22-0.99) but not MSS (HR 0.89, 95% CI 0.40-1.99). SLNB-positive patients had significantly worse OS, MSS, and DFS compared with SLNB-negative patients (Figure 1a-c). **CONCLUSIONS:** Our experience showed no significant improvement in MSS for patients undergoing LND; however, 29.2% of patients undergoing SLNB had nodal disease and SLNB-positive patients had worse OS, MSS, and DFS compared to SLNB-negative patients. These findings emphasize the importance of nodal staging for both prognosis and adjuvant treatment decisions in subungual melanoma.

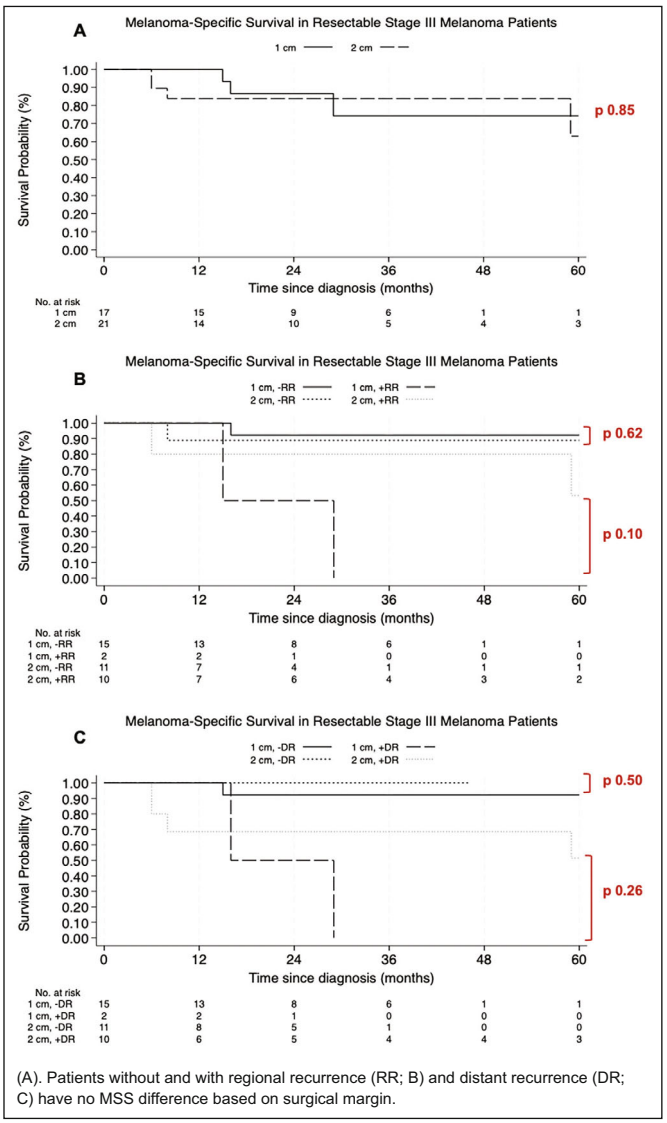
Figure. OS (a), MSS (b), and DFS (c) Comparing SLNB-positive and SLNB-negative patients.



P419. Surgical Management of the Synchronous Primary in Clinical Stage III Melanoma: Do Surgical Margins for the Primary Tumor Matter?

Adrienne B Shannon, MD[1]; Rogerio I Neves, MD PhD[2]; Amod A Sarnaik, MD[3]; Vernon K Sondak, MD[4]; Jonathan S Zager, MD[5]; Matthew C Perez, MD[6]
[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4]Moffitt Cancer Center, Tampa, FL, US; [5]Moffitt Cancer Center, Tampa, FL, US; [6]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: NCCN recommendations for primary melanoma excision margins are based on Breslow's depth, which recommend a 2 cm margin for melanomas >2 mm thick. In the setting of synchronous macroscopic nodal disease, it is not established if margin width impacts local disease control or survival. **METHODS:** Patients with clinically detectable nodal metastasis who underwent concurrent wide excision (WE) of the primary melanoma tumor along with an axillary or inguinofemoral lymph node dissection from 2011 to 2023 were identified. Clinical and treatment characteristics were analyzed using univariate analyses. **RESULTS:** Among 43 patients with clinically detectable nodal metastasis and primary tumors not previously definitively excised, the median age was 65 (interquartile range [IQR] 55-75) years, and the median follow-up was 23 (IQR 12-39) months. Thirteen (30.2%) patients received neoadjuvant immune checkpoint inhibitors (nICI), and 3 (7%) patients received neoadjuvant BRAF/MEK inhibitors; 8 (50%) had complete pathologic response (pCR) in the nodal basin, and 2/8 had a pCR in the nodal basin and primary tumor. Two (12.5%) patients had a mixed response with a pCR In the primary tumor and partial response in the nodal basin. Twenty-one (48.8%) patients had surgical margins of 2 cm. Of the 22 patients who underwent 1 cm margins, 17 (77.3%) patients met NCCN criteria for a wide surgical margin (2 cm) of the primary tumor. Following WE, median tumor thickness was 5 (IQR 2.8-9) mm, and 8 (18.6%) patients had microsatellitosis; 4/8 patients had pre-operative documented microsatellites. Patients with microsatellitosis were more likely to have undergone the recommended 2 cm margin (33.3% vs 5.9%, p 0.04), and nICI patients were less likely to get 2 cm margins (58.8% vs 4.8%, p<0.0001). Two (4.7%) patients, both undergoing 2 cm margins, developed local recurrence (LR; time-to-recurrence 2 months); 1 patient developed ITM recurrence, and 1 patient developed both nodal and distant recurrence (DR). Of nICI patients, 0/13 had LR or DR, and 1/13 (7.7%) had nodal recurrence. Patients who had 2 cm margins were more likely to have regional recurrence (47.6% vs 11.8%, p 0.02) and DR (47.6% vs 11.8%, p 0.02), but when primary tumor pathological factors and receipt of ICI were controlled in multivariate analysis, there was no difference in MSS between patients treated with 1 cm vs 2 cm margins (hazards ratio [HR] 1.06, p 0.95). **CONCLUSIONS:** LR rates in patients with synchronous primary melanoma and macroscopic nodal metastasis are low, with the majority of patients developing regional or distant recurrence. In the patients who underwent narrower primary tumor surgical margins than recommended by the NCCN guidelines, no patients experienced a LR. Wide surgical margins in these patients do not appear to result in oncologic benefit.



(A). Patients without and with regional recurrence (RR; B) and distant recurrence (DR; C) have no MSS difference based on surgical margin.

Figure. Melanoma-specific survival (MSS) in resectable stage III melanoma following synchronous lymph node dissection and excision of the primary tumor with 1 cm versus 2 cm margins

P420. Validation of a melanoma recurrence model in patients undergoing sentinel lymph node biopsy in an academic community care setting

Chris Baliski[1]; Julia Downey[2]; Yue Zhang[3]
[1]BC Cancer, Kelowna, BC, CA; [2]BC Cancer, Kelowna, BC, CA; [3]BC Cancer, Kelowna, BC, CA

INTRODUCTION: Adjuvant treatment of melanoma is increasingly being utilized, with the American Joint Committee on Cancer staging system (AJCC) being the gold standard for determining prognosis and recommendations for treatment. The AJCC may not accurately reflect disease recurrence risk in certain substages, which has led to the development of other predictive models. A recently developed and validated predictive tool has been shown to perform well in academic centers, and may help inform decision making in a diverse community setting. **METHODS:** A retrospective review of patients with AJCC 8th edition T1b or greater melanomas, undergoing sentinel lymph node biopsy at a community referral center between January 1, 2005 and June 30, 2022 were included. Patients were excluded if there was evidence of microsatellitosis. Retrospective review of demographic, pathology, and treatment related factors was performed, and cross referenced with a population based database for disease recurrence. A previously validated tool (Stassen et al.) was assessed for the ability to discriminate for melanoma recurrence when applied to this population utilizing 6 prognostic factors

(Breslow thickness, ulceration, age, tumour location, sentinel lymph node status and maximal diameter of lymph node metastasis). **RESULTS:** There were 494 patients included. The median age was 63 years (IQR: 53-72), with a median Breslow thickness of 1.7 mm (IQR: 1.1-3.0). 105 patients (21.2%) had pathologically positive sentinel lymph nodes with 130 patients (26.3%) developing recurrent disease. When applying this model to our population, the AUC for recurrence free survival was 0.67 (0.65 - 0.70). **CONCLUSIONS:** A previously developed melanoma predictive tool performed well at predicting recurrence in a community setting. The available online calculator may be of benefit to clinicians to advise patients on the merits of adjuvant treatment for melanoma.

P421. An analysis of peritoneal aspirate – Examining the impacts of a 90-minute heated intraperitoneal chemoperfusion in patients with peritoneal malignancy

Neelia E. Abadi[1]; Katherine Horrigan[2]; Jonathan E. Boyson[3]; Seth Harlow[4]; Jessica A. Cintolo-Gonzalez, MD[5]; Conor H. O'Neill[6]
[1]University of Vermont Larner College of Medicine, Burlington, VT, US; [2]University of Vermont Larner College of Medicine, Burlington, VT, US; [3]Division of Surgical Oncology, University of Vermont Medical Center, Burlington, VT, US; [4]Division of Surgical Oncology, University of Vermont Medical Center, Burlington, VT, US; [5]Division of Surgical Oncology, University of Vermont Medical Center, Burlington, VT, US; [6]Division of Surgical Oncology, University of Vermont Medical Center, Burlington, VT, US

INTRODUCTION: Cytoreductive surgery with heated intraperitoneal chemotherapy (HIPEC) is a frequent treatment option for patients with peritoneal malignancies. However, there is a lack of data that reflects how HIPEC acutely impacts a patient's cellular environment over the course of a U.S. standard, 90-minute perfusion. The aim of this project was thus to determine the quantity and viability of cells in peritoneal aspirates from patients that were actively receiving HIPEC, serving as a model to examine the effects of the therapy within a 90-minute timeframe. **METHODS:** A biomarker-based translational study was conducted. Over the course of each enrolled HIPEC, four aspirates were collected from the hyperthermia pump used to lavage the peritoneum. Collection was completed at 30-minute intervals, with the first being immediately prior to chemoperfusion and the last at 90 minutes. Hemocytometry was used to quantify viable and non-viable cells at each time point. **RESULTS:** Aspirates were collected from four participants over a two-month period. Cell counts were highly variable between cases, with the maximum number of cells aspirated at 90 minutes determined to be 96.25 million cells/mL peritoneal fluid and the minimum recorded as 1.73 million cells/mL peritoneal fluid. Despite these discrepancies in cell quantity between unique participants, positive trends in total and viable cell count over the duration of perfusion were identified. Across all four cases, the viable cell counts consistently increased between the four time intervals, with overall percent change from 0 minutes ranging from 223.07% to 2358.33%. This trend indicates an increase in viable cell aspiration over the course of chemoperfusion, with fluctuating magnitudes of such change. The mean non-viable cell counts also reflected a net escalation from 0 to 90 minutes. However, there were variations in non-viable cell quantities at 30 and 60 minutes, and thus the relationship between time and non-viable count was not exclusively positive. On average, the proportion of viable cells present was larger than that of non-viable cells at each time point. **CONCLUSIONS:** It is evident that HIPEC acutely impacts the peritoneal environment. There is a positive relationship between time in HIPEC perfusion and the quantity of viable cells aspirated, with more viable than non-viable cells removed throughout the procedure. Characterizing the cellular contents of aspirate with antibody-specific staining and flow cytometry can allow for the translation of these cellular impacts into clinical understanding.

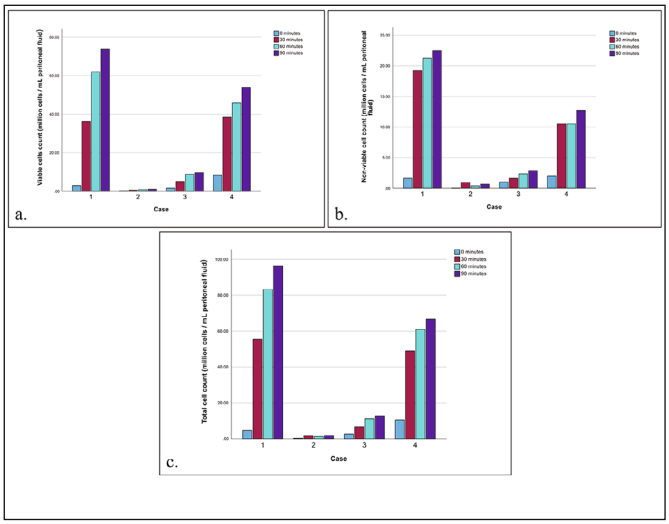
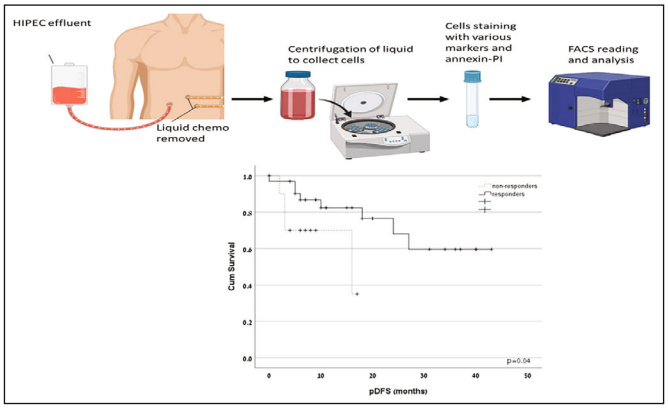


Figure 1. Quantities of cells in peritoneal aspirate over the course of 4 HIPEC perfusions.

P422. Apoptotic Markers in HIPEC Effluent as Predictors of Peritoneal Recurrence: A Novel Biomarker Approach

Eran Nizri[1]; Almog Ben-Yaacov[2]; Yaniv Berger[3]; Aviram Nissan[4]; Guy Lahat[5]; Ravit Geva[6]
[1]Tel-Aviv Sourasky Medical Center, Tel-Aviv, IL; [2]Chaim Sheba Medical Center, Ramat-Gan, IL; [3]Chaim Sheba Medical Center, Ramat Gan, IL; [4]Chaim Sheba Medical Ceter, Ramat-Gan, IL; [5]Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel, IL; [6]Tel-Aviv Sourasky Medical Center, Tel-Aviv, IL

INTRODUCTION: The role of heated intra-peritoneal chemotherapy (HIPEC) following cytoreductive surgery (CRS) in treating peritoneal metastases (PM) remains contentious. Current evaluations of HIPEC efficacy rely on patient-derived tumor tissue and ex vivo measurements of drug activity, which are later correlated with clinical outcomes. This study introduces a novel method to assess HIPEC efficacy by measuring apoptosis in tumor cells present in the HIPEC effluent at the conclusion of the procedure. **METHODS:** We analyzed apoptosis markers using the Annexin V-PI assay on cells collected from HIPEC effluent immediately after the procedure and again 24 hours later. To specifically measure apoptosis in tumor cells, we used positive selection for epithelial cells (EpCam+) and negative selection for inflammatory cells (CD45-). Apoptotic markers were then correlated with long-term clinical outcomes to assess their utility as biomarkers of HIPEC efficacy. **RESULTS:** HIPEC effluent samples were collected from 44 patients (32 females [72.7%], median age 56.2 years, IQR: 49.2–68.7). Tumor origin was: appendix (n=8, 18.2%), colon (n=22, 50%), ovary (n=7, 15.9%), stomach (n=5, 11.4%), and other (n=2, 4.6%). The median peritoneal carcinomatosis index (PCI) was 8.5 (IQR: 3–15.25), and 36 patients (81.6%) achieved complete cytoreduction (CCR=0). To assess chemotherapy-induced apoptosis, post-HIPEC apoptosis markers were compared to pre-HIPEC samples. Patients with a pre- to post-HIPEC apoptosis increase of <5% were classified as non-responders. While no significant differences in disease-free survival (DFS) or overall survival (OS) were observed between responders and non-responders across all tumor types, responders with CCR=0 demonstrated significantly longer peritoneal DFS (median not reached vs. 16 months, p=0.04). This finding remained significant in multivariate analysis, which also accounted for PCI (HR=0.28, p=0.05). **CONCLUSIONS:** Apoptotic markers in HIPEC effluent show promise in predicting peritoneal recurrence. Further studies are warranted to validate these findings and explore whether apoptosis markers could guide treatment intensification, such as the use of early postoperative intraperitoneal chemotherapy, to prevent recurrence. HIPEC effluent represents a novel source of biomarkers, offering insights into chemotherapy effectiveness and residual tumor characteristics.



P423. Balancing Patient Safety and Cost Savings: Immediate Extubation as a Standard of Care after CRS-HIPEC

Yusuf Ciftci[1]; Shannon N Radomski[2]; Nolan M Winicki[3]; Fabian M Johnston[4]; Jonathan B Greer[5]

[1]Johns Hopkins University School of Medicine, Baltimore, MD, US; [2]Johns Hopkins University School of Medicine, Baltimore, MD, US; [3]Johns Hopkins University School of Medicine, Baltimore, MD, US; [4]Wake Forest University School of Medicine, Winston-Salem, NC, US; [5]Massachusetts General Hospital, Boston, MA, US

INTRODUCTION: Immediate extubation in the operating room has been shown to decrease cost, shorten length of stay (LOS), and improve patient outcomes. Patients who undergo cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) may inappropriately remain intubated due to lengthy operative time and provider availability. There are no studies investigating the association between immediate and early extubation on charges and outcomes following CRS-HIPEC. **METHODS:** We performed a retrospective cohort study of patients undergoing CRS-HIPEC from 2016-2022 at a single quaternary center. Our study cohort was divided into two groups based on time to extubation; extubated in the operating room or extubated within 6 hours in the ICU. We performed 1:1 propensity score matching (PSM) to adjust for patient complexity. A multivariable regression was performed to estimate the effect of early extubation on hospital charges and outcomes of CRS-HIPEC. **RESULTS:** Our final matched cohort consisted of 32 patients, with 16 patients in each cohort. Mean age was 54.6 (SD 13.8) and 53% (n=17) were female. After matching, there were no significant differences in operating room and routine (administrative, room and board) charges, LOS (13 days [9.75-15.5] vs. 14 days [9.75-19], p=0.798), and ICU LOS (3.5 days [2-5.25] vs. 3 days [2-4.25], p=0.800). Overall morbidity (n=11, 68% vs. n=9, 56%, p=0.752) and serious complications (n=6, 38% vs. n=6, 38%, p=0.99) were also similar. On multivariable regression analysis, extubation within 6 hours was associated with a significant total charge increase of $35,698 (SE $14,000, 95% CI [$8,259-$63,137], p=0.012) compared to immediate extubation. This difference was driven by routine charges (Estimate $16,648, SE $7,701, 95% CI [$1,554-$31,742], p=0.031). **CONCLUSIONS**: Extubation within 6 hours in the ICU is associated with significantly higher charges and similar outcomes compared to immediate extubation in the operating room. These findings suggest that immediate extubation in the operating room will reduce costs without worsening outcomes for select patients who undergo CRS-HIPEC. Collaboration between providers in the operating room and ICU should be established to promote immediate extubation in the operating room.

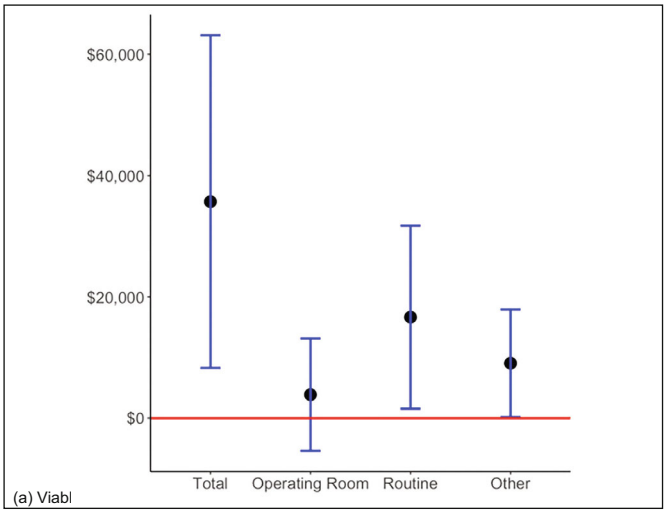


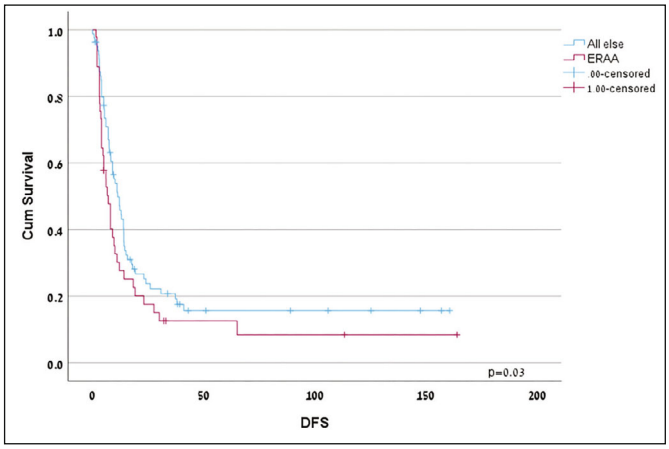
Figure 2: Average Treatment Effect (ATT) of Delayed Extubation on Charges, by Charge Category

P424. Colorectal Peritoneal Metastases Diagnosed Within One Year After Adjuvant Chemotherapy: Association with Poor Prognosis

Jawad Tome[1]; Yossi Maman[2]; Yaniv Berger[3]; Almog Ben-Yaacov[4]; Mordechai Gutman[5]; Aviram Nissan[6]; Guy Lahat[7]; Eran Nizri[8]

[1]Tel-Aviv Sourasky Medical Center, Tel-Aviv, IL; [2]Tel-Aviv Sourasky Medical Center, Tel Aviv, IL; [3]Chaim Sheba Medical Center, Ramat Gan, IL; [4]Chaim Sheba Medical Center, Ramat Gan, IL; [5]Chaim Sheba Medical Center, Ramat Gan, IL; [6]Chaim Sheba Medical Ceter, Ramat-Gan, IL; [7]Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel, IL; [8]Tel-Aviv Sourasky Medical Center, Tel-Aviv, IL

INTRODUCTION: Patients with peritoneal metastases of colorectal cancer (PM-CRC) are treated by cytoreduction and hyperthermic intraperitoneal chemotherapy (CRS HIPEC). However, there is considerable perioperative morbidity and mortality associated with this procedure, making patient selection a crucial determinant of outcomes. We hypothesize that the diagnosis of PM during or within one year after primary resection and adjuvant therapy may indicate a more aggressive variant of the disease. The aim of this study is to compare the clinical outcomes of patients with early recurrence within one year of adjuvant treatment (ERAA) to those diagnosed with PM-CRC at later times or in the lack of adjuvant therapy. **METHODS**: This multicenter retrospective study included patients with pathologically confirmed metachronous PM-CRC who underwent CRS HIPEC (n=175). Clinicopathologic characteristics were retrieved from prospectively maintained databases at participating institutions. Patients with ERAA were compared to those with early recurrence who did not receive adjuvant therapy or patients diagnosed with PM at a later time. **RESULTS:** A total of 175 patients were included in the analysis, of which 56 patients constituted the ERAA group, clinical characteristics such as patient age (59.5 years, IQR: 52–74), gender distribution, and primary tumor location did not significantly differ between groups. The ERAA group had a lower rate of neoadjuvant treatment before CRS-HIPEC (39% vs. 54.1%, p=0.04). Additionally, there was a trend toward a higher N stage in the ERAA group, with 78.8% of patients having N1-N2 disease compared to 68% in all patients. Median DFS was significantly shorter in the ERAA group compared to the rest of patients (7, IQR: 5–9 vs. 11.2 months IQR: 7.8–14.5, p=0.03, respectively). However, overall survival (OS) did not significantly differ between the groups (median OS=37 vs. 41 months, p=0.34). ERAA patients had significantly higher rate of systemic recurrence as compared to all other patients (33.9% vs.18.5%, p=0.01). In the multivariate analysis, ERAA remained an independent predictor of poor prognosis (HR=1.48, p=0.05) along with peritoneal cancer index (PCI) (HR=1.04, p=0.02). **CONCLUSIONS:** The development of peritoneal metastases within one year of completing adjuvant therapy is a strong indicator of aggressive disease biology, as reflected by significantly shorter DFS and systemic recurrence. Future studies should evaluate the effectiveness of neoadjuvant therapy in this specific group, as well as other methods to evaluate extra-abdominal disease such as circulating tumor DNA (ctDNA).



P425. Combined Retroperitoneal Resection with Cytoreductive Surgery and Heated Intraperitoneal Chemotherapy for Metastatic Colorectal Cancer

Shachar Laks[1]; Mohammad Adileh[2]; Yaniv Berger[3]; Aviram Nissan[4]; Almog Ben-Yaacov[5]

[1]Edith Wolfson Medical Center, 62 Ha-Lokhamim St, IL; [2]Hadassah Medical Center, Jerusalem, IL; [3]Chaim Sheba Medical Center, Ramat Gan, IL; [4]Sheba Medical Center, Ramat Gan, IL; [5]Chaim Sheba Medical Center, Ramat Gan, IL

INTRODUCTION: Colorectal peritoneal metastases (CRPM) and retroperitoneal lymphatic metastases (RLM) are each considered poor prognostic indicators in colorectal cancer (CRC). Current data suggests that surgery for each including cytoreductive surgery and heated intraperitoneal chemotherapy (CRS/HIPEC) for CRPM and retroperitoneal resection (RR) for RLM may improve survival. Given the poor prognosis of each finding individually, each condition is generally considered a contraindication to the other. We aim to describe the first series of outcomes of combined RR and CRS/HIPEC. **METHODS**: Retrospective analysis of a prospectively maintained tertiary institution database comparing perioperative and oncological outcomes of combined RR+CRS/HIPEC to CRS/HIPEC only in CRPM. **RESULTS:** Included 280 CRS/HIPEC for CRC patients and divided the cohort to 17 with RR+CRS/HIPEC and 263 with CRS/HIPEC only. Demographic/perioperative characteristics were similar including tumor characteristics and peritoneal cancer index. We found longer operative times in RR+CRS/HIPEC cohort (5 versus 4 hours, p=0.003). Complications were similar except more postoperative bleeding events in the RR+CRS/HIPEC cohort (24% versus 4.2%, p=0.008). This did not translate into longer length of stay, reoperations, or major complications. Similar median disease free and overall survival of 7.9 and 16.6 months, respectively, in the entire cohort (p=0.83 and p=0.7). Less retroperitoneal recurrences occurred after regional lymphadenectomy (12%) compared to mass only resection (44%). **CONCLUSIONS:** Our study demonstrates the safety and oncological efficacy of RR+CRS/HIPEC. We further noted an association with improved local control in patients who underwent regional lymphadenectomies versus mass only resections in the retroperitoneal resection cohort. We believe that RR+CRS/HIPEC in highly selected patients is a suitable option and hope this will lead to larger multi-institutional studies to corroborate these findings.

P426. Comparative Analysis of Patient Body Surface Area and Peritoneal Surface Area: Implications for HIPEC Dosing

Saim Ali[1]; Jun Yu, PhD[2]; Susan Campbell, MD[3]; Jessica A. Cintolo-Gonzalez, MD[4]; Conor H. O'Neill, MD[5]

[1]The Robert Larner, MD College of Medicine at The University of Vermont, Burlington, VT, US; [2]Department of Mathematics & Statistics, University of Vermont, Burlington, VT, US; [3]Division of Surgical Oncology, University of Vermont Medical Center, Burlington, VT, US; [4]University of Vermont Medical Center, Burlington, VT, US; [5]Division of Surgical Oncology, University of Vermont Medical Center, Burlington, VT, US

INTRODUCTION: Cytoreductive surgery and HIPEC for select patients with peritoneal surface malignancy (PSM) remains the best opportunity for cure. Both flat and weight-based chemotherapy dosing regimens are utilized, but the correlation of body surface area (BSA) with the actual treated peritoneal surface area (PSA) is not well established. This study investigates the relationship between PSA and BSA to highlight the need for a more individualized approach in treating PSM. **METHODS:** De-identified abdominopelvic CT scans from our HIPEC registry were processed in 3DSlicer (BWH, Boston, MA). Using Auto3DSeg, an organ segmentation model, intraperitoneal organs were combined into a single segmentation. To isolate the parietal peritoneum, the external contours of the segmentation were wrapped. Multiple wraps were created, and manual editing ensured anatomical accuracy. The liver surface area was substituted for the visceral peritoneum due to its large proportion of the total viscera. Surface area calculations were completed in 3DSlicer. Pearson correlation coefficients were calculated to compare BSA and PSA. Potential dosing rates were calculated by normalizing the average PSA/BSA to a 30 mg flat dose. **RESULTS:** Thirteen HIPEC patients were included in our analysis. There was a discrepancy between possible BSA and flat rate doses, with BSA dosing resulting in an average 92% increase. Following peritoneal segmentation analysis, the mean PSA was 3515.2 cm2. The mean BSA was 1.92 m2. The Pearson correlation coefficient between PSA and actual BSA was r = .72; adjusted BSA r = .69; ideal BSA r = .35. Normalizing a 30 mg flat dose to the average PSA in our dataset returns a rate of 85.3 mg/m2, (rate = 30 mg/(average PSA)). Applying this potential dosing rate to individual PSA values shows a dose variation from -29% to +33% of the 30 mg flat dose. BSA normalization returned a rate of 15.7 mg/m² -35% to +39% of the flat dose. There is only a moderate positive correlation between true PSA and a patient's BSA, with the BSA rate showing higher variability when compared to the PSA rate. **CONCLUSIONS:** The use of BSA in HIPEC may lead to subtherapeutic or toxic doses due to unique anatomy. The lack of a strong correlation found in our analysis underscores the need for a more patient-specific dosing approach for HIPEC. PSA may serve as a more accurate metric, as it directly measures the surface area exposed to chemotherapeutic agents – it was also found to have less variability in potential dosing when compared to BSA. Further investigation is underway, including the development of a library for future machine learning models.

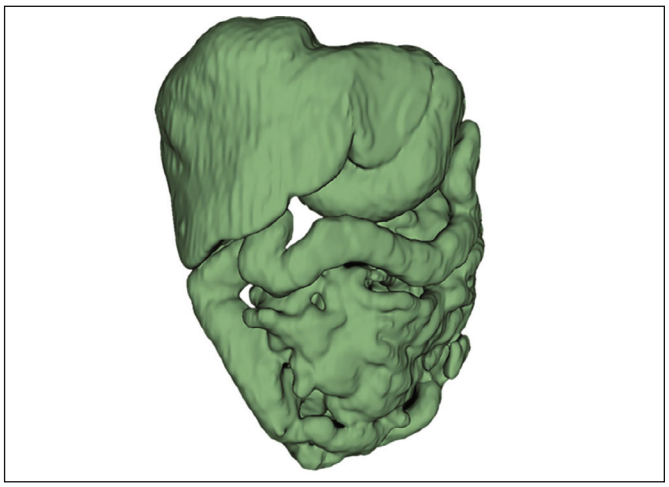


Figure. Example of intra peritoneal organ segmentation prior to wrapping

P427. Discordance between laparoscopic and open assessment of peritoneal disease burden

Dhruv J Patel[1]; Mohammad Mahmoud Noubani[2]; Elizabeth Gleeson, MD, MPH[3]; Phillip Spanheimer, MD[4]; Hong Jin Kim, MD[5]; Jeremiah L Deneve[6]

[1]University of North Carolina, Chapel Hill, NC, US; [2]UNC at Chapel Hill, Chapel Hill, NC, US; [3]University of North Carolina Chapel Hill, Chapel Hill, NC, US; [4]University of North Carolina Chapel Hill - Chapel Hill, NC, Chapel Hill, NC, US; [5]University of North Carolina, Chapel Hill, NC, US; [6]University of North Carolina at Chapel Hill, Chapel Hill, NC, US

INTRODUCTION: Identification of the peritoneal burden of disease in the setting of peritoneal carcinomatosis remains a challenge. Diagnostic laparoscopy (DL) provides a reliable assessment, however, often times additional disease is identified at the time of cytoreduction and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC). We assess the discordance between DL and CRS/HIPEC burden of disease. **METHODS:** A retrospective review was performed for patients who were evaluated for peritoneal carcinomatosis at a single institution between 2017 and 2024. Pts who underwent a staged DL prior to CRS/HIPEC were included. Total burden as defined by the peritoneal cancer

index score (PCI) and location of disease were determined and correlated with outcome. Wilcoxon signed rank test was used to evaluate change in PCI score between DL and CRS/HIPEC while Fisher's exact tests were used to compare changes based on location of involvement. **RESULTS:** Of the 118 patients who were reviewed, 30 patients met inclusion criteria,16 cases of which a PCI score from DL was extrapolated based on both operative findings and preoperative cross-sectional images. The median age was 49.5 years (range, 41-55 years), 60% female and 80% Caucasian. The median PCI at DL was 5 (range, 3-19) while the median PCI at CRS/HIPEC was 16 (range, 8-25). The duration from DL to CRS/HIPEC was 46 days (range, 21-86 days). The most common histology was colon adenocarcinoma (50%) and appendiceal adenocarcinoma (40%). Diaphragm involvement was similarly identified at both DL (30%) and CRS/HIPEC (27%). Furthermore, small bowel serosa involvement was similarly identified at DL and CRS/HIPEC (2.6% and 3.3%, respectively, p=0.07). Small bowel mesentery was identified in 20% of DL procedures and 40% of CRS/HIPEC procedures (p=0.07). The most common reasons for incomplete peritoneal assessment at the time of DL were adhesions, extensive burden of disease and fused abdominal contents. There were no DL-related complications. There were no port site recurrences at DL insertion port sites. **CONCLUSIONS:** While DL may under-represent the exact peritoneal burden of disease compared to CRS/HIPEC, DL does provide a reliable assessment of high-risk areas associated with incomplete cytoreduction such as the small bowel serosa and mesentery. DL remains a useful tool for assessment of the peritoneal disease burden.

Table. Demographic and Oncologic Characteristics for Patients Undergoing Staged Laparoscopy Before Cytoreduction

Variables	Overall Cohort (n=30)
Age*	49.5 (41 - 55.3)
Sex	
Female	18 (60.0%)
Race	
White	24 (80.0%)
PCI at Laparoscopy	5.0 (3.0-19.0)
PCI at Cytoreduction	16.0 (8.0-25.0)
Change in PCI	5.0 (2.0-12.0)
Days between Laparoscopy and Cytoreduction	45.5 (21.0 - 86.3)
Pathology	
colon adenocarcinoma	15 (50.0%)
appendiceal adenocarcinoma	8 (26.7%)
goblet cell adenocarcinoma of the appendix	4 (13.3%)
low-grade appendiceal mucinous neoplasm	1 (3.3%)
peritoneal mesothelioma	2 (3.3%)
infiltrating lobular carcinoma of the breast	3 (3.3%)
Diaphragm Involvement at Laparoscopy	
Right	9 (30.0%)
Left	1 (3.3%)
Bilateral	3 (10.0%)
No Involvement or Unable to Visualize	17 (56.7%)
Diaphragm Involvement at Cytoreduction	
Right	8 (26.7%)
Left	0 (0.0%)
Bilateral	9 (30.0%)
No Involvement or Unable to Visualize	12 (40.0%)
Small Bowel Involvement at Laparoscopy	
Serosal Involvement	2 (6.7%)
Mesenteric Involvement	6 (20.0%)
Both	2 (6.7%)
No Involvement or Unable to Visualize	20 (66.7%)
Small Bowel Involvement at Cytoreduction	
Serosal Involvement	1 (3.3%)
Mesenteric Involvement	12 (40.0%)
Both	10 (33.3%)
No Involvement or Unable to Visualize	7 (23.3%)
Porta Hepatis Involvement at Cytoreduction	
Yes	6 (20.0%)
No	24

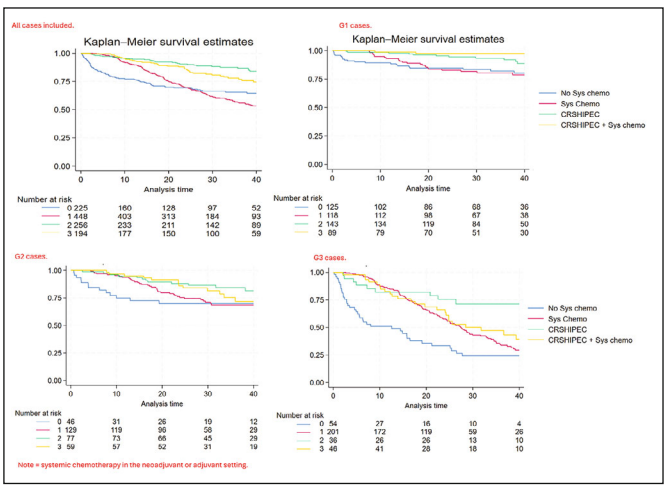
**All numeric variables reported with median and interquartile range*

P428. Does Systemic Chemotherapy Benefit Patients with High-grade Mucinous Appendiceal Neoplasms Undergoing CRS-HIPEC? A National Database Analysis

Salvador Rodriguez Franco, MD[1]; Sumaya Ghaffar, MD[2]; Andrii Khomiak, MD[3]; Benedetto Mungo, MD[4]; Martin D McCarter, MD[5]; Ana L. Gleisner, MD, PhD[6]; Steven Ahrendt, MD[7]

[1]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [2]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [3]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [4]University of Colorado School of Medicine, Aurora, CO, US; [5]University of Colorado School of Medicine, Aurora, CO, US; [6]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [7]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US

INTRODUCTION: The American Joint Committee on Cancer (AJCC) 8th edition introduced a three-tiered grading system (G1–G3) for mucinous appendiceal neoplasms (MAN). Optimal treatment for peritoneal involvement of MAN is cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC). The role of systemic therapy is less well-defined. **METHODS:** We queried the National Cancer Database (2018-2021) for disseminated mucinous appendiceal tumors (histology codes 8470, 8480, 8481, 8490) located at the appendix (C18.1) with complete grading information (G1–G3). Systemic chemotherapy and surgical interventions were compared between grade groups. Survival outcomes were analyzed using adjusted hazard ratios (HR). **RESULTS**: A total of 1,599 patients were included: G1 (n=606), G2 (n=454), G3 (n=539). Systemic chemotherapy utilization (excluding HIPEC) was high across all groups G1 (46%), G2 (73%), G3 (79%). Surgical intervention, including exploratory laparoscopy, was common: G1 (96%), G2 (96%), G3 (84%). Among surgical patients, the sequence of chemotherapy differed between groups. Neoadjuvant chemotherapy (NAC) was administered in G1 (8.6%), G2 (17%), and G3 (18%); adjuvant chemotherapy (ACT) in G1 (34%), G2 (46%), and G3 (50%); and CRS-HIPEC was performed in 36.2% of all patients (578/1599), in all grades, G1 (46%), G2 (41%), and G3 (21%). Adjusted survival analysis showed that higher tumor grade and age ≥60 were predictors of worse survival (G2 HR 2.13, 95% CI: 1.53–2.95; G3 HR 5.66, 95% CI: 4.22–7.58; age ≥60 HR 1.48, 95% CI: 1.20–1.84). Among all patients, the use of CRS-HIPEC was associated with improved survival (HR 0.52, 95% CI: 0.40–0.67), and this benefit persisted when analysis was limited to G2 and G3 patients (HR 0.60, 95% CI: 0.44–0.80 (vs. non CRS-HIPEC surgery and no chemotherapy)). Systemic chemotherapy provided no survival benefit among G1 patients undergoing CRS-HIPEC (HR 0.37 (0.11-1.29)). Furthermore, despite being standard of care the addition of systemic chemotherapy (NAC and/or ACT) in patients undergoing CRS-HIPEC did not improve survival among both G2 (HR 1.32 (0.63-2.74)) and G3 (HR 1.32 (0.63-2.74)) patients. **CONCLUSIONS:** CRS-HIPEC is associated with improved survival in patients with disseminated mucinous appendiceal tumors across all grades, including higher-grade tumors. Systemic chemotherapy is used in a large number of G1 patients without any survival benefit. Despite the widespread acceptance of colon cancer-derived chemotherapy protocols in high-grade MAN, a survival benefit is not present in this population of patients undergoing CRS-HIPEC.

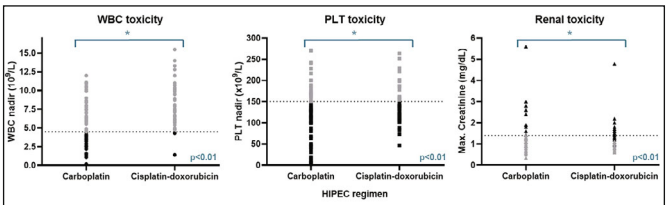


P429. Hyperthermic intraperitoneal chemotherapy (HIPEC) with carboplatin vs. cisplatin-doxorubicin for stage III/IV ovarian cancer

Luis Felipe Falla-Zuniga, MD[1]; Armando Sardi, MD FACS[2]; Mary Caitlin King, BS[3]; Vladislav Kovalik, MD MSPH[4]; Sergei Iugai, MD[5]; Carol Nieroda, MD[6]; Kseniia Uzhegova, MD[7]; Teresa Diaz-Montes, MD FACOG[8]; Vadim Gushchin, MD FACS[9]

[1]Mercy Medical Center, Baltimore, MD, US; [2]Mercy Medical Center, Baltimore, MD, US; [3]Mercy Medical Center, Baltimore, MD, US; [4]Mercy Medical Center, Baltimore, MD, US; [5]Mercy Medical Center, Baltimore, MD, US; [6]Mercy Medical Center, Baltimore, MD, US; [7]Mercy Medical Center, Baltimore, MD, US; [8]Mercy Medical Center, Baltimore, MD, US; [9]Mercy Medical Center, Baltimore, MD, US

INTRODUCTION: Carboplatin has been a common HIPEC agent for advanced ovarian cancer (OC) due to its favorable toxicity profile, heat-synergistic effects, and ongoing evaluation in clinical trials. However, only cisplatin is currently recommended for routine use after primary cytoreductive surgery (CRS) due to its survival benefits. In response, our institution shifted from carboplatin to cisplatin-doxorubicin. We hypothesized that the new regimen would improve safety and survival outcomes for our OC patients. **METHODS:** This quasi-experimental pre-post study compared two HIPEC regimens in newly diagnosed stage III/IV OC patients. The pre-intervention group (G1) included those perfused with carboplatin (800 mg/m2) (5/2014-3/2021). The post-intervention group (G2) received cisplatin-doxorubicin (50-15 mg/m2) (4/2021-2/2024). Hematologic and renal toxicities were assessed for 30-days using the Common Terminology Criteria for Adverse Events. Acute kidney injury (AKI) was evaluated by KDIGO criteria. Surgical morbidity was monitored for 90-days using the Clavien-Dindo classification with grades III-IV considered major complications. Kaplan-Meier progression-free (PFS) and overall survival (OS) were compared via log-rank test. The association of HIPEC regimen with toxicity and survival was assessed by multivariable logistic regression. **RESULTS:** Of 102 patients, 61 (60%) were in G1 and 41 (40%) in G2. Groups were balanced by age, ASA score, Charlson Comorbidity Index (CCI), histology, and peritoneal cancer index. All patients underwent complete CRS (CC-0/1), with comparable surgical complexity scores and number of bowel resections. G1 patients had less renal toxicity (25% vs 54%, p<0.01), but more WBC (41% vs 5%, p<0.01) and platelet toxicity (28% vs 5%, p<0.01) (Fig. 1). No differences were observed in AKI, RBC toxicity, major morbidity or adjuvant chemotherapy completion rates. Median follow-up was 61 months. Median PFS (G1: 19.1 vs G2: 21.4 months, p=0.6) and OS (G1: 65.4 months, vs G2: not reached, p=0.8) were similar between groups. CCI (OR 1.1 [95%CI: 1-1.1], p<0.01) and G2 (OR 0.8 [0.7-0.9], p<0.01) were found to be independent factors affecting WBC toxicity. WBC toxicity was identified as an independent factor influencing PFS (HR 4.4 [95%CI: 1.4–13.4], p<0.01) and OS (HR 6.7 [2.4–18.8], p<0.01). **CONCLUSIONS:** HIPEC with cisplatin-doxorubicin was associated with increased renal, but less WBC and platelet toxicities compared to carboplatin. Survival was not adversely affected. WBC toxicity's impact on survival warrants further investigation.



Dashed lines denote cutoff values for toxicity based on the Common Terminology Criteria for Adverse Events. Black figures denote toxicity grade ≥1 and light gray figures depict absence of toxicity (grade 0). Asterisks denote statistical significance.

CRS: cytoreductive surgery, HIPEC: hyperthermic intraperitoneal chemotherapy, PL T: platelets, Max: maximum, WBC: white blood cells.

Figure 1. Hematologic and renal toxicities monitored for 30-days after CRS/HIPEC.

P430. Is there value in repeat CRS±HIPEC for colorectal cancer peritoneal metastases?

Kailey M. Oppat, MD[1]; Frances J. Bennett, MD[2]; Sameer H. Patel, MD[3]; Mustafa Raoof, MD[4]; Joel M. Baumgartner, MD[5]; Harveshp D. Mogal, MD[6]; Laura A. Lambert, MD[7]; Daniel E. Abbott, MD[8]; Jonathan B. Greer, MD[9]; Travis E. Grotz, MD[10]; Keith F. Fournier, MD[11]; Sean P. Dineen, MD[12]; Mohammad Y. Zaidi, MD[13]; Joshua H. WIner, MD[14]; Maria C. Russell, MD[15]; Charles A. Staley, MD[16]; Jordan M. Cloyd, MD[17]; Shishir K. Maithel, MD[18]; Seth J. Concors, MD[19]

[1]Department of Surgery, Emory University, Atlanta, GA, US; [2]Department of Surgery, Emory University, Atlanta, GA, US; [3]Department of Surgery, University of Cincinnati College of Medicine, Cincinnati, OH, US; [4]Division of Surgical Oncology, Department of Surgery, City of Hope National Medical Center, Duarte, CA, US; [5]Division of Surgical Oncology, Department of Surgery, University of California, San Diego, La Jolla, CA, US; [6]Department of Surgery, Division of General Surgery, Fred Hutch Cancer Center, University of Washingt, Seattle, WA, US; [7]Department of Surgery, Section of Surgical Oncology, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, US; [8]Division of Surgical Oncology, Department of Surgery, University of Wisconsin, Madison, WI, US; [9]Division of Surgical Oncology, Department of Surgery, Massachusetts General Hospital, Boston, MA, US; [10]Division of Hepatobiliary and Pancreas Surgery, Mayo Clinic, Rochester, MN, US; [11]Department of Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, US; [12]Department of Gastrointestinal Oncology, Moffitt Cancer Center, Department of Oncologic Sciences, Mo, Tampa, FL, US; [13]Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA, US; [14]Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute of Emory University, Atlanta, GA, US; [15]Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA, US; [16]Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA, US; [17]Division of Surgical Oncology, Department of Surgery, The Ohio State University Wexner Medical Cente, Columbus, OH, US; [18]Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA, US; [19]Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA, US

INTRODUCTION: Although cytoreductive surgery ± hyperthermic intraperitoneal chemotherapy (CRS±HIPEC) is a treatment strategy for pts with colorectal cancer peritoneal metastases (CRC-PM), the majority recur within one year. We assessed the oncologic value and perioperative safety of repeat CRS±HIPEC after recurrence for this population. **METHODS**: A multi-institutional database of pts treated for CRC-PM from 2009-2024 was reviewed. Pts who underwent initial only or repeat curative-intent CRS±HIPEC, defined as CCR0 or CCR1, were included. Pts who underwent a repeat CRS±HIPEC for recurrent disease were identified; those who underwent >2 procedures were excluded. Primary outcome was overall survival (OS), which was evaluated in three distinct ways. We compared OS from date of index operation of pts who underwent repeat CRS±HIPEC to those who only had one procedure. Next, to assess the value of repeat CRS±HIPEC, we compared OS from the date of the repeat procedure to the OS of the pts who only had one operation. Third, we did a subset analysis of only those pts with a documented recurrence after the index CRS±HIPEC and compared OS of pts who underwent repeat surgery to those who only received systemic therapy and/or best supportive care. Secondary outcome was clinically significant postoperative complication rate (≥Grade 3 adverse events per Common Terminology Criteria for Adverse Events Version 5.0). **RESULTS**: 139 pts with CRC-PM were included. 17 (12%) pts underwent a repeat CRS±HIPEC procedure for recurrence after an index procedure. Mean PCI of 10.8 at repeat surgery was similar to mean PCI of 12.6 at the time of index operation. Repeat CRS±HIPEC was associated with improved median OS compared to those that underwent only one procedure (51 vs 24 mos, p=0.02; Fig 1A). The median OS as measured *after repeat* CRS±HIPEC was similar to that as *after initial* CRS±HIPEC (27 vs 24 mos, p=0.49; Fig 1B). Repeat CRS±HIPEC for recurrence was associated with improved OS compared to systemic therapy alone and/or best supportive care (27 vs 12 mos, p=0.01; Fig 1C). There was no difference in postoperative complications for repeat versus initial CRS±HIPEC (59% vs 61%; p=1.0). **CONCLUSIONS**: Repeat CRS±HIPEC for recurrence is associated with an improved overall survival in pts with CRC-PM compared to those who only undergo one procedure and/or are treated with only systemic therapy/best supportive care. Furthermore, the median OS *after repeat* surgery parallels that of pts after their index operation who only received one surgery. Thus, repeat CRS±HIPEC should be considered in well selected pts.

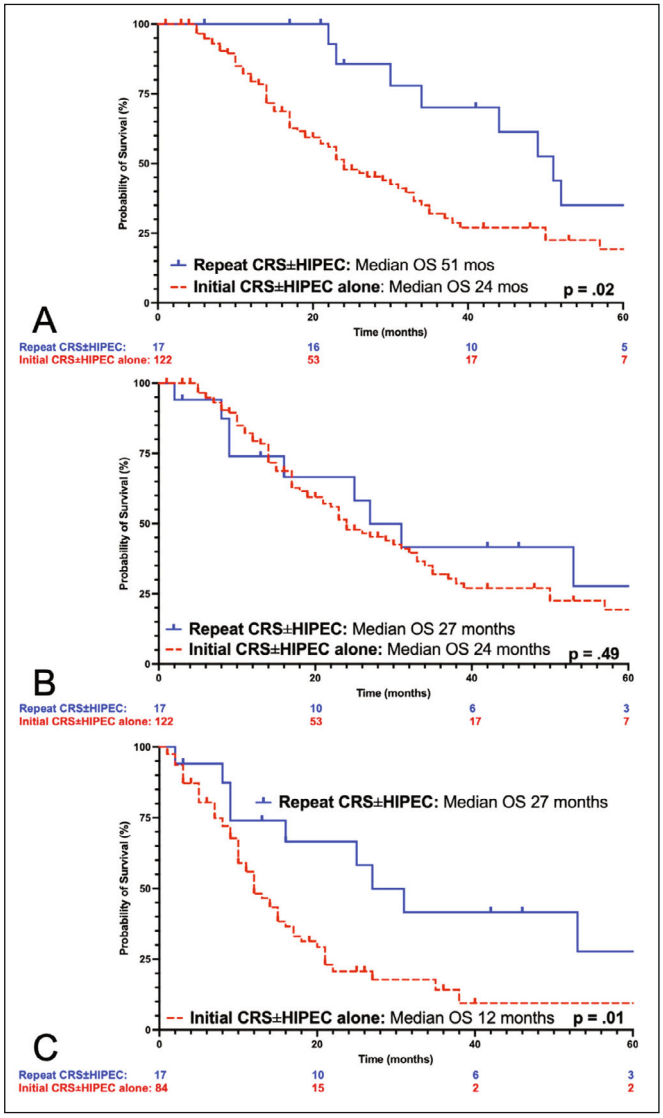


Figure 1. Kaplan Meier (KM) curves demonstrating probability of survival from A. date of initial surgery for both cohorts. B. date of second surgery for the repeat CRS±HIPEC cohort or initial surgery for the cohort who received only one CRS±HIPEC. C. date of second surgery for the repeat CRS±HIPEC cohort or recurrence for the cohort who received only one CRS±HIPEC, among patients with recurrent disease.

P431. Negative Impact of Systemic Therapy on Survival in Patients Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Low-Grade Metastatic Appendiceal Adenocarcinoma

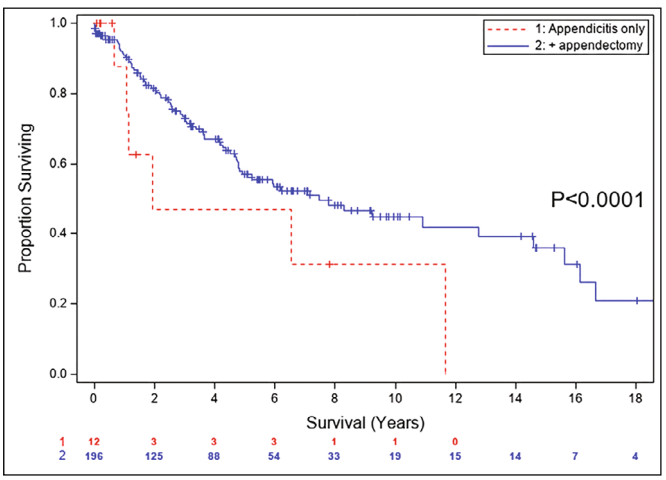
Mason Stillman[1]; Ponnandai Somasundar[2]; N Joseph Espat[3]; Abdul Saied Calvino[4]; Sung Kwon, MD MPH[5]
[1]Columbia University Irving Medical Center, New York, NY, US; [2]Roger Williams Medical Center, Providence, RI, US; [3]Roger Williams Medical Center, Providence, RI, US; [4]Roger Williams Medical Center, Providence, RI, US; [5]Roger Williams Medical Center, Providence, RI, US

INTRODUCTION: Despite studies demonstrating that patients with peritoneal metastases from low-grade appendiceal adenocarcinoma (AA) do not respond well to systemic chemotherapy (SC), patients frequently undergo combination of SC with cytoreductive surgery/hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) regardless of grade. **METHODS:** A nationwide retrospective analysis using the National Cancer Database evaluated patients with AA with peritoneal metastasis from 2016-2021. Cox proportional hazards model was used to evaluate the impact of SC in addition to CRS/HIPEC on overall survival (OS) stratified by tumor grade. **RESULTS:** Total of 1,449 patients were included – 481 low-grade, 428 intermediate-grade, and 540 high-grade tumors. Clinical variables such as age, sex, and comorbidity index were similar across tumor grades. CRS/HIPEC without SC was utilized in 65.73% of low-grade cases compared to 41.01% in intermediate-grade and 11.11% in high-grade cases. SC was utilized alone in 17.74% and with CRS/HIPEC in 16.53% of low-grade cases. In adjusted survival analysis, addition of SC to CRS/HIPEC was associated with worse OS for patients with low-grade AA (HR 2.77, 95% CI 1.18-6.50) but not for intermediate (HR 1.65, 95% CI 0.82-3.35) and high-grade tumors (HR 1.18, 95% CI 0.67-2.45). The addition of time to definitive surgery variable nullified the negative impact of adding SC to CRS/HIPEC in low-grade AA (HR 1.76, 95% CI 0.68-4.53). **CONCLUSIONS:** Negative OS impact of SC may be mediated by delays in effective surgical/intraoperative therapy. If CRS/HIPEC is planned for patients with metastatic low-grade AA, avoiding SC may facilitate earlier surgical intervention and improve survival.

P432. Non-operative management of appendicitis is associated with decreased survival in patients with appendiceal neoplasms

Heidy Cos, MD[1]; Wesley H Iobst[2]; Greg Russell[3]; Rui Zheng-Pywell[4]; Perry Shen, MD[5]; Konstantinos I. Votanopoulos, MD, PhD[6]; Edward Levine, MD[7]
[1]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [2]Wake Forest School of Medicine, Winston Salem, NC, US; [3]Atrium Health Wake Forest Baptist Medical Center, Winston Salem, NC, US; [4]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [5]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US; [6]Wake Forest Institute for Regenerative Medicine, Winston-Salem, NC, US; [7]Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC, US

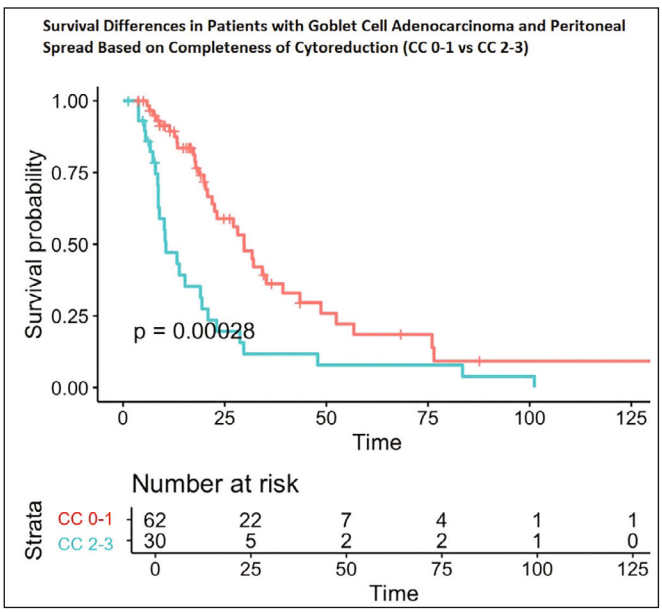
INTRODUCTION: Non-operative management of appendicitis has been widely adopted in the surgical community with reported safe outcomes. However, data are lacking on its impact in diagnosis and management of appendiceal neoplasms. **METHODS:** A prospectively maintained database of 1900 CRS/HIPEC procedures was reviewed and outcomes of 900 patients with appendiceal neoplasms were explored. Kaplan-Meier method was used to estimate overall survival (OS); the log-rank test of the chi-square approximation was used to assess statistical significance. SAS (version 9.4, Cary, NC, USA) was used for all analyses. P-values <0.05 were considered statistically significant. **RESULTS:** 900 patients underwent CRS/HIPEC for appendiceal tumors at our institution from 1993 to 2024. Most patients were female (56.3%) with a mean age of 54.8 (SD=12.1). 208 patients had a diagnosis of appendicitis before their first CRS/HIPEC and out of these, 196 underwent an appendectomy before CRS/HIPEC. Forty-nine percent of patients in the appendectomy group had high grade disease, compared to 58% in the non-operative management group, p=.56. Median OS was significantly higher in patients with appendicitis who underwent appendectomy than for those who underwent non operative management of appendicitis (89.7 months vs 23 months, p<0.05). **CONCLUSIONS:** Non operative management of appendicitis is associated with decreased overall survival in patients with appendiceal neoplasms who undergo cytoreduction and heated intraperitoneal chemotherapy.



P433. Outcomes of CRS and HIPEC in Patients with Peritoneal Metastases from Goblet Cell Adenocarcinoma: A Retrospective Analysis

Vladimir Milovanov, MD[1]; Brendan Moran[2]; Tom Cecil[3]; Faheez Mohamed[4]
[1]Basingstoke and North Hampshire Hospital, Basingstoke, GB; [2]Basingstoke and North Hampshire Hospital, Basingstoke, GB; [3]Basingstoke and North Hampshire Hospital, Basingstoke, GB; [4]Basingstoke and North Hampshire Hospital, Basingstoke, GB

INTRODUCTION: Goblet cell adenocarcinoma (GCA) of the appendix with peritoneal metastases poses significant treatment challenges. Cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) offers a potentially curative approach. This study evaluates the outcomes of patients with GCA undergoing CRS/HIPEC with curative intent. **METHODS:** We retrospectively analyzed data from 92 patients with GCA and peritoneal metastases who underwent CRS/HIPEC. The mean patient age was 58 years (range: 30-82), and 35% were male. The mean operative time was 7 hours (range: 4-10). Tumor classification was based on Tang criteria: Tang A (2 patients), Tang B (39 patients), Tang C (40 patients), and 11 unclassified. The median follow-up was 21 months. **RESULTS:** Survival: The median overall survival (OS) was 23 months, with 1-, 3-, and 5-year survival rates of 76%, 28%, and 19%, respectively. The median OS was 30 months for Tang B patients and 21 months for Tang C patients (p=0.4). Cytoreduction: Complete cytoreduction (CC 0-1) was achieved in 67% of patients, while 33% had incomplete cytoreduction (CC 2-3). The median OS for patients with CC 0-1 was 30 months, compared to 10 months for those with CC 2-3 (p=0.00028). Median progression-free survival (PFS) for CC 0-1 patients was 14 months. Peritoneal Cancer Index (PCI): The mean PCI was 18 (range: 2-39). Patients with a PCI <20 had a median OS of 32 months, whereas those with a PCI >20 had a median OS of 17 months (p<0.0001). Lymph Node Involvement: Positive lymph nodes were found in 67% of patients. The median OS was 27 months for node-negative patients, versus 21 months for node-positive patients (p=0.87). Tumor Markers: Elevated CA 125, CEA, and CA 19-9 levels were observed in 42%, 31%, and 27% of patients, respectively. On univariate analysis of tumor markers, only a tripling of CA 125 levels >105 was associated with worse prognosis (median OS: 7 vs. 28 months, p=0.023). Complications: No perioperative mortality was observed. Complications occurred in 62% of patients, with 3% experiencing grade 3/4 complications. **CONCLUSIONS:** CRS and HIPEC provide a 5-year overall survival of 19% for patients with peritoneal metastases from GCA. Complete cytoreduction, particularly in patients with a PCI <20, results in the best survival outcomes. However, only 67% of patients achieved complete cytoreduction, highlighting the need for improved patient selection criteria to optimize outcomes. Further studies are warranted to refine these criteria and enhance treatment efficacy.



P434. Overall and progression-free survival and treatment of recurrence after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for patients with malignant peritoneal mesothelioma

Zachariah Tman[1]; Andrew M. Lowy, MD, FACS[2]; Jula Veerapong, MD[3]; Joel M. Baumgartner, MD, FACS[4]
[1]UC San Diego Health, La Jolla, CA, US; [2]University of California San Diego, San Diego, CA, US; [3]UCSD Moores Cancer Center, La Jolla, CA, US; [4]University of california san diego, San Diego, CA, US

INTRODUCTION: Malignant peritoneal mesothelioma (MPM) is a rare and aggressive peritoneal surface malignancy, with relatively poor survival despite cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC). Rates and management of recurrence are not well defined. We sought to examine these at our institution. **METHODS:** We retrospectively analyzed patients with MPM who underwent CRS-HIPEC with platinum-based and doxorubicin chemotherapy at our institution from February 2008 to May 2023. Progression-free survival (PFS) and overall survival (OS) were calculated from the time of CRS-HIPEC. In recurrent disease, OS was also calculated from the time of postoperative chemotherapy, immunotherapy, and repeat CRS-HIPEC using the Kaplan Meier method. **RESULTS:** A total of 61 CRS-HIPEC procedures were performed in 60 patients with MPM at our institution in the study period. Demographic details are shown in the Table. Median PFS was 24.3 months (95% CI 10.6, 38.0 months) and median OS was 59.8 months (95% CI, 18.6, 101.0 months), after a median follow-up time of 45.5 months (range: 1.7-94.1 months). Forty (65.6%) patients recurred, for which 26 (42.6%) received chemotherapy, 19 (31.1%) received immunotherapy (checkpoint blockade +/- chemotherapy), and nine (14.8%) underwent repeat CRS +/- HIPEC. Median OS was 17.0 months (95% CI, 2.3, 31.8 months) after chemotherapy, 18.9 months (95% CI, 15.8, 22.1 months) after immunotherapy, and 22.1 months (95% CI no reached) after repeat CRS +/- HIPEC for recurrence. Five patients who received immunotherapy had greater than 24 months of OS, four of which have had no further progression. **CONCLUSIONS:** Patients with MPM had favorable outcomes after CRS HIPEC at our institution. Immunotherapy has potential for improving outcomes after recurrence after CRS-HIPEC.

Table 1. Demographics and Variables

Demographics	**n (%)/median (range)**
N	61
Male	32 (52.5)
Female	29(47.5)
Mean Age	56.8
Histology	
Epithelioid	55 (90.2)
Biphasic	3 (4.9)
Sarcomatoid	1 (1.6)
Unknown	2 (3.3)
Prior Chemotherapy	38 (62.3)
Adjuvant Chemotherapy	6 (9.8)
Post Op Chemotherapy	26 (42.6)
Post Op Immunotherapy	19(31.1)
PCI	15 (5-32)
CC-score	
CC-0	24 (39.3)
CC-1	27 (44.3)
CC-2	10 (16.4)
OR time (min)	432 (196-866)
Estimated Blood Loss (cc)	150 (10-1250)
Num of Visceral Resections	0 (0-4)
Num of Anastomoses	0 (0-4)
Post Operative Variables	
Length of Stay (days)	9 (4-28)
60 day CD ≥ 3	12 (19.7)
60 day Readmission	13 (21.3)
F/u Time (months)	45.5 (1.7-194.1)

Note: PCI – peritoneal cancer index; CC-score – completeness of cytoreduction score; OR – operating room; EBL – estimated blood loss; LOS – length of stay; CD – Clavien Dindo complications

P435. Percutaneous Transesophageal Gastrostomy as an Alternative Approach for Palliative Decompression of Malignant Bowel Obstruction

Kristofor Olson, MD, PhD[1]; F Edward Boas[2]; Bo Liu, MD[3]; Vijay Trisal, MD[4]; Thinzar Lwin, MD, MS[5]
[1]City of Hope, Duarte, CA, US; [2]City of Hope, Duarte, CA, US; [3]City of Hope, Duarte, CA, US; [4]City of Hope, Duarte, CA, US; [5]City of Hope Medical Center, Duarte, CA, US

INTRODUCTION: Percutaneous trans-abdominal gastrostomy (PG) tube placement is commonly utilized for management of malignant bowel obstruction (MBO). In cases where the PTG is contraindicated, a nasogastric approach is used, however these tubes cause significant discomfort and a poor quality of life. The use of the percutaneous trans-esophageal gastrostomy tube (PTEG) offers an alternative for patients who have contraindications for a PG tube placement. This case series explores the clinical indications, outcomes, and longevity of PTEG placement in patients with malignant bowel obstruction, to gain insights into its role as a palliative option. **METHODS:** Single center retrospective chart review was conducted on patients diagnosed with MBO who underwent percutaneous trans-esophageal gastrostomy (PTEG) tube placement for gastric decompression from Jan 2024 – Oct 2024.. Demographic data such as age, gender, and primary cancer were collected. Clinical parameters including prior multidisciplinary consultations and contraindications to percutaneous trans-abdominal gastrostomy (PG) were recorded. Associated outcomes such as technical success of the PTEG procedure, complication rates, time to discharge, code or hospice status upon discharge, and duration of PTEG tube use were documented. **RESULTS:** Five patients with malignant bowel obstruction underwent percutaneous trans-esophageal gastrostomy (PTEG) tube placement. The median age was 52 years (range: 46-73). Cancer types included gastric (n=2), head and neck (n=1), ovarian (n=1), and pancreatic (n=1). Three patients had large volume ascites and two patients had abdominal wall infection as contraindications to PG tube placement. Four patients had additional palliative tubes in place. The technical success rate for PTEG placement was 100%, with no immediate procedure-related mortality. There were 2 patients with soft tissue infection from the PTEG tract site which were treated with antibiotics. Post-procedure length of stay ranged from 4-9 days, 4 patients were discharged home, and 1 to inpatient hospice. The mean duration of PTEG tube use was 75.25 days, and the median duration was 77 days (range:9-138 days). All patients who could tolerate swallowing were returned to clear liquids for oral gratification. **CONCLUSIONS:** PTEG placement demonstrates a high technical success rate with limited complications and moderate durability, enabling discharge to home or hospice in most cases. While previous studies have reported that over 90% of patients died within 30 days of PTEG placement, our case series showed longer tube use and survival, suggesting that PTEG may offer a viable and more comfortable alternative to nasogastric (NG) tubes for gastric decompression in patients with malignant bowel obstruction who are not candidates for percutaneous trans-abdominal gastrostomy. Further studies are needed to assess long-term outcomes and the impact on quality of life in this patient population.

P436. Robotic versus Open Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy: A Propensity Score-Matched Study

Ekaterina Baron, MD[1]; Zhesheng Xu[2]; Alessandro Paro, MD[3]; Andrei Nikiforchin, MD[4]; Jessica A. Wernberg, MD, FACS[5]; Rohit Sharma, MD, FACS[6]
[1]Marshfield Medical Center, Marshfield, WI, US; [2]Pomona College, Claremont, CA, US; [3]Marshfield Medical Center, Marshfield, WI, US; [4]Marshfield Medical Center, Marshfield, WI, US; [5]Marshfield Medical Center, Marshfield, WI, US; [6]Marshfield Medical Center, Marshfield, WI, US

INTRODUCTION: Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is often associated with extensive surgical resection and has traditionally been performed via an open approach. However, in select patients with low tumor burden, a minimally invasive robotic approach can be feasible, yet existing data are limited to case reports. We evaluated surgical safety and oncological outcomes of robotic CRS/HIPEC for peritoneal surface malignancies (PSM). **METHODS:** A single-center propensity score-matched study was conducted using a prospectively collected database (2008-2024). We included PSM patients treated with robotic CRS/HIPEC and selected control subjects with open-CRS/HIPEC in a 1:1 ratio using propensity score matching weighted by age, sex, BMI, histology, and PCI. **RESULTS:** Of 99 cases, 15 robotic and 15 open CRS/HIPECs were identified. After matching, both groups were balanced by age (medians 67 vs 63 years, p=0.17), sex (females 66.7% vs 66.7%, p=1.00), BMI (medians 31.1 vs 30.7 kg/m², p=0.81), diagnosis (p=0.72), prior surgical score 2/3 (73.3% vs 60.0%, p=0.44), and PCI (medians 5 vs 6, p=0.54). Conversion rate in the robotic group was 6.7% (n=1). CC-0/1 rate was comparable between the robotic (100.0%) and open CRS/HIPEC (93.3%) groups (p=1.00). Estimated blood loss was significantly lower in the robotic group (100 mL vs 250 mL, p=0.04). There was no difference in the median length of surgery: 631 vs 516 minutes in robotic and open groups (p=0.17). Median hospital stay was shorter in the robotic group (6 vs 9 days, p=0.05). No differences were found in major complication (26.7% vs 33.3%, p=1.00) and return to the operating room rates (0.0% vs 6.7%, p=1.00). No perioperative mortality was seen in either group. The median follow-up was 54 months. Median overall survival (OS, not reached [NR] vs 52 months, p=0.06) and progression-free survival (PFS, NR vs 42, p=0.41) did not differ in robotic and open groups. 3-year OS was 93% in robotic vs 80% in open HIPEC. In appendiceal tumors (10 in each group), OS was NR in robotic CRS/HIPEC vs 94 months in the open group (p=0.34) and PFS was NR vs 57 months, respectively (p=0.35) (Figure 1). **CONCLUSIONS:** Robotic CRS/HIPEC is not associated with increased morbidity and may offer lower blood loss and shorter hospital stay for patients with low PCI. Oncological outcomes appear similar between robotic and open approaches. Further multi-institutional studies are needed to confirm whether robotic CRS/HIPEC provides additional benefits for PSM patients.

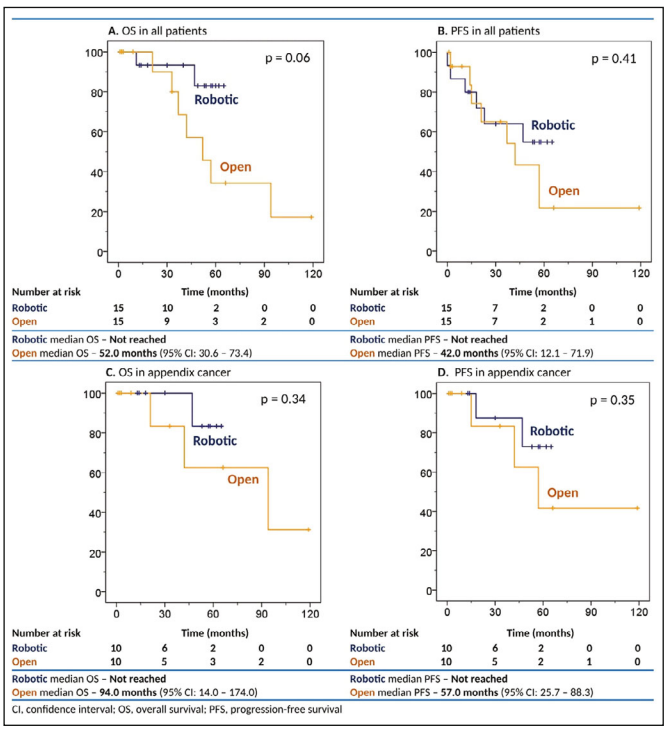


Figure 1. Survival outcomes

P437. Tailored Surveillance for Mucinous Appendix Cancer after Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy

Vladislav Kovalik, MD, MSPH[1]; Armando Sardi, MD, FACS[2]; Mary Caitlin King, BS[3]; Sergei Iugai, MD[4]; Luis Felipe Falla-Zuniga, MD[5]; Kseniia Uzhegova, MD[6]; Carol Nieroda, MD[7]; Vadim Gushchin, MD, FACS[8]
[1]Mercy Medical Center, Baltimore, MD, US; [2]Mercy Medical Center, Baltimore, MD, US; [3]Mercy Medical Center, Baltimore, MD, US; [4]Mercy Medical Center, Baltimore, MD, US; [5]Mercy Medical Center, Baltimore, MD, US; [6]Mercy Medical Center, Baltimore, MD, US; [7]Mercy Medical Center, Baltimore, MD, US; [8]Mercy Medical Center, Baltimore, MD, US

INTRODUCTION: In mucinous appendix cancer (MAC), despite varying recurrence rates across histologic subtypes, the surveillance schedule following cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) remains uniform – typically, every 6 months for 5 years followed by annual follow-up (FU). We aimed to identify time periods that reflect significant changes in the probability of recurrence after CRS/HIPEC for each MAC subtype. **METHODS:** A prospective institutional database (1998-2023) was

used including stage IV MAC patients with low-grade (LGMCP), high-grade (HGMCP), and signet-ring cell (SRC) mucinous carcinoma peritonei treated with initial CRS/HIPEC. Aborted HIPECs were excluded. Kaplan-Meier recurrence-free survival (RFS) from CRS/HIPEC to recurrence or death was compared across histologies using a log-rank test. A piecewise exponential RFS model was employed. Excluding the first 6 months, the post-CRS/HIPEC timeline was divided into periods by knots obtained through a forward selection using Bayesian Information Criterion (BIC) in a histology-adjusted Cox regression model. For each histology, cumulative risk of recurrence (CRR) and 5% decline points (DP) in RFS were estimated during the identified periods. Assuming a constant within-period probability of recurrence, we divided periods into equally spaced intervals based on DPs. **RESULTS:** A total of 385 patients were included: 60.3% (n=232) had LGMCP, 20.8% (n=80) had HGMCP, and 19.0% (n=73) had SRC. Median age was 54 (interquartile range [IQR]: 46-63) years and 64.9% (n=250) were female. Median peritoneal cancer index was 26 (IQR: 9-36) and complete cytoreduction (CC-0/1) was obtained in 98.2% (n=378). Median length of hospital stay was 9 days (IQR: 8-12). Grade III/IV Clavien-Dindo complications occurred in 14.5% (n=56) of patients. Median FU was 92 months (95% confidence interval [CI]: 83, 98). Median RFS was not reached (NR) for LGMCP (95% CI: 109, NR), 30 months (95% CI: 23, 39) for HGMCP, and 23 months (95% CI: 15, 31) for SRC (p<0.001). Knots were selected at 16 and 48 months (BIC=484.4), dividing FU into 3 periods: I – 6 to 16 months; II – 16 to 48 months; and III – 48 to 120 months. The CRR rates and suggested equally spaced FUs within each period are summarized in Figure 1. **CONCLUSIONS:** Each histological subtype of MAC exhibits a distinct recurrence probability at key time periods after CRS/HIPEC, which can be addressed by a tailored FU schedule. HGMCP and SRC subtypes may require a more intensive FU between 16 and 48 months, while for LGMCP a less frequent FU within the same period is adequate.

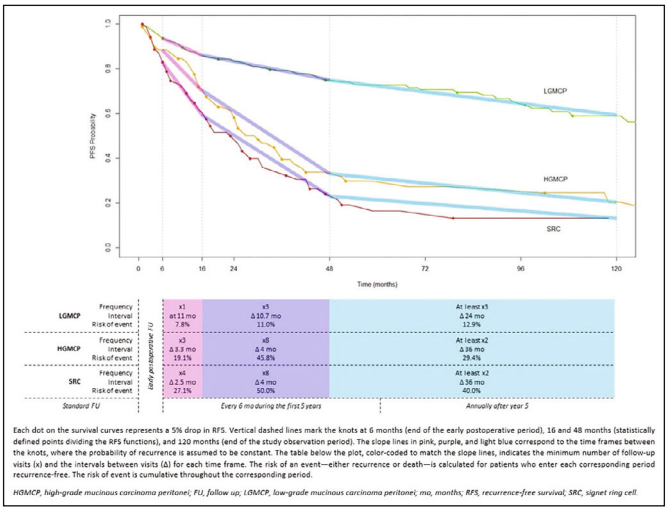


Figure 1. Follow-Up Frequencies to Addressing the Risk of Recurrence across MAC histology

P438. The Atypical Presentation and Delayed Timing of Anastomotic Leak in Patients who Undergo Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy

Colin J Rog, MD[1]; Riom Kwakman, MD[2]; Charlotte van Schooten, MD[3]; Chloe Hanson, MD[4]; Erek Nelson, MD[5]; Joy Sarkar, MD[6]; Matthew GK Benesch, MD PhD[7]; Joseph Skitzki, MD[8]; Mohamed Alassas, MD[9]; Evan Ong, MD[10]
[1]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [2]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [3]Swedish Medical Center, Seattle, WA, US; [4]Swedish Medical Center, Seattle, WA, US; [5]Brooke Army Medical Center, Fort Sam Houston, TX, US; [6]Novant Health Cancer Institute, Charlotte, NC, US; [7]Memorial University of Newfoundland, St. John, NL, CA; [8]Roswell Park Comprehensive Cancer Center, Buffalo, NY, US; [9]Swedish Medical Center, Seattle, WA, US; [10]Swedish Medical Center, Seattle, WA, US

INTRODUCTION: Anastomotic leak (AL) is a devastating complication following cytoreductive surgery/hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) for peritoneal surface malignancies. Anecdotally, leaks can present atypically and later in the postoperative course compared to non-CRS/HIPEC gastrointestinal surgery, but this has not been rigorously described in the literature. **METHODS:** The records of all patients who underwent CRS/HIPEC at two specialty centers were retrospectively reviewed, and patients with AL were identified. Demographics, traditional preoperative risk factors for AL, information pertaining to neoadjuvant therapies, surgical details, and variables describing patient clinical presentation were recorded and analyzed. **RESULTS:** 527 patient charts were reviewed and 32 (6.1%) who experienced AL were identified. The median time at which patients presented with an AL was postoperative day (POD) 15. Using receiver operator characteristic curves and the maximum Youden's index, the point of maximum discrimination was POD10 and patients were hence dichotomized into early (< POD10) (n = 11) and late (≥ POD10) (n = 21) leak groups. Smoking status, pre-existing diagnosis of diabetes, obesity status (BMI ≥ 30), disease histology, receipt of neoadjuvant chemotherapy +/- bevacizumab, preoperative hematocrit, number of hollow viscus resections, number of anastomoses created, and hand-sewn versus stapled technique were similar between groups. All except 1 patient (carboplatin) were perfused with mitomycin C. Preoperative albumin was satisfactory in both groups although was significantly higher in the late group compared to the early group (4.4 +/- 0.3 g/dL vs 3.9 +/- 0.4 g/dL; p = 0.03). A higher proportion of ileocolonic and colorectal anastomoses leaked in the late group whereas a higher proportion of small bowel anastomoses leaked in the early group (p = 0.02). Patients in the late group were more likely to present without fever (p = 0.001), tachycardia (p = 0.02), and hypotension (p = 0.01). WBC count did not differ significantly between the two groups (p = 0.053). Presence of peritonitis on physical exam also did not differ significantly between groups, although interestingly it was only present in 6 (18.8%) patients in the entire cohort (5 focal, 1 diffuse). **CONCLUSIONS:** Patients who experience AL after CRS/HIPEC, particularly of ileocolic or colorectal anastomoses, may present later compared to patients who undergo non-CRS/HIPEC gastrointestinal surgery. Those who leak in a delayed manner are more likely to present without expected clinical signs such as fevers, tachycardia, hypotension, and peritonitis.

P439. Treatment Patterns for Patients with Non-Mucinous Appendix Cancer and Peritoneal Metastases: A National Cancer Database Study

Sergei Iugai, MD[1]; Vadim Gushchin, MD, FACS[2]; Mary Caitlin King, BS[3]; Vladislav Kovalik, MD, MSPH[4]; Luis Felipe Falla-Zuniga, MD[5]; Kseniia Uzhegova, MD[6]; Carol Nieroda, MD[7]; Armando Sardi, MD, FACS[8]
[1]Mercy Medical Center, Baltimore, MD, US; [2]Mercy Medical Center, Baltimore, MD, US; [3]Mercy Medical Center, Baltimore, MD, US; [4]Mercy Medical Center, Baltimore, MD, US; [5]Mercy Medical Center, Baltimore, MD, US; [6]Mercy Medical Center, Baltimore, MD, US; [7]Mercy Medical Center, Baltimore, MD, US; [8]Mercy Medical Center, Baltimore, MD, US

INTRODUCTION: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is the standard of care (SoC) for mucinous appendix cancer (MAC) with peritoneal metastases (PM). However, due to its rarity, the data on existing treatment patterns (TP) for non-mucinous appendix cancer (NMAC) are limited. This study aims to evaluate national trends in the management of advanced NMAC. **METHODS:** A retrospective study using appendix cancer cases (C18.1) between 2004-2021 from the National Cancer Database (NCDB) was conducted. NMAC patients were identified by excluding codes corresponding to MAC and non-epithelial tumors. Stage IV patients were selected using the "Analytic stage," while "CS Mets at Dx"/ "Mets at Dx" categories identified patients with PM. TP were described using data from the "Treatment" section. A stepwise logistic regression was used to identify factors associated with treatment approaches. Survival analysis was performed using the Kaplan-Meier method and log-rank test. **RESULTS:** We identified 10,759 cases of NMAC. Of 2,867 stage IV patients, 1,763 (61.4%) either had or were likely to have PM and were included. Adenocarcinoma, NOS (ADN) was the most common histology (88.6%, n=1562). Of 1,332 (75.5%) patients undergoing surgery, 339 (25.5%) had surgery alone, while 8.9% (n=118), 49.5% (n=660), 3.6% (n=48), and 12.5% (n=167) also received neoadjuvant, adjuvant, perioperative chemotherapy, or HIPEC, respectively. Palliative chemotherapy (PC) alone was administered in 18.1 % (n=319) of patients and 6.4% (n=112) received supportive care (SC) only. Surgery+chemotherapy (S+Ch) was the predominant TP from 2006 to 2021. However, patients diagnosed after 2013 (p<0.001), males (p<0.001), and patients older than 65 years (p=0.015) had the highest likelihood of non-surgical management. Non-ADN histology (p=0.010), private insurance (p<0.001), academic facility (p<0.001), and diagnosis after 2013 (p<0.001) were associated with a higher probability of CRS/HIPEC. The 5-year overall survival (OS) was 33%, 29%, 52%, 49% and 45% for patients undergoing SC, PC, surgery only, S+Ch, and CRS/HIPEC, respectively. While patients treated with a surgery had better OS (p=0.002) than those receiving SC or PC alone, there was no significant difference between surgery, S+Ch

and CRS/HIPEC (p=0.309). **CONCLUSIONS:** Surgery is the most common treatment option for NMAC with PM and associated with prolonged survival. Unlike MAC, the use of CRS/HIPEC is not widespread for NMAC, though its application is growing in academic centers.

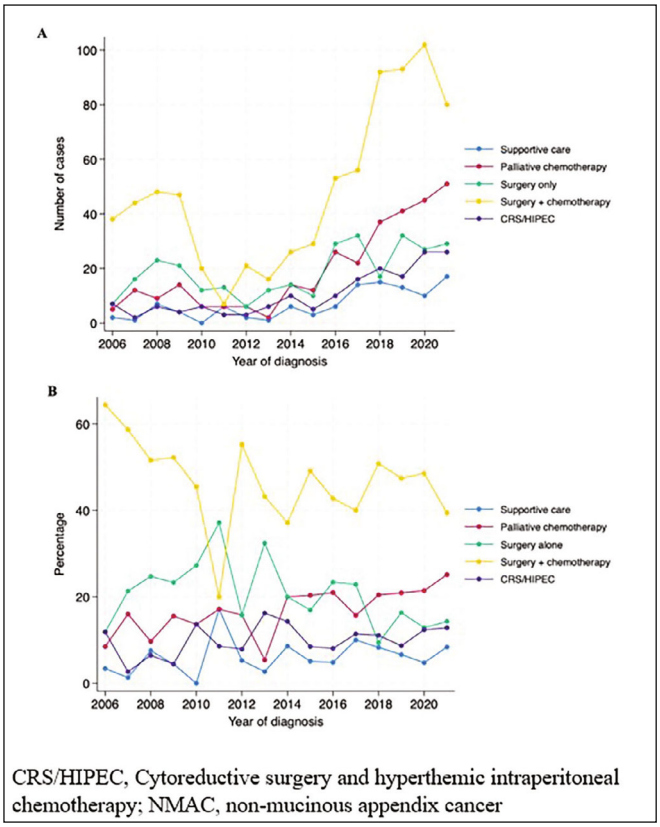


Figure 1. Absolute (A) and relative (B) frequency of different treatment pattems in advanced NMAC by year of diagnosis.

P440. A detailed evaluation of the clockwise anterior-to-posterior double isolation (CAP-DI) approach to portal lymphadenectomy for biliary tract cancers: lymph node yields, anatomical nodal distribution, and oncologic implications

Anastasios Mitsakos, MD[1]; Betzaira Childers[2]; Megan A Satyadi, MD[3]; Andrew J Sinnamon, MD[4]; Gregory Lauwers[5]; Yukihiro Nakanishi[6]; Richard Kim[7]; Daniel A Anaya, MD[8]; Jason Denbo[9]

[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]University of Cincinnati College of Medicine, Cincinnati, OH, US; [4]Moffitt Cancer Center, Tampa, FL, US; [5]Moffitt Cancer Center, Tampa, FL, US; [6]Moffitt Cancer Center, Tamps, FL, US; [7]Moffitt Cancer Center, Tampa, FL, US; [8]Moffitt Cancer Center, Tampa, FL, US; [9]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Portal lymphadenectomy for biliary tract cancers remains a challenging operation with approximately 50% oncological lymph node yield of 6 or more lymph nodes even in high-volume experienced centers. The clockwise anterior-to-posterior double isolation (CAP-DI) approach of portal lymphadenectomy in 6 defined lymph node packages has shown promising results in performing this operation with reproducible oncological outcomes. Goal of this study was to achieve a descriptive analysis of oncological quality metrics after standardizing this method in a single institution. **METHODS:** Retrospective analysis of a prospectively collected database of patients with biliary tract cancers at a single institution in 2021-2024 was performed. Biliary tract cancers of interest included intrahepatic and extrahepatic hilar cholangiocarcinomas and gallbladder cancers. Patients underwent curative operative resection of the primary mass as well as CAP-DI oncological portal lymphadenectomy in an open or robotic fashion. The primary outcomes were total lymph node retrieval, per package lymph node retrieval, and need for major hepatectomy with bile duct resection and reconstruction. Secondary outcomes included preoperative and baseline patients characteristics, as well as intraoperative and postoperative surgical quality metrics. **RESULTS:** A total of 26 patients were included of whom the average age was 66 years old (range 45-86). 27% of the operations were performed using robotic approach, with 1 case requiring conversion to open approach. Total lymph node retrieval from CAP-DI portal lymphadenectomy averaged at 6.3 lymph nodes (range 2-13). 53.8% of patients had 6 or more lymph nodes retrieved. More than 70% of the lymph nodes were retrieved from packages 1, 5, and 6. Regarding preoperative characteristics, only 2 patients (7.7%) had underlying hepatic cirrhosis, and none had evidence of portal hypertension. Average BMI was 28.8 (range 20-40) and average ASA classification 2.8 (range 2-3). 23.1% of patients received preoperative systemic therapy. Intraoperatively, average estimated blood loss was 137 mL and average Pringle maneuver duration was 40 minutes. Overall postoperative complication rate was 23.1%, with no patients experiencing major complications. **CONCLUSIONS:** Despite advances in operative standardized approaches and use of minimally invasive methods, adequate portal lymphadenectomy for biliary tract cancers using the quality metric of 6 or more lymph nodes remains difficult to be attained. However, incremental improvement can be achieved safely and efficiently in a consistent and reproducible manner.

Table. Descriptive analysis of patient factors, operative factors, and post-operative quality metrics of patients undergoing curative liver resection and oncological lymphadenectomy for biliary tract cancers

	Average value or percentage (N=26)
Patient Factors	
Age	66.3 years (range 45-86)
Charlson-Deyo Comorbidity Index	2.46 (range 2-5)
Cirrhosis	7.7% (n=2)
Portal Hypertension	0% (n=0)
BMI	28.8 (range 20-40)
ASA Classification	2.8 (range 2-3)
Preoperative systemic therapy	23.1% (n=6)
Operative Factors	
Operative time	423 minutes (range 200-650)
Blood loss	137 mL (range 25-500)
Pringle maneuver duration	40 minutes (range 0-76)
Robotic approach	27% (n=7)
Major hepatectomy (>2 segments)	42.3% (n=11)
Hepatectomy with bile duct resection and reconstruction	7.7% (n=2)
Post-operative Quality Metrics	
Overall complications	23.1 % (n=6)
Length of stay	4 days (range 1-8)
Total lymph node retrieval	6.3 (range 2-13)
Percentage lymph node retrieval 6 or more	53.8% (n=14)

P441. Analysis of Post-COVID Trends in Upstaging and Treatment within Multiple Cancer Types

Lacey Mead, DO, MS[1]

[1]Lakeland Regional Health, Lakeland, FL, US

INTRODUCTION: The COVID-19 pandemic altered access to healthcare resulting in a decrease number of patients who received cancer screening, prompt evaluation, and care. This significantly increased diagnosis and treatment delays throughout this time. Currently, there is limited information on trends observed after the COVID pandemic and whether these similar practices continue to be observed. Therefore, we set to evaluate patterns of disease staging at diagnosis and treatment within multiple cancer types when comparing pre, during and post COVID eras. We seek to understand whether there is a COVID effect on the current guidelines for diagnosis, treatment and surveillance. **METHODS:** Our retrospective study population was derived from a high-volume, Commission on Cancer institute. We divided the cohorts into Pre-COVID (PreC) (2013-2020), During COVID (DC) (2020-2021) and post-COVID (PosC) (2022-present). Stage at treatment verses non-treatment during the three era was evaluated for each cancer type. Each site was examined independently, therefore, factorial ANOVAs tested these relationships. Further, independent samples t-tests and chi-squares were used to examine the differences between eras in staging and treatment. A p-value of <0.05 was classified as significant. **RESULTS:** Our study population consisted of 16119 individuals. Interestingly, those with breast cancer had a significantly lower stage at treatment DC (1b) compared to PreC era (2a) (<0.001) and no more likely to be treated PosC (1a) compared to DC. Alternatively, Lung cancer had a significant upstage and decrease treatment management DC (3a) when compared to PreC (2b) (<0.001) and no more likely for PosC (3a) treatment compared to DC. Further, there was a significant

increase in patients treated at a higher stage DC (3a) and PosC (3a) when compared to PreC (2b) within prostate cancer (<0.001). This was also reflected in colorectal cancer, with a significant upstage in those first receiving treatment DC (3a) when compared to PreC (2b) (<0.001). This trend persistent in PosC (3a) group. Pancreatic and gastric cancer did not have significant difference in staging amongst the cohorts. **CONCLUSIONS:** Based on results, there appears to be a COVID effect within staging and treatment dependent on cancer type. Some cancers showcase a continuation of the same trend seen during the pandemic of a higher stage at first diagnosis and treatment. This potentially highlights awareness of a changing population and healthcare system after the pandemic and bring to question whether our guidelines are appropriate for current society.

P442. Complex Hepatopancreaticobiliary Surgery Is Safe In A Geriatric Patient Population: A High-volume Community Center Experience

Alexandra E Adams, MD[1]; Kai A Bickenbach, MD[2]; Zubin M Bamboat, MD[3]; Lawrence E Harrison, MD[4]; Eric D Whitman, MD[5]; Irene E Rossmer, MD[6]
[1]Atlantic Health System, Morristown, NJ, US; [2]Atlantic Health System, Morristown, NJ, US; [3]Atlantic Health System, Morristown, NJ, US; [4]Atlantic Health System, Morristown, NJ, US; [5]Atlantic Health System, Morristown, NJ, US; [6]Atlantic Health System, Morristown, NJ, US

INTRODUCTION: Elderly patients have a perceived risk of worse outcomes after complex abdominal surgery. We demonstrate that at a high-volume center, surgical outcomes in older patients undergoing hepatopancreaticobiliary surgery are comparable to younger populations. **METHODS:** Data were extracted from electronic medical record for patients undergoing liver, pancreas, and bile duct resections at a high-volume center (2016-2023). Outcomes in patients >75 years old were compared to those younger than 75. Primary endpoints were in-hospital or 30-day mortality, return to OR, length of stay (LOS), and readmission rate. Secondary endpoint was 5-yr survival. Outcome measures were compared using Fisher's exact or Mann-Whitney test, and survival was compared using log-rank test, with p<0.05 considered statistically significant. **RESULTS:** 264 hepatectomies, 376 pancreatectomies, and 20 bile duct resections were reviewed. There was no statistically significant difference between the groups with respect to post-operative LOS or operative time for any of the surgeries. Return to OR and perioperative mortality were both extremely rare events, and were not observed more frequently in the older population. Readmission rate was higher in older patient hepatectomy group (14.0% vs 4.6%, p=0.02) but did not differ among pancreatectomies (19.0% vs 17.9%, p=0.88) or bile duct resections (25.0% vs 18.8%, p>0.99). Median survival was not reached, but 5-year survival was lower in older patients following hepatectomy (44.2% vs 72.6%, p=0.054) as well as pancreatic and bile duct resection (54.3% vs 75.1%, p=0.01, 37.5% vs 76.6%, p=0.04 respectively). **CONCLUSIONS:** Complex liver, pancreas, and bile duct surgery can be safely performed in elderly patients at a high-volume community center.

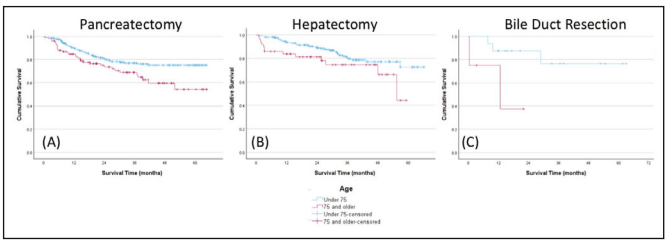


Figure 1. 5 year survival stratified by age groups for patients undergoing (A) Pancreatectomy (log rank test p-value=0.01), (B) Hepatectomy (log rank test p-value=0.054), and (C) Bile Duct Resection (log rank test p-value=0.04)

P443. Creation and utilization of cancer registry in Hawassa, Ethiopia

Taylor J Jaraczewski, MD, MEng, MS[1]; Netsanet Bogale, MD[2]; Syed Nabeel Zafar, MD, MPH[3]
[1]Medical College of Wisconsin, Milwaukee, WI, US; [2]Hawassa University Comprehensive Specialized Hospital, Hawassa, ET; [3]University of Wisconsin - Madison School of Medicine, Madison, WI, US

INTRODUCTION: Cancer is becoming a leading cause of morbidity and mortality throughout the world. Accurate data on cancer burden and outcomes are critical for improving cancer care and resource allocation. In response to this need, we established a comprehensive cancer registry at Hawassa University Comprehensive Specialized Hospital in Hawassa, Ethiopia, - the only cancer center for a catchment population of 20 million in Southwest Ethiopia. We aimed to describe the overall pattern of cancer incidence, presentation, and outcomes for Southern Ethiopia. **METHODS:** We collected data from January 1, 2017 to January 1, 2024 through retrospective chart reviews to enhance the ongoing prospective registry, which began on January 1st 2024. Phone calls were performed to get updated data on survival. All new adult patient with cancer were included. Data points include patient demographics, cancer type, treatment modalities, survival outcomes, and geographic information. Descriptive statistics of registry data are presented as proportions. **RESULTS:** A total of 2,500 patients were included. The median age was 45 years (IQR 35–58). There were 1,153 males (46.1%) and 1,347 females (53.9%). The most common cancer types for men were lymph node (15.1%, N=174), colorectal (12.3%, N=142), and liver/bile duct (9.3%, N=107). Most common for women were breast (30.9%, N=415), colorectal (8.1%, N=109), and lymph node (7.4%, N=100). Most cancers presented with stage IV 41.8% (N=1045) or stage III 36% (N=901) disease with very few with stage II 5.9% (N=147) and stage I 0.5% (N=12) disease. Findings for the most common cancers can be seen in table 1. Patients came from 23 different zones. The most common were Sidama (N=933, 37.5%), Arsi (N=563, 22.6%), and Bale (N=175, 7.0%). A total of 1,071 (42.9%) phone calls were successfully completed to obtain survival data. Five-year survival data was available for 687 (27.5%) of patients. Of this data, five-year survival for breast was 20.8% (N=22), colorectal was 25.6% (N=20), gastric was 9.8% (N=4), and liver/bile duct 3.5% (N=2). Missingness was less than 1%. **CONCLUSIONS:** Initial findings from this registry point to a high prevalence of advanced-stage diagnoses and low median age of disease onset underscoring the urgent need for earlier detection and regionally personalized surveillance. Further, phone calls are a reasonable approach for capturing survival information. Finally, this registry is one of the few registries in the low-income setting with detailed outcomes data; thus, it offers an opportunity to perform analyses that explore cancer trends in an area that has historically been under-researched.

Table 1. General characteristics of 4 most common solid tumors within HUCSH cancer registry

		Breast	Colorectal	Gastric	Liver/Bile Duct
Mean age (SD)		41.9 (13)	43.9 (14.3)	54.3 (15.4)	52.6 (17.1)
Stage					
	1-2	6.6%	12.8%	0%	0%
	3-4	89.6%	74.4%	92.7%	70.2%
Biopsy performed?		34.9%	64.1%	68.3%	5.3%
% Received Chemo		63.2%	56.4%	29.3%	7.0%
% Received Surgery		44.3%	21.8%	29.3%	3.5%
Patients with status obtained through phone call		96.2%	98.7%	97.6%	98.2%
5-year overall survival		20.8%	25.6%	9.8%	3.5%

P444. Cytoreductive Surgery Plus Hyperthermic Intraperitoneal Chemotherapy (CRS+HIPEC) Associated with Sustained Long-term Quality of Life in Patients with Peritoneal Surface Malignancies

Mariaugusta Montealegre[1]; Peter A Borowsky[2]; Kimberly P Gomez[3]; Alexandra E Hernandez[4]; Charles J Cash[5]; Sina Yadegarynia[6]; Heidi Bahna[7]; Mecker Moller[8]
[1]University of Miami, Miami, FL, US; [2]University of Miami, Miami, FL, US; [3]University of Miami, Miami, FL, US; [4]University of Miami, Miami, FL, US; [5]University of Miami, Miami, FL, US; [6]University of Miami, Miami, FL, US; [7]HCA Healthcare JFK Hospital, West Palm Beach, FL, US; [8]University of Chicago Pritzker School of Medicine, Chicago, IL, US

INTRODUCTION: CRS+HIPEC is used to treat peritoneal surface malignancies. This surgery, however, is associated with extensive morbidity, potentially impacting patient satisfaction. This study assessed the long-term impact of CRS+HIPEC on patient-reported quality of life (QoL). **METHODS:** Patients undergoing CRS+HIPEC were prospectively enrolled from 2017-2024 and completed the 26 item World Health Organization (WHOQOL-BREF) QoL questionnaire in the pre- and/or post-operative periods. Questionnaires assessed functionality in physical (PF), psychological (PSY), social (SOC), and environmental (ENV) domains. Mean pre- and post-operative domain scores were compared using t-test analyses. **RESULTS:** 161 of 274 patients were alive at time of assessment, of which 69 (43%) completed QoL analyses. 41, 11, and 17 patients completed postoperative, preoperative, and both surveys, respectively. Mean patient age was 53 ± 12 years. Most patients were white (86%), Hispanic/Latino (51%), female (70%). The most common primary malignancy was appendiceal (55%) followed by colon (23%) and

ECOG status of 0 (45%). Mean preoperative PCI score was 15 (range 0-39). 47 (68%) patients had R_0 resection. Mean hospital length of stay was 11 days. Median follow up time was 23.3 months (range 27 days-145.5 months). Median time from surgery to postoperative QoL survey completion was 30.1 months (82 days-147.5 months). Overall, mean PF, PSY, and ENV scores were higher postoperatively, although this was only significant for PSY scores (p= 0.037). SOC scores remained stable pre- and post-operatively. For patients completing both pre- and post-operative surveys, pre- and post-operative PF, and SOC scores did not differ (p> 0.05); ENV scores were higher preoperatively (p= 0.009). **CONCLUSIONS:** Even more than 30 months postoperatively, patients undergoing CRS+HIPEC can sustain stable long-term QoL. This study includes to our knowledge the longest follow up time for assessment of QoL after CRS+HIPEC. The results suggest patients should be counseled that QoL remains stable, or potentially improved, after CRS+HIPEC despite the known morbidity associated with this procedure.

P445. Days at home after gastrointestinal cancer surgery: Description and validation of a novel patient-centered post-operative outcome

Tiago Ribeiro, MD, MSc[1]; Adom Bondzi-Simpson, MD MSc[2]; Wing C Chan, MSc[3]; Alyson Mahar, PhD[4]; Angela Jerath, MD MSc[5]; Natalie G Coburn, MD, MPH[6]; Julie Hallet, MD MSc[7]

[1]University of Toronto, Toronto, ON, CA; [2]University of Toronto, Toronto, ON, CA; [3]ICES, Toronto, ON, CA; [4]Queens University, Kingston, ON, CA; [5]Sunnybrook Health Sciences Centre, Toronto, ON, CA; [6]University of Toronto, Toronto, ON, CA; [7]Sunnybrook Health Sciences Centre, Toronto, ON, CA

INTRODUCTION: There is a paucity of peri-operative patient-centered data in cancer research, policy, and quality improvement initiatives. Days at home (DAH) after surgery is a novel, patient-centered measure that captures time spent outside health care institutions after surgery. We described patterns of DAH after surgery for gastrointestinal (GI) cancer and examined its concurrent and predictive validity. **METHODS:** We conducted a population-based retrospective cohort study of adults undergoing elective surgery for GI cancer between 2003 – 2021. DAH at 30 (DAH-30), 90, 180 and 365 days after surgery were computed by cancer site and procedure type. DAH was computed as total days minus institution-days (including days in hospital, rehabilitation, nursing home, and emergency department). Concurrent and predictive validity were explored through the association with major morbidity (Clavien-Dindo grade 3-5) and one-year mortality, using logistic regression with restricted cubic splines. **RESULTS:** A total of 91,290 patients were included. Median DAH were: DAH-30 = 23 (interquartile range - IQR 19 – 25), DAH-90 = 82 (IQR 77 – 85), DAH-180 = 172 (IQR 164 – 175), and DAH-365 = 355 (IQR 343 – 359) (Figure), with a left-skewed distribution with a spike at 0 driven by deaths and time spent fully in institutions. DAH-90 was chosen as the primary outcome due to its superior discriminative ability across cancer and procedure types. DAH varied in an expected manner across demographic factors, comorbidities, and treatment factors. Large variability was observed across GI cancer sites. Appendiceal tumors had the highest median DAH-90 of 87 (IQR 84 – 89) and esophageal tumors the lowest, with 76 (IQR 63 – 80). The time spent in institutions was driven primarily by the index post-operative admission. DAH-90 was lower in patients with major morbidity was (median 70, IQR 41-79 vs. 83, IQR, 80 -85; p<0.001). The probability of major morbidity increased with decreasing DAH-90. Patients with one-year mortality had lower DAH-90 compared to those without (median 62, IQR 0 -80 vs. 83, IQR 78 – 85;0.001). The probability of one-year mortality increased with a decreasing DAH-90. **CONCLUSIONS:** DAH varied across cancer site, procedure type, and important treatment and patient characteristics. Concurrent and predictive validity are supported by associations with major morbidity and one-year mortality. DAH represents a valid post-operative outcome measure to assess the burden of surgery for GI cancer. Future work in GI cancer surgery can consider using DAH as a patient-centred post-operative outcome.

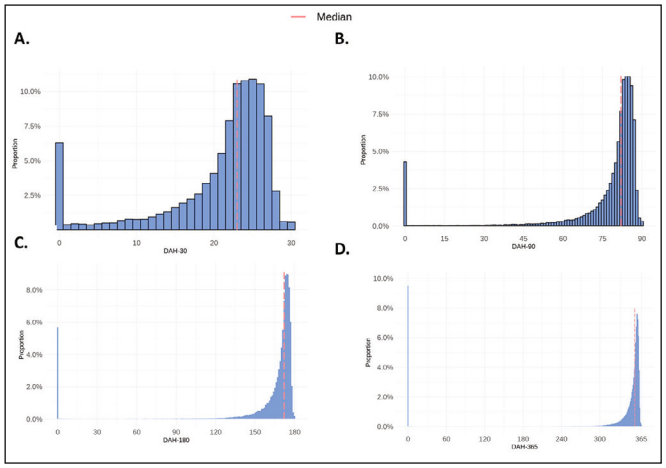


Figure. Days at home after surgery (DAH) for gastrointestinal cancer at 30 (A), 90 (B), 180 (C), and 365 (D) days. DAH represent days spent outside of hospital, rehabilitation, long-term care, and the emergency department.

P446. Development of an Electronic Patient-Reported Outcomes Tool for Discharge Planning in Oncology

Norma E Farrow, MD MHS[1]; Iris H. Wei, MD[2]; Daniela Molena, MD[3]; Jamie Ostroff[4]; Thomas Atkinson[5]; Melissa Assel[6]; Andrew Vickers[7]; Deb Schrag[8]; Sigrid Carlsson[9]; Jennifer Cracchiolo[10]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, US; [2]Memorial Sloan Kettering Cancer Center, New York, NY, US; [3]Memorial Sloan Kettering Cancer Center, New York, NY, US; [4]Memorial Sloan Kettering Cancer Center, New York, NY, US; [5]Memorial Sloan. Kettering Cancer. Center, New York, NY, US; [6]Memorial Sloan Kettering Cancer Center, New York, NY, US; [7]Memorial Sloan Kettering Cancer Center, New York, NY, US; [8]Memorial Sloan Kettering Cancer Center, New York, NY, US; [9]Memorial Sloan Kettering Cancer Center, New York, NY, US; [10]Memorial Sloan Kettering Cancer Center, New York, NY, US

INTRODUCTION: Tools are needed to help coordinate the discharge process and improve communication between the clinical team and patient after oncologic surgery. Integration of Patient-Reported Outcomes (PROs) into surgical oncology care is an evidence-based strategy shown to improve communication and align expectations. We aimed to implement an electronic PROs discharge tool that enhances communication and aligns expectations during hospital admission after oncologic surgery to prevent avoidable prolonged hospital stays. **METHODS:** Utilizing mixed methods with input from multiple patient, clinician and health informatics stakeholders, we developed and implemented the electronic Goals to Discharge (G2D) tool. A focus group with a patient advisory panel was conducted to understand the clinical need to improve inpatient stays and discharge coordination. PRO items were selected involving a stepwise process that included input from clinicians and disease site champions and aligned with existing Enhanced Recovery After Surgery (ERAS) pathways. Patient, disease site, procedure and operational attributes were used to define the initial cohort of surgical patients to receive the G2D tool. The analysis comprised of patients in the initial cohort who received the G2D platform from the initiation of the G2D tool between February 11, 2020 and September 7, 2022 including 3,927 patients who underwent 4,428 qualifying procedures. We analyzed patient and operational factors associated with adoption of the G2D, which was defined as patients submitting at least one G2D survey prior to discharge. **RESULTS:** Qualitative analysis supported a clinical need for novel discharge tools, with our focus group analysis identifying the following themes: fragmented communication during hospitalization, a need for formal expectations, emotional readiness for discharge assessment, and confirmation that an electronic tool will not replace face-to-face communication with the clinical team. The G2D tool was developed and piloted in oncology patients after surgery. We did not see evidence on an effect of responding to the G2D tool and prolonged length of stay (risk reduction 2.3%, 95% CI -0.12%, 4.8%, p-value = 0.062). Patient and operational characteristics contribute to variation in adoption rates. These include factors such as primary language and access to tool education. **CONCLUSIONS:** We developed the G2D tool to improve communication for oncologic surgery patients, and to promote safe and timely discharges. The tool received positive feedback from patients and was associated with decreased length of stay in patients who adopted the platform. The G2D

tool can be used to enhance communication between patients and the clinical team to improve the discharge process after surgery.

P447. Difficult Conversations with Cancer Patients: An Oncologist's Perspective

Beatrice J Sun, MD[1]; Tiffany M Yue, BS[2]; Byrne Lee, MD[3]
[1]Stanford University School of Medicine, Stanford, CA, US; [2]Stanford University School of Medicine, Stanford, CA, US; [3]Stanford University School of Medicine, Stanford, CA, US

INTRODUCTION: Conversations about cancer prognosis, treatment course, and end of life are common in surgical oncology. In this study, we aim to identify the challenging aspects of interacting with cancer patients and explore the experiences from the physician's perspective. **METHODS:** Surveys and semi-structured interviews were conducted with cancer surgeons and medical oncologists at a single tertiary center. Interviews were transcribed and coded by two independent researchers, and qualitative analysis was performed. **RESULTS:** In total, 21 cancer physicians were interviewed: 14 surgeons from various subspecialties (Surgical Oncology/Hepatobiliary, Colorectal, Thoracic, Gynecologic Oncology, Orthopedic Oncology) and 7 medical oncologists. Two-thirds were male, and median experience in practice was 14 years. Physicians identified "helping patients understand their cancer" and "managing treatment expectations" as the hardest topics to discuss with patients. Factors including young age, high symptom burden, unresectable disease, and discordant understanding of prognosis made these discussions particularly difficult. Only 52% of physicians believed that patients generally have a reasonable sense of curability and life expectancy. All medical oncologists and 57% of surgeons routinely discussed prognosis with patients, although most (79%) preferred not to bring it up during the first visit. Participants described prognosis as a "graded process"ongoing conversation" that evolves with time. However, surgeons in particular struggled to convey poor prognosis due to uncertainty and fear of taking away hope from patients. All medical oncologists and 50% of surgeons routinely discussed end of life care and hospice with their patients. Despite recognizing palliative care as a valuable resource, cancer physicians expressed a strong sense of personal responsibility to prepare their patients for the transition to end of life. Physicians emphasized wanting to be a steady presence for their patients in order to minimize feelings of abandonment when broaching topics of palliative care and hospice. **CONCLUSIONS:** Discussions about cancer prognosis and death are some of the most difficult yet impactful physician-patient interactions. As surgery represents a major decision point in cancer treatment, surgeons play an integral role in balancing hope and realistic outlook when offering surgery for cancer, managing postoperative expectations and burden of recurrence, and discussing transition to end of life when treatment options are exhausted. It is therefore crucial for surgeons to integrate and practice these conversations to effectively navigate these challenging topics.

P448. Early and delayed postoperative mortality of total pancreatectomy for malignancy in a contemporary national cohort

Gracia M Vargas, MD[1]; Neha Shafique[2]; Mohammad S. Farooq, MD, MS[3]; Major Kenneth Lee, MD PhD[4]; Charles M Vollmer, MD[5]; John Miura, MD[6]; Giorgos Karakousis, MD[7]
[1]Hospital of University of Pennsylvania, Philadelphia, PA, US; [2]Hospital of University of Pennsylvania, Philadelphia, PA, US; [3]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [4]University of Pennsylvania, Philadelphia, PA, US; [5]University of Pennsylvania, Philadelphia, PA, US; [6]University of Pennsylvania, Philadelphia, PA, US; [7]University of Pennsylvania, Philadelphia, PA, US

INTRODUCTION: Total pancreatectomy (TP) is a rare procedure with high historic morbidity and mortality with scarce contemporary outcomes data. This study uses a large national cohort to identify sociodemographic and facility factors associated with early and delayed mortality from TP for malignancy in a large national cohort. **METHODS:** The National Cancer Database (NCDB) was queried for TP cases from 2010-2020 in patients ≥18 years with Stage I-III disease. Annual volume of all NCDB pancreas cases was calculated for each facility. Univariable and multivariable logistic regressions controlling for patient clinical and oncologic factors were used to identify sociodemographic and facility factors associated with early (≤30 days), delayed (31-90 days), and 90-day mortality. **RESULTS:** 9,808 patients underwent TP for Stage I-III malignancy with 3.17% early mortality, 3.06% delayed mortality, and 6.23% total 90-day mortality. 59.5% of patients had government insurance, 15.5% were in the lowest income quartile, 50.4% had surgery at an academic/research program (ARP), and 27.1% had surgery at a high-volume (top 5th percentile) facility. On univariable analysis, early, delayed, and 90-day mortality were significantly increased with government insurance (p<.001). Early and 90-day mortality were significantly decreased with both ARP (p=.008, p=.001, respectively) and high-volume facility (p<.001 for both). On multivariable analysis, government insurance was associated with increased early mortality (OR 1.57, p=.010) and 90-day mortality (OR 1.37, p=.013). Top income quartile was associated with half the odds of delayed mortality compared to the lowest income quartile (OR 0.56, p=.005). ARP was significantly associated with decreased overall 90-day mortality (OR 0.56, p=.019). High-volume facility was significantly associated with decreased early mortality (OR 0.49, p<.001) and total 90-day mortality (OR 0.62, p<.001), but not delayed mortality (OR 0.73, p=.078). **CONCLUSIONS:** Early and delayed postoperative mortality rates following TP were comparable in this contemporary national cohort, though disparities emerged due to patient resources and institutional factors. Notably, high-volume centers and ARP facilities mitigated the risk of 90-day mortality, predominantly in the early postoperative period. Understanding these variables can guide resource allocation and best practices in both surgical technique and postoperative management strategies to improve outcomes.

Table. Sociodemographic and facility factors associated with early, delayed, and 90-day postoperative mortality following total pancreatectomy for malignancy on multivariable analysis

	Number (%) N = 9,808	Early Mortality 311 (3.17%) OR	p-value	Delayed Mortality 300 (3.06%) OR	p-value	Overall 90d Mortality 611 (6.2%) OR	p-value
Sociodemographic factors							
Insurance Status							
Private insurance	3,607 (36.8)						
Uninsured	224 (2.3)	1.29	0.594	2.04	0.085	1.66	0.100
Government insurance	5,839 (59.5)	1.57	**0.010***	1.09	0.620	1.37	**0.013***
Median Income in Zip Code							
<$46,277	1,306 (15.5)						
$46,277 - $57,856	1,778 (21.1)	1.48	0.091	0.76	0.223	1.04	0.826
$57,857 - $75,062	2,024 (24.1)	1.33	0.214	0.69	0.090	0.92	0.611
$74,063+	3,306 (39.3)	1.05	0.815	0.56	**0.005***	0.75	0.055
Facility factors							
CoC Program Type							
Community Cancer Program	264 (2.8)						
Comprehensive Community Cancer Program	2,545 (26.6)	0.68	0.231	0.79	0.512	0.74	0.235
Academic/Research Program	4,820 (50.4)	0.56	0.071	0.54	0.091	0.56	**0.019***
Integrated Network Cancer Program	1,944 (20.3)	0.71	0.307	0.75	0.446	0.74	0.244
NCDB Annual Pancreas Volume							
<40 (Bottom 75th percentile)	3,052 (31.1)						
40-111 (75-95th percentile)	4,095 (41.8)	0.58	**<0.001***	0.77	0.100	0.65	**<0.001***
≥112 (Top 5th percentile)	2,661 (27.1)	0.49	**<0.001***	0.73	0.078	0.62	**<0.001***

P449. Impact of Cancer Diagnosis on Outcomes in Adult Intestinal Transplantation: A UNOS Database Analysis

Laura M. Cogua, BS[1]; Connor J. Tupper, MD[2]; Meng-Hao Li, PhD[3]; Naoru Koizumi, PhD[4]; Giovani Faddoul[5]; Jorge Ortiz[6]
[1]Creighton University School of Medicine, Phoenix, AZ, US; [2]Department of Orthopedic Surgery, Hofstra/Northwell Zucker School of Medicine, New Hyde Park, NY, US; [3]George Mason University, Fairfax, VA, US; [4]George Mason University, Fairfax, VA, US; [5]Staten Island University Hospital, Staten Island, NY, US; [6]Garnet Health, Middletown, NY, US

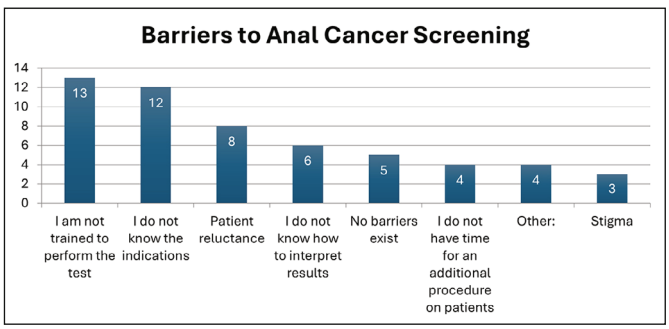
INTRODUCTION: Intestinal transplantation is a life-saving treatment for those with irreversible intestinal failure resulting from a variety of causes including cancer. Despite significant advancements in perioperative management and surgical techniques, outcomes remain understudied. We aim to assess the effect of cancer and other primary diagnoses and their association with recipient mortality and graft failure rates in intestinal transplantation. **METHODS:** A retrospective analysis was performed using the UNOS database between January 1, 1994 and June 30, 2024. Demographic characteristics of both organ recipients and donors were compared using Pearson chi-square tests. Recipient mortality and graft failure were compared among primary diagnosis groups using log-rank tests and Cox regression. **RESULTS:** A total of 896 adult intestinal transplant recipients were included. Primary diagnoses included tumor (n=82/896, 9.2%), Crohn's disease (n=90/896, 10.0%), mesenteric arterial thrombosis or embolus (n=51/896, 5.7%), venous thrombosis (n=40/896, 4.5%), intestinal volvulus secondary to malrotation (n=29/896, 3.2%) and other diagnoses (n=604/896, 67.4%). The cancer group had the greatest proportion of females (65.5%), the shortest wait time (33 days), and the lowest BMI at time of transplant (21.5). Log-rank tests showed no differences in recipient mortality or graft failure by diagnosis. On Cox regression, a cancer diagnosis was not associated with recipient mortality or graft survival. However, retransplantation status was associated with increased recipient mortality (HR=1.783, p<0.001) and graft failure (HR=1.553, p=0.002). **CONCLUSIONS:** These results suggest that a cancer diagnosis does not significantly affect recipient mortality or graft failure in intestinal transplantation. All diagnostic groups demonstrated similar

recipient survival and graft failure rates through five years post-transplant. However, retransplantation status is associated with an increased risk of recipient mortality and graft failure. Given the small sample sizes in this analysis, ongoing evaluation of the effect of cancer and other primary diagnoses on intestinal transplantation outcomes will benefit risk stratification and prognostication.

P450. Improving HPV-Related Anal Cancer Screening: Understanding Physician Barriers

Dharma Ayer, BS[1]; Julia Liporace Hall, NP[2]; Sandra R. DiBrito, MD, PhD[3]
[1]Albany Medical College, Albany, NY, US; [2]Albany Medical Center, Albany, NY, US; [3]Albany Medical College, Albany, NY, US

INTRODUCTION: Human papillomavirus (HPV) infection is the most important risk factor for anal cancer. Though anal Pap smears are an effective initial screening tool, many clinicians under anticipate the patients at risk and face barriers preventing appropriate screening. The objective of this study was to assess physician practices and perceived barriers to HPV-related anal cancer screening to identify areas for improving screening rates and patient care. **METHODS:** Physicians were queried using a brief 7-question survey developed to assess their practices and perceived barriers regarding HPV-related anal cancer screening. The survey included questions about demographics (e.g., specialty, years in practice, practice setting), patient screening factors (e.g., MSM, HIV-positive, immunocompromised), and barriers to screening (e.g., lack of training, time constraints, stigma). It also captured standard practices for anal Pap smears when a patient has a positive cervical Pap result. Surveys were distributed via an anonymous link to providers within the region in different practice settings. The data was then analyzed to assess whether providers perform anal Pap smears, which patient indications prompt screening, and the barriers they encounter. **RESULTS:** Of the 100 surveys distributed, 36 were returned. Most physician respondents were gynecologists (64%) with others including internists (19%), family medicine providers (8%), and other (8%). All respondents had over 4 years of experience in practice with 56% having over 15 years of experience. Out of all respondents, only 6% said they order and perform anal Pap smears when a patient has a positive cervical Pap result. Additionally, 67% reported they believe there are barriers that exist in screening for anal cancer within their practice with the most common being lack of training (43%) and not knowing the indications (40%). Furthermore, many physicians expressed unfamiliarity with the guidelines and referral process in cases where a patient receives a positive anal Pap smear result. **CONCLUSIONS:** There is a clear clinical gap in anal cancer screening with many providers underutilizing anal Pap smears, even for high-risk patients like those with positive cervical Pap results. The main barriers include lack of training and unfamiliarity with screening indications. Given the practical opportunity to screen for anal cancer during cervical Pap exams, providing physicians with better education on screening guidelines and integrating reminders into electronic medical record systems, could improve screening rates and ensure appropriate referrals for specialized care.



P451. Incidence of VTE with Pancreatic Leak following Pancreatectomy for Pancreatic Ductal Adenocarcinoma

Ryan D Lints[1]; Srinivas Kavuturu, MD, FRCS, FACS[2]; Olivia Flessland, DO[3]; Ruxin Shi[4]; Ling Wang, MS, PhD[5]; Linda Qu, MD[6]
[1]Michigan State University College of Human Medicine, East Lansing, MI, US; [2]Michigan State University College of Human Medicine - Department of Surgery, East Lansing, MI, US; [3]University of Michigan Health-Sparrow General Surgery Residency Program, Lansing, MI, US; [4]Michigan State University, East Lansing, MI, US; [5]Michigan State University Division of Occupational and Environmental Medicine, East Lansing, MI, US; [6]Michigan State University, East Lansing, MI, US

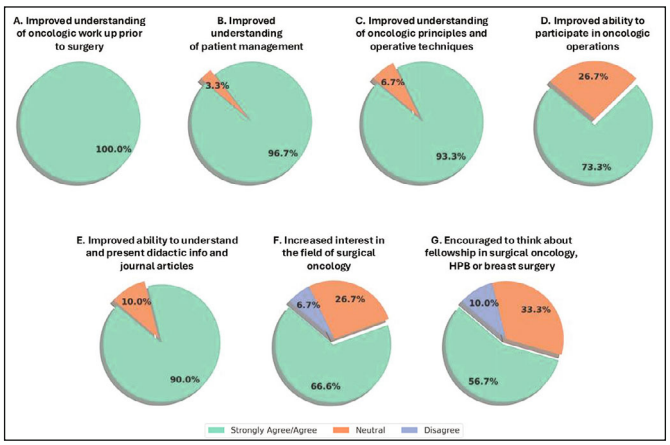
INTRODUCTION: Postoperative pancreatic fistula (POPF) is a potentially morbid complication following pancreatectomy for cancer. In patients with pancreatic ductal adenocarcinoma (PDAC) who are at elevated risk of venous thromboembolism (VTE), the association between POPF and postoperative VTE is poorly defined. **METHODS:** Patients with PDAC who underwent surgical resection from 2014-2021 were retrospectively identified from the ACS NSQIP pancreatectomy-targeted dataset. Patient and clinical factors were evaluated for association with postoperative VTE. Multivariable logistic regression using the Akaike Information Criterion (AIC) for model selection was used to determine risk factors for VTE after the diagnosis of POPF. **RESULTS:** There were 23,791 patients in this study, of which 3401 (14.3%) developed POPF. Of the patients with POPF, 667 (19.6%) had a biochemical leak while 2734 (80.4%) had a clinically relevant pancreatic fistula. Of the patients with POPF, 238 (7%) developed VTE compared to 597 (2.3%) of patients who developed VTE who did not have POPF ($p<0.05$). Using AIC, 11 factors were identified for inclusion in the multivariate regression model. POPF significantly increased the probability of VTE (OR 1.35, $p=0.015$). Other relevant factors associated with VTE included readmission, length of stay, vein resection, blood transfusion, pneumonia, Asian race, surgical site infection, postoperative total transfusion amount, and return to the operating room (all $p<0.05$). Blood transfusion and return to operating room were identified as interaction variables. Return to operating room (OR 0.757, $p=0.012$) was associated with a decreased effect of POPF on the incidence of VTE. Blood transfusion was not significantly associated with an interaction effect (OR 1.345, $p=0.13$). **CONCLUSIONS:** There was a significant positive association between POPF and the incidence of postoperative VTE. Furthermore, returning to the operating room is associated with an interaction effect of POPF on the incidence of VTE. Clinical vigilance and adherence to chemoprophylaxis protocols may help ameliorate VTE in this at-risk population.

P452. Incorporation of Comprehensive Surgical Oncology Curriculum into General Surgery Residency Program

Meher Oberoi, MBBS[1]; Tulio Pacheco[2]; Matthew Krell[3]; Zachary J. Brown, DO[4]; Gary Deutsch[5]; John Allendorf[6]; Eihab N. Abdelfatah, MD[7]
[1]NYU Langone Health - Long Island, Mineola, NY, US; [2]NYU Langone Health - Long Island, Mineola, NY, US; [3]NYU Langone Health - Long Island, Mineola, NY, US; [4]NYU Langone Health, Mineola, NY, US; [5]NYU Langone Health, Mineola, NY, US; [6]NYU Langone Health, Mineola, NY, US; [7]NYU Langone Health, Mineola, NY, US

INTRODUCTION: The field of surgical oncology incorporates complex concepts across multiple disciplines in understanding pathophysiology, patient management and surgical technique. While these patients are often cared for in academic medical centers by general surgical residents, traditional general surgical didactic and educational programs are limited in their ability to address the nuance and complexity of surgical oncological disease, leading to residents feeling that they lack the preparedness and confidence in managing these patients. In this study, we aim to evaluate the benefits of a formalized, comprehensive surgical oncology curriculum during general surgery residency. **METHODS:** A CME-approved, comprehensive surgical oncology education curriculum was instituted at our program in January 2023. This involves a weekly one hour conference progressing through topics in surgical oncology in the format of didactic lectures, case scenarios, journal clubs and demonstration of operative technique. In October 2024, a nine question anonymous survey was sent out to all current residents and recent general surgery graduates to evaluate the effect of the curriculum. Responses were reported as strongly agree, agree, neutral, disagree and strongly disagree. **RESULTS:** The survey was sent to 37 current residents and 5 recent graduates. We received 30 responses (response rate 71%; 6 PGY1s, 8 PGY2s, 4 PGY3s, 3 PGY4s, 6 PGY5s and 3 recent graduates) with a survey completion rate of 100%. 100% of respondents responded strongly agree or agree that the curriculum had resulted in improved understanding of pre-surgery oncologic work up and 97% (29/30) that they had improved understanding of management of patients on the surgical oncology service. Respondents reported strongly agree or agree that the curriculum improved understanding of principles of surgical oncology and operative techniques in 93% (28/30), and improved ability to participate in operations in 73% (22/30) [Figure 1]. Twenty seven (90%) of respondents responded strongly agree or agree that it had also improved their ability to present and analyze didactic information and journal articles. Twenty respondents (67%) reported increased interest in the field of surgical oncology with 19 (63%) reporting that they had attended sessions voluntarily even when not on their scheduled surgical oncology rotation. Seventeen respondents (57%) were encouraged to consider fellowship in surgical oncology, HPB or breast surgery as a result of

the curriculum. This percentage increased to 72% when PGY4-5s and recent graduates were excluded from the analysis. **CONCLUSIONS:** The addition of a dedicated, comprehensive surgical oncology education curriculum allows for improved self-reported resident preparedness in management and surgery for surgical oncology patients and increased interest in surgical oncology and related fields as a fellowship option.

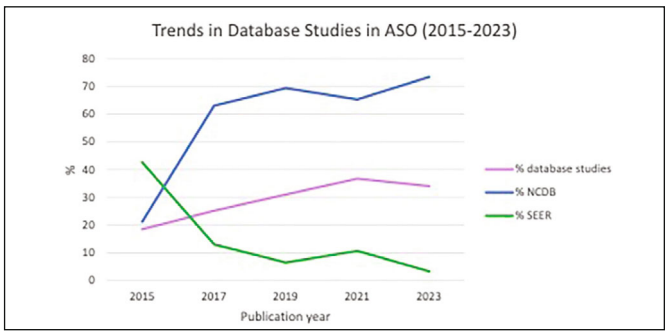


P453. Increasing Utilization of Database Studies in Surgical Oncology Literature

Beatrice J Sun, MD[1]; Tiffany M Yue, BS[2]; Dong Hur, BS[3]; Mason Sakamoto, BS[4]; Alex Doan, BS[5]; Byrne Lee, MD[6]

[1]Stanford University School of Medicine, Stanford, CA, US; [2]Stanford University School of Medicine, Stanford, CA, US; [3]Stanford University School of Medicine, Stanford, CA, US; [4]Stanford University School of Medicine, Stanford, CA, US; [5]Stanford University School of Medicine, Stanford, CA, US; [6]Stanford University School of Medicine, Stanford, CA, US

INTRODUCTION: While large-scale national database studies have important applications, particularly in the research of rare diseases, its utilization has markedly increased across the surgical literature in recent years. We aim to characterize the database publication trends in the leading surgical oncology journal. **METHODS:** The *Annals of Surgical Oncology* (ASO) journal was queried for original research papers originating in the United States between 2015 and 2023. Included publications from odd years were reviewed and stratified as database studies or non-database studies. The most common national databases used were the National Cancer Database (NCDB); Surveillance, Epidemiology, and End Results (SEER); and American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP). **RESULTS:** Of 2,901 original research publications reviewed, 1,239 (43%) were US studies. Common subtopics were Breast (38%), Pancreas (8%), Hepatobiliary (8%), and Endocrine (7%). National database studies comprised 30% of all publications: the majority were from NCDB (62%), followed by SEER (13%), then ACS-NSQIP (5%); 65% reported outcomes or survival data, 24% analyzed 2 or more treatments or interventions, and 10% reported descriptive data only. Additionally, non-database studies included single-institution studies (49%), multi-institutional studies (9%), clinical trials (3%), and basic science/translational research (3%). During the 8-year study period, database publications increased steadily from 18% in 2015 to 34% in 2023 (Figure). In particular, NCDB studies increased dramatically from 4% of publications in 2015 to 16% in 2017 and 25% of all original publications in 2023. In contrast, studies using SEER decreased from 8% in 2015 to 1% in 2023. When compared to non-database studies, the first author of database studies were more often medical students (9% vs 5%, p=0.021) and residents (40% vs 24%, p<0.001), and less often female (47% vs 55%, p=0.012). The senior author of database studies was more likely to be assistant or associate professors (53% vs 37%, p<0.001). **CONCLUSIONS:** The proportion of original research database studies in Surgical Oncology has almost doubled in the last decade. This is primarily driven by the sharp rise in studies using NCDB, while the use of SEER has declined. Despite their ease of use and potential for multiple publications, national databases have inherent limitations. To ensure impactful manuscripts, especially those involving non-randomized data in oncology, mentoring, well-designed studies, and careful result interpretation are essential



P454. Management of Malignant Bowel Obstruction: Can We Do Better?

Neha Shafique[1]; Gracia M Vargas, MD[2]; Mohammad S. Farooq, MD, MS[3]; Ariel Nehemiah, MD, MS[4]; Robert Krouse, MD, MS[5]; Giorgos Karakousis, MD[6]

[1]Hospital of University of Pennsylvania, Philadelphia, PA, US; [2]Hospital of University of Pennsylvania, Philadelphia, PA, US; [3]Hospital of the University of Pennsylvania, Philadelphia, PA, US; [4]Hospital of university of Pennsylvania, Philadelphia, PA, US; [5]University of Pennsylvania, Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, PA, US; [6]University of Pennsylvania, Philadelphia, PA, US

INTRODUCTION: Malignant bowel obstructions (MBO) are a complex clinical entity with significant practice variation in management. This study aimed to characterize the contemporary management of MBO in an academic health system and identify areas of quality improvement. **METHODS:** The electronic health record was queried for patients with an inpatient admission between 2017 and 2023 with a diagnosis code of both disseminated intraperitoneal cancer of appendiceal, colorectal, and gynecologic histologies and intestinal obstruction. Primary tumors of appendiceal and colorectal histologies causing obstruction were excluded. Pearson chi square tests were used to assess the relationship between management and key outcomes of length of stay (LOS) and hospital readmission within 90 days. **RESULTS:** Of 249 patients identified, 15.6% were male, 73.1% identified as White, and had a median age of 61 years (interquartile range [IQR] 49-69). The median length of stay was 8 days (IQR 5-13) and 90 day readmission rates were 55% with 65.7% of readmissions being due to MBO. 158 patients (63.4%) were managed conservatively for their MBO. In these patients, a nasogastric tube was inserted 37.9% of the time with a median time of insertion of 3 days (IQR 2-4) and total parenteral nutrition (TPN) was initiated in the hospital 35.4% of the time. The remaining 91 patients underwent a procedure during admission which involved 37 (40.7%) percutaneous endoscopic gastrostomy placements, 8 (8.8%) other endoscopic procedures, and 46 (50.5%) abdominal operations with 47% being initiated on TPN. Median time to procedure from admission was 4 days (IQR 2-8). A higher proportion of patients who underwent a procedure experienced LOS >10 days (65.3% vs 15.9%, p<0.001) and were discharged to hospice (22% vs 12%, p=0.03). Rates of 90-day readmission were similar between those who underwent a procedure to those who were managed conservatively (52.7% vs 56.3%, p=0.58). Only half the patients (50.2%) received an inpatient palliative consult. There was no association with a palliative consult and undergoing a procedure during admission (54.9% vs 45.1%, p=0.26). Patients with a palliative consult were more likely to have a LOS >10 days (43.2% vs 27.4%, p=0.009) and be discharged to hospice (25.6% vs 5.6%, p<0.001). **CONCLUSIONS:** MBO is a challenging diagnosis with heterogenous management even at a single institution. Streamlining care with multidisciplinary decisions between medical and surgical oncologists, early palliative care consults, and shared decision making about nutritional support and goals of care may help decrease length of stay and frequency of readmissions.

P455. Mood, Anxiety, and Cognitive Alterations in Cancer Patients

Gabriela Noronha Fortes[1]; Marcos Fraga Fortes[2]; Marcos Noronha Fortes[3]; Fernanda Christoffel Gomes[4]; Marilia Cerqueira Leite Seelaender[5]; José Pinhata Otoch[6]

[1]Oncológica Tapajós, Santarém, BR; [2]Brazilian Society of Surgical Oncology, Santarém, Pará, BR; [3]University of Santo Amaro, São Paulo, São Paulo, BR; [4]University of Santo Amaro, São Paulo, São Paulo, BR; [5]University of São Paulo, São Paulo, BR; [6]University of São Paulo, São Paulo, BR

INTRODUCTION: The inflammatory response in cerebrospinal fluid (CSF) may indicate alterations in cancer patients with (CC) and without cachexia

(CWC). This study aims to analyze the cytokine profile in cerebrospinal fluid (CSF), as well as mood, anxiety, and cognition profiles in patients with CC. **METHODS:** The study was conducted in a descriptive, exploratory, and cross-sectional manner. 109 individuals were evaluated, 37 controls, 18 CWC, and 54 CC patients. Assessments included BDI, HADS, Digit Span, FAS-verbal, Animals/WMS-R, Matrix Reasoning and Vocabulary (WASI), and QLQ-C30. CSF inflammatory status was determined through cytokine measures, and systemic inflammation via biochemical assays. **RESULTS:** The CC group exhibited 62.96% depression and probable anxiety/depression, with 75.92% showing attention deficits. The CC and CWC groups demonstrated significant cognitive impairment on the WASI-Vocabulary test (CWC: 13.4±2.2; CC: 15.9±1.1) compared to the control group (Ct: 22.8±1.6; p = 0.0002). In the QLQ-C30 scores, the CC group reported a greater perceived loss of quality of life and health deterioration (score of 17.5 ± 2.6) and lower scores on the Functional Scale (49.8 ± 4.5). The CC group had 18.52% illiteracy, 18.52% incomplete higher education, and 22.22% complete elementary education. The CC group also had lower weight (Ct: 67.8±1.4; CWC: 61.7±3.1; CC: 59.6±1.7; p = 0.0023) and BMI (CC: 21.5 [18.3; 24.8]; Ct: 24.9 [23; 25.8]; p = 0.0021) compared to controls. Cytokines detected in the CSF were MCP-1, VEGF, IL-8, IP-10, and MIP-1β. Higher concentrations of MCP-1 were found in cancer patients (CSC: 571.2±105.8; CC: 399.5±65.9; Ct: 1,477±0.1; p < 0.0001), along with lower levels of MIP-1β (CC: 4,345 [3,060; 7,353]) and VEGF (CC: 48.3±2.0; CWC: 49.8±3.8; Ct: 64.8±3.2; 0.0001). **CONCLUSIONS:** The level of mental impairment correlated with cancer-associated and cachexia-associated inflammation, weight loss, low BMI, elevated CRP, leukocytosis, lymphopenia, anemia, hypoalbuminemia, and low scores on the QLQ-C30 questionnaire. CC group exhibited a higher prevalence of depression/anxiety, a stronger correlation between depression and inflammation, and greater cognitive impairment in attention, reasoning, and language, alongside lower average educational attainment. The low concentration of certain cytokines in the CSF combined with elevated systemic CRP in cancer and cachexia, associated with mental disorders, presents a paradox that requires further investigation. Higher concentrations of the cytokine MCP-1 in cancer patient groups indicated a positive correlation with the preservation of language abilities.

P456. Patients Seeking Second Opinions at an NCI-Designated Comprehensive Cancer Center: A Population Segment with Unique Needs and Preferences

Erin A Strong, MD, MBA, MPH[1]; Paige W Lake, MPH[2]; Shainal Gandhi[3]; Crystalynn G Llamas[4]; Christine E Vinci, PhD[5]; Heather Jim, PhD[6]; Susan Vadaparampil, PhD, MPH[7]; Daniel A Anaya, MD[8]
[1]Moffitt Cancer Center, Tampa, FL, US; [2]Moffitt Cancer Center, Tampa, FL, US; [3]Moffitt Cancer Center, Tampa, FL, US; [4]Moffitt Cancer Center, Tampa, FL, US; [5]Moffitt Cancer Center, Tampa, FL, US; [6]Moffitt Cancer Center, Tampa, FL, US; [7]Moffitt Cancer Center, Tampa, FL, US; [8]Moffitt Cancer Center, Tampa, FL, US

INTRODUCTION: Patients with cancer seeking second opinions on diagnosis and treatment represent a population segment with unique motivations and priorities. The purpose of this study was to characterize this patient segment at a stand-alone cancer center and assess their self-reported needs and preferences. **METHODS:** A 21-item survey was emailed to all patients seen for a second opinion appointment at an NCI comprehensive cancer center from January 2024 through August 2024. Demographic and clinicopathologic features were also captured, and patients were categorized based on having metastatic vs. non-metastatic disease at presentation. **RESULTS:** During the study period, 2,681 patients were evaluated for second opinions; 365 (13.6%) responded to the survey. Mean age was 69 years (SD 11.8), 156 (43%) were women, and 327 (90%) were White. Median distance traveled was 66 miles (IQR 25-110). Study cohort included patients across primary cancer sites, and 45% were visits with a surgical specialty. Median number of visits following the index second opinion visit was 5 (IQR 3-11). While the primary drivers for a second opinion were peace of mind with current treatment plans (38%) and expert review (34%), patients with metastatic disease more frequently sought information about chemo- or immunotherapy (35% vs. 13% for each, p=0.001) or clinical trials (30% vs. 11%, p=0.001). Those with nonmetastatic disease more often sought advice on surgery (33% vs. 22%, p=0.03). Patients with metastatic disease more often wanted an ongoing consulting relationship (23% vs. 13%, p=0.006), while those with nonmetastatic disease were more likely to transfer care (37% vs. 20%, p=0.006). Most patients preferred an in-person visit (76%), fewer preferred virtual appointments (9%). While most sought a second opinion with a specialist (89%), opinions rendered by a multidisciplinary team through tumor boards were also valued, particularly for those with metastatic disease (71 vs. 59%, p=0.05). **CONCLUSIONS:** Patients seeking second opinions at a cancer center represent a well-defined "population segment." While second opinions are often thought of as one-time consultations, in this study patients often required multiple visits to meet their needs. Needs and preferences on visit format varied, highlighting differences even between subsegments, such as patients with metastatic disease. Further studies to better characterize these subsegments can lead to higher value care by matching services with specific needs, while minimizing burden to patients and clinicians derived from repetitive visits.

P457. Preoperative Frailty Screening in Cancer Surgery: Early Findings of a Pilot Study of Feasibility and High-Risk Characteristics

Anthony J Scholer, MD, M.BS, FACS[1]; Michele Abramova, MD[2]; Gabriela Giovannetti, BSN[3]; Kelly Rubino, MSN[4]; Gregory Tiesi, MD, FACS[5]
[1]Jersey Shore University Medical Center Hackensack Meridian, Neptune, NJ, US; [2]Jersey Shore University Medical Center Hackensack Meridian, Neptune, NJ, US; [3]Jersey Shore University Medical Center Hackensack Meridian, Neptune, NJ, US; [4]Jersey Shore University Medical Center Hackensack Meridian, Neptune, NJ, US; [5]Jersey Shore University Medical Center Hackensack Meridian, Neptune, NJ, US

INTRODUCTION: The Centers for Medicare and Medicaid Services Age Friendly Hospital Measure necessitates frailty screening. Our objective was to assess the feasibility of preoperative frailty screening and to identify the prevalence of high-risk characteristics in frail patients. **METHODS:** Frailty screening was implemented in the surgical oncology clinic on January 1, 2023, for patients aged ≥ 75 scheduled for surgery with colorectal (CR) and thoracic (T) cancers. Screening for hepatobiliary and pancreas (HPB) cancers began on September 1, 2023. Screening adhered to the American College of Surgeons Geriatric Verification Program Standard 5.6, encompassing eight domains of frailty through validated instruments (Table 1). Patient demographics, tumor characteristics, and perioperative outcomes were retrospectively reviewed. Feasibility was defined as screening ≥ 75% of eligible patients, while the secondary outcome focused on elucidating high-risk characteristics in frail patients. **RESULTS:** As of September 27, 20024, 88.2% (n=105/119) of eligible patients completed screening (49.5% CR (n=52); 28.6% T (n=30); and 21.9% HBP (n=23)) with more patients being classified as frail than non-frail (63.8% and 36.2%, p=0.00006, respectively). Differences in the frailty domains were observed, with malnutrition and delirium being the most prevalent high-risk characteristics (52.2% and 55.2%, p-0.021, respectively)(Table 1). Frail patients were more likely to have a loss of independence compared to non-frail patients (33.8% and 16.2%, p=0.091, respectively). Preliminary data demonstrated no difference in 30-day morbidity or mortality between the groups. **CONCLUSIONS:** This pilot study demonstrated that preoperative frailty screening in the surgical oncology clinic is feasible. Future research aims to compare frail patients' outcomes to both non-frail patients and NSQIP historic controls to establish novel frailty-related benchmarks. These data will guide a clinical trial focused on the personalization of perioperative optimization strategies targeted at prevalent high-risk characteristics (domains of frailty) to improve the outcomes of vulnerable patients.

Table 1. High-Risk Characteristics in Vulnerable Frail Surgical Oncology Patients

	Overall	HPB	Thoracic	Colorectal	
Preoperative Frailty Screening	(n=105)	(n=23)	(n=30)	(n=52)	
Frail patients, % (n)	63.8% (n=67)	78.3% (18)	40.0% (12)	71.2% (37)	
Non-frail patient, % (n)	36.2% (n=38)	21.7% (5)	60.0% (18)	28.8% (15)	
	0.00006	0.00013	0.121	0.000016	**p-value**
	All Frail	**HPB Frail**	**Thoracic Frail**	**Colorectal Frail**	
Domains of Frailty, % (n)	63.8% (n=67)	(n=18)	(n=12)	(n=37)	
Age ≥ 85 years old	37.3% (n=25)	5.5% (1)	50.0% (6)	43.2% (16)	
Cognition	22.4% (n =15)	1.7% (3)	25.0% (3)	32.4% (12)	
Delirium	52.2% (n=35)	72.2% (13)	33.3% (4)	48.6% (18)	
Activities of Daily Living	28.4% (n=19)	22.2% (4)	8.3% (1)	37.8% (14)	
Mobility	37.3% (n=25)	22.2% (4)	16.7% (2)	51.4% (19)	
Dysphagia	7.5% (5)	5.5% (1)	16.7% (2)	5.4% (2)	
Malnutrition	55.2% (n=37)	55.5% (10)	33.3% (4)	62.2% (23)	
Palliative Care	22.4% (n=15)	33.3% (6)	8.3% (1)	21.6% (8)	
	0.021	0.568	0.779	0.584	**p-value**
Loss of Independence at Discharge, % (n)					
Frail patients, % (n)	33.8% (n=22/65)	38.9% (7)	8.3% (1)	40.0% (14)	
Non-frail patient, % (n)	16.2% (n=6/37)	20.0% (1)	5.6% (1)	28.6% (4)	
	0.091	0.8	1	0.656	**p-value**
30 Day Morality, % (n)					
Frail patients, % (n)	2.99% (2)	0	0	5.4% (2)	
Non-frail patient, % (n)	2.63% (1)	0	0	6.7% (1)	
	1	N A	N A	1	**p-value**
	Overall	**HPB**	**Thoracic**	**Colorectal**	
30 Day Morbidity, % (n)	(n=105)	(n=23)	(n=30)	(n=52)	
Frail patients, % (n)	19.4% (13)	16.7% (3)	16.7% (2)	21.6% (8)	
Non-frail patient, % (n)	15.8% (6)	0	16.7% (3)	20.0% (3)	
	0.843	0.819	1	1	**p-value**

P458. Safety and Feasibility of Transcutaneous Electrical Nerve Stimulation for Delayed Gastric Emptying after Pancreaticoduodenectomy: A Pilot Study

Hannah Liefeld[1]; Jason Aubrey[2]; Jesse Kelley[3]; Mariam Khan[4]; M. Mura Assifi, MD[5]; G. Paul Wright, MD[6]; Mathew Chung, MD[7]
[1]Corewell Health West/Michigan State University, Grand Rapids, MI, US; [2]Corewell Health West/Michigan State University, Grand Rapids, MI, US; [3]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [4]Corewell Health West/Michigan State University, Grand Rapids, MI, US; [5]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [6]Corewell Health West - Michigan State University, Grand Rapids, MI, US; [7]Corewell Health West - Michigan State University, Grand Rapids, MI, US

INTRODUCTION: One of the most frequent complications after pancreaticoduodenectomy (PD) is delayed gastric emptying (DGE), with an incidence quoted between 10-30%. Transcutaneous electrical nerve stimulation (TENS) initially emerged as a non-pharmacologic treatment for chronic pain; however, its application has reached beyond treating pain. We aimed to examine the safety and feasibility of TENS to reduce the incidence of DGE after PD. **METHODS:** Patients who underwent PD between August 2023 to August 2024 at a single institution were recruited for the study prospectively. The primary aim was to investigate if TENS could be used safely in post-PD patients. Our secondary aim was to determine the rate of DGE in patients undergoing TENS treatment following PD. DGE was defined as the inability to return to standard diet by the first postoperative week or reinsertion of a nasogastric tube beyond postoperative day 3. A TENS 7000 device with two electrode pads was applied on both sides of the patient's midline incision or on the patient's mid-lower back. The TENS device was configured to setting 2 intensity level, 100 Hertz frequency and pulse width of 250 milliseconds for two, 30-minute treatments daily. Treatments were continued until postoperative day 7 or until discharge. Return of bowel function, resumption of a normal diet, adverse events and patient satisfaction scores were recorded. **RESULTS:** Of the 29 patients who were recruited for the study, 20 patients (69%) completed the entirety of the treatment course. Six patients were excluded based on predefined criteria and three declined to participate in the study after PD. For the patients who completed the TENS treatment course, the average age at the time of surgery was 67.5 years with an average Charlson Comorbidity Index score of 5 points. There was a median return of bowel function on post-operative day 5 and an average length of stay of 7.35 days. Four (20%) patients experienced a complication unrelated to TENS usage. Two (10%) patients developed delayed gastric emptying despite TENS usage. One patient required reinsertion of a nasogastric tube beyond postoperative day 3, while the other patient was unable to return to a standard diet prior to postoperative day 7. Both patients eventually discharged home on a soft-food diet. No patient experienced TENS related complications or reported discomfort related to initiation of the device. **CONCLUSIONS:** Our study confirms safe usage of the TENS device in post-PD patients. A low rate of DGE (10%) was observed, however, more questions on ideal treatment parameters remain that warrant further study.

P459. The Development of a Median Survival Calculator for Pancreatic Adenocarcinoma Using Artificial Intelligence: An Application of the Surveillance, Epidemiology, and End Results Program

Gowri Warikoo[1]; Samuel J Kim[2]; Praneet Khanna[3]; Saad Khan[4]; Sarah Ding[5]; Raabia Qureshi[6]; Robert Zhang[7]; Sreeja Ponnam[8]; Anshal Vyas[9]; Bianca Ituarte[10]; Steven Nyugen[11]; Patrick Weldon[12]; Nathan Carpenter[13]; Sara Trompeter[14]; An-Lin Cheng[15]; Cuthbert Simpkins[16]
[1]University of Missouri Kansas City SOM, Kansas City, MO, US; [2]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [3]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [4]UMKC SOM, Kansas City, MO, US; [5]UMKC SOM, Kansas City, MO, US; [6]UMKC SOM, Kansas City, MO, US; [7]UMKC SOM, Kansas City, MO, US; [8]UMKC SOM, Kansas City, MO, US; [9]UMKC SOM, Kansas City, MO, US; [10]UMKC SOM, Kansas City, MO, US; [11]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [12]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [13]UMKC SOM, Kansas City, MO, US; [14]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [15]University of Missouri-Kansas City School of Medicine, Kansas City, MO, US; [16]University of Missouri-Kansas City, Kansas City, MO, US

INTRODUCTION: Pancreatic adenocarcinoma (PA) is an incurable and highly insipidus tumor with 10-year survival rates of 10%. Katz and colleagues have developed a clinical calculator of conditional survival estimates for PA based on the Surveillance, Epidemiology, and End Results (SEER) Program database. Despite this, the calculator only includes 7 variables and was last updated in 2012. With the advent of socioeconomic determinants of health (SDOH) and recent advances in chemoradiation, this study has developed a new calculator using artificial intelligence (AI). Data was extracted from 17 registries between 2000-2020 for pancreatic adenocarcinoma based on ICD-O-histology codes. Median survival times were calculated and compared by sex, age, primary site, race, histology, grade, radiation, chemotherapy, and metastasis to distant sites via analysis of variance (ANOVA) testing. Results were inputted into ChatGPT 4o, weighed, and coded via ChatGPT 1o-preview models. A total of 39,107 patients with pancreatic adenocarcinoma were analyzed. All categories showed significant differences in median survival months ($p<0.0001$). The tool has been developed as a web-based calculator utilizing ChatGPT 4o for primary analysis and ChatGPT 1o-preview for more advanced coding. The median survival calculator successfully provided accurate survival estimates using patient data, enhancing prognostic capabilities in pancreatic cancer within a user-friendly interface and is available on Github (https://github.com/SamJoeKim/Pancreatic-Adenocarcinoma-Calculator). This investigation utilized the SEER database and basic statistics to generate a median survival months calculator for PA patients. The developed median survival calculator provides an accessible and user-friendly tool for estimating survival in these patients. Further validation of the tool and progressive use for patient education should be pursued. National guidelines recommend surgery when pathology analysis of a malignant colorectal polyp reveals high-risk features: positive margin/piecemeal resection (PM/PR), lymphovascular/perineural invasion (LVI/PNI), poor differentiation (PD), or tumor budding (TB). However, some patients choose to avoid surgery, with its morbidity and quality-of-life implications, despite the risk of residual disease. **METHODS:** This single-center cohort study determined the rates of luminal or lymph node disease and distant metastasis in patients who underwent surgery and patients who underwent observation following removal of a malignant colorectal polyp with high-risk features between 2015 and 2022. **RESULTS:** Of 336 patients who underwent a malignant polypectomy in the colon (n = 226) or rectum (n = 110), 312 had a PM/PR, 96 had LVI/PNI, 47 had PD, and 45 had TB; 208 patients (62%) underwent surgery, and 128 (38%) underwent observation. Patients with a malignant polyp in the rectum were more likely to undergo observation than patients with a malignant polyp in the colon (79 [72%] vs. 49 [22%] patients; $P < 0.01$). In the surgery group, 19 patients (9%) had residual luminal disease, 39 patients (19%) had lymph node disease, and 5 patients (2%) had distant metastasis. In the observation group, disease was identified in 14 patients (11%): regrowth in the lumen, 7 patients (9%); regrowth in lymph nodes, 5 patients (6%); distant metastasis, 1 patient (1%); regrowth with distant metastasis, 1 patient (1%). The 12 cases of regrowth (lumen and lymph node) were salvaged: resection, 4 patients; local excision, 2 patients; chemoradiotherapy, 6 patients. **CONCLUSIONS:** The risk of residual disease following removal of a malignant colorectal polyp with high-risk features is considerable. Patients concerned about the morbidity of surgery and postsurgery quality of life should be counseled about this risk, as well as the availability of effective salvage options.

P460. The Impact of the COVID-19 Pandemic on Gastrointestinal Cancer Treatment and Outcomes

Divya Ventarapragada[1]; Evelyn Gardolinski[2]; Raag Patel[3]; Siddarth Satuluru[4]; Queen Abure[5]; Isabela Pavkov[6]; Yazmin Reategui[7]; Steven Colquhoun[8]; Alicia Arnold[9]; Daniel Milgrom[10]; Danny Yakoub[11]
[1]Medical College of Georgia, Augusta, GA, US; [2]Medical College of Georgia, Augusta, GA, US; [3]Medical College of Georgia, Augusta, GA, US; [4]Medical College of Georgia, Augusta University, Augusta, GA, US; [5]Medical College of Georgia, Augusta, GA, US; [6]Medical College of Georgia, Augusta, GA, US; [7]Medical College of Georgia, Augusta, GA, US; [8]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US; [9]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US; [10]Wellstar Medical College of Georgia at Augusta University, Augusta, GA, US; [11]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US

INTRODUCTION: The COVID-19 pandemic disrupted healthcare systems globally limiting availability and access to gastrointestinal (GI) cancer treatment which includes esophageal, gastric, liver, gallbladder, pancreatic, colon, rectal, and anal cancers. We aim to characterize the effects of the pandemic on GI cancer stage distribution, time to treatment, lymphovascular invasion, and ratio of positive lymph nodes harvested. **METHODS:** A retrospective analysis using the National Cancer Database (NCDB) was conducted on GI cancer data to

compare patients from 2018 (prepandemic) to patients from 2020 (pandemic) and assess variation between COVID-19 positive (C19+) and COVID-19 negative (C19-) patients within the pandemic group. Descriptive statistics were used to compare groups. There were no significant differences in the number of patients between the pre-pandemic and pandemic periods, nor in age, sex distribution, or comorbidity. Patients with missing data were excluded. **RESULTS:** Across most GI cancers, there was a noticeable increase in advanced-stage cases during the pandemic not linked to C19 status. Specifically, there was an increase in stage 4 esophageal adenocarcinoma (p<0.001), overall stage 4 gastric cancer (p<0.001), stage 3 and 4 hepatocellular carcinoma and cholangiocarcinoma (p<0.001), overall stage 4 gallbladder cancer (p<0.001), and stage 3 anal squamous cell carcinoma (p<0.001). C19+ patients experienced significantly longer times to initial treatment in pancreatic (46 days C19+ vs 36 days C19- , p<0.001), rectal (46 days C19+ vs 40 days C19- p<0.01), and colon cancer (27.85 days C19+ vs 23.91 days C19-, p<0.05). Moreover, surgery delays increased for gastric (122 vs 116 days, p<0.01), gallbladder (54.8 vs 28.7 days, pancreatic (96 vs 82 days, p<0.001; 118 vs 97 days for C19+, colon (46.4 vs 40.2 days, and rectal cancers (176 vs 151 days, p< 194 vs 176 days for C19+, p<0.05). Surprisingly, liver cancer saw shorter surgery times. Lymphovascular invasion was unchanged across periods and C19 status, except for decreased Stages 1, 2, and 4 gastric cancers (p<0.05) and increased Stage 3 C19+ anal cancer (p<0.05). Higher lymph node ratios were found in Stage 3 C19+ pancreatic (p<0.01), colon (p<0.05), and rectal cancers (p<0.001). **CONCLUSIONS:** Overall, the data highlights that the COVID-19 pandemic led to significant delays in treatment and increased disease severity for GI cancer patients likely not attributed to the COVID-19 infection itself.

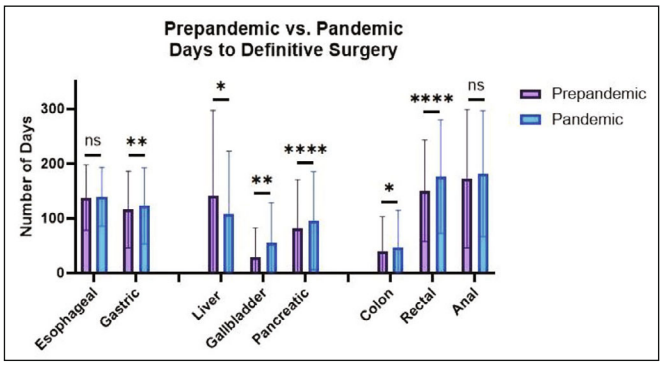


Figure 1. Days to definitive surgery comparisons in pre-pandemic vs. pandemic cohorts

P461. Wide variation in parental leave allowances during Society of Surgical Oncology fellows: Due for change

Sara Ardila, MD[1]; Kristin Lupinacci, DO[2]; Qurat Ul Ain Sabih, MD[3]; Jennifer Steiman, MD[4]; Kathrine Kelly, DO[5]; Priscilla F. McAuliffe, MD, PhD[6]; Erin M. Bayley, MD, MSc[7]

[1]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [2]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [3]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [4]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [5]Universtiy of Pittsburgh Medical Center, Pittsburgh, PA, US; [6]University of Pittsburgh Medical Center, Pittsburgh, PA, US; [7]University of Pittsburgh Medical Center, Pittsburgh, PA, US

INTRODUCTION: The Society of Surgical Oncology (SSO) oversees both the Breast and Complex General Surgical Oncology (CGSO) clinical fellowship training programs. Despite the fact that surgical and subspecialty training periods are the most likely times of having a child throughout one's medical education and career, SSO does not have a parental leave policy for its fellowship programs to guide fellows and programs regarding leave allowances and graduation requirements. **METHODS:** A survey was developed to better understand fellow parental leave requests, approvals, and considerations, as well as perceived policies governing leaves. The survey was distributed via social media targeting only fellowship-trained breast and CGSO surgeons. Only those who (A) trained in SSO/American Society of Breast Surgeons fellowship programs and (B) had a child during fellowship training were included. Having a child during fellowship was defined as childbirth, child by partner-birth, adoption, or surrogacy. **RESULTS:** A total of 15 eligible responses were collected from 13 current/past breast and 2 CGSO fellows. Graduates included those from 2018 to 2025 (planned). Respondents were birthing parents in 13 (87%) instances, partner/non-birthing parents in 1 (7%) case, and adoptive parents in 1 (7%) case. Two (13%) birthing parents reported not requesting any leave; leave was requested for the remaining 13 (87%) respondents, and varied in duration from <4-9 weeks (Table). When asked which resources were used by program leadership to determine leave allowance, policies of the institution (6, 46%), SSO (2, 15%), American Board of Surgery (1, 8%), and ACGME (1, 8%) were cited, while 4 (31%) respondents said program leadership referenced no policy at all. For their part, fellows reported not being able to find any policy guiding leave allowances in most instances (13/15, 87%). One fellow who took 9 weeks off and graduated on time, was told to "keep it hush," while another fellow who took 7 weeks off was required to graduate 4 weeks late "to be fair." One respondent said their program was "extremely supportive," while another said their program director was "not supportive and [was] annoyed" by her pregnancy during fellowship. **CONCLUSIONS:** A wide variety of practices exist across Society of Surgical Oncology Breast and CGSO fellowship training programs with respect to allowed parental leave and work requirements for graduation. We believe the Society of Surgical Oncology should develop a parental leave policy, consistent with the American Board of Surgery and America Board of Medical Specialties, to guide fellowship programs and fellows, and ultimately support working parents in subspecialty surgical training.

Program	Child By	Any Leave?	Leave Duration (Weeks)	Delay in Graduation?	Graduation Delay Duration
Breast	Birth	No	0	--	--
Breast	Birth	No	0	--	--
CGSO	Partner birth	Yes	<4	No	--
Breast	Adoption	Yes	4	No	--
Breast	Birth	Yes	6	No	--
Breast	Birth	Yes	6	No	--
Breast	Birth	Yes	6	No	--
CGSO	Birth	Yes	7	No	--
Breast	Birth	Yes	7	Yes	4-5 weeks
Breast	Birth	Yes	8	No	--
Breast	Birth	Yes	8	Yes	2-3 weeks
Breast	Birth	Yes	8	Yes	2-3 weeks
Breast	Birth	Yes	8	Yes	4-5 weeks
Breast	Birth	Yes	8	Yes	4-5 weeks
Breast	Birth	Yes	9	No	--

P462. Building a multidisciplinary team: The impact of sarcoma-trained pathologists on diagnostic outcomes of patients with retroperitoneal masses

Laura E Kerr, MD, FRCSC[1]; Laura Nguyen[2]; Tim Ramsay[3]; Alex Lee[4]; Kristin Ambacher[5]; Bibianna Purgina[6]; Carolyn Nessim, MD, MSc[7]

[1]University of Ottawa, Ottawa, ON, CA; [2], US; [3], US; [4], US; [5], US; [6], US; [7]The Ottawa Hospital (General Campus), Ottawa, ON, CA

INTRODUCTION: Soft tissue sarcomas are a relatively rare heterogeneous group of neoplasms that make up only 1% of adult neoplasms;15% of these are retroperitoneal sarcomas. Their low incidence highlights the need for subspecialty care for these patients. Initial diagnosis is critical to treatment planning but complex, owing to the diversity of histological subtypes within the class. This retrospective study looks at the impact on diagnostic yield and accuracy of the addition of sarcoma-trained pathologists to the multidisciplinary team at a Canadian academic centre. **METHODS:** This study is a retrospective chart review, comparing biopsies performed prior to January 2010 to biopsies performed after January 2010, at which point a sarcoma-trained pathologist was hired. Patient characteristics and biopsy technique were compared. Primary outcome was diagnostic yield and diagnostic accuracy between biopsies in these two cohorts. Diagnostic yield was assessed based on the entire population; diagnostic accuracy was further assessed on all patients who proceeded to surgical resection. **RESULTS:** A total of 212 retroperitoneal lesion biopsies were included; 59 were performed between October 1999 and January 2010 and 153 biopsies were performed between January 2010 and September 2021. Patient and lesion characteristics were compared using continuous variables. The diagnostic yield of the biopsies performed prior to Jan 2010 was 76.3% (45/59) compared with 80.4% (123/153) performed after Jan 2010 (p=0.51). However, there was only 63.6% (21/33) accuracy for diagnosing malignancy in biopsies performed prior to Jan 2010 compared to 84.9% (79/93; p=0.009) in biopsies performed after Jan 2010. In biopsies performed prior to Jan 2010, the diagnosis at time of biopsy was incorrect in class and grade in 5.9%, correct class but wrong grade in 29.4%, and correct in class and grade in 35.3% of all specimens. In biopsies performed after Jan 2010, the class and grade were incorrect in 10.4%, correct class but wrong grade in 16% and correct class and

grade in 55.2% (p = 0.03). **CONCLUSIONS:** While there were not statistically significant differences in diagnostic yield before and after January 1, 2010, there was significant difference in the accuracy of diagnosis, which affects treatment planning. These results demonstrate that dedicated sarcoma trained pathologists are key members of, and should be prioritized when planning a multidisciplinary team, as they have a paramount role in facilitating accurate diagnosis of patients.

P463. Does Surgery Improve Outcomes in Metastatic Gastrointestinal Stromal Tumors (GISTs) in All Sites?

Christina H Bae, Medical Student[1]; Christopher Vakkur, Medical Student[2]; Justin Abes, Medical Student[3]; Jonathan Vainer, Medical Student[4]; Alicia Arnold[5]; Daniel Milgrom[6]; Steven Colquhoun[7]; Danny Yakoub[8]

[1]Medical College of Georgia, Augusta, GA, US; [2]Medical College of Georgia, Augusta, GA, US; [3]Medical College of Georgia, Augusta, GA, US; [4]Medical College of Georgia, Augusta, GA, US; [5]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US; [6]Wellstar Medical College of Georgia at Augusta University, Augusta, GA, US; [7]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US; [8]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US

INTRODUCTION: Outcomes of Gastrointestinal stromal tumors (GISTs) vary depending on the primary site and metastatic disease. This study aims to evaluate the impact of surgical intervention on overall survival (OS) in patients with metastatic GISTs at different primary GI sites and metastatic locations. **METHODS:** The National Cancer Database (NCDB 2004-2018) was queried for cases of metastatic GISTs originating from different GI sites. Kaplan-Meier survival analyses, log-rank tests, and Cox proportional hazard models were used to evaluate the impact of surgical intervention on OS across GI site groups. **RESULTS:** A total of 2,489 patients with metastatic GISTs across all GI sites were identified. Patients who underwent primary debulking surgery (PDS) had a significantly longer median OS compared to those who received systemic therapy only (77.0 months vs. 36.47 months, p<0.001). Further subgroup analysis demonstrated that PDS combined with systemic therapy yielded the longest median OS compared to PDS alone and systemic treatment alone (82.83 months, 61.83 months, and 38.67 months respectively, p<0.001). GI organ-specific analyses revealed significantly better OS for patients with gastric (91.96 months) and small intestinal (73.23 months) GISTs compared to esophageal (46.85 months), colonic (35.32 months), and rectal (25.2 months) GISTs (p<0.001). Furthermore, patients who underwent both PDS and metastatic site debulking across all GI sites had a significantly longer OS compared to those who had PDS alone (83.98 months vs. 72.94 months, p=0.02). Specifically, liver metastasectomy combined with PDS significantly improved survival for small intestinal (88.08 months, p=0.033) and colonic (61.83 months, p=0.043) GISTs compared to PDS and liver metastasectomy in gastric GISTs (p=0.61). **CONCLUSIONS:** Overall, surgical resection improves OS in metastatic GISTs, especially when combined with systemic therapy. Liver metastasectomy particularly further improved OS in metastatic GISTs of the small intestine and colon. Further studies are warranted to evaluate metastasectomy of other sites.

P464. Factors Associated with Refusal of Surgery in Stage I-III Primary Bone and Joint Cancers and Their Effect on Survival

Jonathan Palmer[1]; Malek Moumne[2]; Evelyn Gardolinski[3]; Ryan Quisling[4]; Brian Kye[5]; Anusha Aiyar[6]; Luke Guy[7]; Gustavo Capo[8]; Sohawm Sengupta[9]; Carter Quinn[10]; Yagni Patel[11]; Caroline Hana[12]; Kelly Homlar[13]; Daniel Milgrom[14]; Steven Colquhoun[15]; Danny Yakoub[16]

[1]Medical College of Georgia, Augusta, GA, US; [2]Medical College of Georgia, Augusta, GA, US; [3]Medical College of Georgia, Augusta, GA, US; [4]Medical College of Georgia, Augusta, GA, US; [5]Medical College of Georgia, Augusta, GA, US; [6]Medical College of Georgia, Augusta, GA, US; [7]Medical College of Georgia, Augusta, GA, US; [8]Medical College of Georgia, Augusta, GA, US; [9]Medical College of Georgia, Augusta, GA, US; [10]Medical College of Georgia, Augusta, GA, US; [11]Medical College of Georgia, Augusta, GA, US; [12]Department of Hematology/ Oncology, Medical College of Georgia, Augusta, GA, US; [13]Department of Orthopedics, Medical College of Georgia, Augusta, GA, US; [14]Division of Surgical Oncology, Department of Surgery, Medical College of Georgia, Augusta, GA, US; [15]Division of Surgical Oncology, Department of Surgery, Medical College of Georgia, Augusta, GA, US; [16]Division of Surgical Oncology, Department of Surgery, Medical College of Georgia, Augusta, GA, US

INTRODUCTION: Surgical resection of bone and joint cancers has reported survival benefits for select subsets of patients; however, some patients refuse surgery despite physician recommendations. This study aims to assess the factors associated with surgery refusal and evaluate its impact on overall survival (OS) in this patient population. **METHODS:** The NCDB (2004-2017) was examined for patients with stage I-III bone and joint cancers who were recommended surgery. Histologies included were osteosarcoma, chondrosarcomas, and other. Patients who underwent surgery were compared to those who refused it. Logistic regression was used to identify predictors of surgery refusal. Propensity scored matching (PSM) was implemented to produce comparable groups based upon demographics, disease characteristics, and treatment. Kaplan-Meier and Log-Rank analysis were used to determine the effect of surgery refusal on OS. A Cox-Proportional Hazard Model was implemented to investigate factors influencing OS. **RESULTS:** Out of the 14,479 patients who were offered surgery, 1.0% (152) refused it. Multivariate logistic regression identified the following factors as predictors of refusing surgery: residence in rural areas (OR=7.48), treatment in non-academic centers (OR=1.61), tumor location in pelvic bones (OR=3.77), anaplastic or undifferentiated grade tumors (OR=2.60), opting for palliative care (OR=5.63), and refusal of radiation (OR=3.69) or chemotherapy (OR=9.09). Factors associated with a decreased probability of surgery refusal included having private insurance (OR=0.22), residing more than 200 miles from the care center (OR=0.52), and tumor location in the skull (OR=0.18) or in the sternum, clavicle, or ribs (OR=0.23). All variables met statistical significance (P<0.01). Kaplan-Meier and Log-Rank analysis of PSM groups showed a decrease in OS in patients who refused surgery versus patients that received surgery (35.3 vs. 85.9 mos. HR=1.77, P<0.01) (Fig.1). On multivariate analysis of survival in patients who refused surgery, a Charlson-Deyo comorbidity score of 2+ (HR=2.48, P<0.01) was associated with decreased survival. **CONCLUSIONS:** Patients who refuse surgery for primary bone and joint cancers have a decrease in OS compared to those who have surgery. Certain socioeconomic factors, such as rural living or insurance status, play a major role in the decision to refuse or accept surgery. Addressing these factors with targeted interventions and multidisciplinary management may improve outcomes in these patients.

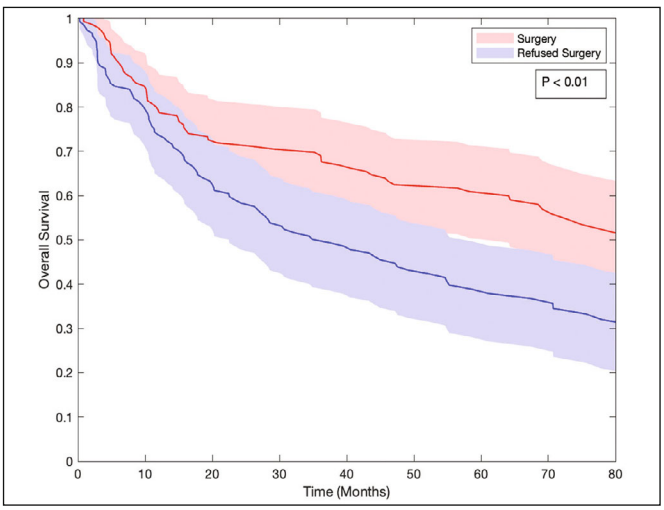


Figure 1. Kaplan Meier survival curves for the overall survival of patients with stage I-III bone and joint tumors who either received or refused surgery.

P465. Identifying the Path to Soft Tissue Sarcoma: The Validation of Multimorbidity Disease Trajectories

Neha Malik, MD, MS[1]; Liwei Wang[2]; Rui Li[3]; Andrew Wen[4]; Qiuhao Lu[5]; Jinlian Wang[6]; Matthew H.G. Katz, MD[7]; Christina L. Roland, MD, MS, FSSO[8]; Hongfang Liu[9]; Heather Lyu, MD[10]

[1]MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas Health Science Center at Houston, Houston, TX, US; [3]The University of Texas Health Science Center at Houston, Houston, TX, US; [4]The University of Texas Health Science Center at Houston, Houston, TX, US; [5]The University of Texas Health Science Center at Houston, Houston, TX, US; [6]The University of Texas Health Science Center at Houston, Houston, TX, US; [7]MD Anderson Cancer Center, Houston, TX, US; [8]MD Anderson Cancer Center, Houston, TX, US; [9]The University of Texas Health Science Center at Houston, Houston, TX, US; [10]MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: Understanding longitudinal disease progression patterns at the population level is critical to identifying unexpected associations between diseases. Signature disease trajectories in rare cancers such as soft tissue sarcoma (STS) can provide crucial data regarding associated conditions at the time of diagnosis. The aim of this study was to describe our approach to discovering signature disease trajectories for STSs leveraging large-scale EHR data. **METHODS:** The IQVIA Oncology Electronic Medical Record database is an international database with deidentified patient-level oncology data from 2015-2023. Two separate cohorts based on tumor location were created, sarcoma-trunk/extremity and sarcoma-abdomen/retroperitoneum. Statistically significant diagnosis pairs were defined as pairs in which the occurrence probability in patients with sarcoma was higher than that of the general population. These were identified through a series of computations starting with the extraction of the first sarcoma diagnosis followed by a comparison of disease pair occurrence with a cohort of patients with the same gender and age. Directionality within the diagnosis pairs was established through a right-tailed binomial hypothesis test and disease trajectories were plotted using Gephi, an open source platform for visualizing large networks. Data from a UTHealth database was used to validate the model. **RESULTS:** 110 statistically significant diagnosis pairs were identified for the trunk/extremity sarcoma cohort and 95 diagnosis pairs were identified for the abdomen/retroperitoneum sarcoma cohort. For the trunk/extremity group, 103 pairs displayed directionality, with 5 pairs starting from sarcoma and 69 pairs leading to sarcoma. Seven pairs were undirected. For the abdomen/retroperitoneum group, 90 pairs displayed directionality, with 61 pairs leading to sarcoma. Five disease pairs were undirected. Disease progression patterns differed between the two cohorts with the most common diagnoses leading to trunk/extremity sarcomas being essential hypertension, soft tissue disorders, and joint disorders compared to the most common diagnoses leading to abdominal/retroperitoneal sarcomas being essential hypertension, other anemias, and iron deficiency anemia. **CONCLUSIONS:** Our study demonstrates the feasibility of using real world data to discover and validate signature disease trajectories. Analyzing disease progression patterns can be used to generate new hypotheses and in primary care settings to help all clinicians identify STS patients at early stages of disease.

P466. Immunohistochemistry and Cytogenetics Do Not Impact Survival in Ewing's Sarcoma Family of Tumors of the Pancreas: A Systematic Review and Survival Analysis

Kaiser O'Sahil Sadiq, MBBS[1]; Rishab Belavadi, MBBS[2]; Swetha Lakshminarayanan, MBBS[3]; Patricia Ruiz Cota, MD[4]
[1]Plexus Neuro and Stem Cell Research Centre, Bangalore, IN; [2]Mayo Clinic Arizona, Phoenix, AZ, US; [3]Sri Ramachandra Institute of Higher Education and Research, Chennai, IN; [4]UC San Diego, La Jolla, CA, US

INTRODUCTION: Ewing's Sarcoma Family of Tumors (ESFT), formerly classified as Ewing's sarcomas and primitive neuroectodermal tumors, consists of undifferentiated small round cell sarcomas of bone and soft tissue with common cytogenetic and histological traits. Pancreatic involvement is extremely rare, and its nonspecific clinical presentation makes diagnosis challenging, often necessitating cytogenetic analysis. This review examines the cytogenetic and immunohistochemical (IHC) characteristics of pancreatic ESFT and evaluates their impact on survival outcomes. **METHODS:** This systematic review and meta-analysis was registered on PROSPERO (CRD42024585711) and followed PRISMA guidelines. The Cochrane Library, Embase, PubMed, and Pubmed Central were last searched in August 2024 without time or language restrictions and included all studies with data that could be pooled for analysis. R 4.4.1 was used to calculate inferential statistics. **RESULTS:** Out of 812 studies retrieved, 71 were included, totaling 89 unique patients. Ages ranged from 2 to 78 (median, 23) with 55.1% male and 43.8% female. Pancreatic involvement occurred in the head (57.1%), uncinate process (10.4%), body (39.0%), and tail (31.2%) (Fig. 1A). Maximum diameter ranged from 1.8 to 33.0 cm (median, 7.75 cm). 11 were secondary tumors, 25 were necrotic, calcification was seen in one, local invasion was observed in 26, and 19 were metastatic. Testing for IHC markers was inconsistent; 100% were positive for CD99 (n=45), 91.7% for NKX2.2 (n=11), 75% for FLI-1 (n=6), 80% for INI-1 (n=4), 96.3% for vimentin (n=26), 40.4% for synaptophysin (n=19), 15.9% for chromogranin-A (n=7), 81.8% for neuron-specific enolase (n=18), 34.5% for S-100 (n=10), 6.7% for CD10 (n=1), 42.3% for CD56 (n=11), 71.4% for CD117 (n=5), 100% for Cyclin-D1 (n=4), 61.5% for β-catenin (n=8), 33.3% for BCL-2 (n=2), 55.6% for EMA (n=5), 100% for CAM5.2 (n=2), and 100% for Leu7 (n=2). Cytogenetic analysis was only performed in 50.1% (n=45); 55.6% with fluorescence in situ hybridization (n=25) and 33.3% with RT-PCR. 55.6% (n=25) had a t(11;22)(q24;q12) translocation producing an EWS-FLI1 fusion oncogene and results of 35.6% (n=16) were unspecified. On follow-up, disease progressed in two cases, recurred in two, and metastasized in six. Survival outcomes were unavailable for 18 cases, mortality was 38.0% for the remaining and 46.5% had no evidence of disease. Patients were followed up for a maximum of 120 months (median, 12 months). Univariate analysis of Cox regression models of overall survival (OS) and disease-free survival (DFS) did not produce statistically significant hazard ratios for any immunohistochemical markers or cytogenetic abnormalities. **CONCLUSIONS:** Pancreatic ESFT is rare, predominantly affecting patients under 40, with a slight male predominance. The most commonly positive IHC markers are CD99, vimentin, and NKX2.2. Cytogenetic analysis is performed in approximately 50% of cases, with the EWS-FLI1 fusion oncogene being the most frequent abnormality. However, neither DFS nor OS was significantly influenced by the reported cytogenetic or IHC markers.

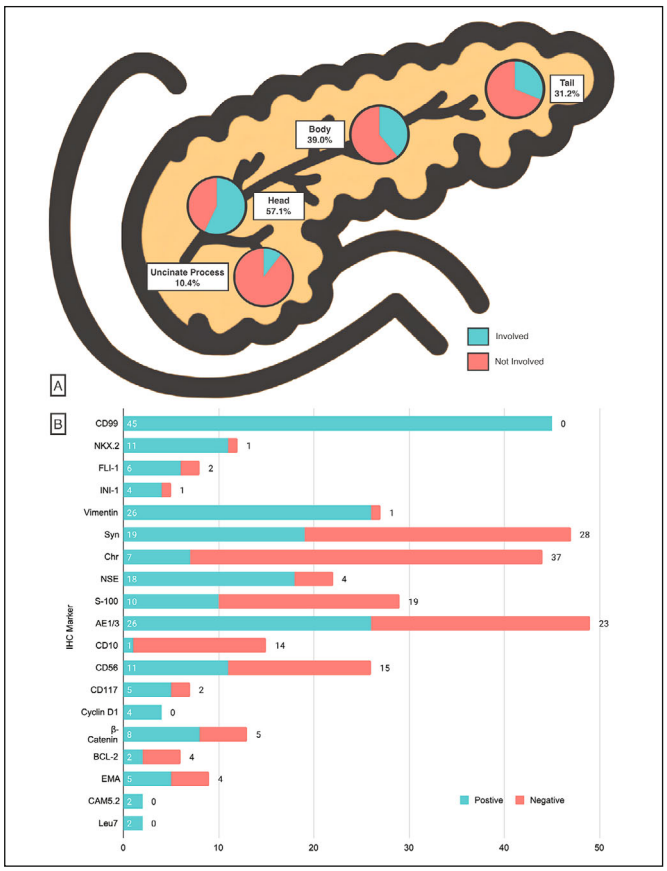


Figure 1. (A) Distribution of anatomic locations, and (B) Immunohistochemistry analysis results of Ewing's Sarcoma Family of Tumors involving the pancreas.

P467. Intravascular Leiomyomatosis: The Smooth Criminal of the Uterus

Brittany L Powell, MD, MPP, MBA[1]; Patrick V Heindel, MD, MPH[2]; Ashraf A Sabe, MD[3]; Elizabeth J. Lilley, MD, MPH[4]
[1]Brigham and Women's Hospital, Boston, MA, US; [2]Brigham and Women's Hospital, Boston, MA, US; [3]Brigham and Women's Hospital, Boston, MA, US; [4]Brigham and Women's Hospital, Boston, MA, US

INTRODUCTION: Intravascular leiomyomatosis (IVL) is a rare, benign smooth muscle neoplasm characterized by tumor originating from the uterus and propagating within veins. While histologically benign, IVL may behave aggressively, extending into the inferior vena cava (IVC) and heart, or can embolize, resulting in benign metastases. We sought to (1) determine the rates of extension to IVC/heart and benign metastasizing disease; and (2) describe tumor and operative characteristics in presentation and management of IVL extending to the IVC/heart. **METHODS:** This retrospective cohort study used data from the Research Patient Data Repository from 1990-2024. We included patients who underwent surgery at two large academic centers with pathology confirming intravascular leiomyomatosis, adenomyomatosis, or uterine smooth muscle tumor of uncertain malignant potential. Natural language processing

was used to extract tumor characteristics from pathology reports. Additional patient and operative data were abstracted from electronic health records. **RESULTS:** We identified 107 cases: 90.7% were confined to uterus/adnexa, 5.6% extended to IVC/heart, and 3.7% were benign metastasizing disease. Among those with disease in IVC/heart (n=6), all were symptomatic: 50% with acute symptoms ≤2 weeks, 16.7% with chronic symptoms >2 weeks, and 33.3% unspecified. Cardiac symptoms (83.3%) were most common at presentation. Tumor extended to the IVC and RA in 100% of cases and to the RV in 50%. 50% were single operations and 50% were staged. Of the staged operations, 33.3% were intended to be single stage, but were aborted and returned to the OR due to bleeding. One case (16.7%) had recurrence, 10.8 years after initial presentation, as an asymptomatic benign metastasizing leiomyoma in the lung. All patients remain alive (median 118.5 months since index surgery, range 4 to 354 months). See Table 1 for patient and tumor characteristics and management characteristics when IVL extends to the IVC/heart. **CONCLUSIONS:** This study provides important insights into the clinical behavior and management of IVL that extends to critical vascular and cardiac structures. The necessity for staged operations in half of these cases, due to intraoperative bleeding, underscores the complexity of operative planning and management of this uncommon neoplasm. Overall, these results contribute to a better understanding of IVL's clinical spectrum and may serve as the basis for developing a workup, treatment, and surveillance algorithm for this rare tumor entity.

Table 1. Patient and tumor characteristics and management characteristics when IVL extends to the IVC/heart

	IVC/heart (n=6)
Patient/tumor characteristics	
History of leiomyoma	6 (100%)
History of surgery for leiomyoma	5 (83.3%)
Symptoms at presentation	6 (100%)
Acute ≤ 2 weeks	3 (50%)
Chronic >2 weeks	1 (16.7%)
Unspecified	2 (33.3%)
Cardiac symptoms	5 (83.3%)
Pelvic or abdominal symptoms	2 (33.3%)
Diagnostic modality	
Echo	3 (50%)
CT	2 (33.3%)
Intra-operative during fibroid surgery	1 (16.7%)
Extent of disease includes	
IVC	6 (100%)
Right atrium	6 (100%)
Right ventricle	3 (50%)
Recurrence	
No	5 (83.3%)
Yes	1 (16.7%)
Management characteristics	
Number of operations	
1 (single stage)	3 (50%)
2 (staged)	2 (33.3%)
3 (staged)	1 (16.7%)
Specialists involved	
Cardiac Surgery	6 (100%)
Vascular Surgery	6 (100%)
Surgical Oncology	3 (50%)
OBGYN/Gynecologic Oncology	3 (50%)
Urology	2 (33.3%)
Procedures performed	
Laparotomy, sternotomy, atriotomy, cardiopulmonary bypass	6 (100%)
IVC venotomy and IVC reconstruction	3 (50%)
Other major pelvic venotomy	3 (50%)
Tricuspid valve repair	1 (16.7%)
Hysterectomy	3 (50%)
Bilateral salpingo-oophorectomy	3 (50%)
Unilateral salpingo-oophorectomy	1 (16.7%)
Adjuvant treatment	
Letrozole	1 (16.7%)
Leuprolide acetate	1 (16.7%)

P468. Multiplex immunofluorescent characterization of inter-patient and intra-patient heterogeneity in multi-metastatic SDH-deficient GIST

Rachael Lowney, MD[1]; Shelby Johnson[2]; Noemi Kedei, MD[3]; Leila Sarvestani, MD[4]; Shruthi R Perati, MD[5]; Ashley Rainey[6]; Jennifer Matta[7]; Andrew Warner[8]; Jiyeun Kim[9]; Jeremy L. Davis, MD[10]; Jonathan M Hernandez, MD[11]; Markku Miettinen, MD[12]; Sun A Kim, MD[13]; Andrew M Blakely, MD[14]

[1]National Institutes of Health/National Cancer Institute, Bethesda, MD, US; [2]National Institutes of Health/National Cancer Institute, Bethesda, MD, US; [3]National Institutes of Health/National Cancer Institute, Spatial Imaging Technology Resources, Bethesda, MD, US; [4]National Institutes of Health/National Cancer Institute, Bethesda, MD, US; [5]National Institutes of Health/National Cancer Institute, Bethesda, MD, US; [6]National Institutes of Health/National Cancer Institute, Bethesda, MD, US; [7]National Institutes of Health, Molecular Histopathology Lab, Frederick, MD, US; [8]National Institutes of Health, Molecular Histopathology Lab, Frederick, MD, US; [9]National Institutes of Health, Molecular Histopathology Lab, Frederick, MD, US; [10]National Institutes of Health/National Cancer Institute, Bethesda, MD, US; [11]National Institutes of Health, Bethesda, MD, US; [12]National Institutes of Health/National Cancer Institute, Bethesda, MD, US; [13]National Institutes of Health, Bethesda, MD, US; [14]National Institutes of Health, Bethesda, MD, US

INTRODUCTION: Gastrointestinal tumors (GISTs) are mostly driven by KIT/PDGFRA mutations, but ~10% instead result from succinate dehydrogenase deficiency (SDH-def). SDH-def GISTs are more likely to metastasize and be resistant to conventional tyrosine kinase inhibitor (TKI) therapy. We aimed to characterize tumor immune microenvironment (TIME) differences in multi-metastatic SDH-def GIST. **METHODS:** Patients with histologically confirmed SDH-def GISTs were enrolled on NCT04557969 and underwent complete cytoreductive surgery for multi-metastatic GIST. Formalin-fixed/paraffin-embedded tissue sections of gastric lesions, lymph node metastases, and liver metastases were selected from two patients for pilot 8-plex immunofluorescence (IF) staining. HALO image analysis software was used to quantify differences in immune cell prevalence and location. **RESULTS:** Patient A presented 7 years after index operation and had progression on multiple TKI therapies with peri-gastric local recurrence and concomitant liver and lymph node metastases. Patient B had no prior medical therapy and presented with a gastric primary and synchronous liver and lymph node metastases. GIST tissue from each demonstrated loss of SDHB on immunohistochemical staining. On multiplex IF, T cells emerged as a predominant immune cell type across tumor sites. In both patients, tissue from liver metastases demonstrated a greater predominance of T cells (identified by CD3E) than the peri-gastric recurrence/gastric primary samples. The liver metastasis in Patient B (untreated) was significantly immune-rich (as identified by CD45, a pan-immune marker) and had diffuse T cell predominance, as compared to the relatively fewer T cells (in clusters) seen in the post-TKI treatment liver metastasis and peri-gastric recurrence in Patient A. Patient B's gastric primary sample (untreated) has the lowest proportion of T cells across both patients' samples. **CONCLUSIONS:** In this two-patient pilot study, the stark differences in relative immune cell, and specifically T cell, prevalence suggest a potential role of T cells in the development of liver metastasis in SDH-def GIST. Additionally, the decreased prevalence of T cells in post-TKI treatment samples suggests that TKI therapies may have a role in inhibiting T cell activity in recurrent and metastatic sites. These novel findings enhance our understanding of GIST tumor biology and may ultimately help in furthering immunomodulating treatment strategies for SDH-def GIST.

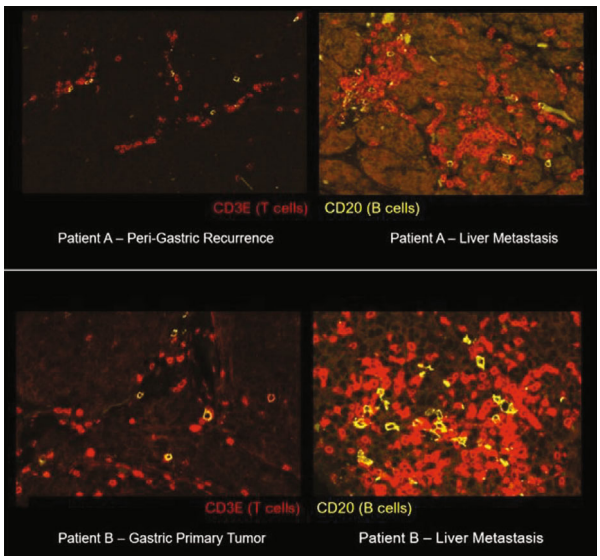


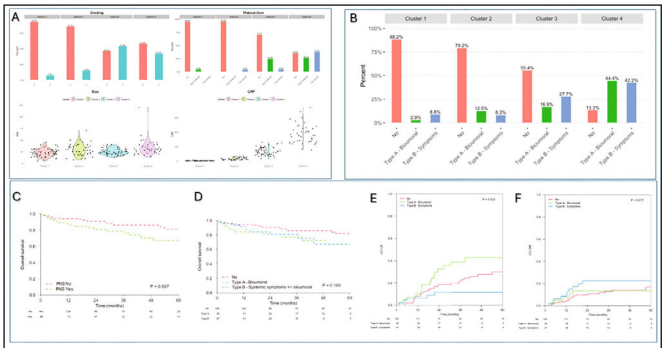
Figure. Multiplex IF images (20X magnification) of SDH-deficient GIST tumor sections from two patients with multi-metastatic disease. To further classify immune cell subtypes, the following markers are illustrated here: CD3E for T-cells and CD20 for B cells.

P469. Paraneoplastic Syndrome in Dedifferentiated Liposarcoma of the Retroperitoneum: an Under-Appreciated Clinical Scenario

Alessandro Delcarro[1]; Sara Iadecola[2]; Sandro Pasquali[3]; Dario CallegaroMD[4]; Roberta Sanfilippo[5]; Valentina Zuco[6]; Chiara Colombo[7]; Stefano Radaelli[8]; Marco Baia[9]; Rossella Bertulli[10]; Rosalba Miceli[11]; Alessandro Gronchi[12]; Marco Fiore[13]

[1]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [2]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [3]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [4]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [5]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [6]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [7]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [8]Fondazione IRCC Istituto Nazionale dei Tumori, Milan, IT; [9]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [10]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [11]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [12]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [13]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT

INTRODUCTION: Patients with retroperitoneal DDLPS often appear unwell at diagnosis. Paraneoplastic syndrome (PNS), a nonmetastatic systemic alteration caused by tumors, occurs in many malignancies, with fever being the most common symptom, though the presentation is highly variable. The specific incidence of PNS in DDLPS and its impact on prognosis and treatment compliance remain unknown. **METHODS:** All consecutive patients with primary localized DDLPS operated in 2016-2022 were included. Clinical data from a prospectively maintained database were reviewed, along with electronic records, to identify any PNS at diagnosis. Aside from fever, sweating and blood test abnormalities (anemia, leucocytosis, piastrinosis, hyponatriemia, hypercalcemia, eosinophilia, hypercortisolemia), no other significant dermatologic, neurologic, musculoskeletal, autoimmune, or gastrointestinal signs were found. PNS was therefore classified as follows: No PNS, Type A = bioumoral abnormalities, Type B = Systemic symptoms +/- bioumoral abnormalities. Unsupervised model-based clustering analysis was performed on the following tumor-related and clinical variables to explore potential correlations with PNS: age, sex, grade, size, postoperative complications, baseline C-reactive protein, malnutrition, pain at diagnosis. The association between PNS and overall survival (OS), local recurrence crude cumulative incidence (LR-CCI), distant metastasis CCI (DM-CCI) was explored, as well as the distribution of PNS among clusters and the rate of neoadjuvant treatment interruption. **RESULTS:** The study included a total of 226 patients, with a median follow up of 38 months (IQR, 21.7-56.8). PNS was found in 86 (38.0%) patients: Type A in 39 (17.3%), Type B in 47 (20.8%). The cluster analysis identified tumor grade, size, C-reactive protein and malnutrition as important variables contributing to the structure of 4 clusters. The combinations of the selected variable levels allowed retrospectively classifying these clusters as representing increasing levels of prognostic risk. Type and prevalence of PNS significantly differed across the 4 clusters (p-value <0.001, see Figure 1B). The 5-year OS was 67.3% (95% CI: 55.1–82.0) for patients with PNS and 81.5% (95% CI: 73.2–90.8) for patients without PNS (p = 0.057), with no difference between PNS Type A and B. Type A group had higher LR-CCI (P = 0.023), Type B had higher DM-CCI (P = 0.317). Overall, 12/102 (11.8%) patients interrupted neoadjuvant treatment: 3/102 (2.9%) for PD, 9/102 (8.8%) for toxicity. Rate of interruption was 10.0% for patients without PNS, 26.7% for PNS Type A, 23.8% for PNS Type B. Notably, no patient exhibiting both paraneoplastic bioumoral abnormalities and symptoms was offered with neoadjuvant treatments. **CONCLUSIONS:** For retroperitoneal DDLPS, clinical scenarios cluster around tumor grade, size, malnutrition and elevated C-reactive protein. This is also associated with different types of paraneoplastic syndrome that overall affected 38% of patients, influencing treatment compliance. The presence of PNS was linked to worse outcomes and will deserve further research for better understanding of underlying mechanisms and clinical implication.



(Panel A); Type of Paraneoplastic Syndrome observed in the 4 different clusters (Panel B); OS according to the presence and type of Paraneoplastic Syndrome (Panel C-D); LR-CCI and DM-CCI according to type of Paraneoplastic Syndrome (Panel E-F)

Figure 1. Distribution of tumor grade (FNCLCC grade 2 and grade 3), Malnutrition (No, Moderate, Severe), tumor size (cm, continuous), C-reactive protein (mg/L, continuous) in 4 different clusters.

P470. Performance of a second preoperative Inflammatory-Immunologic-Metabolic Biomarkers Score originally built for Lung Cancer to predict overall survival also in Primary Retroperitoneal Sarcoma

Giulia Avogadro[1]; Camilla Valsecchi[2]; Rosalba Miceli[3]; Chiara Colombo[4]; Dario Callegaro, MD[5]; Stefano Radaelli[6]; Marco Baia[7]; Silva Ljevar[8]; Ugo Pastorino[9]; Alessandro Gronchi[10]; Marco Fiore[11]

[1]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [2]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [3]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [4]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [5]Istituto Nazionale dei Tumori, Milano, IT; [6]Fondazione IRCC Istituto Nazionale dei Tumori, Milan, IT; [7]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [8]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [9]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [10]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [11]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT

INTRODUCTION: Inflammatory biomarkers are used as a prognostic tools in many cancer types, and C-reactive protein (CRP) is one of the most common. We previously described an Inflammatory Biomarker Prognostic Index (IBPI) including Hemoblogin, NLR, PLR and Monocytes that predicted overall survival (OS) in retroperitoneal sarcoma (RPS). Unfortunately, CRP was not available on that series. A similar score (Routine Blood Test, RBT) also including CRP and glicemic index is already available and tested to be prognostic for lung cancer. We aimed to verify on a more recent series of RPS whether RBT is effective across different malignancies, and specifically if its performance may be better than IBPI. **METHODS:** Primary localized RPS operated at between 2017-2021 were included. IBPI (score range 0-4) and RBT (classified as low, intermediate and high risk) were calculated based on preoperative blood tests. A modified RBT algorithm (RBTrps) was also tested by re-estimating the optimal cut-off point for each blood parameter. Primary aim was performance of IBPI, RBT and RBTrps in predicting 5-yr OS and DFS. The discriminatory power of the 3 models was assessed by ROC curves and their AUC. **RESULTS:** 294 patients were included, with median follow-up of 3.9 years. IBPI identified 32 pts (12%) with score 0, 102 (38%) score 1, 98 (36%) score 2, 39 (14%) score 3, none score 4. RBT identified 64 pts (24%) with low risk, 88 (32%) with intermediate risk, and 119 (44%) with high risk. RBTrps identified 93 (34%) with low risk, 90 (33%) with intermediate, and 88 (33%) with high risk. The 5-yr OS was 68.4%, 72%, 58%, and 53% according to IBPI score, respectively(p-value=0.0202). According to RBT risk, the 5-yr OS was 90%, 56%, and 54% respectively (p-value<.0001). According to RBTrps risk, 5-yr OS was 88%, 54%, and 48% respectively (p-value<.0001) (Figure 1). For DFS, no significant differences were found according to IBPI (p-value=0.0757), while both RBT and RBTrps showed significant differences between groups (p-value=0.0068, p-value=<.0001, respectively). Between the 3 tested models, RBTrps performed with the highest prognostic value, with an AUC of 0.7034. The better performance of RBTrps was maintained at a secondary analysis that excluded glicemic index from the score (data not shown). **CONCLUSIONS:** RBT is an inflammatory – immunologic – metabolic score with prognostic value across different

malignancies (lung cancer and RPS), although disease-specific modifications to thresholds are needed. Factoring in the addiction of C-reactive protein, resulted in an improved performance both in OS and DFS prognosis.

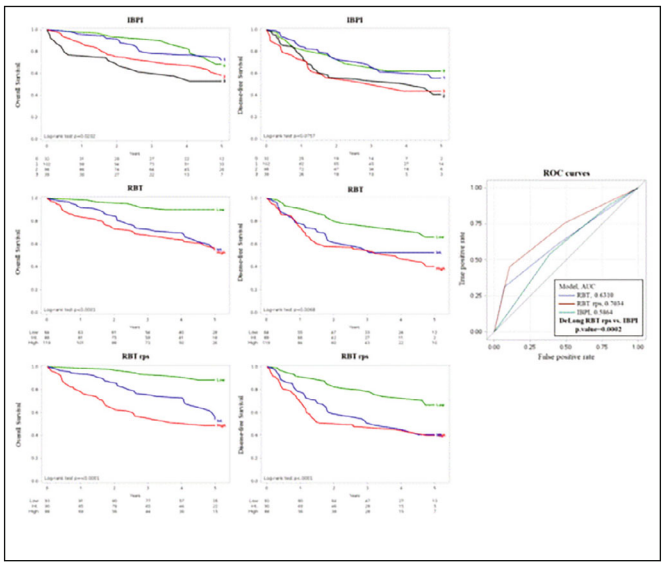


Figure 1. Overall Survival and Disease-free Survival in primary Retroperitoneal Sarcoma according to 3 different models of preoperative blood test score.

P471. Population-based experience of neoadjuvant treatment for patients with gastrointestinal stromal tumors (GIST)

Emily Heath[1]; Omar Khan[2]; Lloyd Mack[3]
[1]University of Calgary, Calgary, AB, CA; [2]Alberta Health Services, Calgary, AB, CA; [3]Alberta Health Services, Calgary, AB, CA

INTRODUCTION: Surgical resection remains the mainstay of treatment for localized GIST. When R0 resection is not feasible or has significant morbidity neoadjuvant therapy may be indicated. We aim to describe the population and tumor characteristics for GIST patients treated with neoadjuvant imatinib in Alberta, and to evaluate treatment, surgical and survival outcomes. **METHODS:** We retrospectively reviewed patients diagnosed with GIST from 2008-2022 treated with neoadjuvant imatinib therapy. Data were abstracted from the provincial cancer registry and chart review including patient, tumor and treatment (imatinib prescriptions/dosing) characteristics. CT and/or MRI and pathology reports were used to capture tumor size (largest dimension) and surgical details/outcomes. Response was evaluated using RECIST criteria, comparing tumor on initial imaging to surgical pathology. Recurrence was captured via oncology progress notes and follow up imaging. **RESULTS:** 693 GIST cases were identified from 2008-2022. Of these, 42 had primary nonmetastatic disease and received neoadjuvant imatinib. Median age was 63 and 64.3% were male. 71.4% were diagnosed in 2016-2022. Tumor characteristics are shown in Table 1. Most patients (54.8%) had primary gastric tumors, 61.9% were 5-10cm and 73.8% were high risk by NIH criteria. Neoadjuvant therapy was started a median of 33.5 days (range 3-123) after diagnosis and median duration was 283.5 days (80-526). Median cumulative imatinib dose was 113g (33-244) with starting dose of 400mg/day in 88.1%. Five patients (11.9%) had dose escalation above 400mg/day while 16 (38.1) required reduction or pause. At time of surgery 21 (50%) patients had partial response, 18 (42.9%) had stable disease and three (7.1%) had progressive disease. 1/23 with gastric GIST underwent total gastrectomy, eight subtotal gastrectomy. 6/8 with rectal GIST underwent APR. No patients with small bowel GIST required a Whipple. R0 resection was achieved in 85.7%. Number of organs resected ranged 0-6 with 57% having only one organ resected. Median follow up was 55.7 months (13.1-137.9). Five (11.9%) patients died, six (14.3%) had local recurrence, seven (16.7%) had distant metastases on imaging and 64.2% remain disease-free. **CONCLUSIONS:** Use of neoadjuvant imatinib in Alberta for primary nonmetastatic GIST has increased in the past eight years. Duration and cumulative dose are individualized, facilitating R0 resection in most, with favorable surgical and long-term outcomes.

Table 1. Tumour characteristics for patients with primary nonmetastatic GIST receiving neoadjuvant imatinib therapy.

	n (proportion) (N=42)
Tumour Location	
Esophagus or GEJ	3 (7.1%)
Gastric	23 (54.8%)
Small Intestine	8 (19.0%)
Colon	0 (0%)
Rectal	8 (19.0%)
Tumour Size at Diagnosis	
<2cm	0 (0%)
2-5cm	3 (7.1%)
5-10cm	26 (61.9%)
>10cm	13 (31.0%)
Mitotic Count (/50 HPF)	
≤5	16 (38.1%)
6-10	2 (4.8%)
>10	7 (16.7%)
Not reported	17 (40.1%)
NIH Risk Category	
Very Low	0 (0%)
Low	0 (0%)
Intermediate	9 (21.4%)
High	31 (73.8%)
Indeterminate	2 (4.8%)
Molecular Pathology	
c-KIT exon 9 mutation	2 (4.8%)
c-KIT exon 11 mutation	23 (54.8%)
c-KIT exon 13 mutation	1 (2.4%)
PDGFRA exon 18 mutation	3 (7.1%)
No c-KIT/PDGFRA mutation identified	2 (4.8%)
Data not available	11 (26.0%)

P472. Preoperative Inflammatory Biomarkers Prognostic Index (IBPI) as a prognostic score in Extremity and Superficial Trunk Soft Tissue Sarcomas.

Marco Fiore, FACS, FEBS[1]; Silva Ljevar[2]; Marco Baia[3]; Daniele Morelli[4]; Dario Callegaro, MD[5]; Chiara Colombo[6]; Stefano Radaelli[7]; Rosalba Miceli[8]; Alessandro Gronchi[9]
[1]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [2]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [3]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [4]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [5]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [6]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [7]Fondazione IRCC Istituto Nazionale dei Tumori, Milan, IT; [8]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT; [9]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, IT

INTRODUCTION: An Inflammatory Biomarkers Prognostic Index (IBPI) including neutrophil-to-lymphocyte ratio (NLR), monocytes, hemoglobin, and platelets-to-lymphocyte ratio (PLR) has been designed for retroperitoneal sarcoma and used as readily available prognostic tool for overall survival in addition to the Sarculator nomogram. We aimed to test the same inflammation-related index in extremity and superficial trunk soft tissue sarcoma (ESTS). **METHODS:** All consecutive patients with primary localized ESTS operated between 2008 and 2017 were included. Preoperative hemoglobin, monocytes, NLR, PLR were retrieved and analyzed both individually and combined into a prognostic index (IBPI). Correlation with clinicopathologic variables was studied, as well as postoperative morbidity according to IBPI risk categories. The association between overall survival (OS), distant metastasis crude cumulative incidence (DM-CCI) and biomarkers and, in addition, the Sarculator linear predictor for 5-yr OS/DM (lpOS/DM) was analyzed using univariable and multivariable Cox models. **RESULTS:** In the study period 1232 patients were identified. Of them 1215 had complete data. The median follow-up was 84.9 months. The median NLR was 2.7 (IQR, 1.9–4.0). 475 (39%) had an IBPI score of 1; 483 (40%) of 2; 200 (16%) of 3; 57 (4.7%) of 4. None had IBPI=0. Among considered biomarkers Hemoglobin and PLR independently predicted OS (Hemoglobin: OR 0.78; 95%CI 0.63-0.94, P .0152; PLR: OR 1.66, 95%CI 1.09-2.51, P .0356). The IBPI showed good discrimination for subgroups at different OS (log-rank test P < .0001), and this was also significant for DM-CCI (Figure 1). 5-year OS was 89.7% (95% CI 86.9-82.6%) for IBPI=1, 80.5% (76.9.84.2%) for IBPI=2, 61.0% (54.3-68.5%) for IBPI=3 and 56.8% (44.9-71.8%) for IBPI=4. The multivariable Cox model showed that IBPI remained significant even after inclusion of the Sarculator lpOS (p-value <.0001) e lpDM (p-value <.0001). IBPI was also associated with the risk of serious postoperative complications (P < .001). **CONCLUSIONS:** IBPI is an independent prognostic factor for OS also in extremity and superficial trunk STS, as well as distant metastasis and severe complications. IBPI values tend to be higher than in retroperitoneal sarcoma. This inflammatory index may

be used as a readily available tool based on preoperative routine blood test to predict surgical morbidity and complement the prognostic prediction of the Sarculator nomogram in ESTS.

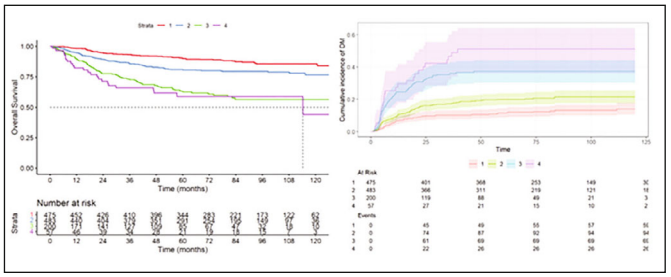


Figure 1. Overall Survival from surgery and Distant metastasis crude cumulative Incidence, according to preoperative IBPI score.

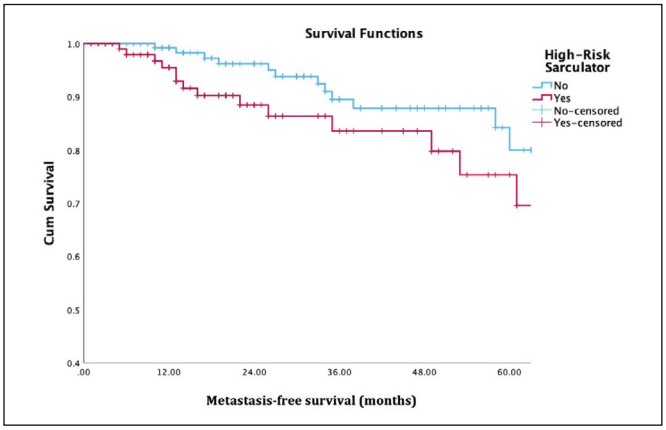
P473. Prognostic Indicators of Early Metastasis in Soft Tissue Sarcomas: The Impact of Sarculator in Patient StratificationSoft tissue sarcomas (STS) are rare tumors, representing 1-2% of all solid malignancies, with an incidence of 1.8 to 5 cases per 100,000 p

Dorian Yarih Garcia-Ortega, MD, PhD[1]; Maria Isabel Hernandez Salcedo[2]; Ana Paulina Melendez-Fernandez[3]; Sylvia Veronica Villavicencia-Valencia[4]; Itzel Elizabeth Vidal-Sánchez[5]; Gabriela Concepcion Alamilla-Garcia[6]

ROC curve for comparing performance between the models is shown on the right panel.

[1]National Cancer Institute (Mexico), Tlalpan, Ciudad de México, MX; [2]National Cancer Institute (Mexico), Tlalpan, MX; [3]National Cancer Institute (Mexico), Tlalpan, MX; [4]National Cancer Institute (Mexico), Tlalpan, MX; [5]National Cancer Institute (Mexico), Tlalpan, MX; [6]National Cancer Institute (Mexico), Tlalpan, MX

INTRODUCTION: Soft tissue sarcomas (STS) are rare tumors, representing 1-2% of all solid malignancies, with an incidence of 1.8 to 5 cases per 100,000 per year. Typically presenting at a median age of 54 years, STS affects the extremities in 60% of cases and the trunk in 10%. Histologically, over 150 subtypes exist, with liposarcoma, pleomorphic undifferentiated sarcoma, and leiomyosarcoma being the most common. Early metastasis, defined as occurring within 12 months, significantly impacts overall survival. While various prognostic factors are known, risk factors for early metastasis remain understudied. **METHODS:** This retrospective, observational cohort study included 182 patients diagnosed with STS of the extremities and trunk between 2010 and 2020. Inclusion criteria involved patients aged 18 years or older with histologically confirmed STS, excluding those with metastatic disease at diagnosis. Variables such as histological subtype, tumor size, grade, and resection margins were evaluated. The Sarculator nomogram was utilized to predict survival and stratify patients into risk groups. Early metastasis was defined as metastasis occurring within 12 months post-treatment. **RESULTS:** Among the 182 patients, the median age was 54 years, with the most common histological subtypes being pleomorphic undifferentiated sarcoma (28%), leiomyosarcoma (12%), and synovial sarcoma (10%). Most tumors were located in the lower extremities (65%); the mean tumor size was 24.86 cm (SD: 10.50 cm). High-grade (G3) and deep-seated tumors were significantly associated with early metastasis ($p<0.01$). Early metastasis occurred in 26% of patients, primarily affecting the lungs (71%), followed by bone (17%) and lymph nodes (6%). Patients with early metastasis had poorer overall survival than those without metastasis (median survival of 21.5 vs. 89.1 months, $p<0.01$). Sarculator effectively stratified patients by risk, with high-risk patients (predicted survival <60%) demonstrating a higher rate of early metastasis (32%) compared to low-risk patients (12%) ($p<0.001$). Sarculator's predictive accuracy for early metastasis was 82%, aiding in more precise follow-up and adjuvant treatment decisions. **CONCLUSIONS:** Critical factors associated with early metastasis in STS include large tumor size, high histological grade, and deep-seated location. Sarculator proved valuable in stratifying high-risk patients, enabling clinicians to adopt personalized treatment strategies. However, further refinement of nomograms may improve the prediction of early metastatic events, potentially enhancing patient outcomes.



P474. Wild type vs. non-wild type gastrointestinal stromal tumors of gastric and small bowel origin: are tumor-specific factors associated with overall survival?

Shruthi R Perati, MD[1]; Bima J Hasjim, MD[2]; Rachael Lowney, MD[3]; Oliver S Eng, MD[4]; Andrew M Blakely, MD[5]

[1]National Institutes of Health/National Cancer Institute, Bethesda, MD, US; [2]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [3]National Institutes of Health/National Cancer Institute, Bethesda, MD, US; [4]Division of Surgical Oncology, Department of Surgery, University of California Irvine Medical Center, Orange, CA, US; [5]National Institutes of Health, Bethesda, MD, US

INTRODUCTION: Wild type (WT) and non-WT gastrointestinal stromal tumor (GIST) are distinct entities with unique medical treatment paradigms. Yet, the Modified National Institutes of Health (NIH) Criteria, which account for tumor size, mitotic rate, and gastric vs. non-gastric origin, are used to estimate recurrence risk for all GISTs. We sought to evaluate whether tumor-specific factors may correlate with OS outcomes for patients with WT GIST of gastric or small bowel origin. **METHODS:** This was a retrospective analysis of cases of gastric and small bowel GISTs in the National Cancer Database (NCDB), 2009-2019. WT GISTs were defined as tumors lacking *KIT* or *PDGFRA* mutations. Anatomic origin approximated WT GIST subtype, as gastric WT GIST is predominantly SDH-deficient, whereas small bowel WT GIST are largely *NF1*-mutant. Univariable and multivariable Cox proportional hazard regression analyses were performed to identify associated risk factors with OS. **RESULTS:** Among 33,365 patients with GIST, 231 (0.7%) were WT. Compared to patients with non-WT GIST, those with WT GIST were younger (median age 60 years [IQR 49-69] vs 65 years [IQR 56-74]; $p<0.001$) and more likely male (57% vs 50%, $p=0.043$), non-Hispanic White (71% vs 64%, $p=0.001$), and privately insured (49% vs 40%, $p=0.001$). WT GISTs arose from the stomach less frequently (59% vs 71%, $p<0.001$) and had lower mitotic rate (≤5 mitoses per 5 mm2: 63% vs. 38%, $p<0.001$), but were more multifocal (15% vs 4%, $p<0.001$) and larger (>5 cm in size: 57% vs 46%, $p=0.001$). Patients with WT GIST had higher rates of lymph node involvement (6% vs 2%, $p<0.001$) and distant metastasis (10% vs 5%, $p<0.001$). OS of WT vs non-WT GIST patients was not significantly different for both gastric and small bowel primary tumors. On multivariable subset analysis of WT GIST, tumor size and mitotic count were not associated with OS of patients with gastric WT GIST. In contrast, among patients with small bowel WT GIST, both mitotic count (>5 mitoses per 5 mm2: HR 9.9, [2.6-37.9], $p=0.001$) and tumor size (diameter >10 cm: HR 14.8, [1.7-129.5], $p=0.015$) were independently associated with OS. **CONCLUSIONS:** Patients with non-WT or WT GIST had similar OS. Upon stratification of WT GISTs by site (gastric vs small bowel), increased size and mitotic count were associated with OS among patients with small bowel WT GIST, but not for those with gastric WT GIST. This suggests that WT GIST, and in particular those that are SDH-deficient (gastric primaries), may have a distinct biology from non-WT GIST.

Table 1. Cox-regression analysis of tumor-specific factors predicting overall survival of wild type GIST patients with gastric and small bowel primary tumors.

		Wild Type GIST (Multivariable hazard ratios, confidence interval, p-value)		
		Overall	Gastric primary	Small bowel primary
Size (diameter) of primary tumor	<5cm	-	-	-
	5-10cm	1.38 (0.64-2.99, p=0.412)	0.50 (0.17-1.49, p=0.213)	5.90 (0.93-37.32, p=0.059)
	>10cm	2.32 (1.05-5.12, p=0.038)	0.88 (0.27-2.90, p=0.836)	14.75 (1.68-129.51, p=0.015)
Mitotic rate of primary tumor	5 or fewer mitoses	-	-	-
	>5 mitoses	3.53 (1.86-6.70, p<0.001)	2.05 (0.76-5.52, p=0.154)	9.89 (2.58-37.94, p=0.001)
Multifocal disease at presentation	Yes	-	-	-
	No	1.23 (0.47-3.19, p=0.670)	0.79 (0.15-4.29, p=0.788)	1.70 (0.18-16.30, p=0.644)
	Not specified	1.43 (0.44-4.62, p=0.549)	1.25 (0.16-9.87, p=0.835)	2.50 (0.12-50.56, p=0.550)
Clinical nodal stage	cN0	-	-	-
	cN1	1.70 (0.54-5.34, p=0.366)	1.05 (0.21-5.41, p=0.950)	28.70 (0.82-1000.97, p=0.064)
	cNX	1.40 (0.46-4.30, p=0.556)	1.13 (0.22-5.72, p=0.881)	2.54 (0.24-26.77, p=0.437)
Clinical metastasis stage	cM0	-	-	-
	cM1	2.16 (1.00-4.68, p=0.051)	2.44 (0.71-8.39, p=0.156)	2.10 (0.32-13.56, p=0.437)

P475. Management for N2-positive Non-small Cell Lung Cancer in the Military Health System

Andrew Marthy, MD[1]; Sarah Darmon, PhD[2]; Yvonne Eaglehouse, PhD, MPH[3]; Jie Lin, PhD, MPH[4]; Craig Shriver, MD, FACS[5]; Kangmin Zhu, PhD[6]
[1]Albany Medical Center, Albany, NY, US; [2]Uniformed Services University of the Health Sciences, Bethesda, MD, US; [3]Uniformed Services University of the Health Sciences, Bethesda, MD, US; [4]Uniformed Services of the Health Sciences, Bethesda, MD, US; [5]Uniformed Services University of the Health Sciences, Bethesda, MD, US; [6]Uniformed Services University of the Health Sciences, Bethesda, MD, US

INTRODUCTION: The management of locally advanced (N2) Non-small Cell Lung Cancer (NSCLC) continues to evolve, with an increasing use of multi-modality therapy. We investigated the management of mediastinal positive NSCLC in association with overall survival, among beneficiaries of the U.S. Military Health System (MHS). **METHODS:** We used the MilCanEpi database, which contains information on patients diagnosed or treated for cancer from the Department of Defense's cancer registry and medical encounter data, to study patients diagnosed with pathologically confirmed NSCLC and positive mediastinal nodes (pN2). Patient demographics, co-morbidities, and cancer treatment were examined. Patients were stratified into 3 groups for statistical analysis, those who received chemotherapy only, surgery only, or multi-modality therapy, specifically neoadjuvant or adjuvant chemotherapy with surgical resection. Cox regression was performed to assess the impact of therapeutic management on survival. **RESULTS:** Among 753 patients with pN2 disease, 436 patients had chemotherapy only, 289 patients had surgery only, and 78 patients had multi-modality therapy (chemotherapy and surgery). The case fatality rate was 76.6 %. Logistic regression analysis revealed no significant differences in race and ethnicity as well as age and comorbidity index between surgery only and chemotherapy, or multi-modality treatment and chemotherapy, respectively . Women were more likely than men to receive multi-modality therapy (aOR= 2.30, 95% CI= 1.33-4.00). In survival analysis, surgical resection alone (aHR= 0.81, 95% CI= 0.66-0.99) and multi-modality therapy (aHR = 0.66, 95% CI= 0.45-0.96) were associated with improved survival when compared with definitive chemotherapy. However, women had an improved survival than men (aHR= 0.71, 95% CI= 0.59-0.87), while patients of Hispanic ethnicity had an associated worse survival than non-Hispanics (aHR= 1.64, 95% CI= 1.08-2.50) when controlled for treatment received and other potential confounders. **CONCLUSIONS:** Although national guidelines recommend neoadjuvant chemotherapy for positive mediastinal disease in NSCLC, there remain areas for quality improvement for ensuring guideline directed care. As demonstrated, multi-modality therapy for N2 disease is associated with improved survival and represents an important treatment paradigm for beneficiaries of the MHS. We also found no racial differences between different treatment modalities, demonstrating universal access to care in the DoD on reducing racial disparities found in the private health care system.

Table 3. Overall survival analysis

Characteristic	Alive (N = 204)	Dead (N = 549)	aHR
Treatment	No. (%)	No. (%)	
Chemo Only	84 (19.3)	351 (80.7)	1.00 (reference)
Surgery	78 (32.0)	166 (68.0)	0.81 (0.66, 0.99)
Surgery with Chemo	42 (57.5)	31 (42.5)	0.66 (0.45, 0.96)
Age at Diagnosis			
18-54	44 (38.9)	69 (61.1)	0.79 (0.60, 1.05)
55-64	76 (26.6)	210 (73.4)	1.00 (reference)
65-74	64 (27.1)	172 (72.9)	1.06 (0.87, 1.31)
75+	20 (17.1)	97 (82.9)	1.23 (0.96, 1.57)
Sex			
Men	117 (23.0)	392 (77.0)	1.00 (reference)
Women	87 (35.8)	156 (64.2)	0.71 (0.59, 0.87)
Marital Status			
Married	155 (26.5)	430 (73.5)	1.00 (reference)
Not Married	49 (29.3)	118 (70.7)	0.93 (0.75, 1.16)
Race			
White	142 (25.0)	427 (75.0)	1.00 (reference)
Black	31 (30.1)	72 (69.9)	0.87 (0.67, 1.13)
Other/Unknown	31 (38.8)	49 (61.3)	0.92 (0.68, 1.25)
Ethnicity			
Not Hispanic	174 (26.5)	482 (73.5)	1.00 (reference)
Hispanic	6 (20.0)	24 (80.0)	1.64 (1.08, 2.50)
Unknown	24 (36.4)	42 (63.6)	0.85 (0.62, 1.18)
Grade			
I	8 (30.8)	18 (69.2)	0.79 (0.48, 1.30)
II	54 (35.1)	100 (64.9)	0.77 (0.60, 1.00)
III	59 (26.6)	163 (73.4)	1.00 (reference)
IV	3 (25.0)	9 (75.0)	1.01 (0.51, 2.01)
Unknown	80 (23.7)	258 (76.3)	1.03 (0.84, 1.26)
Elixhauser Comorbidity			
0	176 (27.5)	463 (72.5)	1.00 (reference)
1-2	13 (24.1)	41 (75.9)	1.25 (0.90, 1.74)
3+	15 (25.4)	44 (74.6)	1.27 (0.93, 1.75)
Care Source of Diagnosis			
Direct	100 (21.5)	365 (78.5)	1.00 (reference)
Private Sector	104 (36.2)	183 (63.8)	0.73 (0.61, 0.88)

P476. Mediastinal Lymph Node Positivity in Patients Undergoing Robotic Esophagectomy

Maren Thomas, MS[1]; Jamie Huston, MS[2]; Ravi Shridhar[3]; Kenneth Meredith[4]
[1]Florida State University, Sarasota, FL, US; [2]Sarasota Memorial Healthcare System, Sarasota, FL, US; [3]Advent Health, Orlando, FL, US; [4]Sarasota Memorial Health Care System, Sarasota, FL, US

INTRODUCTION: Esophageal cancer is increasing in incidence worldwide. Robotic approaches have quickly become mainstream due to the improved visualization and possible increase in nodal harvest. There remains significant debate on the utility of mediastinal lymph node dissection in esophageal cancer patients. We sought to analyze the incidence of mediastinal lymph node positivity and to evaluate its impact on survival in patients with esophageal cancer undergoing robotic assisted trans-thoracic esophagectomy (RATE). **METHODS:** Utilizing a prospectively maintained esophageal database, we identified patients who were diagnosed with EC and underwent RATE between 2009-2024. We then identified patients with positive lymph nodes and stratified by location (celiac or mediastinal). Baseline univariate comparisons were made for continuous variables using both the Mann-Whitney U and Kruskal Wallis tests. Pearson's Chi-square test was used to compare categorical variables. Survival analysis was performed via Kaplain-Meier method. **RESULTS:** We identified 201 patients who underwent RATE with a median age of 70 (41-91). There were 160 (79.6%) males and 41 (20.4%) females. The mean BMI was 26.5 ± 5.5 and mean ASA score was 3.1 ± 0.6. Adenocarcinoma was the predominate histology at 162(80.6%). Locally advanced T3/T4 tumors were identified in 53 (26.4%) patients and 63(31.3%) had clinical node + disease. Neoadjuvant therapy was utilized in 159(79.1%) patients. The median lymph nodes resected 18 (14 – 22), and length of hospitalization 8 (7 – 11) days. The 30 and 90-day mortality were 2.2% and 2.6% respectively. R0 resections was performed in 200 (99.5%) of patients and the pathologic complete response rates were 42.1%. The incidence of mediastinal lymph node positive was 6.3% vs 76.3% abdominal. There were 17.6% of patients that had both mediastinal and abdominal lymph nodes positive. The median survival was 23 months for abdominal LN+, 19.5 months for mediastinal LN+ p=0.23. Multivariate analysis revealed that age, neoadjuvant radiation, nodal positivity were predictors of survival. **CONCLUSIONS:** The incidence of mediastinal positive lymph nodes are much higher than previously reported. Perhaps the improved visualization and manipulation of tissue with robotic approaches have enhanced our ability to resect these nodes. Mediastinal lymph node positivity is a poor prognostic

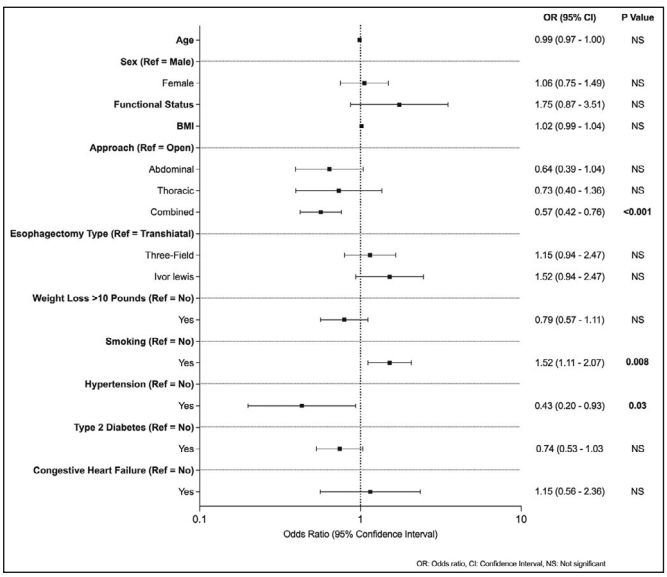
factor for survival in patients undergoing robotic esophagectomy. Given these findings, we would continue to support aggressive nodal resection in patients diagnosed with esophageal cancer.

P477. The Minimally Invasive Approach confers Improved Outcomes in Frail Cancer Patients Undergoing Esophagectomy

Amr I. Al Abbas, MD[1]; Morgan F Pettigrew[2]; Jennie Meier[3]; Raghav Chandra, MD[4]; Sam Wang, MD[5]; Scott I. Reznik[6]; Inderpal Sarkaria[7]; Herbert J Zeh, MD[8]; Matthew Porembka, MD[9]

[1]UT Southwestern Medical Center, Dallas, TX, US; [2]UT Southwestern, Irving, TX, US; [3]UT Southwestern, Dallas, TX, US; [4]UT Southwestern Medical Center, Dallas, TX, US; [5]UT Southwestern Medical Center, Dallas, TX, US; [6]UT Southwestern Medical Center, Dallas, TX, US; [7]University of Texas Southwestern Medical Center, Dallas, TX, US; [8]UT Southwestern Medical Center, Dallas, TX, US; [9]UT Southwestern Medical Center, Dallas, TX, US

INTRODUCTION: The rates of morbidity and mortality after esophagectomy have improved. More surgeons are offering older and more frail patients resection. While these patients are known to have higher complications, the impact of the minimally invasive approach (MIE) is unknown. In this work, we aim to evaluate the impact approach on outcomes in frail cancer patients. **METHODS:** Elective non-emergent esophagectomies from the 2016-2022 American College of Surgeons National Surgical Quality Improvement Project Esophagectomy-specific Participant User File (PUF) were included. Patients were considered frail if their modified frailty score (mFI-5) was greater than or equal to 2. Outcomes included mortality, any complication, major complication, prolonged length of stay (pLOS), non-home discharge and leak. **RESULTS:** A total of 7,887 elective non-emergent esophagectomies were performed. Only, 1,462 were considered frail and after excluding benign etiologies,246 patients entered the analysis. Of these, 173 (14.1%) were trans-hiatal (THE), 874 (71.2%) were Ivor-Lewis (ILE) and 179 (14.6%) were three-field (MCK). In terms of operative approach, 533 (55.4%) were completely MIE, whereas 139 (13.5%) had some MIE component and 289 (30%) were open. Postoperatively, patients undergoing completely MIE had lower rates of any complication, major complication and pLOS (P<0.05). On multivariable analysis, undergoing completely MIE was independently associated with lower odds of any complication (OR: 0.64, 95% CI: 0.47-0.89), and major complication (OR:0.63, 95% CI: 0.46-0.87). **CONCLUSIONS:** MIE conferred lower rates of complications in frail patients undergoing esophagectomy for cancer. Minimally invasive esophagectomy may be of benefit to frail cancer patients and efforts should be made to investigate this in prospective randomized studies.



P478. Turning the Clock Back: Seven Year Experience of Pulmonary Metastatectomy from a Single Centre

John J Alapatt, MS (General surgery), Dr NB Surgical Oncology), FEBS, MRCS (Edinburgh)[1]

[1]MVR Cancer Centre and Research Institute, Kozhikode, Kerala, IN

INTRODUCTION: Pulmonary metastatectomy is a accepted treatment option for patients who develop metastases in the lung from a wide range of solid tumors. The oligometastatic paradigm in a subset of solid tumors provide a therapeutic opportunity to offer a potential for longer overall survival and sometimes even cure. In this study we describe our seven year tryst with pulmonary metastatectomy and assessed the survival outcomes and the prognostic factors which impacted survival in our patients. **METHODS:** We did a retrospective cohort study of all patients who underwent pulmonary metastatectomy in our tertiary care cancer centre from April 2017 – January 2024. All patients who defaulted treatment and who were lost during follow up were excluded from the study. The parameters analysed were the primary site of tumour, disease free interval, number of metastases, margins of resection, mediastinal nodes and the survival. The analysis was carried out using IBM SPSS version 25. **RESULTS:** The total number of patients included in the study were 80.The mean age of the patients was 50 years. The most common primary site of tumour in the study was colorectal, n= 34 (42.5%) followed by soft tissue sarcoma, n= 21 (26.2 %).The disease free interval was less than 1 year in 26 patients (32.5%) and more than 1 year in 54 patients (67.2%).The majority of cases, 62 patients (77.1%) had a solitary site of metastases. The most common procedure done was a wedge resection in 68 patients (85%). We achieved R0 resection in 77 patients (96.3%).The median tumour size was 1.5 cm. The median duration of hospital stay was 3 days and only two patients developed Clavien Dindo Grade 3 complications. There was no post operative mortality in the entire group of patients. The median duration of follow up was 22.9 months. The median survival of patients with colorectal primary and sarcoma was 48 and 36 months respectively. On further analysing individual predictors for prognostic significance and impact on survival ,the site of primary and tumour size, showed a trend towards significance. In the group 41 patients (50%) had a recurrence, out of which 2 patients underwent a repeat metastatectomy. **CONCLUSIONS:** Pulmonary metastatectomy has the potential to prolong survival and this procedure can be done safely with low morbidity and a short hospital stay in a established and dedicated thoracic unit. The key points in this intervention are preserving maximum lung parenchyma (by wedge resection as margins do not affect the prognosis) and careful patient selection (longer DFI, smaller tumor sizes and a favourable primary site).

CHARACTERISTICS	PERCENTAGE
Disease Free Interval < 1 year	32.8
Disease Free Survival >1 year	67.2
Solitary tumor	77.1
Metastasectomy	85
Lobectomy	15
Synchronous	20
Staged Metastasectomy	11
Negative final Histopathology	17.5
Median tumor size	1.5cm
R 0 Resection	96.3
Mediastinal Sampling	6
Mediastinal node Positivity	2
Median duration of hospital stay	3 days
Post operative complications	2
Post operative mortality	0

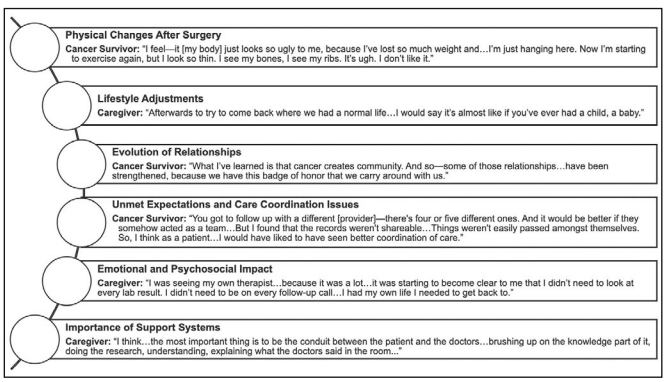
P479. Understanding the "new normal": A thematic analysis of patient and caregiver perspectives on challenges faced in recovery after esophagectomy

Steven Tohmasi, MD, MPHS[1]; Meera Muthukrishnan, PhD, MPH[2]; Nikki E. Rossetti, MD, MSc.[3]; Mary C. Politi, PhD[4]; Brendan T. Heiden, MD, MPHS[5]; Whitney S. Brandt, MD[6]; Varun Puri, MD, MSCI[7]; Benjamin D. Kozower, MD, MPH[8]; Aimee James, PhD, MPH[9]; Bryan F. Meyers, MD, MPH[10]

[1]Washington University School of Medicine, St. Louis, MO, US; [2]Washington University School of Medicine, St. Louis, MO, US; [3]Washington University

School of Medicine, St. Louis, MO, US; [4]Washington University School of Medicine, St. Louis, MO, US; [5]Washington University School of Medicine, St. Louis, MO, US; [6]Washington University School of Medicine, St. Louis, MO, US; [7]Washington University School of Medicine, St. Louis, MO, US; [8]Washington University School of Medicine, St. Louis, MO, US; [9]Washington University School of Medicine, St. Louis, MO, US; [10]Washington University School of Medicine, St. Louis, MO, US

INTRODUCTION: Esophagectomy can impact patients' health-related quality of life (HR-QOL). We explored physical and psychosocial challenges faced by patients and caregivers following esophagectomy to identify intervention targets for improving the recovery process. **METHODS:** We conducted semi-structured interviews with esophageal cancer survivors and caregivers to explore their recovery experiences after esophagectomy. We used purposive sampling to recruit adult participants from our institution and the Esophageal Cancer Education Foundation, an organization that hosts support groups for adults affected by esophageal cancer. Open-ended interview questions explored perceived changes in HR-QOL and coping strategies for overcoming postoperative challenges. Interviews were audio-recorded and transcribed verbatim. Two trained qualitative research experts conducted interviews, inductively coded transcripts, and used thematic analysis to identify relevant themes and representative quotes. **RESULTS:** We interviewed 10 cancer survivors and 9 caregivers. Emerging themes and representative quotes are shown in Figure 1. Survivors reported significant lifestyle changes after surgery, including strict dietary monitoring, physical activity challenges, sleep disruption, altered responsibilities, and difficulty maintaining normalcy in hobbies/work. Body image concerns were prevalent, with survivors expressing sadness over eating difficulties, weight changes, and altered self-perception. Participants reported having unclear expectations after surgery, leading to increased stress, and they suggested the need for clearer communication about post-surgery expectations and improved care coordination to address ongoing needs. Caregivers played a crucial role during recovery by providing physical and emotional support and serving as patient advocates. Survivor and caregiver relationships evolved after surgery, with survivors feeling increased dependence on caregivers and caregivers taking on new emotional burdens. The psychological challenges faced by participants after surgery include fear of cancer recurrence and loss of control after surgery. Participants mentioned that support groups provide valuable information, psychological benefits, and foster a sense of community. **CONCLUSIONS:** Survivorship care after esophagectomy should encompass a comprehensive, multidisciplinary approach to address the complex physical and psychosocial needs of patients and their caregivers.

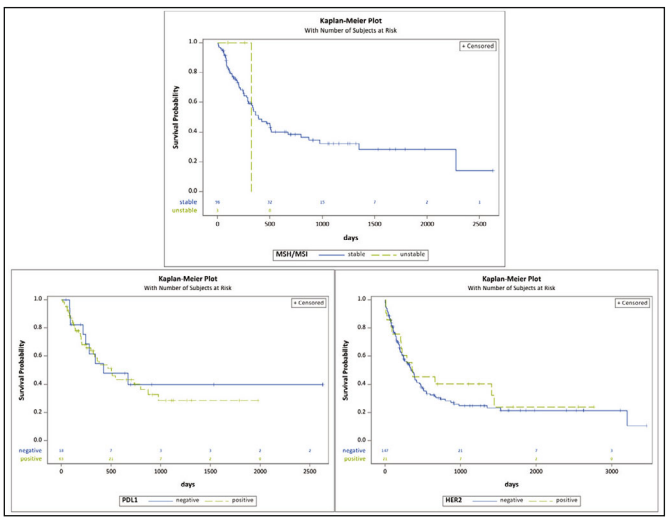


P480. Clinicopathologic and prognostic significance of biomarker expression in gastric cancer in a predominately Hispanic population

Ashley Montgomery, DO[1]; Chen-Pin Wang[2]; Alexander A. Parikh, MD, MPH[3]; Caitlin A McIntyre[4]; Colin M Court[5]; Mio Kitano, MD, MPH[6]

[1]Mays Cancer Center, University of Texas Health San Antonio, San Antonio, TX, US; [2]Univeristy of Texas Health Science Center, San Antonio, TX, US; [3]University of Texas Health Science Center San Antonio MD Anderson Cancer Center, San Antonio, TX, US; [4]University of Texas Health Science Center San Antonio, San Antonio, TX, US; [5]University of Texas Health Science Center San Antonio, San Antonio, TX, US; [6]University of Texas Health San Antonio, San Antonio, TX, US

INTRODUCTION: Identification of molecular biomarkers in gastric adenocarcinoma (GC) has led to marked advancements in targeted therapy. The prevalence and prognostic significance of biomarkers within Hispanic population has not been well defined. In this study, the expression of human epidermal growth factor receptor 2 (HER2), programmed cell death ligand 1 (PD-L1), and microsatellite instability (MSI) were investigated to define the prevalence, clinicopathologic characteristics, and outcomes in a predominately Hispanic population. **METHODS:** The immunohistochemistry profile of HER2, PD-L1, and MSI in a prospective cohort of 174 patients from a single institution were analyzed and the prevalence of each biomarker was defined. The association between the biomarker expression with demographics, clinicopathologic status, and outcomes were analyzed utilizing chi-squared test, Fishers exact test, or 2-sample T-test as appropriate. Kaplan-Meier curve and Cox proportional hazards model were performed to determine the influence of HER2, and MSI on survival time. **RESULTS:** Of the 174 patients, 81% (140) identified as Hispanic. The prevalence of biomarker expression was identified as 12.5% for HER2, 78% for PD-L1, and 3% for MSI-H. Analysis did not identify an association between age, gender, histologic subtype, tumor location, nodal status, or clinical staging with PDL-1 or MSI-H expression. An association between HER-2 and a higher incidence of moderately differentiated subtype was identified ($p<0.001$). Within the Hispanic subgroup, the mean age at diagnosis was 57 years-old, 51% were male, 73% had poorly differentiated histology, 73% had nodal positive disease, and 74% were late stage (III-IV). HER2 expression and lack of PDL-1 expression showed trends towards higher survival probability, however, none of the biomarkers were significant on the Cox model. **CONCLUSIONS:** HER2 expression was lower in this population than documented in literature among predominantly Caucasian and Asian populations, 12.5% vs 22%. PDL-1 expression was higher at 78% vs 12-73% and MSI-H was comparable at 3% vs 4%. The only relationship identified with biomarker expression and clinicopathologic status was HER2 status and histologic grade. Biomarker expression appears independent of clinicopathologic status. Immune checkpoint inhibitors may be promising therapeutic option in this population with GC with high PD-L1 expression. As immune checkpoint inhibitors are relatively new therapy for GC, further longitudinal studies are needed to elucidate long-term outcomes.



P481. Factors Associated with Surgery Refusal in Patients with Stage I-III Esophageal Cancer and Their Effect on Survival

Luke Guy[1]; Malek Moumne[2]; Gustavo Capo[3]; Yagni Patel[4]; Carter Quinn[5]; Jonathan Palmer[6]; Sohawm Sengupta[7]; Ryan Quisling[8]; Alicia Arnold[9]; Steven Colquhoun[10]; Daniel Milgrom[11]; Danny Yakoub[12]

[1]Medical College of Georgia, Augusta, GA, US; [2]Medical College of Georgia, Augusta, GA, US; [3]Medical College of Georgia, Augusta, GA, US; [4]Medical College of Georgia, Augusta, GA, US; [5]Medical College of Georgia, Augusta, GA, US; [6]Medical College of Georgia, Augusta, GA, US; [7]Medical College of georgia, Augusta, GA, US; [8]Medical College of Georgia, Augusta, GA, US; [9]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US; [10]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US; [11]Wellstar Medical College of Georgia at Augusta University, Augusta, GA, US; [12]Surgical Oncology Clinical Outcomes Research Group (SOCORG), Division of Surgical Oncology, Departme, Augusta, GA, US

INTRODUCTION: Surgery remains a primary treatment for non-metastatic EC, but many patients refuse. We investigated factors linked to surgery refusal and its impact on overall survival (OS). **METHODS:** The NCDB (2004-2019) was queried for patients with stage I-III EC who were recommended surgery. Patients who underwent surgery were compared to those who refused it. Logistic regression was used to identify predictors of surgery refusal. Propensity-scored matching (PSM) produced comparable groups regarding demographics, disease characteristics, and treatment. Kaplan-Meir and Log-Rank analysis determined the effect of surgery refusal on OS. A Cox-Proportional Hazard Model was used to investigate factors influencing OS. **RESULTS:** Among 51,215 patients recommended for surgery, 2,192 (4.3%) refused. Multivariate logistic regression revealed several factors associated with an increased probability of surgery refusal: age over 50 (OR=2.38), female sex (OR=1.31), non-Hispanic black race (OR=1.69), a Charleson Deyo comorbidity score (CDCS) of 2 or greater (OR=1.23), treatment in a non-academic center (OR=1.79), opting for palliative care (OR=2.57), radiation refusal (OR=2.46), chemotherapy refusal (OR=7.72) stage II (OR=1.24) and III disease (OR=1.23). Factors associated with a decreased probability of surgery refusal included patients with private insurance (OR= 0.41), median income $63,333 + (OR=0.67), southern residence (OR= 0.74), midwestern residence (OR= 0.88), distance from care 50-200 (OR =0.48), tumors in the middle (OR= 0.55), and lower third of the esophagus (OR= 0.41). All variables met statistical significance (P<0.01). Kaplan-Meier and Log-Rank analysis of PSM groups showed decreased OS for those refusing surgery across all stages: Stage I [57.6 vs 22.3 mos. HR=1.88, P<0.01], Stage II [36.61 vs 25.24 mos. HR=1.39, and Stage III [23.71 vs 22.2 mos. HR=1.18, P<0.01]. In the multivariate survival analysis for patients that refused surgery, CDCS 2+ (HR=1.23), non-academic center (HR=1.16), stage II (HR=1.23) and III (HR=1.39), tumor size (2-4 cm HR=1.36; 4+ cm HR=1.54), opting for palliative care (HR=1.62), and refusal of radiation (HR=2.05) were linked to decreased OS. Non-Hispanic black race (HR=0.77) and private insurance (HR=0.70) were associated with improved OS (P<0.01). **CONCLUSIONS:** Surgery is associated with improved OS in stage I-III EC, and patients should be counseled as such. Interventions should address factors related to surgery refusal to improve outcomes.

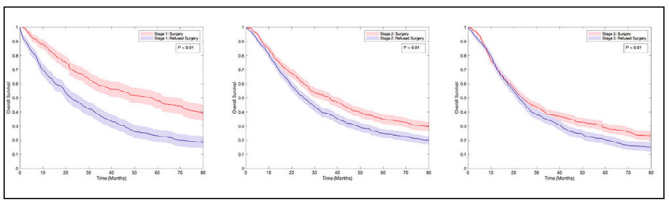


Figure 1. Overall Survival for Stage I-III Esophageal Cancer among patients who underwent vs refused surgery

P482. Gastric Cancer among California's Hispanic Population: Highlighting Epidemiological Disparities

Amir Ashraf Ganjouei[1]; Carlos U. Corvera, MD[2]; Mohamed A. Adam, MD[3]; June S. Peng, MD[4]; Eric K. Nakakura, MD, PhD[5]; Kenzo Hirose, MD[6]; Ajay Maker, MD[7]; Adnan Alseidi[8]; Lucas W. Thornblade, MD, MPH[9]

[1]University of California San Francisco, San Francisco, CA, US; [2]University of California, San Francisco, San Francisco, CA, US; [3]University of California, San Francisco, San Francisco, CA, US; [4]University of California, San Francisco, San Francisco, CA, US; [5]University of California, San Francisco, San Francisco, CA, US; [6]University of California, San Francisco, San Francisco, CA, US; [7]University of California San Francisco, San Francisco, CA, US; [8]University of California San Francisco, San Francisco, CA, US; [9]University of California, San Francisco, San Francisco, CA, US

INTRODUCTION: Recent reports indicate a shift in the epidemiology of gastric cancer in the United States, with marked disparities in incidence and mortality among ethnic and racial groups. Notably, there is an increasing trend in the incidence rates among young and Hispanic patients. This study investigates this trend specifically among patients in California. **METHODS:** A retrospective cohort study of adults with gastric adenocarcinoma was conducted using the California Cancer Registry (2000-2020). Incidence rates were calculated among age and racial groups. Joinpoint regression was employed to compute the annual percent change (APC) in cancer incidence. Multivariable Cox regression was utilized to examine overall survival. **RESULTS:** Of 53,595 patients with gastric cancer, the percentage of Hispanic patients rose from 22.5% to 35.6%, (APC 2.2%, p<0.001) (Figure 1), matching 2.1% APC in the California Hispanic population over that period (US Census). Compared with other racial/ethnic groups, Hispanics were more likely to present before 40 (8.5% vs. 2.5%), have signet ring/poorly cohesive pathology (25% vs. 18%), present at an advanced stage (47% vs. 40%), and have no health insurance (4.5% vs. 1.8%, all p<0.001). Multivariable analysis indicated that Hispanic ethnicity (HR: 1.19, 95% CI: 1.12-1.26) or Asian race (HR: 1.09, 95% CI: 1.01-1.13) were independently associated with worse overall survival. **CONCLUSIONS:** Matching population trends, there has been a dramatic increase in the proportion of gastric cancers among Hispanics in California. Hispanics present younger, with less favorable pathology, more often metastatic, and experience greater burden of uninsured status. Controlling for these social and biologic determinants, Hispanics with gastric cancer display worse survival. Causes for this outcome are unknown, raising the critical need for screening and solutions to care access disparities in this population.

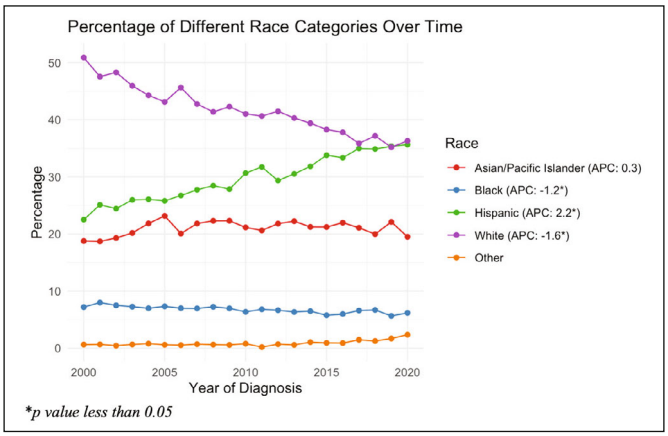


Figure 1. Trends in Gastric Cancer Incidence by Race in California (2000-2020)

P483. Gastric Cancer in the United States: How Can We Do Better?

Gregory Sigler, MD[1]; Brittany Walker[2]; Patrick Varley, MD[3]; Syed Nabeel Zafar, MD, MPH[4]; Daniel Abbott, MD[5]; Sharon Weber, MD[6]; Sean M Ronnekleiv-Kelly, MD[7]; Kaitlyn Kelly, MD, MAS[8]

[1]University of Wisconsin, Madison, WI, US; [2]University of Wisconsin, Madison, WI, US; [3]University of Wisconsin, Madison, WI, US; [4]University of Wisconsin - Madison School of Medicine, Madison, WI, US; [5]University of Wisconsin, Madison, WI, US; [6]University of Wisconsin - Madison School of Medicine, Madison, WI, US; [7]University of Wisconsin-Madison, Madison, WI, US; [8]University of Wisconsin, Madison, WI, US

INTRODUCTION: The United States (U.S.) is a low-incidence country for gastric cancer and screening is not performed. As a result, patients most commonly have advanced-stage disease at diagnosis. We evaluated a comprehensive U.S. dataset to assess patient presentation and identify opportunities for earlier diagnosis. **METHODS:** We reviewed all gastric cancer diagnoses at a single academic center over the past 11 years and reviewed demographics, presenting signs and symptoms, diagnostic evaluations, stage at diagnosis, and outcomes. **RESULTS:** We identified 249 patients with gastroesophageal junction (GEJ) or gastric adenocarcinoma. The median age at diagnosis was 66 years (range 19 to 95). 216 patients (86%) were white, 12 (5%) were Asian, 13 (5%) were African American, and race was not reported for 8 (3%). 133 patients (53%) had a family history of cancer and 7 (2%) had a predisposing germline mutation. 41 patients (17%) had stage I disease at diagnosis, 109 (43%) had stage II/III, and 99 (40%) had stage IV. The presence of GI-related symptoms at diagnosis was statistically-significantly associated with more advanced disease (p<0.001), and symptoms differed across stages. The most common presenting symptoms for stage I patients were reflux, GI bleed, abdominal pain, and unintentional weight loss (Table). For all patients, the median self-reported duration of symptoms prior to first endoscopy was 2 months (range 0 to 35). 185 patients (74%) were participating in colon cancer screening. 181 (73%) had undergone a recent colonoscopy and 9 patients (4%) had a Cologuard test within 3 years of the gastric cancer diagnosis. 4 (45%) of these 9 had a positive Cologuard result with negative colonoscopy. 2 of these 4 patients (50%) had stage I gastric cancer on endoscopy to work up the positive Cologuard result. The median survival (MS) of the entire cohort was 23.0 mo [95% CI 14.4, 31.6] and was not reached for stage I patients. MS was 47 mo [24.3, 69.7] for stage II, 23.0 mo [19.9, 26.3] for stage III, and 11.0 mo [6.6, 15.4] for stage IV; (p<0.001). **CONCLUSIONS:** Discussion: The presence of symptoms is not a reliable indicator of early-stage gastric cancer. 74% of patients in this cohort were participating in colon cancer screening and in 2 asymptomatic

patients, stage I gastric cancer was able to be detected by a stool-based DNA assay. Novel protocols such as more comprehensive GI cancer screening with addition of endoscopy to colonoscopy, or broader use of a DNA-based stool assay, should be investigated in the U.S.

Table. Percentage of Gastric Cancer Patients with Symptoms at Diagnosis Across Stage Groups

Symptoms	Stage I (%) N=41	Stage II (%) N=86	Stage III (%) N=23	Stage IV (%) N=99	P
Any	65.9	88.4	100.0	94.9	**<0.001**
Nausea / vomiting	14.6	19.8	13.0	27.3	0.237
Reflux	19.5	24.4	39.1	19.2	0.209
GI Bleed	19.5	14.0	21.7	11.1	0.446
Anemia	14.6	17.4	8.7	11.1	0.556
Abdominal pain	19.5	38.4	65.2	58.6	**<0.001**
Dysphagia	9.8	31.4	13.0	33.3	**0.010**
Weight loss	19.5	52.3	59.1	69.7	**<0.001**

P484. Impact of Lymph Node Ratio in Patients with Esophageal Cancer

Parker Wilson[1]; Jamie Huston, MS[2]; Ravi Shridhar[3]; Kenneth Meredith, Chief of Surgical Oncology[4]
[1]Florida State University, Sarasota, FL, US; [2]Sarasota Memorial Healthcare System, Sarasota, FL, US; [3]Advent Health, Orlando, FL, US; [4]Sarasota Memorial Health Care System/ Florida State University, Sarasota, FL, US

INTRODUCTION: Esophageal cancer is a leading cause of mortality worldwide. Neoadjuvant therapy followed by surgery remains the best option for durable survival. The lymph node (LN) ratio, defined as the ratio of positive lymph nodes to the total number of lymph nodes removed, has emerged as a prognostic marker in various cancers. This study examines the effect of LN ratio on overall survival in patients with esophageal cancer. **METHODS:** Utilizing the National Cancer Database we identified patients diagnosed with esophageal cancer who underwent esophagectomy. A propensity score matching (PSM) approach was employed to balance baseline characteristics between the two treatment groups. Median overall survival and 5-year overall survival rates were compared across LN ratio strata (0, 0.01-0.10, 0.11-0.40, >0.40) for adenocarcinoma and squamous histology's. Kaplan-Meier survival analyses were conducted, with p-values calculated to assess statistical significance. **RESULTS:** We identified 14,954 esophageal cancer patients (1,658 receiving neoadjuvant chemotherapy(NCT) and 13,296 receiving Neoadjuvant chemoradiation(NCR) with a median age of 63 (19-89). The majority were adenocarcinoma's 90% vs 10% and GE junction or lower esophagus were the most common locations. Lymph nodes removed and LN + were both higher in the NCT vs NCR, p<0.001 and p<0.001. R0 resections were higher in the NCR, 94.3% vs 88%, p<0.001. In the non-PSM cohort, patients receiving NCR had significantly more favorable LN ratios compared to those receiving NAC (p<0.001). LN ratio was strongly associated with OS in both adenocarcinoma and squamous cell carcinoma. Among adenocarcinoma patients, the 5-year overall survival rate decreased from 54% in patients with 0 LN involvement to 16% in those with an LN ratio >0.40 (p<0.001). Similarly, squamous cell carcinoma patients showed a decline in 5-year OS from 59% to 26% with increasing LN ratio (p<0.001). These trends were confirmed in the PSM cohort, where a higher LN ratio continued to predict worse survival outcomes (p<0.001). **CONCLUSIONS:** LN ratio is a critical prognostic factor in esophageal cancer patients treated with neoadjuvant therapy. Both adenocarcinoma and squamous cell carcinoma patients with a higher LN ratio exhibited significantly worse survival outcomes. These findings underscore the importance of LN ratio as a potential stratification tool for risk assessment and guiding post-operative management in esophageal cancer patients.

P485. Intensive versus Standard Neoadjuvant 5-Fluorouracil, Leucovorin, Oxaliplatin, and Docetaxel (FLOT) for Gastric Cancer: A Retrospective Analysis

Josh G Kim, BA[1]; Judy Li[2]; Allen T Yu, MD, PhD[3]; Umut Sarpel, MD, MSc[4]; Daniel Labow, MD[5]; Benjamin Golas, MD[6]; Camilo Correa-Gallego, MD[7]; Spiros Hiotis, MD, PhD[8]; Sofya Pintova, MD[9]; Noah A. Cohen, MD[10]
[1]Icahn School of Medicine at Mount Sinai, New York, NY, US; [2]Icahn School of Medicine at Mount Sinai, New York, NY, US; [3]Icahn School of Medicine at Mount Sinai, New York, NY, US; [4]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, US; [5]Nuvance Health, Danbury, CT, US; [6]Icahn School of Medicine at Mount Sinai, New York, NY, US; [7]Icahn School of Medicine at Mount Sinai, New York, NY, US; [8]Icahn School of Medicine at Mount Sinai, New York, NY, US; [9]Icahn School of Medicine at Mount Sinai, New York, NY, US; [10]Icahn School of Medicine at Mount Sinai, New York, NY, US

INTRODUCTION: Patients with locally advanced gastric cancer are recommended to receive perioperative 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT) typically administered as 4 preoperative and 4 postoperative cycles, and curative-intent gastrectomy. Few studies have investigated the pathologic and clinical outcomes of patients who receive >4 cycles of preoperative FLOT. **METHODS:** A retrospective study was conducted on patients diagnosed with gastric adenocarcinoma between 2017 and 2023 who received any number of cycles of neoadjuvant FLOT prior to curative-intent gastrectomy. Groups were defined as those receiving ≤ 4 cycles (standard group) and > 4 cycles (intensive group) of preoperative FLOT. Patient demographics, operative outcomes, pathologic characteristics, and survival were compared by chi-square analysis, independent t-test, Mann-Whitney U test, and log-rank test. **RESULTS:** In total, 87 patients met inclusion criteria, with 37 (42.5%) patients in the intensive group (median preoperative FLOT 6 [range 5-12] vs 4 cycles [range 1-4], $p < 0.001$). Median duration of follow-up was 24.5 months [range 1-80] in the intensive group and 21 months [range 4-54] in the standard group. Patients in the intensive group were younger (mean 58 ± 12 vs 63 ± 12 years old, $p < 0.05$). The intensive group completed more total chemotherapy cycles than the standard group (median 8 [range 5-14] vs 7 [range 1-8] cycles, $p < 0.001$). There were no differences in rates of dose reduction required. Recurrence-free survival (RFS, $p = 0.268$) and overall survival (OS, $p = 0.697$) were similar between the groups. The 24-month RFS rate was 73.1% in the standard group and 67.5% in the intensive group. The 24-month OS rate was 83.2% in the intensive group and 86.3% in the standard group. Operative characteristics were similar between groups. There were no differences in 30-day postoperative complications, nor 90-day readmission and reoperation rates. Rates of pathologic complete response and lymph node positivity were similar. **CONCLUSIONS:** Overall, these data demonstrate that patients in the intensive group received more total cycles of chemotherapy without any difference in pathologic findings, recurrence or survival. However, long-term survival outcomes should be investigated further in follow-up studies with larger study populations.

Table. Comparison of Pathologic and Postoperative Outcomes After Neoadjuvant Therapy for Gastric Adenocarcinoma

	Standard (N=50)	Intensive (N=37)	Overall (N=87)	*p*-value
Age at diagnosis (mean, SD)	63 ± 12	58 ± 12	61 ± 12	<0.05
Median follow-up time (months) (range)	24.5 [1, 80]	21 [4, 54]	23 [1, 80]	0.323
Median number of neoadjuvant chemotherapy cycles completed[A] (range)	4 [1, 4]	6 [5, 12]	4 [1, 12]	<0.001
Median number of adjuvant cycles completed[B] (range)	4 [0, 6]	2 [0, 7]	3 [0, 7]	<0.001
Median number of total chemotherapy cycles completed[B] (range)	7 [1, 8]	8 [5, 14]	8 [1, 14]	<0.001
Time from completion of NAT to surgery (days, mean, SD)	40 ± 12	45 ± 18	42 ± 15	0.187
Required dose reduction?				
Yes	26 (52.0)	18 (48.6)	44 (50.6)	0.304
No	20 (40.0)	12 (32.4)	32 (36.8)	
Unknown	4 (8.0)	7 (18.9)	11 (12.6)	
Type of surgery				
Total gastrectomy	11 (22.0)	13 (35.1)	24 (27.6)	0.393
Proximal gastrectomy	2 (4.0)	1 (2.7)	3 (3.4)	
Distal gastrectomy	37 (74.0)	23 (62.2)	60 (69.0)	
Treatment effect				
Present	28 (56.0)	23 (62.2)	52 (59.8)	0.428
Absent	15 (30.0)	12 (32.4)	27 (31.0)	
Unavailable	7 (14.0)	2 (5.4)	8 (9.2)	
Histologic type (Lauren)				
Diffuse	17 (34.0)	17 (45.9)	34 (39.1)	0.225
Intestinal	23 (46.0)	9 (24.3)	32 (36.8)	
Mixed	4 (8.0)	4 (10.8)	8 (9.2)	
Unavailable	6 (12.0)	7 (18.9)	13 (14.9)	
Pathologic grade				
Complete response	5 (10.0)	2 (5.4)	7 (8.0)	0.531
Well differentiated	3 (6.0)	1 (2.7)	4 (4.6)	
Moderately differentiated	10 (20.0)	5 (13.5)	15 (17.2)	
Poorly differentiated	32 (64.0)	29 (78.4)	61 (70.1)	
Lymph nodes positive for disease (mean, SD)	3.0 ± 5.4	2.7 ± 4.7	2.9 ± 5.1	0.757
Lymph nodes inspected (mean, SD)	26 ± 13	36 ± 12	26 ± 13	0.976
30 Day Postoperative Complications[C]				
Grade I	6 (12.0)	4 (10.8)	10 (11.5)	0.863
Grade II	7 (14.0)	7 (18.9)	14 (16.1)	0.567
Grade III	5 (10.0)	4 (10.8)	9 (10.3)	0.902
Grade IV	0 (0)	2 (5.4)	2 (2.3)	0.178
Grade V	2 (4.0)	0 (0)	2 (2.3)	0.505
Unexpected readmission				
Within 30 days	4 (8.0)	5 (13.5)	9 (10.3)	0.486
Within 90 days	7 (14.0)	7 (18.9)	14 (16.1)	0.567
Unexpected reoperation				
Within 30 days	1 (2.0)	2 (5.4)	3 (3.4)	0.572
Within 90 days	3 (6.0)	1 (2.7)	4 (4.6)	0.633

[A] All patients received FLOT. 8 patients (6 in standard, 2 in intensive) received FOLFOX or CAPEOX in addition due to FLOT toxicity.
[B] 3 cases excluded from standard group and 1 case excluded from intensive group due to missing adjuvant chemotherapy data.
[C] Complications graded by Clavien-Dindo classification.

P486. Intermediate-term Mortality for Esophagogastric Malignancy: Implications for Shared Decision Making?

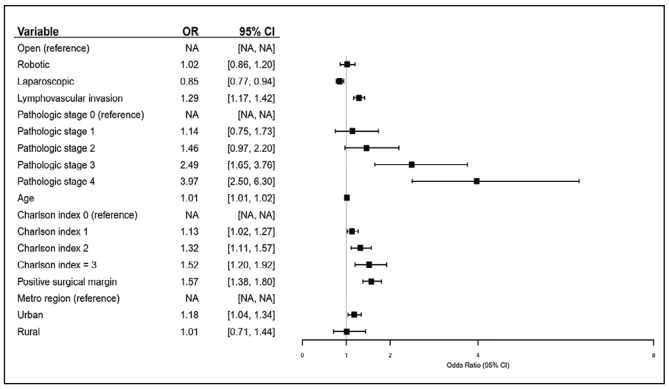
Andrew D Folkerts, MD[1]; Lauren Janczewski, MD[2]; Mina Seals[3]; David Bentrem[4]; David Odell[5]; Mitchell Posner[6]; Ryan P Merkow, MD, MS[7]
[1]University of Chicago, Chicago, IL, US; [2]Northwestern Medicine, Chicago, IL, US; [3]University of Chicago, Chicago, IL, US; [4]Northwestern, Chicago, IL, US; [5]University of Michigan, Ann Arbor, MI, US; [6]University of Chicago, Chicago, IL, US; [7]University of Chicago, Chicago, IL, US

INTRODUCTION: Esophagogastric cancer remain in the top 10 malignancies by incidence and mortality worldwide. While short-term (0-3 months) mortality is well appreciated, intermediate-term (3-6 months) mortality following surgical resection remains insufficiently recognized. Our objectives were to (1) characterize the incidence of intermediate-term mortality, (2) assess unique predictors of intermediate-term mortality, and (3) evaluate hospital-level variation in intermediate-term mortality following resection for esophagogastric cancer in the United States. **METHODS:** Patients undergoing curative intent resection for stage 1A-3C esophagogastric adenocarcinoma were identified from the National Cancer Database (2010-2020). Multivariable logistic regression identified predictors of intermediate-term mortality and assessed differences between short-term and intermediate-term mortality. Intermediate-term mortality hospital-level quartiles were analyzed using firth logistic regression. **RESULTS:** Of the 13,386 patients that underwent esophagogastric resection, 1,194 (8.9%) died within 6-months of surgery, of which 463 (39%) occurred in the intermediate term. Intermediate-term mortality occurred in 4.6% of esophagectomies, 3.6% of total gastrectomies, and 3.1% of partial gastrectomies. Roughly half of the deaths within 6 months occurred in the intermediate term for patients less than 50 (56%) and at high-volume centers (47%). Factors predictive of intermediate-term mortality vs. short-term mortality were age less than 50 (vs. over 75, OR=2.65, p=0.004), integrated facility type (vs. community, OR= 2.36, p=0.015) and any adjuvant or neoadjuvant therapy (vs. no systemic therapy, OR=1.86 for neoadjuvant and 5.17 for adjuvant, p<0.001). At the hospital level, intermediate-term mortality ranged from 0 to 100% (IQR 0%-5%). Factors predicting intermediate-term mortality at the hospital level included any non-community facility (vs. community), any non-west region (vs. west), esophagus (vs. gastric), and positive margins (vs. negative) (all p<0.05). **CONCLUSIONS:** Nearly 1 in 10 patients undergoing esophagogastrectomy for cancer died within 6 months of surgery with over one-third of deaths occurring in the intermediate term. Intermediate-term mortality was more common in younger patients with more advanced, and wide hospital-level variation exists. These data emphasize the importance of including intermediate-term mortality in shared decision-making discussions.

P487. Management and Outcomes of Gastric Adenocarcinoma in the United States Over 17 Years: Analysis of National Cancer Database

Ali Esparham[1]; Zahra Shafaee[2]
[1]Mashhad University of Medical Sciences, Mashhad, Iran, Mashhad, IR; [2]Department of Surgery Elmhurst Hospital Center , Icahn School of Medicine, New York, NY, US

INTRODUCTION: In the recent years, efforts have focused to improve management and outcomes of gastric adenocarcinoma (GAC). In the current study, we aimed to investigate the trends of management and outcomes of GAC over a period of 17 years in the United States. **METHODS:** We analyzed adult GAC patients from the National Cancer Database (2004-2021), divided into three groups: 2004-2009 (P1), 2010-2015 (P2), and 2016-2021 (P3). Multivariate Cox regression was used to identify predicating factors of mortality. **RESULTS:** 177,069 GAC patients were included. Stage IV of disease significantly increased in P3 (40.7%) compared to two other periods (P1: 23.3%, P2: 29.7%). Immunotherapy and chemotherapy utilization significantly increased (P1: 0.1%, P2: 2.2%, P3:10% and P1: 44.8%, P2: 54.8%, P3: 59, respectively). The use of single-agent chemotherapy decreased significantly (P1: 21.4%, P2: 13.1%, P3: 8.1%), while multi-agent chemotherapy increased (P1: 66.1%, P2: 78.8%, P3: 88.1%). In term of systemic therapy sequence, neoadjuvant therapy (P1: 7.3%, P2:12.5%, and P3: 14.0%) and using both neoadjuvant and adjuvant therapy (P1:1.4%, P2:2.9%, P3: 5.8%) significantly increased while adjuvant therapy significantly decreased (P1: 14.2%, P2:10.3%, P3:7%). Despite increase in metastatic disease (P1: 39.1%, P2: 30.5%, P3: 74.4%), 3-years overall survival significantly increased from 13.3% in P1 to 21.3% in P2 and 23.1% in P3. Thiry day unplanned readmission (P1: 3.2%, P2: 3.1%, P3: 2.4%), 30-day mortality (P1: 5.3%, P2: 3.9%, P3: 3%), and 90-days mortality (P1:11%, P2:7.9%, P3:5.9%) significantly decreased across the periods. Robotic approach (P2:1.6%, P3: 4.9%) and laparoscopic (P2:11.1% P3:13.3%) significantly increased, while open approach significantly decreased (P2:25.3% P3:15.2%). Length of hospital stay after surgery decreased significantly (P1: 11.56 ± 11.84 days, P2: 10.15 ± 10.54 days, P3: 8.55 ± 9.75 days). The number of lymph nodes examined increased (P1: 14.51 ± 10.75, P2: 16.95 ± 11.34, P3: 20.53 ± 12.57), and the time from diagnosis to surgery lengthened (P1: 43.94 ± 54.2 days, P2: 68.16 ± 65.94 days, P3: 90.26 ± 75.82 days). Positive surgical margin significantly decreased (P1: 15.2%, P2: 13.0%, P3: 11.4%). Figure 1 shows the results of multivariate COX regression. **CONCLUSIONS:** 3-years overall survival in patients with GAC significantly improved in recent years that can be due to increase utilization of minimally invasive surgery, immunotherapy, neoadjuvant therapy, multi-agent chemotherapy, together with reduced positive margins.



P488. Multidisciplinary tumor board discussion improves survival in patients with gastric and gastroesophageal cancer

Ricardo E. Nunez-Rocha, MD[1]; Morgan F Pettigrew, MD[2]; Ryan T Heslin, MD[3]; Samy Castillo-Flores, MD[4]; Nafeesah Fatimah, MD[5]; Andres A, Abreu, MD[6]; John C Mansour, MD[7]; Cecilia G Ethun, MD[8]; Amanda Dann, MD[9]; Alex Kim, MD, PhD[10]; Patricio M. Polanco, MD[11]; Adam Yopp, MD[12]; Herbert J Zeh, MD[13]; Scott I. Reznik[14]; Inderpal Sarkaria[15]; Timothy Brown, MD[16]; Suntrea T.G. Hammer, MD[17]; Sam Wang, MD[18]; Matthew Porembka, MD[19]
[1]University of Texas Southwestern Medical Center, Dallas, TX, US; [2]UT Southwestern, Irving, TX, US; [3]UT Southwestern, Dallas, TX, US; [4]University of Texas Southwestern, Dallas, TX, US; [5]UT Southwestern, Dallas, TX, US; [6]University of Texas Southwestern Medical Center, Dallas, TX, US; [7]UT Southwestern Medical Center, Dallas, TX, US; [8]UT Southwestern Medical Center, Dallas, TX, US; [9]The University of Texas Southwestern Medical Center, Dallas, TX, US; [10]UT Southwestern Medical Center, Dallas, TX, US; [11]University of Texas Southwestern Medical Center, Dallas, TX, US; [12]UT Southwestern Medical Center, Dallas, TX, US; [13]UT Southwestern Medical Center, Dallas, TX, US; [14]UT Southwestern Medical Center, Dallas, TX, US; [15]University of Texas Southwestern Medical Center, Dallas, TX, US; [16]University of Texas Southwestern Medical Center, Dallas, TX, US; [17]UT Southwestern Medical Center, Dallas, TX, US; [18]UT Southwestern Medical Center, Dallas, TX, US; [19]UT Southwestern Medical Center, Dallas, TX, US

INTRODUCTION: Multidisciplinary tumor board (MTB) discussion has been associated with increased receipt of guideline-concordant care (GCC) in gastrointestinal (GI) cancers; however, the impact of MTB on survival in GI cancers is not well-delineated. In 2018, we began bi-weekly gastroesophageal MTB including providers from surgical, medical, and radiation oncology as well as GI pathology. We sought to evaluate the effect of MTB presentation on survival outcomes in patients with gastric cancer (GC) and gastroesophageal junction cancer (GEJ). **METHODS:** We retrospectively reviewed GC and GEJ patients treated from 2020 to 2024. Patients discussed at MTB were compared to those who were not. Primary outcome was overall survival (OS). Secondary outcomes were receipt of GCC, time to treatment initiation, and receipt of multimodal treatment (MMT), which was defined as concomitant receipt of neoadjuvant therapy and surgery. **RESULTS:** Of 411 patients included, 219 (52%) had GC, and 192 (47%) had GEJ. 28 (8%) patients had early-stage disease, 125 (34%) had locally advanced disease, and 215 (58%) had metastatic disease. There were no differences in age or sex in patients who were discussed at MTB. GEJ were presented more often than GC (53% versus 47%; p = 0.01). Early (9-4% vs 5.3%) and locally advanced (39.8% vs. 26.9%) stages had higher MTB presentation rates compared to metastatic disease (50.7% vs. 57.6%) (p = 0.004). There was no difference in receipt of GCC (p =

0.35) or time to treatment initiation (p = 0.48). Patients discussed at MTB were more likely to receive MMT (34% versus 20%; p = 0.001). In multivariable analysis, non-metastatic stage (HR = 0.43, p = 0.03), tumor board presentation (HR = 0.64, p = 0.01), and receipt of multimodal treatment (HR = 0.61, p = 0.01) were associated with improved survival. MTB presentation was associated with longer OS (22 vs 15 months; p = 0.006). When stratified by stage, presentation of locally advanced patients was associated with prolonged median OS (30.8 mo vs. 16.4 mo; p=0.03). There was no difference in early and metastatic disease. Receipt of MMT was associated with longer OS (24.3 mo vs.16.2 mo; p=0.002). **CONCLUSIONS:** In patients with locally advanced GC and GEJ, MTB presentation was associated with receipt of MMT and prolonged survival. MTB presentation should be standard for all patients with GC and GEJ.

P489. Outcomes of Neoadjuvant Chemoradiation in Early Esophageal Cancers with Signet Ring Histology

Sumaya Ghaffar, MD[1]; Andrii Khomiak, MD[2]; Haley C Perkins, Medical Student[3]; Keiko Fox, Medical Student[4]; Alison Mungo, MD[5]; Elizabeth David, MD[6]; Simran Randhawa, MD[7]; Akshay Chauhan, MD[8]; Robert Meguid, MD MPH[9]; John D Mitchell, MD[10]; Ana L. Gleisner, Md, PhD[11]; Martin D McCarter, MD[12]; Benedetto Mungo, MD[13]

[1]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [2]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [3]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [4]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [5]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [6]University of Colorado School of Medicine, Aurora, CO, US; [7]University of Colorado School of Medicine, Aurora, CO, US; [8]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [9]University of Colorado School of Medicine, Aurora, CO, US; [10]University of Colorado School of Medicine, Aurora, CO, US; [11]University of Colorado Denver | Anschutz Medical Campus, Aurora, CO, US; [12]University of Colorado School of Medicine, Aurora, CO, US; [13]University of Colorado School of Medicine, Aurora, CO, US

INTRODUCTION: Signet ring cell (SRC) histology has been associated with significantly worse clinical outcomes in esophageal cancers. The role of neoadjuvant treatment in clinical early-stage esophageal cancer in the presence of SRC remains controversial. **METHODS:** We utilized the National Cancer Database from 2004 to 2017 to evaluate early-stage esophageal cancers (cT1N0, cT1N1, and cT2N0) with SRC histology that were surgically resected. Patients who received neoadjuvant chemoradiation (NA-CRT) were compared to those who underwent upfront surgery. M1 disease was excluded. Differences in categorical variables were assessed using the Chi-Square test. Kaplan-Meier survival analysis was performed to estimate survival probabilities, and Cox regression analysis was used to calculate Hazard Ratios (HR). **RESULTS:** A total of 198 patients were identified, with 88 (44.5%) receiving NA-CRT and 110 (55.5%) undergoing upfront surgery. The median age was 64 years, with the majority being male (88.4%) and white (98.0%). There were no significant differences in baseline characteristics, including the type of facility where treatment was received (Academic vs Community, p = 0.90). The median time from diagnosis to surgery was 4.4 months in NA-CRT vs. 1.8 months in the upfront surgery group. When evaluating the final pT stage, a higher proportion of patients in the NA-CRT group had pT3 disease compared to the non-CRT group (27.3% vs 20.0%, p<0.001), suggesting potential upstaging. No differences were observed in the proportions of pN0 and pN+ cases. Adjuvant therapy was received by 4 (4.5%) patients in the NA-CRT group vs. 31 (28.2%) in the upfront surgery group (p < 0.001). No significant differences were noted in short-term outcomes, including 90-day mortality and readmission rates. In multivariate analysis, factors negatively impacting survival included the receipt of preoperative chemoradiation [HR 1.62 (95%CI 1.09-2.39), p = 0.015], age at diagnosis, clinical stage group, and positive margins. Patients who received NA-CRT had worse median overall survival compared to those who did not receive CRT (36.0 months vs. 68.1 months, p = 0.031). **CONCLUSIONS:** Neoadjuvant chemoradiation may not offer a survival benefit for patients with early-stage esophageal cancer and signet ring cell histology. These patients may instead benefit from upfront surgical resection and could potentially avoid the toxicity associated with chemotherapy and radiation regimens, as well as delays in treatment administration.

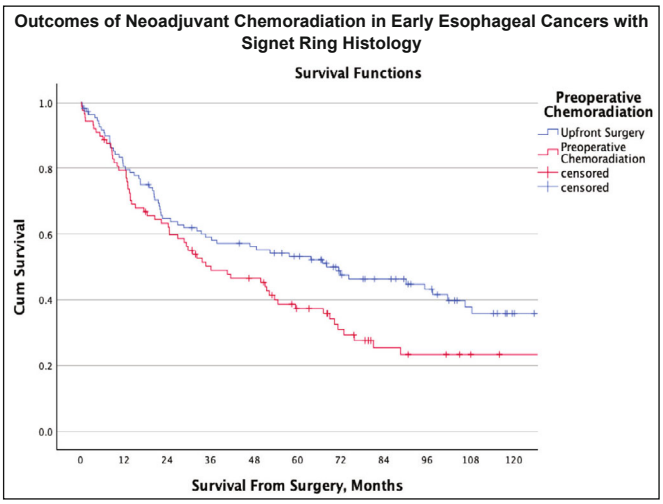


Figure 1. Kaplan Meyer Survival Analysis of Early-Stage Esophageal Cancer with Signet Ring Cell Histology: NA-CRT vs Non-CRT (Upfront surgery) Outcomes.

P490. Outcomes of Neoadjuvant Chemotherapy Versus Chemoradiation For Esophageal Adenocarcinoma

Kenneth Meredith, Chief of Surgical Oncology[1]; Jamie Huston[2]; Ravi Shridhar, MD[3]

[1]Sarasota Memorial Health Care System/Florida State University, Sarasota, FL, US; [2]Sarasota Memorial Healthcare System, Sarasota, FL, US; [3]Advent Health, Orlando, FL, US

INTRODUCTION: While neoadjuvant chemoradiation (NCRT) has been the acceptable standard of care, recent trials have shown that neoadjuvant chemotherapy (NAC) are either equivalent or superior to NCRT. We sought to examine the outcomes of NAC versus NCRT in esophageal cancer. **METHODS:** Utilizing the National Cancer Database, we identified esophagectomy patients with esophageal adenocarcinoma (EAC) who underwent multiagent NAC versus multiagent NCRT. Overall Survival (OS) was analyzed with the Kaplan-Meier method and univariate (UVA) and multivariate analysis (MVA) was performed to identify predictors of OS. Propensity score matching (PSM) was used to correct for baseline differences between groups. **RESULTS:** After PSM, we identified 1007 patients in each group. Groups were equally balanced in age, gender, T/N stage, grade, and facility volume. There was improved lymphadenectomy and higher use of adjuvant therapy in NAC patients. There were significant improvements in R0 resection and pathologic response associated with NCRT patients. There was a significant improvement in OS in NCT versus NCRT. The median and 5-year OS was 42.7 months and 42%, respectively in NCT patients versus 34.2 months and 35%, respectively in NCRT patients (p = 0.001). On MVA, improved survival was associated with female gender, pathologic N0, >10 nodes removed, pathologic partial or complete response, R0, well/moderate grade, NCT, adjuvant chemotherapy, and higher facility volume. **CONCLUSIONS:** Despite higher R0 and pathologic response associated with NRT, NCT was superior to NCRT for OS in EAC patients. NCRT needs to be re-examined in its role as a treatment recommendation for operable EAC patients.

P491. Preoperative frailty and associated outcomes after esophagectomy, a single center experience

Kristina Fraser, DO[1]; Anthony Easterday[2]; Jared Reyes[3]; Ali Ahmad[4]

[1]The University of Kansas School of Medicine Wichita, Wichita, KS, US; [2]University of Kansas School of Medicine-Wichita, Wichita, KS, US; [3]University of Kansas School of Medicine-Wichita, Wichita, KS, US; [4]University of Kansas School of Medicine-Wichita, Wichita, KS, US

INTRODUCTION: With greater than 60% of individuals with esophageal cancer over the age of 65 years, frailty is of concern when weighing the risk of morbidity and mortality associated with esophagectomies. However, outcomes have changed since the introduction of minimally invasive surgery. The purpose of this study was to evaluate the association between frailty and operative outcomes for open and minimally invasive esophagectomies. **METHODS:** A retrospective review was conducted including patients undergoing esophagectomy for esophageal cancer between 2016 and 2020 at a single

community hospital. The 5-Factor Modified Frailty Index was used to define patient frailty. Data was collected on patient demographics, tumor pathology and stage, comorbidities, complications, ICU days, total hospital days, readmission within 30 days of discharge, in-hospital mortality, and mortality at 30, 90 days, and one year post discharge. **RESULTS:** Our analysis included 95 patients with an average age of 64.4 years. A majority of our patients were white, non-Hispanic males, who underwent neoadjuvant chemotherapy and radiation, and indication for esophagectomy was for esophageal adenocarcinoma (88%). The most common comorbidities were hypertension (61%), coronary artery disease (30.5%), and diabetes mellitus (29.5%). When taking into account the severity of frailty, the need for post-operative mechanical ventilation ($p<0.05$) and reintubation ($p<0.05$) was significantly higher in severely frail patients, and as the severity of frailty increased in our population, the less likely the patient was to return home ($p<0.05$). There was no significant difference in outcomes as severity of frailty increased in post-operative in-hospital mortality ($p=0.491$), anastomotic leak ($p=0.061$), acute kidney injury ($p=0.556$), and acute respiratory distress syndrome ($p=0.300$; Table 1). Between laparoscopic, robotic and open, there was no significant difference in post-operative anastomotic leak ($p=0.413$), ARDS ($p=0.598$), sepsis ($p=0.702$), pneumonia ($p=0.702$), and in-hospital mortality ($p=0.206$). Additionally, as frailty increased there was no difference in the varying surgical modalities when it came to hospital length of stay ($p=0.390$) or ICU days ($p=0.156$). **CONCLUSIONS:** Our single center population did not have increased mortality with increasing frailty; however, there was a significant chance of postoperative respiratory support and need for discharge to facility rather than home. We were also able to demonstrate the feasibility and safety of minimally invasive esophagectomy when comparing our results to open esophagectomy results, even in the setting of increasing frailty.

Table 1. Complications and Outcomes by Frailty*

	0 Conditions (n=22)	1 Condition (n=39)	≥ 2 Conditions (n=34)	P Value
Myocardial Infarction	0.0% (0)	10.3% (4)	2.9% (1)	.283
Acute Respiratory Distress Syndrome	9.1% (2)	20.5% (8)	26.5% (9)	.300
Pneumonia	13.6% (3)	28.2% (11)	35.3% (12)	.200
Acute Kidney Injury	4.5% (1)	12.8% (5)	14.7% (5)	.556
Need for Dialysis	0.0% (0)	5.1% (2)	0.0% (0)	.343
Anastomotic Leak	4.5% (1)	20.5% (8)	29.4% (10)	.061
Sepsis	13.6% (3)	25.6% (10)	39.4% (13)	.118
Pulmonary Embolus	0.0% (0)	2.6% (1)	3.0% (1)	>.999
Reoperation	0.0% (0)	7.7% (3)	3.0% (1)	.547
ICU Length of Stay (days)	5 (3.75-7)	5 (3-10)	7 (4-13.25)	.156
Hospital Length of Stay (days)	9 (8-12)	10 (8-15)	11.5 (8.75-19)	.390
In-Hospital Mortality	4.5% (1)	15.4% (6)	14.7% (5)	.491

*Frailty was categorized as in Weaver et al. (2019). Each patient was stratified by how many of the following conditions they had: congestive heart failure, diabetes mellitus, chronic lung disease, hypertension, and partial or total dependence.

P492. Psychometric Validation of a new MD Anderson Symptom Inventory Survey for Patients with Upper Gastrointestinal Cancers: MDASI-UGI-Surg

Paula M. Smith, MD, PhD[1]; Koichi Tomita, MD, PhD[2]; Yuki Hirata, MD[3]; Samuel Cass[4]; Cong Pan[5]; Shu-En Shen[6]; Xuemei Wang[7]; Xin Shelley Wang[8]; Lori Williams[9]; Melissa Aryide[10]; Connie To[11]; Ravi Rajaram[12]; David Rice[13]; Wayne Hofstetter[14]; Mara Antonoff[15]; Reza Mehran[16]; Ara Vaporcivan[17]; Gerett Walsh[18]; Jessica E. Maxwell, MD MBA[19]; Rebecca A. Snyder, MD, MPH[20]; Michael P. Kim, MD[21]; Ching-Wei D. Tzeng, MD[22]; Brian Badgwell, MD, MS[23]; Paul Mansfield, MD[24]; Matthew H.G. Katz, MD[25]; Jeffrey E. Lee, MD[26]; Stephen Swisher[27]; Naruhiko Ikoma, MD[28]

[1]MD Anderson Cancer Center, Houston, TX, US; [2], US; [3], US; [4], US; [5]The University of Texas Health Science Center at Houston, Houston, TX, US; [6], US; [7], US; [8], USUS; [10], US; [11], US; [12], US; [13], US; [14], US; [15], US; [16], US; [17], US; [18], US; [19]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [20]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [21]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [22]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [23]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [24]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [25]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [26]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [27], US; [28]UT MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: The MD Anderson Symptoms Inventory (MDASI) is a well-established, validated survey designed to assess patient-reported outcomes (PROs) for cancer patients, enabling comprehensive symptom assessment in clinical care and providing an instrument to track PROs in clinical research. Multiple MDASI "modules" have been developed and validated to tailor the survey to specific cancer- and treatment-types, each adding questions that are cancer- or treatment-specific. We sought to develop and validate an MDASI survey specific to patients with upper gastrointestinal cancer (MDASI-UGI-Surg), including for patients with pancreatic and gastroesophageal (PGE) cancers, and which captures dynamic changes in quality of life (QoL) through the phases of multidisciplinary treatment, including surgery. **METHODS:** Phase 1 included qualitative interviews with PGE cancer patients who underwent surgical resection. Interview transcripts were analyzed, and symptoms ranked by frequency reported. In phase 2, an expert panel assessed symptom relevance, and those that were commonly reported and reached a threshold relevancy score were added to the MDASI-UGI-Surg module. In phase 3, the new MDASI-UGI-Surg module was psychometrically validated in a population of 169 consecutive patients undergoing surgical resection for PGE cancer. **RESULTS:** In phase 1, 17 patients with gastric (n=6), esophageal (n=5), or pancreatic (n=6) cancers underwent qualitative interviews. In phase 2, an expert panel determined that 9 symptoms (difficulty swallowing, heartburn/reflux, diarrhea, constipation, flushing/sweating, stomach feeling full, malaise, dizziness, feeling cold) reached threshold relevancy and these were added to the MDASI-UGI-Surg module. In phase 3, 145 of the 169 patients enrolled were deemed evaluable (6 patients failed to complete a survey, 18 patients' operations were cancelled or aborted). The primary disease sites were 43 (19.7%) esophagus, 26 (17.9%) stomach, and 76 (52.4%) pancreas. Ninety-one (62.8%) patients underwent neoadjuvant chemotherapy, 54 (37.2%) underwent neoadjuvant radiation therapy, and 5 (3.5%) underwent neoadjuvant immunotherapy. Cronbach alpha values were 0.83 and 0.92 for symptoms severity items and interference items, respectively. Sensitivity was supported by the ability of MDASI-UGI-Surg to detect significant differences in symptom and interference levels according to performance status. **CONCLUSIONS:** The new MDASI-UGI-Surg is a new, psychometrically validated tool that can be used to capture dynamic changes in QoL through phases of multidisciplinary treatment in patients with PGE cancers.

P493. Treatment and Outcomes for Patients with Inadequate Lymphadenectomy after Resection of Stage II Small Bowel Adenocarcinoma

Jackson Baril, MD[1]; Karl Y Bilimoria, MD,MS[2]; Eugene P Ceppa, MD[3]; Michael G House, MD[4]; Anita A Turk, MD[5]; Thomas K Maatman, MD[6]; Alex M Roch, MD, MS[7]; C. Max Schmidt, MD, PhD[8]; Ryan J Ellis, MD,MS[9]

[1]Surgical Outcomes and Quality Improvement Center (SOQIC), Department of Surgery, Indiana University, Indianapolis, IN, US; [2]Surgical Outcomes and Quality Improvement Center (SOQIC), Department of Surgery, Indiana University, Indianapolis, IN, US; [3]Division of Surgical Oncology, Department of Surgery, Indiana University, Indianapolis, IN, US; [4]Division of Surgical Oncology, Department of Surgery, Indiana University, Indianapolis, IN, US; [5]Division of Hematology/Oncology, Department of Medicine, Indiana University, indianapolis, IN, US; [6]Division of Surgical Oncology, Department of Surgery, Indiana University, Indianapolis, IN, US; [7]Division of Surgical Oncology, Department of Surgery, Indiana University, Indianapolis, IN, US; [8]Division of Surgical Oncology, Department of Surgery, Indiana University, Indianapolis, IN, US; [9]Surgical Outcomes and Quality Improvement Center (SOQIC), Department of Surgery, Indiana University, Indianapolis, IN, US

INTRODUCTION: Adjuvant chemotherapy (AC) is considered for patients with Stage II small bowel adenocarcinoma (SBA) with an inadequate lymphadenectomy. However, the selective use of AC based on high-risk features (e.g., T4 primary, positive margin, poorly differentiated, or lymphovascular invasion) is not well established. The objectives of this study were to (1) describe

utilization of AC after inadequate lymphadenectomy for patients with Stage II SBA, (2) identify factors associated with receipt of AC, and (3) examine the association between AC and survival with or without other high-risk features. **METHODS:** Patients with upfront surgery for pathologic Stage II SBA (T3-T4 N0 M0) were identified in the National Cancer Database from 2004 to 2021. An inadequate lymphadenectomy was defined as <5 lymph nodes for tumors of the duodenum and <8 for other small bowel locations. Factors associated with receipt of AC (within 12 weeks of surgery) were assessed using multivariable logistic regression. Survival was assessed by Kaplan-Meier method and Cox proportional hazards. **RESULTS:** Of 15,491 patients who had upfront surgery for SBA, 5,105 (33.0%) had pathologic Stage II cancer. Of those, 1,921 (38.3%) had inadequate lymphadenectomy (mean age 66.6 years; 45.5% female). Of this final cohort,123 had additional high-risk features (58.5%), and 525 received AC (27.3%). Several clinicopathologic features were associated with receiving AC, including T4 tumor (vs T3; aOR 1.97, 95%CI 1.50-2.57; p<0.001), poorly differentiated tumor (vs moderately; aOR 1.42, 95%CI 1.07-1.89; p=0.02), and positive resection margin (vs negative; aOR 1.62, 95%CI 1.12-2.35; p=0.01). Patients aged 70-79 (aOR 0.37, 95%CI 0.59-1.17;0.001) were less likely to receive AC than those aged 50-59. Receipt of AC was associated with higher 5-year adjusted survival (54.3% vs 44.6%; Hazard Ratio for mortality (HR) 0.78, 95%CI 0.66-0.94; p=0.007). When stratified by the presence of additional high-risk features, receipt of AC was associated with higher 5-year survival in patients with additional high-risk features (49.3% vs 34.2%; HR 0.72, 95%CI 0.59-0.89; p=0.003) but not in patients with no additional high-risk feature (65.6% vs 55.3%; HR 0.92, 95%CI 0.66-1.30; p=0.65) (Figure 1). **CONCLUSIONS:** AC is not routinely administered to patients with Stage II SBA and inadequate lymphadenectomy. Receipt of AC was associated with improved survival in patients with additional high-risk features on adjusted analyses. High-risk pathologic features may assist in recommending AC in Stage II SBA with inadequate lymphadenectomy.

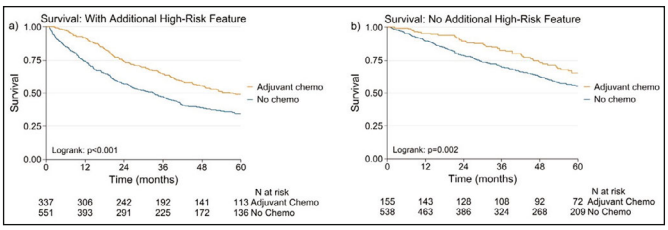


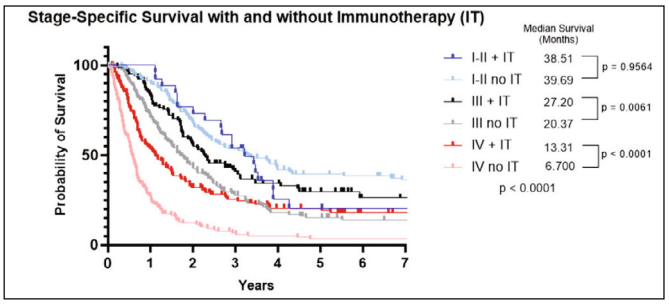
Figure 1. Kaplan-Meier survival curves among patients with Stage II small bowel adenocarcinoma and any additional high-risk features (a) and with no additional high-risk feature (b) stratified by receipt of adjuvant chemotherapy.

P494. A Novel Patient-Derived Xenograft Model of Inflammatory Breast Cancer

Tiffany C. Cheung, DO[1]; Monica Khattak, DO[2]; Yun Yun Sun, MD[3]; Pushpinder K Bains, PhD[4]; Daniel Campo, PhD[5]; Patrick McIntire, MD[6]; Alexander Ring, MD, PhD[7]; Gregor Krings, MD, PhD[8]; Karin List, PhD[9]; Ruth Keri[10]; Julie Lang, MD[11]

[1]Cleveland Clinic, Cleveland, OH, US; [2]Cleveland Clinic - South Pointe Hospital, Warrensville Heights, OH, US; [3]University of Southern California, Los Angeles, CA, US; [4]University of Southern California, Los Angeles, CA, US; [5]Next Bioinformatics, Los Angeles, CA, US; [6]Cleveland Clinic, Cleveland, OH, US; [7]University of Southern California, Los Angeles, CA, US; [8]Cleveland Clinic, Cleveland, OH, US; [9]Wayne State University, Detroit, MI, US; [10]Cleveland Clinic, Cleveland, OH, US; [11]Cleveland Clinic, Cleveland, OH, US

INTRODUCTION: Inflammatory breast cancer (IBC) is one of the most aggressive forms of breast cancer, but few models exist for studying experimental therapeutics. The objective of our study was to establish a novel patient-derived xenograft (PDX) from a HER2 positive IBC patient refractory to neoadjuvant chemotherapy to better understand the biology of IBC resistance. **METHODS:** A novel PDX was derived from a patient with hormone receptor negative, HER2 positive IBC refractory to neoadjuvant chemotherapy with Docetaxel, Carboplatin, Trastuzumab, and Pertuzumab (TCHP). Tumor was implanted into NOD SCID gamma mice and used for serial propagation of PDX. We performed short-tandem repeat (STR) profiling, immunohistochemistry (IHC), and plotted tumor growth curves for mice treated with alpelisib/everolimus (AE) vs untreated. Paired Student's t-tests were used to compare tumor growth curves. We used 10X genomics for single cell transcriptome analysis of 1000 cells derived from the PDX, ctDNA, whole exome and RNA sequencing to further characterize the genetic landscape of the PDX model. **RESULTS:** Tumor next generation sequencing (NGS) showed a hotspot mutation in PIK3CA (H1047R), a variant associated with resistance to HER2 targeted therapy and chemotherapy, but sensitivity to everolimus. Using STR profiling, we confirmed that the PDX and primary tumor were derived from the same patient. By the 3rd generation transplant, 15/15 orthotopically transplanted mice produced PDX. The mean tumor size was 619 mm3. Five mice were then treated with a combination of AE for 20 days to block signaling of the PI3K/AKT/mTOR pathway. Tumor growth was compared over 21 days (Figure 1). After treatment with AE, the tumor size decreased significantly (869.9mm3 vs. 45.8mm3, p = 0.006). No mice (0/15) had metastasis on necropsy at the time of meeting humane endpoints. We performed IHC to assess the protein expression in treated vs untreated tumors. All tumors strongly expressed JAK2. Receptor expression changed after neoadjuvant TCHP (from HER2 positive to triple negative). The group treated with AE had higher expression of PIK3CA, CD24, and HER2. **CONCLUSIONS:** We established a novel PDX of a HER2 positive IBC tumor with a PIK3CA hotspot mutation (H1047R) refractory to trastuzumab. Few PDX models have been created to study IBC. AE decreased tumor growth in our model. JAK2 was strongly expressed in both treated and untreated tumors. TCHP resistant tumor cells downregulated HER2 expression, which was re-expressed after treatment with AE. Targeting the PI3K/mTOR pathway may be useful to overcome resistance in HER2 positive IBC with a H1047R mutation in PIK3CA.



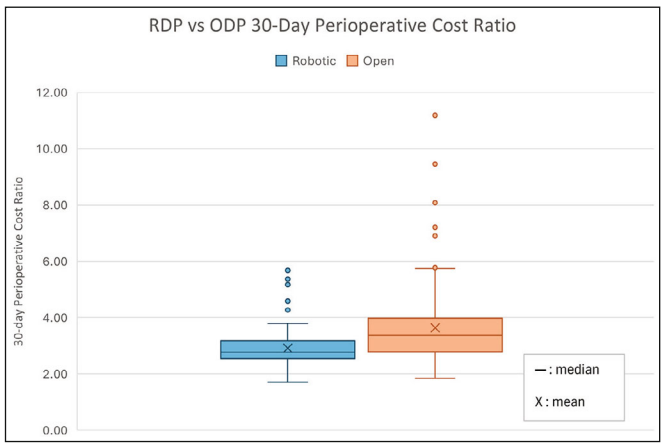
P495. Short-Term Outcomes and Costs of Robotic vs. Open Distal Pancreatectomy in the First 5 Years of a Robotic Surgical Oncology Program at a U.S. Cancer Center

Anneliese Hierl[1]; Jessica E. Maxwell, MD MBA[2]; Elsa M Arvide[3]; Morgan Bruno[4]; Whitney Dewhurst[5]; Laura Prakash[6]; Yi-Ju Chiang[7]; Rebecca A. Snyder, MD, MPH[8]; Michael P. Kim, MD[9]; Hop S. Tran Cao, MD[10]; Ching-Wei D. Tzeng, MD[11]; Matthew H.G. Katz, MD[12]; Naruhiko Ikoma, MD[13]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [4]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [5]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [6]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [7]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [8]MD Anderson Cancer Center, Houston, TX, US; [9]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [10]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [11]The University of Texas MD Anderson Cancer Center, Houston, TX, US; [12]MD Anderson Cancer Center, Houston, TX, US; [13]UT MD Anderson Cancer Center, Houston, TX, US

INTRODUCTION: The robotic approach is increasingly popular in pancreatic surgery, yet its safety and cost-effectiveness, particularly during early surgeons' early experience, are not well established. We compared 90-day outcomes and costs of robotic distal pancreatectomy (RDP) and open distal pancreatectomy (ODP), including the initial phase of our robotic program at a cancer center. **METHODS:** We identified all patients who underwent RDP or ODP at our center from January 2018 to May 2024, including initial robotic pancreatectomy cases. Clinical data and 90-day outcomes were collected from a prospective department database. Cost data were obtained from the financial department then converted to ratios relative to average ODP costs and limited to 30 days postoperatively to exclude adjuvant chemotherapy. A 1:1 propensity score matching (PSM) method was used to compare cohorts, matching on sex, age, BMI, ASA, and surgery indication. **RESULTS:** We identified 119 RDP and 164 ODP patients (283 total); 202 were included after PSM (101/group). Median age was 65 years (19-86 years) and median BMI 27.6 kg/m2 (16.6-55.3 kg/m2). Comparisons

of the matched cohorts demonstrate that RDP patients had lower estimated blood loss (median, 50 vs 200 cc; p<0.001), shorter length of stay (median, 3 vs 5 days;0.001), fewer total inpatient oral morphine equivalents (OME) used (median, 68 vs 143; and discharge OME prescribed (median 12.5 vs 25;0.001). RDP and ODP groups had no significant differences in Accordion grade >3 complications (10% vs 17%; p=0.214), infectious complications (11% vs 18%; p=0.228), pulmonary complications (4% vs 5%; p=1), pulmonary embolisms (0% vs 3%; p=0.246), cardiac complications (6% vs 4%; p=0.748); length of surgery (median 4.4 vs 4.5 hours; p=0.948), or readmissions within 90-days (17% vs 17%; p=1). RDP patients had a higher rate of biochemical leaks (35% vs 22%; p=0.06) but similar rates of grade B postoperative pancreatic fistula (12% vs 19%; p=0.241). One death in the ODP, but none in the RDP group, occurred within 90-days. Intraoperative cost ratio was significantly higher for RDP (1.30 vs 1.00;0.001). However, perioperative and 30-day perioperative cost ratio were significantly lower for RDP (1.27 vs 1.83;0.001 and 2.77 vs 3.37;0.001, respectively). **CONCLUSIONS:** RDP was safe with 90-day outcomes comparable to ODP in our early robotic program. Although intraoperative costs were higher, RDP costs were significantly lower in the 30-day perioperative period. More research is needed on quality-of-life benefits and patient selection for RDP.



ABSTRACTS

Participating in the

GLOBAL PARTNER POSTERS PROGRAM

SSO 2025 ANNUAL MEETING

Society of Surgical Oncology

March 27-29, 2025

GPP1. Clinical outcomes in patients with synchronous bilateral breast disease who received neoadjuvant chemotherapy

Soong June Bae, MD[1]; Minji Lee, MD[2]; Seung Ho Baek, MD[3]; Yoonwon Kook, MD[4]; Sung Gwe Ahn, MD, PhD[5]; Joon Jeong, MD, PhD[6]

[1]Gangnam gu Gagnam severance hospital, Seoul, Republic of Korea; [2], , , ; [3], , , ; [4]Department of Surgery, Gangnam gu, Seoul, Republic of Korea; [5]Seoul, Republic of Korea; [6]Department of Surgery Gangnam Severance Hospital, Seoul, Republic of Korea

INTRODUCTION: The application of neoadjuvant chemotherapy (NAC) has increased for downstaging tumors and tailoring adjuvant treatment in patients with early breast cancer. However, evidence on the clinical implications for the patients with synchronous bilateral breast disease undergoing NAC remain limited. **METHODS:** In the neoadjuvant setting, we retrospectively analyzed the characteristics of the synchronous bilateral breast disease compared to the unilateral invasive breast cancer. Patients with synchronous bilateral breast disease were defined as those having invasive cancer in both breasts or having unilateral invasive cancer with contralateral ductal carcinoma in situ (DCIS). Subtype concordance and treatment response in this subpopulation was also evaluated. **RESULTS:** Among the 1,576 patients who received NAC, 26 (1.6%) had synchronous bilateral breast disease. Of these, 18 (69.2%) had bilateral invasive cancer, while 8 (30.8%) patients had unilateral invasive cancer with contralateral DCIS. The HR+HER2- subtype proportion was significantly higher in the bilateral disease group (59.1% vs. 30.5%), yet no significant differences in treatment response and survival outcomes between the unilateral and bilateral disease groups. The concordance rate of subtypes between both breast diseases was 44.4% (8 of 18) in patients with bilateral invasive cancer and 25.0% (2 of 8) in patients with unilateral invasive cancer and contralateral DCIS. The majority of patients (90% [9 of 10]) with concordant subtypes between both breast lesions had HR+HER2- disease. There were no bilateral pathologic complete response (pCR) cases in patients with bilateral invasive cancer. Additionally, in patients with unilateral invasive cancer and contralateral DCIS, the contralateral DCIS often remained after NAC, regardless of the response of the invasive cancer. **CONCLUSIONS:** Bilateral excellent response to NAC was rare in patients with synchronous bilateral invasive breast cancer, likely due to the high rate of subtype discordance and the predominance of the HR+HER2- subtype. Furthermore, contralateral DCIS often persisted post-NAC. Nevertheless, the patients with synchronous bilateral breast disease exhibited survival comparable to those with unilateral invasive cancer.

GPP2. Additional colectomy after endoscopic excision of malignant polyps: is it really necessary?

Mariana E Marques[1]; Mariana Peyroteo[2]; Luís Lencastre[3]; André V Guimarães[4]; Maria J Cardoso[5]; Paula F Pinto[6]; José C Pereira[7]; Flávio Videira[8]; Joaquim Abreu de Sousa[9]

[1]Portuguese Institute of Oncology - Oporto.; [2]Portuguese Institute of Oncology - Oporto.; [3]Portuguese Institute of Oncology - Oporto.; [4]Portuguese Institute of Oncology - Oporto.; [5]Portuguese Institute of Oncology - Oporto.; [6]Portuguese Institute of Oncology - Oporto.; [7]Portuguese Institute of Oncology - Oporto.; [8]Portuguese Institute of Oncology - Oporto.; [9]Portuguese Institute of Oncology - Oporto.

INTRODUCTION: Colonic malignant polyps are identified in 1% of colonoscopies performed for positive fecal occult blood tests. Oncological surgery is recommended after incomplete excision and/or in the presence of recognized risk factors. However, there has been some debate as to whether additional surgery is truly necessary for these lesions. The objective of this study was to evaluate the short and long-term results of surgery following endoscopic excision of malignant colon polyps. **METHODS:** We present a 6-year retrospective observational study, in a tertiary oncology center, analyzing all patients diagnosed with malignant colonic polyps after endoscopic excision, submitted to posterior oncological surgery, whose histology revealed pT=2, treated at the Institution, between January 2015 and December 2020. Patients with history of familial syndromes were excluded. **RESULTS:** 124 patients were included. 4 underwent polypectomy of 2 malignant polyps at the same time. Additional data can be found in table 1. Of the 128 endoscopic excision specimens, the majority were located at the sigmoid colon (75%) and most of them (80.5%) also demonstrated more than one histological risk factor, namely, deep submucosal invasion – DSI (>1000 µm), tumor budding, grade 2 or 3, lymphatic, venous or perineural invasion. In 51 (40%) of the endoscopic resection specimens, margins were R1, R2, or not safely assessable. Of the remaining 77 (R0 endoscopic resection), 25 had a single histological risk factor, majority of which (76%) only had DSI. Of these 25 specimens, none had residual disease in the surgical specimen (local or nodal), and none had disease recurrence. Of the 124 surgical specimens, 13 (10.5%) revealed residual disease: 6 (4.84%), local disease in the colon – 4 of which had non-evaluable or R1 margins after endoscopic resection; and 8 (6.5%), lymph node disease. All pN+ patients had = 2 histological risk factors or insufficient margins on the endoscopic specimen. Major morbidity (CTCAE 3 or 4) was recorded in 11 (8.9%) patients. No cases of mortality were recorded. 3 patients presented systemic relapse (median follow-up of 59 months); 2 of which pN+; and the other, pN0, with R1 endoscopic margin and a single histological risk factor - histological grade 2. **CONCLUSIONS:** In our findings, 10.5% of patients presented disease in the surgical specimen after endoscopic excision, which is in accordance with the literature. Furthermore, of the patients who presented with only 1 risk factor after a R0 endoscopic resection (the majority with only DSI), none had residual disease in the surgical specimen, and none relapsed. The low rate of disease in the surgical specimen after endoscopic excision, particularly in patients with a single risk factor, suggests that there is scope for further refinement in the indication for radical surgery after endoscopic excision of malignant polyps.

GPP3. Association of neighborhood socioeconomic status and ethnic diversity with receipt of adjuvant chemotherapy in stage III colon cancer: a population-based cohort study

Julie Hallet, MD, MSC[1]; Adom Bondzi-Simpson, MD MSc[2]; Ramy Behman, MD PhD[3]; Tiago Ribeiro, MD[4]; Sheron Perera, MD, PhD[5]; Aisha Lofters, MD PhD[6]; Rinku Sutradhar, PhD[7]; Vivian Aghanya, MPH[8]; Andrea Covelli, MD PhD[9]; Rebecca A. Snyder, MD MPH[10]; Callisia N. Clarke, MD MS[11]; Natalie G. Coburn, MD MPH[12]

[1]Department of Surgery, Sunnybrook Health Sciences Centre, Canada; [2]Department of Surgery, University of Toronto, Toronto, Ontario, Canada; [3]Department of Surgery, University of Toronto, Toronto, Ontario, Canada; [4]Department of Surgery, University of Toronto, Toronto, Ontario, Canada; [5]Division of Medical Oncology, Odette Cancer Centre – Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada; [6]Peter Gilgan Centre for Women's Cancers, Women's College Hospital, Toronto, Ontario, Canada; [7]Institute of Health Policy Management and Evaluation, University of Toronto, Toronto, Ontario, Canada; [8]ICES, Toronto, ON, Canada; [9]Department of Surgery, University of Toronto; [10]Departments of Surgical Oncology and Health Services Research, University of Texas MD Anderson Cancer Center, Houston, Texas, US; [11]Division of Surgical Oncology, Department of Surgery, Medical College of Wisconsin, Milwaukee, WI, US; [12]Department of Surgery, University of Toronto, Toronto, Ontario, Canada

INTRODUCTION: In eligible patients, adjuvant chemotherapy decreases cancer recurrence and improves overall survival. Barriers to accessing such care may contribute to inequity in oncological outcomes. We examined the association between neighborhood socioeconomic status (SES) and ethnic diversity on receipt of adjuvant chemotherapy in stage III patients with colon cancer. **METHODS:** We conducted a population-based retrospective cohort study of adults undergoing surgery for stage III colon cancer (2007- 2020). The primary exposures were SES and ethnic diversity defined by ecologic measures from census data, both measured as quintiles. Outcomes were receipt of medical oncology consultation and adjuvant therapy, within 3 months after surgery. Logistic regression measured the association between each exposure and outcomes while adjusting for confounders. A sub-group analysis examined the receipt of adjuvant therapy restricted to patients who received a medical oncology consultation post-surgery. **RESULTS:** Of 14,511 patients included, 10,973 (76.5%) received medical oncology consultation and 8,814 (61.4%) adjuvant chemotherapy within 3 months of surgery. After adjusting for age, sex, surgical approach, and comorbidities, SES and ethnic diversity were not associated with medical oncology consultation. However, both the lowest SES quintile and the highest ethnic diversity quintile were associated with lower odds of adjuvant chemotherapy (OR – 0.70; 95% confidence interval – CI 0.62-0.80 and OR 0.72; 95% CI 0.64-0.82 respectively). When extending outcomes to 6 months after surgery, these associations persisted. When restricted to patients who had a medical oncology consultation, both the lowest SES quintile and highest ethnic diversity quintile were associated with lower odds of adjuvant chemotherapy (OR 0.70; 95% 0.62-0.79 and OR 0.73; 95% CI 0.65-0.83). **CONCLUSIONS:** Lower SES and higher ethnic diversity were independently associated with lower odds of adjuvant chemotherapy but not medical oncology consultation. These findings outline equal processes but different outcomes for marginalized patient groups within a universal healthcare system which may translate to inequity in oncologic care.

GPP4. Understanding the Correlation Between Social Determinants of Delays in Diagnosis, Management and Outcomes for Solid Cancers in Tamil Nadu - A Multicentric Mixed Method Study

Rajkumar K. Seenivasagam, MS, MCh, FRCSEd, FACS[1]; Saranya Rajamanickam, MD CCEBDM[2]; Subbiah Shanmugam, MS MCh[3]; Ramesh Muthuvelu, MS MCh[4]; Marimuthu Saravanamuthu, MS MCh[5]; Sudha Ramalingam, MD[6]; Arulmurgan Ramalingam, MS MCh[7]; Sandhiya Venkatesan, MD[8]; Gurumurthy A. Narayanasamy, MS MCh[9]; Kirubakaran S., MD[10]; Vijaykumar R., MD[11]; Abinaya S., MD[12]

[1]PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India; [2]PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India; [3]Govt. Royapettah Hospital & Kilpauk Medical College, Chennai, Tamil Nadu, India; [4]Govt. Rajaji Hospital & Madurai Medical College, Madurai, Tamil Nadu, India; [5]Thanjavur Medical College, Thanjavur, Tamil Nadu, India; [6]PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India; [7]PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India; [8]PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India; [9]Govt. Rajaji Hospital & Madurai Medical College, Madurai, Tamil Nadu, India; [10]Govt. Omandurar Medical College, Chennai, Tamil Nadu, India; [11]PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India; [12]PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India

INTRODUCTION: Geographical and social barriers to healthcare contribute to delays in diagnosis and treatment of cancers and therefore impact cancer outcomes. Identifying these determinants will help address health care gaps, decrease delays and improve cancer outcomes. Aim of study was to understand the correlation between social determinants of delays in cancer diagnosis and management for patients with oral cavity (including lip), lung and Gastrointestinal cancers in Tamil Nadu, India. **METHODS:** The study was Multicentre, Mixed Methods operational research done (Quantitative and Qualitative) in 2076 patients with oral cavity, lung and Gastrointestinal cancers and 10 oncologists from 32 cancer hospitals in Tamilnadu. Socioeconomic and demographic profile of patients, geographic distances from healthcare facilities, delays in cancer diagnosis and management (in days) and patient reported reasons for delays were collected from hospital records and patient interviews. Delays more than 4 weeks for diagnosis and 8 weeks for treatment were considered significant. Quantitative analysis was done using SPSS 24.0. Delays were correlated with socio-demographic and health-system-related factors using multivariate linear regression. Pearson correlation > 0.3 was suggestive of strong correlation. P-value < 0.05 was considered statistically significant. Key Informant Interviews (KII) were undertaken with purposefully selected doctors from study areas and transcribed for qualitative analysis. A grounded theory-influenced approach was used to explore participants' experiences in cancer delays based on a Thematic analysis. **RESULTS:** Significant cancer delays were identified – patient related delay (54.6%), referral delay (26.1%), diagnostic delay (45%) and treatment delay (10%). Most common patient reported reasons for delays were patient awareness, referral delays by primary care doctors, second opinions and financial barriers. These delays strongly correlated with distance from treating hospital, availability of oncologists, number of doctors/hospitals visited, elderly/single/widowed patients, relationship of primary caregiver, family income, and patients living in certain districts of Tamil Nadu. Qualitative analysis identified certain patient centric factors like fear and denial, financial barriers, impact of alternative therapy, lesser awareness and acceptance of screening; and healthcare system challenges like infrastructure, oncologist accessibility, insurance barriers, referral and treatment pathway streamlining and standardisation challenges. **CONCLUSIONS:** This was the first multicentric operational research study done on cancer delays in Tamil Nadu and was led by surgical oncologists. Based on the results from the study, recommendations were given to Tamil Nadu government for implementation.

GPP5. Clinical Impact of Conversion Surgery After Induction Therapy for Esophageal Cancer with Synchronous Distant Metastasis: A Multi-institutional Retrospective Study

Keijiro Sugimura[1]

[1]Department of Surgery, Kansai Rosai Hospital, Amagasaki, Hyogo, JP

INTRODUCTION: The standard treatment for advanced esophageal cancer with synchronous distant metastasis is systemic chemotherapy or immunotherapy. Conversion surgery is not established for esophageal cancer with synchronous distant metastasis. This study aimed to investigate the clinical impact of conversion surgery for esophageal cancer with synchronous distant metastasis after induction therapy. **METHODS:** This multi-institutional retrospective study enrolled 66 patients with advanced esophageal cancer, including synchronous distant metastasis, who underwent induction chemotherapy or chemoradiotherapy followed by conversion surgery between 2005 and 2021. Short- and long-term outcomes were investigated. **RESULTS:** Distant lymph node (LN) metastasis occurred in 51 patients (77%). Distant organ metastasis occurred in 15 (23%) patients. There were 41 patients with metastatic para-aortic LNs, and 10 patients with other metastatic LNs. Organs with distant metastasis included the lung in seven patients, liver in seven patients, and liver and lung in one patient. For 61 patients (92%), R0 resection was achieved. The postoperative complication rate was 47%. The in-hospital mortality rate was 1%, and the 3- and 5-year overall survival (OS) rates for all the patients were 32.4% and 24.4%, respectively. The OS rates were similar between the patients with distant LN metastasis and the patients with distant organ metastasis (3-year OS: 34.9% vs. 26.7%; P = 0.435). Multivariate analysis showed that pathologic nodal status is independently associated with a poor prognosis (hazard ratio, 2.43; P = 0.005). **CONCLUSIONS:** Conversion surgery after chemotherapy or chemoradiotherapy for esophageal cancer with synchronous distant metastasis is feasible and promising. It might be effective for improving the long-term prognosis for patients with controlled nodal status.

GPP6. Multi-Sample Approach for Breast Cancer Prognostic Biomarkers via Microbiome Profiling

Jeongshin An, MD, PhD, Professor[1]

[1]Institute of Convergence Medicine Research, Ewha Womans University Mokdong Hospital, College of Medicine, Ewha Womans University

INTRODUCTION: Breast cancer is the most common malignancy among women worldwide. With the rising incidence of breast cancer, managing risk factors that influence its prognosis has become essential. Recent evidence suggests that the microbiome has the potential to contribute to breast cancer development and holds promise as a potential prognostic biomarker. **METHODS:** Blood, urine, and stool samples were collected from breast cancer patients diagnosed with stages 0 to 3, but excluding stage 4. Samples were obtained after histological confirmation of breast cancer and before chemotherapy, radiotherapy, or surgery. Bacterial extracellular vesicles (EVs) were isolated from blood samples for microbiome profiling. Comparative analysis of the microbiome across different sample types was conducted, along with subgroup analysis targeting specific breast cancer risk factors. **RESULTS:** Microbiome profiling across different sample types revealed distinct expression patterns, with initial changes observed in the digestive tract, particularly in fecal samples. These changes were followed by subsequent impacts on the blood or lymphatic system and eventual excretion through urine, providing insights into the gut-breast axis. Further analysis focused on specific breast cancer risk factors, such as elevated fasting glucose and high low-density lipoprotein (LDL) cholesterol levels, both of which are associated with increased breast cancer risk. Subgroup analysis identified several candidate microbiome groups correlated with these factors. Notably, the analysis demonstrated a significant correlation between high LDL cholesterol and elevated glucose levels, which were further associated with high BMI. These metabolic risk factors also showed a potential link to fatty liver based on microbiome findings. The observed associations between these risk factors offer a potential explanation for how the microbiome may contribute to breast cancer progression. Among the identified microbiome groups, the family Christensenellaceae was significantly linked to breast cancer prognosis. Patients with Christensenellaceae levels exceeding 0.01% showed improved disease-free survival, supported by a log-rank P value of 0.045. **CONCLUSIONS:** This study identified potential prognostic biomarkers through microbiome analysis, suggesting that microbiota-targeted interventions could influence breast cancer prognosis. Further research is required to validate these findings and develop microbiome-based tools for clinical application.

GPP7. A competent Pancreatico Jejunostomy After Pancreaticodoudenectomy

Medhat Khafagy[1]

[1]National Cancer Institute Cairo University, Cairo, EG

INTRODUCTION: Background: Pancreatic anastomosis is the corner stone of pancreaticoduodenectomy. Postoperative pancreatic fistula is a major cause of morbidity and mortality. The optimal method of pancreatic remnant reconstruction is controversial and no single technique has shown to be superior. The aim of this work was to present the results of a novel technique for pancreaticojejuonostomy in 36 patients after pancreaticoduodenectomy. **METHODS:** Method: Our anastomosis is a two layers anastomosis. First layer was done with interrupted transverse mattress sutures with 4/0 PDS

including the whole thickness of the pancreas and whole thickness of the jejunum (not duct to mucosa only). Sutures are taken over a 14 G stent inserted in the pancreatic duct and jejunum. A second interrupted mattress sutures were taken between the seromuscular coat of the jejunal stump and the outer half thickness of the pancreas. **RESULTS:** Results: 36 patients underwent pancreaticoduodenectomy from 2000 to 2018 for malignant or benign diseases. All underwent pancreaticojejunostomy for reconstruction of the pancreas. The age ranged from 17 to72 years with a median of 58 years. The tumour size ranged from 1 to 6 cm. There was no postoperative leakage from pancreaticojejunostomy. The postoperative morbidity rate was 25 % (9 / 36). The postoperative complications were wound infection which occurred in 5.56 % (2 / 36), stress gastric ulcer and hematemesis which occurred in 8.33 % (3 / 36), Delayed gastric empting which occurred in also 8.33 % (3 / 36) and pulmonary embolism which occurred in 2.78 % (1 / 36). The postoperative mortality occurred only in 2 patients (5.56 %), one due to myocardial infarction and the other due to cerebrovascular stroke. **CONCLUSIONS:** Conclusion: Performing small aperture in the jejunal stump is crucial in preventing leakage after pancreaticojejunostomy and was performed in this study with a 14 G trocar. Keywords: pancreaticodudenectomy, pancreaticojejunostomy, postoperative pancreatic fistula, pancreatic surgery.

GPP8. Awareness of hereditary breast cancer and genetic testing among patients with breast cancer in Nigeria: A multi-centre study

Funmilola O Wuraola, MBBS, ChM[1]; Jenine Ramruthan, Msc[2]; Emma Reel, MSW[3]; Agodirin Olaide, MBBS, MSc[4]; Nneka Sunday-Nweke, MBBS[5]; Mary Ogunyemi[6]; Olawale Boladuro[7]; Saheed Lawal[8]; Olusegun I Alatise, MBChB, MS[9]; Tulin D Cil, MD[10]

[1]Department of Surgery, Faculty of Clinical Sciences, Obafemi Awolowo University Ile-Ife, Nigeria; [2]Department of General Surgery, University Health Network; [3]Department of General Surgery, University Health Network; [4]Department of Surgery, University of Ilorin, Ilorin, Nigeria; [5]Department of Surgery, University of Ilorin, Ilorin, Nigeria; [6]African Research Group on Oncology; [7]Department of Surgery, Alex Ekwueme Federal University Teaching Hospital, Abakaliki, Nigeria; [8]African Research Group on Oncology; [9]Department of Surgery, Obafemi Awolowo University Teaching Hospital Complex; [10]Department of Surgery, University of Toronto,

INTRODUCTION: Breast cancer remains a significant public health concern in Nigeria, often diagnosed at advanced stages due to delayed presentation and limited awareness. Understanding patient knowledge of breast cancer is essential to improve early detection and outcomes. This study aimed to assess the demographic and clinical characteristics of breast cancer patients across three Nigerian hospital centres and evaluate their knowledge of breast cancer risk factors, hereditary breast cancer, and genetic testing. **METHODS:** A cross-sectional study was conducted among 230 newly diagnosed patients with breast cancer attending three major teaching hospitals in Ile-Ife, Ilorin, and Abakaliki in Nigeria. Data on demographics, tumour characteristics, and molecular subtypes were collected. Knowledge of breast cancer symptoms, risk factors and hereditary breast cancer was assessed using a structured questionnaire. Univariable and multivariable linear and logistic regression analyses identified factors associated with knowledge scores. **RESULTS:** The mean age of participants was 48.3 years; the majority were female (99.1%); most patients were traders (51.1%) and of low socioeconomic status (66.5%). Educational levels varied, with 33.0% having tertiary education. A large proportion presented at advanced stages (Stage III: 51.7%, Stage IV: 21.3%), with 64.3% having triple-negative breast cancer. Knowledge of risk factors was low, with higher knowledge associated with tertiary education ($p = 0.004$) and higher socioeconomic status ($p = 0.020$), while older age (=65) was linked to lower scores ($p = 0.091$). Participants from Ilorin had lower knowledge of breast cancer symptoms than those from Ile-Ife ($p < 0.001$). Regarding hereditary breast cancer, only 11 patients (4.8%) had heard of BRCA genes; of these, most had a tertiary education. Willingness to undergo BRCA1/2 genetic testing was high (95.7%), with 93.9% willing to inform siblings and 96.5% willing to encourage genetic testing for family members. **CONCLUSIONS:** Awareness of hereditary breast cancer was low despite high willingness for genetic testing. Higher education and socioeconomic status remained strong predictors linked to higher knowledge of breast cancer risk factors. Knowledge gaps were more pronounced among older, less educated patients and those with lower socioeconomic status. Our findings highlight the need for targeted education to improve the understanding of hereditary breast cancer and genetic testing in this setting.

GPP9. Evaluation of the Expression of Soluble Coestimulatory Molecules of Lymphocyte Activation sOX40, sOX40L, s4-1BB and sICOS in Gastric Cancer

Cecilia Araújo Carneiro Lima[1]; Mário Rino Martins, MD, PhD[2]; Nora Manoukian Forones, MD, PhD[3]; Leuridan Cavalcante Torres, PhD[4]

[1]Hospital Israelita Albert Einstein, São Paulo, Brazil and Hospital de Câncer de Pernambuco, Recife,, , , BR; [2]Hospital de Câncer de Pernambuco, Recife, BR; [3]Department of Digestive Surgery, Universidade Federal de São Paulo (UNIFESP), São Paulo, BR; [4]Translational Research Laboratory Prof CA Hart (IMIP), Instituto de Medicina Integral Prof. Fernando, Recife, BR,

INTRODUCTION: T cells play a central role in antitumor immunity in gastric cancer (GC). Previous studies have demonstrated that soluble forms of T-cell costimulatory molecules OX40 (sOX40), OX40L (sOX40L), 4-1BB (s4-1BB) and ICOS (sICOS) interact with immune cells and may participate in immune evasion by tumors in various cancers. The role of the soluble forms of these molecules in GC remains unclear. To evaluate the expression of OX40, OX40L, 4-1BB, and ICOS in their soluble form in the serum of patients with GC, and to analyze them according to clinical and anatomical-pathological variables. **METHODS:** A cross-sectional, exploratory, and translational study conducted at the Pernambuco Cancer Hospital and the Translational Research Laboratory at the Institute of Integral Medicine Prof. Fernando Figueira. The study evaluated 83 patients with gastric cancer and 20 healthy controls. Serum levels of sOX40, sOX40L, s4-1BB, and sICOS were analyzed using the enzyme-linked immunosorbent assay (ELISA). **RESULTS:** Patients with metastatic GC had elevated levels of sOX40 compared to those with advanced stage III ($p=0.0003$) and early stages I/II ($p=0.005$). Patients with high levels of sOX40 had more deaths ($p=0.0230$). Patients in early stages I/II had higher levels of s4-1BB and sICOS compared to those with advanced tumors ($p=0.003$ and $p=0.005$, respectively). Compared to the control group, patients with GC had reduced levels of sICOS ($p<0.0001$) and elevated levels of sOX40L ($p=0.0231$). Patients with higher levels of sICOS, s4-1BB, and sOX40L had better clinical and anatomical-pathological prognostic features. **CONCLUSIONS:** Serum levels of co-stimulatory molecules are associated with metastatic disease in GC and may represent biomarkers of advanced disease. These findings could guide future therapies for GC.

GP1. Addressing Global Inequities in Breast Cancer Genetic Testing, Counselling, and Management Among Breast Cancer Patients in Nigeria

Colleen Kerrigan, MD[1]; Funmilola Wuraola[2]; Jenine Ramruthan[3]; Emma Reel[4]; Andrea Covelli, MD[5]; Anna Dare, MD[6]; Jeanna McCuaig[7]; Larissa Peck[8]; Emily Thain[9]; Janet Papadakos[10]; Danielle Rodin, MD[11]; Michelle Jacobson, MD[12]; Olusegun I Alatise, MD[13]; Tulin D Cil, MD[14]

[1]Department of Surgery, University of Toronto; [2]Obafemi Awolowo University Teaching Hospital, Ife, Osun, NG; [3]Department of General Surgery, University Health Network; [4]Department of General Surgery, University Health Network; [5]Department of Surgery, University of Toronto, Toronto, Ontario, Canada; [6]Department of Surgery, University of Toronto; [7]Department of Molecular Genetics, University of Toronto; [8]Department of Genetics, Princess Margaret Cancer Centre; [9]Department of Genetics, Princess Margaret Cancer Centre; [10]Department of Cancer Education, Princess Margaret Cancer Centre; [11]Department of Radiation Oncology, University of Toronto; [12]Department of Obstetrics and Gynaecology, Women's College Hospital; [13]Department of Surgery, Obafemi Awolowo University Teaching Hospital Complex; [14]Department of Surgery, University of Toronto

INTRODUCTION: Breast cancer (BC) is a significant health challenge in Nigeria, characterized by early onset, late-stage diagnosis, and prevalent triple-negative tumors. While North America offers widespread genetic testing (GT) and counselling for BC risk and management, our recent data in Nigeria show that GT access and knowledge is limited. This study aims to develop and evaluate a hybrid educational training curriculum for Nigerian healthcare providers (HCPs). **METHODS:** From June to September 2023 an international oncology team developed a 4-module curriculum on hereditary BC genetics. Twenty-five HCPs completed the online curriculum, followed by in-person training in Nigeria. Pre and post knowledge scores were assessed using 10 standardized questions. **RESULTS:** Participants demonstrated significant knowledge improvement across all modules. Module 1 had marked improvement in interpreting BC incidence in Sub-Saharan Africa and disparities in survival. Module 2 showed knowledge enhancement in understanding implications of BRCA1/2 mutations, risk of secondary BC, and GT outcomes ($p = 0.0048$, $p = 0.02$, $p = 0.0175$). Module 3 showed increased understanding

in communicating variant of uncertain significance test results (p = 0.0013). Module 4 had considerable knowledge improvement with a 30.86-fold higher likelihood of identifying the tumor subtype of a BRCA1 carrier and an 11.56-fold higher likelihood of knowing the appropriate age for high-risk breast screening in women with a BRCA mutation (p = 0.0011, p = 0.0003, respectively). **CONCLUSIONS:** Our study demonstrates the hybrid training model effectively improved knowledge of hereditary BC genetics among Nigerian HCPs. This collaboration underlines the importance of accessible education for equitable BC care globally.

GP2. Experience of Targeted Axillary Surgery with Magseed® Localisation after Neoadjuvant Systemic Anti-Cancer Therapy

Akriti Nanda[1]; Evelyn Marshall[2]; Dalal Alaradi[3]; Jennifer Rusby[4]; Katherine Krupa[5]; Marios Tasoulis[6]; Peter Barry[7]; William Allum[8]; Radhika Merh[9]; Gerald Gui[10]; Rachel O'Connell[11]

[1]Royal Marsden NHS Foundation Trust, Breast Surgery, London, United Kingdom; [2]Royal Marsden NHS Foundation Trust, Breast Surgery, London, United Kingdom; [3]Royal Marsden NHS Foundation Trust, Breast Surgery, London, United Kingdom; [4]Royal Marsden NHS Foundation Trust, Breast Surgery, London, United Kingdom; [5]Royal Marsden NHS Foundation Trust, Breast Surgery, London, United Kingdom; [6]Royal Marsden NHS Foundation Trust, Breast Surgery, London, United Kingdom; [7]Royal Marsden NHS Foundation Trust, Breast Surgery, London, United Kingdom; [8]Royal Marsden NHS Foundation Trust, Breast Surgery, London, United Kingdom; [9]Royal Marsden NHS Foundation Trust, Breast Surgery, London, United Kingdom; [10]Royal Marsden NHS Foundation Trust, Breast Surgery, London, United Kingdom; [11]Royal Marsden NHS Foundation Trust, Breast Surgery, London, United Kingdom

INTRODUCTION: Targeted axillary dissection (TAD) is used to selectively remove marked metastatic axillary lymph node(s) alongside a sentinel lymph node biopsy (SLNB) to stage the axilla after neoadjuvant systemic anti-cancer therapy (NSACT). We share our experience of using Magseed® in marking nodes in women who are found to have metastatic node(s) at diagnosis who went on to have NSACT. **METHODS:** A retrospective analysis was conducted on 129 women with breast cancer who underwent NSACT with utilisation of Magseed® to mark an abnormal lymph node between October 2018 and December 2022. The presence and localisation of Magseed® in axillary lymph nodes were evaluated, as well as concordance between pre-operative imaging response and post operative pathological complete response (pCR). **RESULTS:** All 129 Magseed® were retrieved. In 107 (83%) the Magseed® was within a lymph node (LN). In 16 (12%) the Magseed® was not within a LN, but adjacent to one. In 6 (5%) this was not documented in neither the operation notes nor histopathology result. Radiologic complete response (rCR) on end of treatment ultrasound was observed in 77/129 (60%) of patients. pCR was achieved in 69/129 (53%) (30 via one step nucleic amplification (OSNA), 31 from OSNA and histopathology combined and 8 through histopathology alone) of patients. Imaging was concordant with OSNA/histopathology in 89/129 cases (69%). 53/77 (69%) of those with rCR had pCR and 16/52 (30%) with an incomplete imaging response had histological pCR. Of those with pCR, 67 had TAD+SLNB only and were spared axillary dissection by employing TAD. The breakdown of pCR according to molecular subtype is summarized in Table 1. Molecular subtype Pathological Complete Response Yes No Triple negative 24 12 HER2+ve 41 21 ER+ve/HER2-ve 4 27 Total 69 60 All patients were followed up with a median follow up of 22 months. 6 patients were stage IV on presentation and therefore excluded from further analysis. 18/123 (14.6%) patients developed a recurrence of disease. 1 supraclavicular (SCL) node recurrence, 4 ipsilateral breast recurrence, 10 distant recurrences, 3 patients had distant and loco-regional recurrence. There were no axillary recurrences. **CONCLUSIONS:** The findings demonstrate that Magseed®offers benefit in TAD after NSACT to de-escalate surgery by avoiding axillary dissection. There were no axillary recurrences in our dataset, though we acknowledge the follow up is short. Further long term follow up is required to assess longer term outcomes. rCR was not completely concordant with pCR, indicating the ongoing need for axillary surgery to stage the axilla after NSACT to help inform adjuvant treatment decision making.

GP3. Investigating the effectiveness and safety of volume displacement and replacement techniques in oncoplastic breast-conserving surgery

Loretta E Nyirády[1]; Jakub Hoferica[2]; Péter Fehérvári[3]; Péter Hegyi[4]; Attila Szijártó[5]; Zoltán Klárik[6]

[1]Department of Surgery, Transplantation and Gastroenterology, Semmelweis University, Budapest, Hungary; [2]Centre for Translational Medicine, Semmelweis University, Budapest, Hungary; [3]Centre for Translational Medicine, Semmelweis University, Budapest, Hungary; [4]Centre for Translational Medicine, Semmelweis University, Budapest, Hungary; [5]Department of Surgery, Transplantation and Gastroenterology, Semmelweis University, Budapest, Hungary; [6]Department of Surgery, Transplantation and Gastroenterology, Semmelweis University, Budapest, Hungary

INTRODUCTION: Oncoplastic breast-conserving surgery (OBCS) encompasses a variety of surgical techniques aimed at improving both aesthetic outcomes and safety in the treatment of early breast cancer. However, obscurity remains in the understanding of satisfaction rates and safety parameters associated with different OBCS techniques. This study endeavors to address this by undertaking a systematic review and meta-analysis to assess risk factors, satisfaction rates, and oncological safety parameters associated with different OBCS techniques. **METHODS:** A systematic exploration of the medical literature was conducted across three prominent databases – PubMed, Embase, and Cochrane Library (CENTRAL) – until November 2023. Original articles reporting quantitative satisfaction rates, frequencies of oncological safety indicators (such as recurrence rate, re-excision rate, positive margins, and distant metastases), and common complications (including hematoma, seroma, wound infection, and fat necrosis) were included. **RESULTS:** The systematic search yielded 17,374 records, from which 80 eligible studies were identified, with 46 providing quantitative data. Overall, all OBCS techniques exhibited high satisfaction rates (Proportion: 0.89; Confidence Interval [CI]: 0.85-0.92), with the volume displacement group demonstrating the highest satisfaction (Proportion: 0.93; CI: 0.85-0.97). Complications were generally infrequent, though volume replacement techniques showed slightly increased incidences of fat necrosis (Proportion: 0.07; CI: 0.04-0.12) and seroma (Proportion: 0.10; CI: 0.05-0.19). Nonetheless, both techniques displayed comparable safety profiles concerning oncological parameters such as overall recurrence (Proportion: 0.02; CI: 0.02-0.03) and re-excision rates (Proportion: 0.05; CI: 0.04-0.07). **CONCLUSIONS:** Oncoplastic breast-conserving surgeries emerge as a safe therapeutic option for treating early-stage breast cancer, characterized by low associated risks and high satisfaction rates. Tailoring surgical approaches to individual patient requirements and anatomical considerations is imperative for optimizing outcomes and minimizing complications.

GP4. Minimally invasive intraoperative ultrasound guided oncoplastic breast conservative surgery for multifocal breast cancers reduce volume excised and mastectomy rates compared to needle localization guided surgery

Antonio J Esgueva[1]; Carolina Sobrido[2]; María J Lucena[3]; Beatrice Pisillo[4]; Mauricio Cambeiro[5]; Teresa Iscar[6]; Fernando Martinez-Regueira[7]; Natalia R Spiteri[8]; Begoña Olartecoechea[9]; Luis J Pina[10]; Arlette Elizalde[11]; Marta Gimeno[12]; Marta Abengozar[13]; Isabel T Rubio[14]

[1]Breast Surgical Unit. Clínica Universidad de Navarra; [2]Breast Imaging. Clínica Universidad de Navarra; [3]Breast Imaging. Clínica Universidad de Navarra; [4] , , ,; [5]Department of Oncology. Clínica Universidad de Navarra; [6]Pathology Department. Clínica Universidad de Navarra; [7]Breast Surgical Unit. Clínica Universidad de Navarra; [8]Breast Surgical Unit. Clínica Universidad de Navarra; [9]Breast Surgical Unit. Clínica Universidad de Navarra; [10]Breast Imaging. Clínica Universidad de Navarra; [11]Breast Imaging. Clínica Universidad de Navarra; [12]Department of Oncology Clínica Universidad de Navarra; [13]Pathology Department. Clínica Universidad de Navarra; [14]Breast Surgical Unit. Clínica Universidad de Navarra

INTRODUCTION: Multicentric/multifocal breast cancer (MMBC) has been considered a relative contraindication for breast-conserving surgery (BCS). Results from the ACOSOG Z11102 trial report that it is safe to perform BCS in multiple ipsilateral breast cancer. For MMBC there are scarce data on the benefits of intraoperative ultrasound (IOUS) guided BCS. The aim of this study is to evaluate the use of IOUS in improving surgical outcomes in MMBC. **METHODS:** Women diagnosed with invasive or in situ breast cancer presenting with MMBC were eligible. Patients underwent BCS guided by IOUS using minimally invasive technique or wire localization (WL) followed by whole breast radiation with single/multiple boost. **RESULTS:** 150 women were enrolled between February 2018 and October 2013. Mean age was 55.1 years

(range, 29-82 years), mean initial tumor size was 19.69 mm (range, 2-100 mm). 130 patients (86.5%) had multifocal tumors and 20 (13.5%) patients had multicentric tumors. Mammogram and ultrasound diagnosed MMBC in 73 patients (diagnostic rentability 48.67%), while magnetic resonance found 100% of the cases (p<0.001). Age, breast density, cup size, estrogen receptor (ER) status and HER2 status, use of neoadjuvant treatment (NAT) were not indicators of missing tumoral foci in mammogram. For multifocal tumors, 51 patients (39.23%) underwent IOUS and 79 (60.77%) underwent WL. For multicentric tumors, 18 patients (90%) underwent IOUS and 2 (10%) received WL. Multifocal tumors were excised en bloc while multicentric tumors were excised in separate lumpectomies. In multifocal tumors, patients undergoing IOUS had smaller volume of excision (mean 34.8cm 3) than those guided by WL (mean 92.9 cm 3)(p<0.001). This difference remained significant after adjusting for tumor size, ER/HER2 status or NAT. In multicentric patients, there were no significant difference in volume excised (IOUS-20.64 cm 3 vs. WL-40.58 cm 3 , p=0.12). 14 (10.76%) patients with multifocal tumors had positive margins requiring a second surgery, 10 (71.42%) underwent margin re-excision while 4 (28.58%) received a mastectomy. Of the 14 re-excisions, 8 (57.14%) were in the WL group vs. 6 (42.86%) in the IOUS group (p=0.80). All 4 mastectomies were in WL patients, showing a strong statistical trend (p=0.07). No second surgeries were observed in the multicentric group (p=0.02). At a median follow-up of 18.4 months (range, 1-61.8 months), 1 patient in the multifocal group (0.67%) developed a local recurrence (this patient refused radiation therapy or any other medical treatment), p=0.99. Age, breast density, ER/HER2 status, en-bloc or multiple lumpectomy, use of MRI and pT/pN were not associated with LR risk. **CONCLUSIONS:** Minimally invasive IOUS guided BCS is safe in MMBC. In multifocal tumors, IOUS guided BCS achieved lower surgical volume of excision and probably less mastectomy rates than WL guided.

GP5. Patient-Reported Outcomes Following Breast Cancer Surgery: A Study Using the BREAST-Q Module.

Shubhashree Muralidhar, MCh[1]; Giridhar CM, MCh[2]; M S, Ganesh, McH[3]
[1]ydehi Institute of Medical Sciences and Research centre; [2]Vydehi Institute of Medical Sciences and Research Centre; [3]Vydehi Institute of Medical Sciences and Research Centre

INTRODUCTION: Breast cancer treatments involve surgical interventions such as Breast Conservation Surgery (BCS) andMastectomy, which can significantly impact a patient's psychological, sexual, and physical well-being. As most of the studies regarding quality of life after breast surgery are analyzed in western population, there is a paucity of such data in India with diverse social,cultural, ethnic and economic background. This study aims to evaluate these aspects, as well as breast satisfaction, in breast cancer patients using the BREAST-Q module. The objective is to understand how different surgical interventions influence patients' quality of life and satisfaction with their breast surgery. **METHODS:** A total of 81 breast cancer patients who underwent either BCS or Mastectomy at a tertiary care center between 2021 and 2023 were surveyed prospectively. The BREAST-Q module was administered postoperative to gather data regarding their psychological, sexual, and physical well-being, as well as their satisfaction with their breasts. **RESULTS:** The cohort consisted of 51 patients who underwent mastectomy and 30 patients who underwent BCS. More than 70% of women who underwent BCS reported feeling confident in social settings and emotionally capable of daily activities, with over 60% feeling feminine and attractive. In contrast, less than 2% of mastectomy patients felt confident socially, and less than 10% felt emotionally capable of performing desired activities. Breast satisfaction was higher in the BCS group, with over 90% satisfied with their appearance compared to about 30% in the mastectomy group. Additionally, 90% of BCS patients reported their operated breast looked similar to their normal breast. In terms of physical well-being, more than 70% of mastectomy patients experienced chest pain or arm movement difficulty, while around 60% of BCS patients reported some discomfort, and only 20% had arm movement issues. Only four BCS patients provided information on sexual well-being and none from the mastectomy group. **CONCLUSIONS:** The study highlights the significant differences in psychological, physical, and sexual well-being, as well as breast satisfaction, between breast cancer patients who underwent BCS and mastectomy using the Breast Q module, one of the first studies in India. These findings underscore the importance of considering the impact of different surgical interventions on patients* quality of life and overall satisfaction.

GP6. Can mutational analysis of naïve non muscle invasive bladder cancer reveal aggressive traits and improve clinical evaluations?

Dimple Gupta[1]; Hari PS[2]; Durgadevi Veeraiyan[3]; Ambili Narikot[4]; Rekha V Kumar[5]; B S Srinath[6]; Aruna K[7]; Srivatsa N[8]
[1]Sri Shankara Cancer Hospital and Research Centre; [2]Sri Shankara Cancer Hospital and Research Centre; [3]Sri Shankara Cancer Hospital and Research Centre; [4]Sri Shankara Cancer Hospital and Research Centre; [5]Sri Shankara Cancer Hospital and Research Centre; [6]Sri Shankara Cancer Hospital and Research Centre; [7]Sri Shankara Cancer Hospital and Research Centre; [8]Sri Shankara Cancer Hospital and Research Centre

INTRODUCTION: Intravesical instillation of Bacillus Calmette-Guerin(BCG) in non-muscle invasive bladder cancer(NMIBC) helps reduce the risk of progression and recurrence but it is not more than 33-50%. Furthermore, BCG instillation is fraught with serious side effects and leads to a crippling quality of life for the patients receiving it. There are many scoring systems like EORTC and CUETO for stratifying NMIBC to guide the treatment but they are at best 70 % accurate. In this study, we have done whole exome sequencing and identified the genes which can add to clinicopathological factors and try to evaluate if it can increase the positive predictive value of the existing scores and guide treatment options. **METHODS:** It is a retrospective subset analysis of prospectively accrued data of 23 patients undergoing treatment uniformly for NMIBC at our institute from 2018 to 2021. We analysed the tissue obtained for histopathological examination for treatment naïve patients. The samples underwent whole exome sequence analysis. **RESULTS:** 150 women were enrolled between February 2018 and October 2013. Mean age was 55.1 years (range, 29-82 years), mean initial tumor size was 19.69 mm (range, 2-100 mm). 130 patients (86.5%) had multifocal tumors and 20 (13.5%) patients had multicentric tumors. Mammogram and ultrasound diagnosed MMBC in 73 patients (diagnostic rentability 48.67%), while magnetic resonance found 100% of the cases (p<0.001). Age, breast density, cup size, estrogen receptor (ER) status and HER2 status, use of neoadjuvant treatment (NAT) were not indicators of missing tumoral foci in mammogram. For multifocal tumors, 51 patients (39.23%) underwent IOUS and 79 (60.77%) underwent WL. For multicentric tumors, 18 patients (90%) underwent IOUS and 2 (10%) received WL. Multifocal tumors were excised en bloc while multicentric tumors were excised in separate lumpectomies. In multifocal tumors, patients undergoing IOUS had smaller volume of excision (mean 34.8cm 3) than those guided by WL (mean 92.9 cm 3)(p<0.001). This difference remained significant after adjusting for tumor size, ER/HER2 status or NAT. In multicentric patients, there were no significant difference in volume excised (IOUS-20.64 cm 3 vs. WL-40.58 cm 3 , p=0.12). 14 (10.76%) patients with multifocal tumors had positive margins requiring a second surgery, 10 (71.42%) underwent margin re-excision while 4 (28.58%) received a mastectomy. Of the 14 re-excisions, 8 (57.14%) were in the WL group vs. 6 (42.86%) in the IOUS group (p=0.80). All 4 mastectomies were in WL patients, showing a strong statistical trend (p=0.07). No second surgeries were observed in the multicentric group (p=0.02). At a median follow-up of 18.4 months (range, 1-61.8 months), 1 patient in the multifocal group (0.67%) developed a local recurrence (this patient refused radiation therapy or any other medical treatment), p=0.99. Age, breast density, ER/HER2 status, en-bloc or multiple lumpectomy, use of MRI and pT/pN were not associated with LR risk. **CONCLUSIONS:** NMIBC treatments options are limited to TURBT and instillations of intravesical chemotherapy and BCG , which is associated with significant adverse reactions, multiple visits to the hospital and compliance issues. This is primarily guided by the histopathology and cystoscopy findings. Knowledge of the mutational landscape of bladder cancer may help in identifying patients which may benefit from early cystectomy as compared to subjecting them to repeated instillations of various drugs. This is particularly important where cost and compliance to treatment are major concerns.

GP7. A prospective randomized pilot study to compare long-course chemo-radiotherapy followed by surgery and adjuvant chemotherapy versus total neoadjuvant therapy followed by surgery in locally advanced rectal cancer

Saumyta Mishra[1]; Sundeep Kumar[2]; Navin Kumar[3]; Manisha Singh[4]; Vinita Trivedi[5]; Rakesh K. Barath[6]
[1]Mahavir Cancer Sansthan and Research Centre; [2]Mahavir Cancer Sansthan and Research Centre; [3]Mahavir Cancer Sansthan and Research Centre; [4]Mahavir Cancer Sansthan and Research Centre; [5]Mahavir Cancer Sansthan and Research Centre

INTRODUCTION: Colorectal cancer (CRC) is the fourth most frequently diagnosed cancer and the second leading cause of cancer death in the United States. Rectal cancer cases were about 732,210 cases and 339,022 deaths in the year 2020.(1)This represents about 3.8% of all new cancer cases in 2020. Second most commonly occurring cancer in women (571000 cases,9.4%of all cancer cases). (1) When Indian statistics are considered, rectal cancer is the 16th most common cancer diagnosed in India with 28,260 cases in 2020, forms 2.1% of total cancers and causes 16149 deaths. Aims And Objectives Primary End Point 1. To compare the rate of pathological response in patients receiving treatment in conventional long-course chemoradiotherapy with a total neoadjuvant treatment regimen in locally advanced mid to lower rectal cancer in Indian settings. Secondary End Point 1. To compare other prognostic factors in patients receiving treatment in both arms. 2. To compare the rate of completion of full treatment in each group. **METHODS:** The trial is designed to have 80 % power to detect the difference in primary endpoint, and the pathological response after the surgery, considering iTNT(experimental arm) non-inferior to Long course CTRT (standard arm). Sealed Envelope | power calculator for binary outcome non -inferiority trial84 is been used for sample size calculation. .in this Prodige 23 considered as reference study. **RESULTS:** Between October 2022, and March 2024, 69 patients were randomly assigned to either the induction total neoadjuvant therapy group (iTNT) Arm A (n=34) or the standard-of-care group Arm B (n=34). Maximum patients in Arm A is between 31-40 years (29.4%) and Arm B is 21-30 years (25.7%). The incidence of colorectal cancer was higher in males than in females in our study out of 69 Of the patients enrolled in the study 55.9% were male and 44.1% were females, male to female ratio of (1.8:1). Maximum cases enrolled in the study were of lower rectum 76.8 %. Considering TNM staging, The maximum number of patients in both Arm A (20) and Arm B (20) were of Stage IIA. All the enrolled patients Arm A and Arm B completed radiotherapy. On Restaging, Overall, 91.3% of cases were down-staged by Neo adjuvant therapy, 94.1% of patients in Arm A (iTNT) were downstaged, 5.9% had the progressive local disease and 3.0% of patients had developed distant metastasis. In Arm B - 88.6 % of cases had been downstaged, 11.4% had the progressive local disease, and 2.9 % developed distant metastasis (p- 0.129). 44.61% of operable patients had undergone abdominal-perineal resection (APR). In ArmA (iTNT) 32.25% of patients had APR, 12.9% had ELAPE, 32.25% had LAR and 13 % had ULLAR, 3.2% each had both ISR and posterior exenteration. In Arm B (nCRT) also the maximum number of patients underwent APR 50%, followed by LAR 23.5% and ULLAR, ELAPE 12.9% each, and 2.9% had ISR. Sphincter preservation was better seen in Arm A (iTNT) in terms of number, but not statistically significant (p-value 0.918). Equal margin positivity was seen in both Arms but is not statistically insignificant (p-0.468). Overall Complete Pathological Response (pCR) was seen in 23.1% of total patients treated. In Arm A (iTNT) 29.0% of patients and 17.6% of patients in Arm B (nCRT) had complete pathological response (p value.0.449). Overall treatment completion- there was no statistically significant difference between the treatment completion in both arms of this study, Arm In Arm A(iTNT) 91.2% vs 85.7% Arm B completed (p- 0.479). **CONCLUSIONS:** Total Neoadjuvant treatment, which combines chemotherapy and radiotherapy before surgery, tends to achieve better rates of complete tumor response, a higher likelihood of attaining tumor-free margins (R0 resection), and generally higher response rates (Requires a large multicentric study of our population). These factors may improve patients* long-term survival and quality of life. Additionally, delivering systemic chemotherapy earlier in the treatment sequence might help prevent distant metastases, offering an advantage over CRT alone. This mode of treatment can be suitable for Indian settings.

GP8. Evaluating the effectiveness of high-resolution anoscopy screening for anal cancer in HPV- and HIV-positive patients

Stefania Ferrari[1]; Marco Scarpa[2]; Davide Leoni[3]; Maria Mazzitelli[4]; Annamaria Cattelan[5]; Salvatore Pucciarelli[6]; Cesare Ruffolo[7]; Gaya Spolverato[8]
[1], , , , ; [2]Azienda Ospedaliera di Padova; [3], , , ,; [4], , , ,; 5, , , ,; [6], , , ,; [7], , , ,; [8], , ,

INTRODUCTION: The incidence of human papillomavirus (HPV)-related anal cancer is increasing, particularly in high-risk populations, necessitating the implementation of screening programs. Screening modalities such as anal cytology and high-resolution anoscopy (HRA) are crucial for early detection and management of precancerous lesions. This study aims to evaluate the effectiveness of screening with HRA in patients with HPV and HIV infection, in line with recent recommendations and to assess whether there is a significant association between high-risk HPV infection and the presence of HSILs, compared with low-risk HPV infection. **METHODS:** This retrospective study, conducted between June 2022 and June 2024, included 257 patients co-infected with HIV and HPV, aged =18 years, attending our tertiary care center. Anal cytology, performed by infectious disease specialists, and HRA, performed by three colorectal surgeons, served as primary screening tools. Rectal swabs were tested for HPV genotypes, including HPV16. Biopsies were taken for histopathologic examination during HRA. Sensitivity, specificity, and accuracy of cytology and combined methods were calculated using the McNemar test to assess concordance. Univariate logistic regression identified predictors for biopsy-confirmed lesions. **RESULTS:** Of 257 patients (median age 53 years, 65.8% male), 208 (81.0%) tested positive for high-risk HPV and 30 (11.7%) were positive for HPV16. The median duration of HIV infection was 157 months. Cytology alone had a sensitivity of 50%, specificity of 64.8%, and accuracy of 53.9%. Combined cytology and HRA improved accuracy to 58.3% (p = 0.0025). Among the patients undergoing biopsy, 7 HSILs and 5 LSILs were confirmed histologically, with 4 of the HSILs detected in patients with negative cytology. No other clinical or demographic variables, including age, gender, or HIV infection duration, were found to be significantly correlated with lesion detection. HPV16 significantly increased the risk of HSIL (RR = 7.57; CI: 1.47-38.9). No invasive anal cancer was observed during follow-up. **CONCLUSIONS:** This study demonstrates the improved diagnostic value of combining cytology with HRA in high-risk populations. The strong association between HPV16 and HSIL underscores the need for HPV genotyping in risk stratification. Limitations in screening accuracy and predictive factors highlight the importance of developing advanced molecular biomarkers and machine learning-based predictive models to refine individualized screening protocols. Further large-scale prospective studies are essential to validate findings and optimize screening pathways for anal cancer prevention.

GP9. Immunoreact 16: Role of Undernourishement in Immunosurveillance of Rectal Cancer

Lavinia Ceccarini[1]; Federico Scognamiglio[2]; Valerio Pellegrini[3]; Andromachi Kotsafti[4]; Astghik Stepanyan[5]; Gaia Tussardi[6]; Michiele Antoniutti[7]; Barbara Di Camillo[8]; Imerio Angriman[9]; Gaya Spolverato[10]; Ignazio Castagliuolo[11]; Luca Saadeh[12]; Matteo Fassan[13]; Melania Scarpa[14]; Marco Scarpa[15]

INTRODUCTION: Nutrition, immunosurveillance and cancer are closely linked. The present study (IMMUNOREACT 16) aimed to assess the differences in the immune microenvironment in the healthy rectal mucosa between undernourished and normal overnourished patients with rectal cancer. **METHODS:** We evaluated retrospectively the difference in terms of immune surveillance gene expression in the healthy mucosa surrounding rectal cancer in the cohort of patients enrolled in the IMMUNOlogical microenvironment in Rectal Adenocarcinoma Treatment (IMMUNOREACT) trial. Only therapy-naïve patients were included while those with metastatic disease were excluded. Patients were categorized based on Body Mass Index and Onodera Prognostic Nutritional Index (OPNI). **RESULTS:** A total of 249 patients were selected and divided in two groups based on BMI. Patients with BMI < 20 had lower Tbet expression (p 0.04), higher CD8/foxp3 ratio (p 0.05), higher CD25+Foxp3+ cell rate (p 0.05) and CD25+Foxp3+ mean fluorescence intensity (p 0.02) compared to patients with BMI over 20. Among 249 patients 194 had a calculated OPNI. This group of 194 patients was further divided based on OPNI cut off of 45: 49 patients had Onodera index 45. The undernourished group, had higher values of HLA-ABC mean fluorescence intensity (p 0.03), lower CD8 CD38 cell rate (p 0.049) and higher expression of epithelial CD80 (p 0.08). **CONCLUSIONS:** According to our results malnutrition could affect the tumor microenvironment impairing the immune response against rectal cancer. In patients with OPNI lower than 45, despite a high antigenic presence and a strong activation of epithelial cells acting as antigen presenting cells, a low cytotoxic lymphocytes response was observed, suggesting a less effective immune response against cancerous cells.

GP10. Long-term incidence of depression in rectal cancer patients with or without stoma: a population-based cohort study

Sunseok Yoon, MD[1]; Kwang dae Hong, MD, PhD[2]; Junwon Um, MD, PhD[3]; Woong Bae Ji, MD, PhD[4]
[1]Department of colocrecatl surgery, Korea University Ansan Hospital, Ansan, Gyunggido, South Korea; [2]Department of colocrecatl surgery, Korea University Ansan Hospital, Ansan, Gyunggido, South Korea; [3]Department of colocrecatl surgery, Korea University Ansan Hospital, Ansan, Gyunggido, South Korea; [4]Department of colocrecatl surgery, Korea University Ansan Hospital, Ansan, Gyunggido, South Korea

INTRODUCTION: Significant improvements have been made in the surgical treatment of rectal cancer with a higher sphincter-saving rate without compromising oncologic results. There have been studies about the quality of life of rectal cancer patients after surgery. However, no study has reported the long-term annual incidence of depression after rectal cancer surgery according to stoma status. The objective of this study was to determine the annual incidence of depression after rectal cancer surgery and the factors affecting it, especially the prevalence of depression according to the presence or duration of a stoma. **METHODS:** Using the Korea National Health Insurance Service database, patients who underwent radical surgery for rectal cancer from 2002 to 2019 were searched. We analyzed the incidence and risk factors of depression in patients who underwent radical surgery for rectal cancer according to stoma status. **RESULTS:** Annual incidence of depression in rectal cancer patients was decreasing annually for 15 years after surgery. There was no statistically significant difference in the incidence of depression according to the stoma status. However, the diagnosis of depression within 1 year after surgery was statistically significantly increased in the permanent stoma group. **CONCLUSIONS:** There was no difference in the overall incidence of depressive disorders among patients with rectal cancer based on their stoma status. However, a permanent stoma seems to increase the incidence in the first year after surgery. Education and intensive assessments of depressive disorders in patients with permanent stoma within 1 year after surgery are needed, particularly for female patients who are under 50 years old.

GP11. The impact of postoperative surgical complications after primary colon cancer surgery on long-term outcomes

Eva Rademaker, MD[1]; B.C. Aktas, BSc[2]; Esther C.J. Consten, MD, PhD[3]; Pieter J Tanis, MD, PhD[4]; Henderik L. van Westreenen, MD, PhD[5]

[1]Department of Surgery, Isala, Zwolle, the Netherlands / Department of Surgical Oncology and Gastrointestinal Surgery, Erasmus MC Cancer Institute, Rotterdam, the Netherlands; [2]Department of Surgical Oncology and Gastrointestinal Surgery, Erasmus MC Cancer Institute, Rotterdam, the Netherlands; [3]Department of Surgery, University Medical Centre Groningen, Groningen, the Netherlands / Department of Surgery, Meander Medical Centre, Amersfoort, the Netherlands; [4]Department of Surgical Oncology and Gastrointestinal Surgery, Erasmus MC Cancer Institute, Rotterdam, the Netherlands; [5]Department of Surgery, Isala, Zwolle, the Netherlands

INTRODUCTION: It is widely acknowledged that postoperative complications after colon cancer resection are associated with postoperative mortality, but the association with long-term outcomes is controversial. This study examined the impact of postoperative surgical complications on locoregional recurrence, defined as any intra-abdominal recurrence including peritoneal metastases, and overall survival. **METHODS:** This nationwide, population-based cross-sectional cohort study was carried out in 49 Dutch hospitals. Patients who underwent a curative colon cancer resection between January 2014 and December 2015 were eligible. Long-term outcomes were assessed in patients without synchronous metastases and a minimum follow-up of 6 months using logistic regression, Kaplan-Meier, log-rank test, and Cox regression analyses. **RESULTS:** A total of 8936 patients were included with a median follow-up of 59.6 months (IQR 28.0-65.6). Any complication occurred in 2649 (29.6%) patients, of whom 1576 (17.6%) had surgical complications (806 (9.0%) requiring reintervention) and 1791 (20.0%) non-surgical complications. In the selected stage 1-3 colon cancer patients with a minimum follow-up of 6 months, 7.6% of patients without postoperative surgical complications experienced locoregional recurrent colon cancer versus 9.2% with complications (p=0.069). Independent risk factors for locoregional recurrence were surgical approach (laparotomy OR 0.7 (95% CI 0.5-0.9)), emergency resection (OR 2.4 (95% CI 1.8-3.2)), right-sided tumour site (OR 1.3 (95% CI 1.1-1.6)), tumour site perforation (OR 1.8 (95% CI 1.2-2.7)), higher pT-stage (pT4 OR 9.5 (95% CI 6.3-14.3)), higher pN-stage (pN2 OR 3.3 (95% CI 2.6-4.2)), and microscopic positive resection margins (OR 2.8 (95% CI 1.5-5.1)). Five-year overall survival probability was 79.2% versus 71.7% for patients with or without surgical complications respectively (p<0.001), which remained significant in multivariable analysis (HR 1.31, 95%Cl 1.16-1.48). **CONCLUSIONS:** Postoperative surgical complications in patients with stage I-III colon cancer resulted in a worse overall survival than patients without. However, postoperative surgical complications did not increase the risk of locoregional recurrence.

GP12. The Oncogenic Role of Midkine in Promoting Colorectal Cancer Progression and Metastasis

Jeongyun Hwang[1]; Young-Sool Hah, PhD[2]; Seung-Jun Lee[3]; Seung-Jin Kwag, MD, PhD[4]

[1]Department of Convergence Medical Science, Gyeongsang National University; [2]Biomedical Research Institute, Gyeongsang National University Hospital; [3]Department of Convergence Medical Science, Gyeongsang National University; [4]Department of Surgery, Gyeongsang National University Hospital

INTRODUCTION: Colorectal cancer (CRC) is one of the most common cancers with a high mortality rate worldwide. Midkine (MDK) is a cytokine showing high expression levels in various cancer patients* tissue, blood, and urine. However, the roles of MDK in phenotypic changes and related signaling pathway mechanisms in CRC remain unknown. **METHODS:** We conducted several public clinical database analyses and performed in vitro and in vivo functional studies to investigate the role of MDK in CRC progression and metastasis. **RESULTS:** In the public clinical database analyses, MDK showed significantly higher expression levels in CRC tissues compared to normal tissues, and CRC patients' overall survival was negatively associated with MDK expression levels. CRC patients-derived tissue microarray analysis showed high MDK expressed tissues were more highly expressed in cancerous tissues compared to non-cancerous tissues. In vitro studies revealed that MDK overexpression enhanced CRC cell viability, clonogenic activity (1.5- to 2-fold increase), migration (approximately 2-fold increase), and invasiveness ability (approximately 2-fold increase). Western blot analysis demonstrated decreased expression levels of E-cadherin and Zo-1, which are known as some of the tight-junction proteins. Conditioned media from MDK-overexpressed CRC cells enhanced the proliferation of other CRC cells, indicating the potential paracrine activity in CRC. In vivo xenograft mouse modeling with the HCT116 cell line confirmed that MDK overexpression significantly promoted tumor growth. **CONCLUSIONS:** In this study, our results showed that MDK promotes CRC cell viability, clonogenic activity, migration, invasion, and tumor growth. These findings indicate that MDK plays oncogenic roles in CRC and exhibits paracrine activity. Furthermore, according to these results, MDK could be considered a potential biomarker and therapeutic target in CRC.

GP13. Exploring the use of the AURA 10 mobile PET/CT-camera for intraoperative imaging of surgical specimens of the (para)thyroid and/or cervical lymph nodes

Valérie Vergucht[1]; Amelie Decock[2]; Charlotte Gabriel[3]; Marianne Rottieres[4]; Mieke Coppens[5]; Dieter Berwouts[6]; Bieke Van Den Bossche[7]; Bieke Lambert[8]

[1]Maria Middelares hospital, Gent, Belgium; [2]Maria Middelares hospital, Gent, Belgium; [3]Maria Middelares hospital, Gent, Belgium; [4]Maria Middelares hospital, Gent, Belgium; [5]Maria Middelares hospital, Gent, Belgium; [6]Maria Middelares hospital, Gent, Belgium; [7]Maria Middelares hospital, Gent, Belgium; [8]Maria Middelares hospital, Gent, Belgium

INTRODUCTION: We evaluated the AURA mobile PET/CT camera, designed by XEOS (Belgium) to capture submillimeter resolution images of surgical specimens. The PET/CT-camera is integrated in a cart and can safely acquire PET/CT-images in the operating room. We explored the added value of the PET/CT-scan of the resected tissue in patients referred because of parathyroid adenoma, thyroid cancer, or lymph node resection for a diagnostic oncological work-up. **METHODS:** This investigator-initiated study assessed the safe implementation of the AURA PET/CT in the surgical room. Surgeons were wearing electronic dosimeters to monitor their radiation exposure. In thyroid carcinoma cases, 4 MBq/kg FDG was intravenously injected 1h before surgery. For resection of suspicious metabolic active cervical lymph nodes in patients undergoing a oncological work up, who did not have a final diagnosis yet, we injected 0.8-4 MBq/kg FDG prior surgery. For parathyroidectomy, 2-4 MBq/kg F18-Choline was administered > 10 minutes before surgery. The device captured images of the surgical specimen within 10 minutes, allowing immediate review of PET/CT-images by the surgeon in the operating room. Specimen PET/CT images were compared with pathology findings. **RESULTS:** We tested the mobile PET/CT in 4 procedures involving thyroid carcinomas: 1 total thyroidectomy with lymphadenectomy and 3 interventions for lymph node recurrence, with/without local thyroid recurrence. The technique facilitated margin assessment for recurrent thyroid carcinoma. Assessment of lymphadenectomy specimens, when compared with pre-operative FDG PET/CT images, aided in confirming complete lymph node removal. We also explored its use in 4 patients referred to have a diagnostic lymph node resection to establish a final (oncological) diagnosis. We selected patients who presented with a metabolic active cervical lymph node on pre-operative FDG PET/CT, without palpable lymphadenopathy. The peroperative PET/CT was correctly confirmed that the correct node was sent for anatomopathology. The mobile PET/CT was also evaluated in 3 patients undergoing parathyroidectomy. Within 10 minutes post-resection, the device assessed F18-Choline avidity of

the suspected parathyroid adenoma. High uptake values correctly predicted adenoma removal. The surgeon*s absorbed doses ranged from 10-197 μSv per procedure. **CONCLUSIONS:** We report our initial exploration of the peroperative use of the mobile AURA PET/CT camera for imaging surgical specimens of parathyroid adenoma, thyroid carcinoma and cervical lymph node metastasis in the operating room. The device demonstrated significant utility in all 3 clinical scenarios. In the future lower PET-tracer activity will be used, allowing reduction the radiation burden for the patient and surgeons

GP14. Fluorescently labeled nanobodies targeting EGFR for tumor delineation in head and neck cancer, a canine dose-escalation study

Jens M Debacker, MD, PhD[1]; Nayra H do Valle, DVM[2]; Sofie Pollenus, [3]; Hilde De Cock, DVM, PhD[4]; David Creytens, MD, PhD[5]; Simone Janssen, DVM[6]; Ingeborgh Polis, DVM, PhD[7]; Sophie Hernot, PhD[8]; Hilde de Rooster, DVM, PhD[9]

[1]Vrije Universiteit Brussel (VUB), Molecular Imaging and Therapy research group (MITH), Brussels, Belgium; [2]Vrije Universiteit Brussel (VUB), Molecular Imaging and Therapy research group - MITH, Brussels, Belgium; [3]Vrije Universiteit Brussel (VUB), Molecular Imaging and Therapy research group (MITH), Brussels, Belgium; [4]Ghent University - Faculty of Veterinary Medicine, Small Animal Department, Merelbeke, Belgium; [5]Ghent University Hospital, Department of Pathology, Ghent, Belgium; [6]Vrije Universiteit Brussel (VUB), Molecular Imaging and Therapy research group - MITH, Brussels, Belgium; [7]Ghent University - Faculty of Veterinary Medicine, Small Animal Department, Merelbeke, Belgium; [8]Vrije Universiteit Brussel (VUB), Molecular Imaging and Therapy research group - MITH, Brussels, Belgium; [9]Ghent University - Faculty of Veterinary Medicine, Small Animal Department, Merelbeke, Belgium

INTRODUCTION: Complete surgical resection remains one of the hallmarks of cancer therapy, with clean surgical margins positively impacting the patient*s survival. We here propose a fluorescently labeled nanobody targeting the epidermal growth factor receptor (EGFR) for its use in FGS. To evaluate its clinical potential, we first performed a trial in dogs with spontaneous HNC. **METHODS:** A prospective clinical 3+3 dose-escalation study was designed with the dog-human cross-reactive EGFR-targeting Nb 7D12 labeled with the near-infrared (NIR) fluorophore s775z. Canine patients diagnosed with HNC, scheduled for tumor resection were eligible for inclusion. The dogs received 7D12-s775z intravenously one hour before surgery. Then, an open-field NIR imaging device was used to image uptake in the malignancy in situ, followed by surgical resection of the tumor and imaging of the tumor bed. Back-table ex vivo imaging was performed using the same camera as well as a flatbed fluorescence scanner, followed by standard histopathological processing and EGFR immunohistochemistry to correlate fluorescent signal and EGFR overexpression on the target tissue. **RESULTS:** Five canine patients with squamous cell carcinomas (n=3), follicular thyroid carcinoma (n=1) and salivary adenoma (n=1) were included. The first group of three patients received 1.74mg/m² and two patients included in the second group received 3.49mg/m² of 7D12-s775z. No adverse events were identified, displaying the safety of the compound. In situ fluorescence imaging allowed identification of the neoplastic tissue in all patients but was relatively weak in the lowest dose whereas adequate signal was observed in the highest dose. Ex vivo imaging using both handheld and flatbed fluorescent imaging displayed compound accumulation in regions macroscopically identified as malignant. This specific accumulation was subsequently confirmed on histopathological analysis. On the histopathological slides, fluorescence was increased in regions with increased EGFR expression, confirming the high specificity of the compound. **CONCLUSIONS:** We here display the first results of a fluorescent Nb targeting EGFR in canine patients undergoing surgery for HNC. Specific fluorescent signal was observed as early as one hour after injection, even in the lowest dose group. The results obtained in this spontaneous cancer model display the high potential for future clinical translation of fluorescently labeled EGFR-targeting nanobodies to improve intraoperative margin assessment in EGFR-expressing malignancies in humans.

GP15. Preserving the reverse flow in Facial Artery: A novel technique to prevent marginal necrosis associated with midline lip-split incisions.

Bhagyashree Deshmankar, MS[1]; Prashant Sharma, MCH[2]

[1]Bhagwan Mahaveer Cancer Hospital and Research Center; [2]Bhagwan Mahaveer Cancer Hospital and Research Center

INTRODUCTION: Midline lip split incision is the most preferred incision in head and neck surgeries for acceptable cosmetic and functional outcomes. However, it is sometimes associated with ipsilateral marginal necrosis. Here we propose a novel technique to avoid this complication by preserving the reverse flow in Facial artery. **METHODS:** We performed careful in vivo dissection of facial artery during raising the skin flap with analysis of its routine path in our cases and noticed an interesting pattern. **RESULTS:** We noticed an interesting pattern at modiolus just posterolateral to the angle of mouth. We named this segment of facial artery as Jaipur junction (JJ) which was a junction of facial artery with its branches namely Inferior labial artery, Superior labial artery, Lateral nasal artery and Angular artery and some branches from Internal maxillary artery. These arteries anastomose with their counterparts from the opposite side thus forming a rich anastomotic network. If we draw an imaginary plane joining the two angles of mouth, facial blood supply can be divided into an upper arterial territory and a lower arterial territory. We named this plane as Deshmankar's plane and JJ forms a connection between the upper and lower arterial territories. During our head and neck surgeries when we put a midline lip split incision and when the facial artery is ligated, the ipsilateral skin flap is dependent on reverse flow of facial artery for its blood supply via JJ. But if the JJ is also compromised during surgery due to disease involving the angle of mouth then the skin flap acts as a random pattern flap thus highly prone to marginal necrosis. Careful preservation of JJ provides good blood supply via reverse flow to the elevated cheek flap including parts of lip and chin and prevents its necrosis. And if the disease compromises the angle of mouth and thus JJ then midline lip split incision should be avoided. **CONCLUSIONS:** Jaipur Junction (JJ) is a sacred landmark in head and neck surgery, and should be taken into consideration during flap elevation to prevent marginal necrosis.

GP16. Worst pattern of invasion: A novel histopathological parameter that impacts adverse prognostic factors, recurrence patterns and survival in oral cancers.

Dhiraj H Kachare, MBBS, MS General Surgery MRCS (Eng)[1]

[1]Department of Surgical Oncology National Cancer Institute

INTRODUCTION: Introduction: Multiparametric histological risk assessment has been reported to predict the survival of patients and differentiate between high and low risk patients. An important and novel pathological parameter is Worst pattern of Invasion (WPOI) that may be associated with worse prognosis and survival. This study was done to assess the impact of WPOI on other adverse risk factors, survival and recurrence patterns in oral cancers. Aims: (1) To find out the distribution of different types of WPOI across cases; (2) To find out correlation of WPOI with Nodal stage; (3) To find out impact of WPOI on Disease Free Survival; (4) To find out Correlation of WPOI with Recurrence (any kind) or metastases; (5) To find out inter-rater reliability (amongst pathologists) in the assessment of WPOI. **METHODS:** A prospective observational study carried out between January 2020 and May 2023, including patients with oral cancers who underwent curative surgery, with or without adjuvant radiotherapy. 529 diagnosed and operated cases of OSCC were evaluated for various histopathological parameters. Clinicodemographic and histopathological details were recorded from electronic medical records. In all cases, WPOI was recorded by 2 experienced pathologists. For comparison of inter-rater reliability of WPOI, 3 pathologists independently recorded their findings in 489 cases. Survival analysis was carried out on eligible 226 patients with minimum post-treatment follow-up of 12 months. Statistical analysis was done using SPSS. Descriptive statistics were done using Chi square and t tests; survival was plotted using Kaplan-Meier curves and compared using Log rank test. Inter-rater reliability between pathologists was found using Fleiss's Kappa co-efficient. **RESULTS:** The most common type of WPOI was type 3 (44.4%). Significant correlation of WPOI was found with histopathological grading ($p<0.05$), peri neural invasion ($p<0.5$), lymph node metastasis ($p<0.5$), and also increasing DOI (p3 were found to be associated with metastatic nodes more than WPOI<3 ($p<0.05$). Patients with WPOI types 4 and 5 were more likely to have recurrence (any kind) or distant metastases. Statistically significant difference in survival and WPOI was observed ($P<0.05$). WPOI Types 4 and 5 had worse survival (DFS) than Type 3, which had worse survival than Types 2 and 1 Regarding inter-rater reliability, the Fleiss Kappa value was 0.911 (p 0.000), which signified 'Excellent Strength of Agreement' between raters. **CONCLUSIONS:** This is the largest Indian study evaluating WPOI in OSCC. This study highlights the importance WPOI as an independent prognostic factor in these cancers. We found that worse WPOI (3,4 and 5) was associated with aggressive tumor biology, nodal metastasis, increased recurrence and decreased DFS. Patients with WPOI 4, 5 had a poorer oncological outcome in terms of disease-free survival irrespective of stage and adjuvant treatment. Patients with WPOI 4, 5 may be considered for treatment intensification especially in early-stage tumors. Inclusion of WPOI in tumor staging may help better treatment

planning, reduce locoregional failure and improve long-term survival in OSCC. Further studies may incorporate WPOI in risk strategy nomograms or consider inclusion as a biological factor in cancer staging systems.

GP17. Implications of portal vein/superior mesenteric vein involvement in pancreatic cancer: A comprehensive correlation from preoperative radiological assessment to resection, pathology, and long-term outcomes

Hyeong Seok Kim, MD, MS[1]; Hochang Chae, MD, MS[2]; Soo Yeun Lim, MD[3]; HyeJeong Jeong, MD, MS[4]; So Jeong Yoon, MD, PhD[5]; Sang Hyun Shin, MD, PhD[6]; In Woong Han, MD, PhD[7]; Jin Seok Heo, MD, PhD[8]; Hongbeom Kim, MD, PhD[9]

[1]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [2]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [3]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [4]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [5]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [6]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [7]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [8]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [9]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea

INTRODUCTION: The incidence of portal vein/superior mesenteric vein (PV/SMV) resection during pancreatoduodenectomy is increasing in clinical practice. This study investigated the clinical significance of preoperative PV/SMV assessment and intraoperative resection and their correlation with pathological results and long-term survival outcomes. **METHODS:** We analyzed 443 patients undergoing pancreatoduodenectomy at a tertiary center from 2012 to 2017 based on PV/SMV resection. Subgroup analyses were performed based on preoperative PV/SMV involvement, resection, and margin status. **RESULTS:** Total 441 patients were analyzed; 175 had PV/SMV involvement on preoperative radiological assessments and 128 underwent PV/SMV resection. True pathological invasion was observed in 78 patients (60.9%), with 34.3% showing no invasion and negative margins. The positive predictive value for preoperative PV/SMV involvement was 61.7%, with a false-negative value of 28.9%. Overall survival of patients who underwent PV/SMV resection were worse than those who did not (2-year survival rate, 38.1% vs. 54.9%, p<0.001). Patients without PV/SMV resection with an rR1/R1 margin showed no decrease in survival compared to those with PV/SMV resection and R0 margins (54.9% vs. 40.3%, p=0.029). Prognostic factors included hypertension, PV/SMV resection, PV/SMV R2 margin, T stage, N stage, cell differentiation, adjuvant treatment and recurrence. **CONCLUSIONS:** PV/SMV resection could ensure R0 resection but may lead to unnecessary resection. Careful consideration is essential in determining the need for PV/SMV resection. Poor survival in such patients highlights the need for tailored treatments, including neoadjuvant therapy, for those who are expected to undergo PV/SMV resections.

GP18. Prognostic accuracy of ypTNM stage in patients with pancreatic cancer in the era of modern neoadjuvant therapy

Hyeong Seok Kim, MD, MS[1]; Hochang Chae, MD, MS[2]; Soo Yeun Lim, MD[3]; HyeJeong Jeong, MD, MS[4]; So Jeong Yoon, MD, PhD[5]; Sang Hyun Shin, MD, PhD[6]; In Woong Han, MD, PhD[7]; Jin Seok Heo, MD, PhD[8]; Hongbeom Kim, MD, PhD[9]

[1]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [2]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [3]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [4]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [5]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [6]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [7]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [8]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [9]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea

INTRODUCTION: The AJCC 8th edition TNM staging, which provided ypTNM for neoadjuvant therapy (NAT) patients, has not been comparatively assessed against pTNM for prognosis in pancreatic cancer. This study aimed to compare the prognosis between ypTNM and pTNM stages. **METHODS:** Analysis of clinicopathological data and propensity score-matched (PSM) analysis for survival factors was conducted on 586 patients who underwent pancreatic cancer surgery at a tertiary center between 2018 and 2022. **RESULTS:** The analysis included 541 patients (100 ypTNM, 441 pTNM). A comparable overall survival (OS) was observed between the two groups (2-year survival rate (YSR): 76.8% vs. 66.7%, p=0.094). Subgroup analysis by stages I (82.4% vs. 76.2%, p=0.577), II (68.8% vs. 61.6%, p=0.715), and III (53.0% vs. 49.8%, p=0.596) revealed similar survival rates. Multivariate analysis identified factors influencing OS: age >65 (HR 1.763, p150 U/mL (HR 1.439, p=0.014), preoperative biliary drainage (HR 1.405, p=0.029), pathologic T2 stage (HR 1.961, p=0.004) and T3/4 stage (HR 2.830, p<0.001) versus T0/1 stage, lymphovascular invasion (HR 2.220, p<0.001), and adjuvant treatment (HR 0.251, p<0.001). After PSM analysis, stages I (2YSR, 82.4% vs. 82.4%, p=0.790), II (68.8% vs. 63.3%, p=0.744), and III (53.0% vs. 51.0%, p=0.696) exhibited no significant difference between the groups. **CONCLUSIONS:** This study confirms comparable survival outcomes between ypTNM and pTNM stages in surgically resected pancreatic cancer, affirming the applicability of the TNM staging system after NAT. Consistent survival results, even after PSM analysis, highlighted the reliability of TNM staging for guiding therapeutic decisions, even in patients with NAT.

GP19. Spatial transcriptomics revealed perineural invasion signatures in biliary tract cancer.

Sung Hwan Lee, MD, PhD[1]

[1]Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, CHA Bundang Medical Center, CHA University School of Medicine, Seongnam, Korea

INTRODUCTION: Perineural invasion is a well-known predictive pathologic factor associated with poor prognosis in pancreaticobiliary cancers. Recently, a new emerging technology, spatial transcriptomics, has emerged in cancer research to reveal complex tumor biology harboring in situ pathologic information of tumor microenvironment. This study aims to identify specific transcriptomic signatures for perineural invasion using the spatial transcriptomic technique with temporally collected patient samples. **METHODS:** Formalin-fixed paraffin-embedded blocks from initial biopsy and post-mortem autopsy samples (gallbladder, liver, peritoneum, lung) were enrolled in this study. Twenty-four areas of interest from six immunofluorescence slides with four morphology markers from the patient's FFPE blocks were selected and the RNA sample for tumor, stroma, and tumor-infiltrating lymphocytes from each AOI was sequenced using GeoMx Human Whole Transcriptome Atlas platform. **RESULTS:** Tumor stroma and TILs showed distinct gene expression patterns according to their unique tumor microenvironments. Interestingly, the tumor samples showing perineural invasion have unique and discriminative transcriptomic profiles with differentially expressed gene sets. Inter and intra-tumoral heterogeneity with distinct tumor phenotypes were identified using single-sample gene-set enrichment analysis from comprehensive pathway analysis. The in-silico analysis for drug response prediction showed differential responses for currently available cancer therapeutics according to temporal tumor progression and spatial tumor context with their unique environments specific to perineural invasion. **CONCLUSIONS:** Spatiotemporal transcriptomic analysis reveals clinically relevant tumor heterogeneity for perineural invasion in advanced biliary tract cancer. Inter and intra-tumoral heterogeneity showing different therapeutic opportunities warrant translational research for clinically relevant molecular deciphering with clinical samples in the era of precision surgical oncology.

GP20. ProMise classifier-defined mutational landscape of endometrial cancer in India: A multicenter observational analysis

Harish N. Lakshmi, MBBS, MS, MCh, PDCR, FMAS[1]; Suruchi Aggarwal, PhD[2]; Chinnababu Sunkavalli, MBBS, MS, MCh, PDCR[3]; Shikhar Kumar, MBBS, MD, DM, ECMO[4]

[1]Yashoda Hospitals; [2]MedGenome Labs; [3]Yashoda Hospitals; [4]Yashoda Hospitals

INTRODUCTION: Endometrial cancer (EC) is the most common gynecological malignancy worldwide, affecting approximately 0.4 million women annually. Though high incidence, there are limited comprehensive studies from India on its mutational profile. Molecular subtyping of EC, particularly through markers such as POLE mutations, p53 mutations, and MMR status, has been shown to classify tumors into prognostically relevant groups, which we evaluated In this study marking the largest report from our subcontinent. **METHODS:** Formalin-fixed, paraffin-embedded (FFPE) tissue blocks with tumor content greater than 10% were selected for this study. Retrospective study where 128 samples were analyzed Inclusion criteria required a diagnosis of endometrial cancer, while samples from patients with concurrent malignancies in other organs were excluded. Next-generation sequencing (NGS) was performed to analyze endometrial carcinoma related genes, including POLE, TP53, and MMR genes. **RESULTS:** The study analyzed 128 FFPE endometrial cancer samples using next-generation sequencing. Endometrioid cancer was found in 87% of cases. The mean age of the study group was 59.2 years with endometrioid cancer being seen in 87% of our patients. 57% of patients had Stage I tumors. The mutational landscape were p53 wild type with non specific mutation profile seen in : 56 patients (43.75%), p53 mutated type seen in 32/109 (24.22%) followed by MMRd in 22/109 (18%) and POLE mutated type with best prognostic type seen in 5/109 (3.9%). **CONCLUSIONS:** This comprehensive genomic study on endometrial cancer, the largest of its kind in India, underscores the feasibility of integrating genomic data alongside clinicopathologic parameters in the management of endometrial cancer. The incorporation of p53 and MSI testing enhances precision oncology by improving prognostication and expanding treatment options, including the feasibility of immunotherapy.

GP21. Trends in hospitalization in patients with malignant bowel obstruction secondary to incurable gastrointestinal cancer: A retrospective cohort study using multi-state models

Tiago Ribeiro, MD, MSc[1]; Calvin Diep, MD, MSc[2]; Adom Bondzi-Simpson[3]; Wing C Chan, MPH[4]; Natalie Coburn, MD, MPH[5]; Julie Hallet, MD, MSC[6]

[1]University of Toronto, Toronto, ON, CA; [2]Institute of Health Policy Management and Evaluation, University of Toronto, Toronto, Ontario, Canada; [3]University of Toronto, Toronto, ON, CA; [4]Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada; [5]Department of Surgery, University of Toronto, Toronto, Ontario, Canada; [6]Department of Surgery, Sunnybrook Health Sciences Centre, Canada

INTRODUCTION: Malignant bowel obstruction (MBO) is a common clinical presentation with significant life impact in patients with incurable gastrointestinal (GI) cancer. We employed multi-state models to evaluate the impact of patient, cancer and treatment factors on hospital admissions, home time, and death. **METHODS:** This was a population-based retrospective cohort study of adults with incurable gastric, pancreatic, or colorectal cancer over 2010-2019 admitted with MBO. Multi-state models were run to evaluate trends in hospitalization and the impact of defined patient, cancer and treatment factors. The four states defined were: MBO admission, non-MBO admission, home, and death. Transition intensities, sojourn time and total time in each state was identified in multivariable models. **RESULTS:** Of 4642 patients, the majority of patients had incurable colorectal cancer (2,642, 57%), followed by rectal cancer (845, 18%), pancreas cancer (652, 14%) and gastric cancer (503, 11%). By the end of the observation window 4120 (89%) patients had died, 20% of which died during their first admission. After adjusting for age, sex, material deprivation, comorbidities, cancer site, MBO treatment, inpatient palliative care and number of MBO, patients with incurable GI cancer were found to be 3 times more likely to be re-admitted for non-MBO indications versus MBO, however spend 50% more time in hospital for MBO than non-MBO. In addition, admission to hospital for MBO had a 1.5 times lower rate of discharge home compared to non-MBO. After adjusting for covariates, surgical and procedural interventions were associated with a 64% (CI: 60–68%) and 43% (CI: 56–74%) reduction, respectively, in MBO re-admission rates compared to supportive care. **CONCLUSIONS:** MBO in patients with incurable GI cancer result in significant time toxicity. Both procedural and surgical interventions are associated with a reduced rate of re-admission for MBO supporting these interventions in appropriately selected patients.

GP22. The impact of neoadjuvant chemotherapy on radiotherapy associated angiosarcoma (RAAS) of the breast: a retrospective single center study

Stijn J.C. van der Burg[1]; Sophie J.M. Reijers[2]; Anke Kuijpers[3]; Lotte Heimans[4]; Astrid N. Scholten[5]; Rick L.M. Haas[6]; Hester van Boven[7]; Willemijn M Kolff[8]; Marie-Jeanne T.F.D. Vrancken Peeters[9]; Martijn Kerst[10]; Beatrijs A. Seinstra[11]; Neeltje Steeghs[12]; Winette T.A. van der Graaf[13]; Yvonne M Schrage[14]; Winan J van Houdt[15]

[1]Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL), Department of Surgical Oncology, Plesmanlaan 121, Amsterdam, The Netherlands; [2]Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL), Department of Surgical Oncology, Plesmanlaan 121, Amsterdam, The Netherlands; [3]Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, , NL; [4]Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL), Department of Medical Oncology, Plesmanlaan 121, Amsterdam, The Netherlands; [5]Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL), Department of Radiotherapy, Plesmanlaan 121, Amsterdam, The Netherlands; [6]Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL), Department of Radiotherapy, Plesmanlaan 121, Amsterdam, The Netherlands; [7]Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL), Department of Pathology, Plesmanlaan 121, Amsterdam, The Netherlands; [8]Amsterdam University Medical Centre, Department of Radiotherapy, Meibergdreef 9, Amsterdam, The Netherlands; [9]Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL), Department of Surgical Oncology, Plesmanlaan 121, Amsterdam, The Netherlands; [10]Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL), Department of Medical Oncology, Plesmanlaan 121, Amsterdam, The Netherlands; [11]Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL), Department of Radiology, Plesmanlaan 121, Amsterdam, The Netherlands; [12]Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL), Department of Medical Oncology, Plesmanlaan 121, Amsterdam, The Netherlands; [13]Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL), Department of Medical Oncology, Plesmanlaan 121, Amsterdam, The Netherlands; [14]Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL), Department of Surgical Oncology, Plesmanlaan 121, Amsterdam, The Netherlands; [15]Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL), Department of Surgical Oncology, Plesmanlaan 121, Amsterdam, The Netherlands

INTRODUCTION: Radiotherapy associated angiosarcoma (RAAS) of the breast is a rare malignancy with poor survival. Optimal treatment strategies remain uncertain due to a lack of data, and vary between surgery alone and a combination of surgery with (neo)adjuvant chemotherapy (NACT) and/or re-irradiation. The aim of this study was to evaluate the potential benefit of taxane based NACT. **METHODS:** In this retrospective single center study, all patients with RAAS of the breast treated between 1994 and 2024 are included. Since 2018, NACT is considered a treatment option for this patient population in our institute. The difference in oncological outcomes of patients with and without NACT were compared. **RESULTS:** Thirty-five women were included. Thirteen (37%) received NACT of which five (39%) also had neoadjuvant re-irradiation with hyperthermia. Eleven patients (85%) received paclitaxel, the other two (15%) had doxorubicine/docetaxel. Complete pathological response was found in 69% (n=9). Median follow up was 41 months (range 24-56) for patients with NACT and 44 (range 20-108) for patients without. In the NACT group, one patient developed a recurrence after 6.5 years. Patients with NACT had better oncological outcomes than patients without NACT in terms of 3-year local recurrence free survival (100%vs.63.9%, p=0.14), distant metastasis free survival (100% vs. 47.5%, p=0.005), and overall survival (100%vs.56.1%, p=0.016). **CONCLUSIONS:** This retrospective analysis of RAAS of the breast showed a trend towards improved oncological outcomes in patients treated with NACT compared to no NACT. Larger, prospective studies can validate these findings and establish the role of NACT in the management of this rare malignancy.

GP23. Intraoperative Revision of a Positive Proximal Resection Margin is Associated with Improved Survival in Patients Undergoing Resection for Gastroesophageal Junction and Proximal Third Gastric Cancer

Kaival Gundavda, MCh[1]; Narayan Rajavelu, MCh[2]; Amit Chopde, MCh[3]; Pallavi R, MSc[4]; Vikas Ostwal, DM[5]; Anant Ramaswamy, DM[6]; Shivakumar Gudi, MD[7]; Rajiv Kaushal, MD[8]; Kedar Deodhar, MD[9]; Vikram Chaudhari, DNB[10]; Shailesh V. Shrikhande, MS, MD, FRCS (hon), FASA (hon)[11]; Manish S, Bhandare, MCh[12]

[1]Department of Gastrointestinal and Hepato-pancreato-biliary Surgery, Department of Surgical Oncology, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India; [2]Department of Gastrointestinal and Hepato-pancreato-biliary Surgery, Department of Surgical Oncology, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India; [3]Department of Gastrointestinal and Hepato-pancreato-biliary Surgery, Department of Surgical Oncology, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India; [4]Department of Statistics, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India; [5]Department of Medical Oncology, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India; [6]Department of Medical Oncology, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India; [7]Department of Radiation Oncology, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India; [8]Department of Pathology, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India; [9]Department of Pathology, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India; [10]Department of Gastrointestinal and Hepato-pancreato-biliary Surgery, Department of Surgical Oncology, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India; [11]Department of Gastrointestinal and Hepato-pancreato-biliary Surgery, Department of Surgical Oncology, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India; [12]Department of Gastrointestinal and Hepato-pancreato-biliary Surgery, Department of Surgical Oncology, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India

INTRODUCTION: Positive proximal resection margins following resection for gastro-esophagal junction (GEJ) and proximal third stomach portend poor survival. Although associated with unfavourable tumour biology rather than technical insufficiency, the benefit of re-resecting intraoperatively encountered positive proximal margin, especially in locally advanced gastric cancers, is uncertain. **METHODS:** Three hundred eighty-eight (388) consecutive patients with proximal third gastric and GEJ adenocarcinoma undergoing radical resection between 2010 and 2022 were analysed for R1 resection rates and the impact of margin conversion from R1 to R0 on long-term survival. **RESULTS:** 91 patients (23%) had an initial positive proximal resection margin, of which, 69 patients (75%) were converted to R0 after frozen section analysis. Twenty-two patients (5.6%) had persistent R1 margins on final pathology. The R0 resection group fared best, with a 3-year-OS of 70%, while in the R1 to R0 resection group, the 3-year-OS was 55%. Patients with R1 resection fared poorly with a 3-year-OS of 36%. The median DFS for the R0, R1 to R0 and R1 groups was 42 months, 28 months, and 18 months respectively. Among the node-positive patients, we found a significant OS benefit for margin revision in N1 disease (p 0.036), but not in N2 or N3 disease (p 0.51). **CONCLUSIONS:** A positive resection margin is an independent poor prognostic factor, regardless of the tumour stage. Conversion of an intraoperatively encountered R1 margin to a R0 resection status is associated with improved survival and should be performed even in locally advanced gastric cancers, especially in N0 and N1 disease.

GP24. Response of Gastric Adenocarcinoma to Neoadjuvant Chemotherapy with Respect to the Presence or Absence of HER2 Overexpression: A Prospective Observational Study

Pratap K. Deb[1]; Samir Bhattacharyya[2]; Subrata K. Sahu[3]; Arnab Gupta[4]

[1]Saroj Gupta Cancer Centre and Research Institute, Kolkata, West Bengal; [2]Surgical Oncology, Saroj Gupta Cancer Centre and Research Institute, Kolkata, West Bengal; [3]Saroj Gupta Cancer Centre and Research Institute, Kolkata, West Bengal; [4]Saroj Gupta Cancer Centre and Research Institute, Kolkata, West Bengal

INTRODUCTION: Neoadjuvant chemotherapy has established itself as a standard therapeutic approach for gastroesophageal junction (GEJ) and gastric cancers. A notable subset of these malignancies exhibits overexpression of the human epidermal growth factor receptor 2 (HER2). Despite this, the current neoadjuvant chemotherapy regimens do not typically incorporate HER2-targeted therapies. Given the prevalence of HER2 overexpression in GEJ and gastric ca. exhibiting this biomarker. Furthermore, it is critical to evaluate the therapeutic efficacy of conventional neoadjuvant chemotherapy in this specific subgroup. Should it be determined that patients with HER2 overexpression consistently demonstrate suboptimal responses to standard neoadjuvant chemotherapy, the justification for subjecting these patients to the associated toxicities and potential risk of tumor progression needs to be critically re-considered. **METHODS:** Present study was conducted over a period of one year on forty (40) patients with histologically confirmed Gastric or gastroesophageal junction adenocarcinoma; (cT2–4 or cN+) according to the AJCC 8.0 staging system, as verified by enhanced CT, or PET/CT who received standard Neoadjuvant chemotherapy with FLOT [consisting of docetaxel (60 mg/m2), oxaliplatin (85 mg/m2), leucovorin (200 mg/m2), and 5-fluorouracil (2,600 mg/m2 as a 24 hr infusion), all given on day 1(2 weekly over 8 weeks)], XELOX (oxaliplatin 130 mg/m2 on day 1; xeloda 1,000 mg/m2 twice a day, on day 1–14), SOX (oxaliplatin 130 mg/m2 on day 1; tegafur 40 mg/m2 twice a day, or FOLFOX6 (oxaliplatin 85 mg/m2, leucovorin 200 mg/m2 on, and 5-fluorouracil 2,600 mg/m2) regimens; followed by surgery (total, subtotal, or distal gastrectomy based on the primary tumor size and location with D2 lymph node dissection). The response to the Neoadjuvant chemotherapy in the study is quantified by the assessment of the Tumour aregression Grade, (Becker et al) by the amount of therapy induced fibrosis in relation to residual tumor or the estimated percentage of residual tumor in relation to the previous tumor site. The HER2 status was be mainly assessed by immunohistochemistry (IHC) [modification proposed by Hofmann et al that has been assimilated by CAP and FDA] and in equivocal cases, by the Fluorescent insitu hybridization F(ISH) assays. The response to the Neoadjuvant chemotherapy as graded by the tumour regression score was then matched against the Her 2 expression status in the gastrectomy specimens and the values were them statistically analysed to find significant correlation the pathological response to Neoadjuvanttherapy with respect to presence or absence of overexpression of Her 2 receptors. **RESULTS:** Among 40 subjects(30 men and 10 women), Her 2 over expression was seen in 9 (22.5%). TRG 1 response (Complete regression of tumour or 50% residual tumour] was observed in 6 out of 9 her 2 over expressing patients(66.6%) but only 5 out of 31 subjects(16.12%) in the non her 2 over expressing group; the difference being statistically significant with p value at .03 ($p<0.05$). Also, if we consider TRG 1 and 2 together as favourable or acceptable response to Neoadjuvant chemotherapy and TRG 3 as unfavourable response, then only 3 out of 9 her 2 over expressing patients showed partially favourable response compared to 26 of 31 non her 2 over expressing patients. Also her 2 overexpressing cohort contributed to 6 of the 11 patients in the unfourable group with poor response to Neoadjuvant systemic therapy. The difference in this response was found to be statistically significant at p value of .0027($p<0.05$). Study groups showed no statistically significant difference in terms of Nodal Staging, Tumour Differentiation and LVI/PNI status when matched according to their her 2 over expression. **CONCLUSIONS:** Though limited in its sample size, the outcomes of this study shows that further introspection is required in this area to consider optimized and tailored treatment protocols, thereby either incorporating HER2-targeted therapies to improve clinical outcomes for this patient population or to consider upfront surgery in operable gastric cancers which have strong her2 overexpression which seems to be a significant predictor of poor response to the presently practised neoadjuvant systemic therapy regimes. Thus, it may be rightly said that though limited in its capacity, this study may be a stepping stone to the possibility that holds the potential of a paradigm shift in the neoadjuvant therapy considerations in treating gastric cancers.

GP25. Endobronchial Ultrasound trans bronchial aspiration versus surgical Mediastinoscopy for diagnosis of Mediastinal Lesions (Egyptian Experience)

Amr Rizk[1]; Galal Ghaly[2]; Mohamed Rahouma[3]; Eugene Shostak[4]; Khaled M Kamel[5]; Abdelrahman Mohamed[6]

[1]Surgical Oncology department, National Cancer Institute, Cairo University, Egypt; [2]Surgical Oncology department, National Cancer Institute, Cairo University, Egypt; [3]Cardiothorcic Surgery Department, Weill Cornell Medicine,NewYork,NY,USA; [4]Cardiothorcic Surgery Department, Weill Cornell Medicine,NewYork,NY,US ; [5]Chest Department, Faculty of Medicine, Cairo University, Egypt; [6]Surgical Oncology department, National Cancer Institute, Cairo University, Egypt

INTRODUCTION: Pathological evaluation of mediastinal lymphadenopathy and mediastinal masses is a crucial step in treatment. Traditionally, mediastinoscopy is considered as gold standard in mediastinal biopsies. Given its invasiveness and costly nature, the need for the development of

minimally invasive techniques for sampling mediastinal lesions was raised. Endobronchial ultrasound-transbronchial ultrasound is a minimally invasive method of mediastinal biopsy under ultrasound guidance. **METHODS:** This is a prospective study on patients with mediastinal lesions or staging for lung cancer over a period of two years was done from Aug 2020 to Aug 2022. Mann Whitney and Fisher exact tests were used. **RESULTS:** 21 patients (median age: 45 [Q1-Q3:35-55], 52.4% were females) were included and presented with isolated mediastinal lymphadenopathy (57.1%), mass (28.6%), generalized lymphadenopathy (9.5%), and lung cancer staging (4.8%).EBUS-TBNA and mediastinoscopy were done in 20 and 12 patients respectively with 11 patients had both.Of the eleven patients who had both procedures, 2 only were inadequate in the EBUS group. **CONCLUSIONS:** Compared to Mediastinoscopy, EBUS-TBNA is accepted minimally invasive procedure in assessing mediastinal lesions and staging lung cancer with advantage of real-time U/s guidance.

GP26. Multifocality does not improve predictability of recurrence in patients with papillary thyroid carcinoma.

Hyungju Kwon, MD, PhD[1]
[1]Department of Surgery, Ewha Womans University Medical Center

INTRODUCTION: Multifocal tumors are commonly found in papillary thyroid carcinoma (PTC) and have a prevalence rate of 18–87% among the cases. Many studies indicate that multifocality is associated with high-risk features of PTC, such as aggressive histologic subtype, extrathyroidal extension (ETE), lymph node (LN) involvement, and distant metastases. However, it is still unclear whether multifocality improves the predictability of recurrence in patients with PTC. **METHODS:** This retrospective cohort study included 1288 consecutive patients with PTC, who underwent total thyroidectomy between 2012 and 2019. Patient demographics and tumor characteristics data pertaining to multifocality, tumor size, ETE, LN metastasis, resection margin statue, and coexisting Hashimoto thyroiditis were collected. The primary endpoint of this study was 10-year disease-free survival. We performed 1:1 propensity score matching to minimize biases from possible confounders. The area under the receiver operating curve (AUROC) was used to evaluate the relative predictability of prediction scores. Time-dependent AUROC analysis was used to compare AUROCs from each prediction model. **RESULTS:** Of the 1249 patients enrolled, 487 patients (39.0%) had multifocal PTCs and 762 (61.0%) had unifocal tumor. Thyroid cancer in patients with multifocal PTCs showed a higher rate of ETE (67.3% vs. 57.3%; $p < 0.001$) and a microscopic resection margin involvement (4.5% vs. 2.4%; $p = 0.035$) than in patients with unifocal tumor. LN metastasis was also more common in the multifocality group than in the unifocality group ($p = 0.007$). Recurrences were found in 21 patients (4.3%) in patients with multifocal PTCs, and 15 patients (2.0%) with unifocal tumor developed recurrence ($p = 0.013$). 10- year DFS was significantly lower in the multifocality group (93.3% vs. 97.1%; $p = 0.011$) than in the unifocality group. Multivariate Cox regression analysis indicated that male sex (HR 2.185, 95% CI 1.047–4.559), tumor size (HR 1.806, 95% CI 1.337–2.441), N1b LN metastasis (HR 3.603, 95% CI 1.207–10.76), and multifocality (HR 1.986, 95% CI 1.015–3.888) were independent predictors of recurrence. Using these factors, we formulated prediction scores using Cox hazards regression models. Predictability as measured by the AUROC of each prediction model indicated that models based on multifocality (AUROC of 0.718) was more powerful than that based on other clinical factors (AUROC of 0.716). However, these models showed comparable overall predictability of recurrence ($p = 0.946$). **CONCLUSIONS:** Although multifocality was an independent predictors of recurrence, it did not improve the predictability of recurrence. A simpler prediction model without multifocality may be sufficient.

GP27. Predictive Value of C-Reactive Protein for Infectious Complications after Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: A Single-Center Prospective Study

Janyssa Charbonneau[1]; Alexandre Brind'Amour, MD, FRCSC[2]; Lucas Sideris, MD, FRCSC[3]; Sabrina Piedimonte, MD, MSc, FRCSC[4]; Mikaël Soucisse, MD, FRCSC[5]; Narcisse Singbo, MSc[6]; Jean-François Tremblay, MD, FRCSC[7]; Guy Leblanc, MD, FRCSC[8]; Suzanne Fortin, MD, FRCSC[9]; Lara De Guerké, MD, FRCSC[10]; Marie-Hélène Auclair, MD, FRCSC[11]; Mai-Kim Gervais, MD, FRCSC[12]
[1]CHU de Québec - Université Laval, Québec, QC, CA; [2]Division of Surgical oncology, Department of Surgery, Hotel-Dieu de Québec, Université Laval, Quebec city, QC, Canada; [3]Division of Surgical oncology, Department of Surgery, Maisonneuve-Rosemont Hospital, Université de Montréal, Montreal, QC, Canada; [4]Division of gynecology oncology, Department of Surgery, Maisonneuve-Rosemont Hospital, Université de Montréal, Montreal, QC, Canada; [5]Division of Surgical oncology, Department of Surgery, Maisonneuve-Rosemont Hospital, Université de Montréal, Montreal, QC, Canada; [6]Centre Hospitalier Universitaire de Québec – Université Laval, Québec, QC, Canada; [7]Division of Colorectal surgery , Department of Surgery, Maisonneuve-Rosemont Hospital, Université de Montréal, Montreal, QC, Canada; [8]Division of Surgical oncology, Department of Surgery, Maisonneuve-Rosemont Hospital, Université de Montréal, Montreal, QC, Canada; [9]Division of Gynecology oncology, Department of Surgery, Maisonneuve-Rosemont Hospital, Université de Montréal, Montreal, QC, Canada; [10]Division of Gynecology oncology, Department of Surgery, Maisonneuve-Rosemont Hospital, Université de Montréal, Montreal, QC, Canada; [11]Division of Gynecology oncology, Department of Surgery, Maisonneuve-Rosemont Hospital, Université de Montréal, Montreal, QC, Canada; [12]Division of Surgical oncology, Department of Surgery, Maisonneuve-Rosemont Hospital, Université de Montréal, Montreal, QC, Canada

INTRODUCTION: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) can be associated with significant morbidity and prolonged hospital stay. Postoperative infections account for a high burden of these complications. This study aimed to assess the predictive value of postoperative C-reactive protein (CRP) levels for overall infectious complications and anastomotic leaks. **METHODS:** This is a single-center prospective study of patients undergoing CRS and HIPEC for peritoneal metastases between 2018 and 2020 at Maisonneuve-Rosemont Hospital in Montreal, Canada. CRP levels were measured daily for ten days following surgery. A comparison was made between patients with infectious complications and those without. **RESULTS:** Ninety-nine patients were included. Thirty patients had infectious complications (30.3%), and four patients presented an anastomotic leak (4%). CRP levels were significantly higher in patients with infectious complications from postoperative day 2 to 10. Daily cut-off values most accurately predicted infectious complications on day 8 (94.3mg/L, AUC 0.85, SE 76.2%, SP 94.7%, PPV 88.9%, NPV 87.8%, $p<0.0001$) and day 9 (72.7mg/L, AUC 0.89, SE95.2%, SP81.8%, PPV 76.9%, NPV 96.4%, $p<0.0001$). Patients with infectious complications had longer operative time, higher peritoneal cancer index, and a higher number of intestinal anastomoses, while their baseline characteristics were comparable. **CONCLUSIONS:** Measurement of CRP helps predict infectious complications following CRS and HIPEC particularly on postoperative days 8 and 9. Cut-off values are more accurate after the first postoperative week, especially in ruling out infectious complications.

GP28. Intralesional interleukin-2 based therapy is effective in the treatment of high-risk cutaneous squamous cell carcinoma

Dejan Vidovic, MD[1]; Brianne Cruickshank, MD[2]; Lucy Helyer, MD[3]; Carman Giacomantonio, MD[4]
[1]Division of General Surgery, Department of Surgery, Dalhousie University, Halifax, NS, Canada; [2]Division of General Surgery, Department of Surgery, Dalhousie University, Halifax, NS, Canada; [3]Division of General Surgery, Department of Surgery, Dalhousie University, Halifax, NS, Canada; [4]Division of General Surgery, Department of Surgery, Dalhousie University, Halifax, NS, Canada

INTRODUCTION: Non-melanoma skin cancers, particularly cutaneous squamous cell carcinoma (cSCC), are often under-recognized in Canada due to gaps in tumor registry reporting and the in-office treatment of small lesions without histological confirmation. While most cSCCs are surgically manageable, tumors in sensitive anatomical locations, or those that are recurrent or locally advanced, can pose significant treatment challenges. Systemic immunotherapy is a current option for inoperable or metastatic cSCC but carries the risk of severe immune-related toxicities, particularly in elderly or medically complex patients. This study evaluates the outcomes of locally advanced cSCC patients treated with intralesional interleukin-2 (IL2), with or without topical imiquimod, aiming to minimize systemic toxicities in this patient population. **METHODS:** Patients with locally advanced or recurrent cSCC, significant comorbidities limiting surgical options, or tumors located in anatomically sensitive areas were referred to our immunotherapy program. Treatment involved intralesional IL2, with or without the addition of imiquimod. Responses to therapy were documented prospectively between 2017 and 2024, with clinical, histological, and radiographic data collected and analyzed. **RESULTS:** Over the study period, 19 patients with cSCC underwent treatment with intralesional IL2, with five also receiving imiquimod. The cohort's average age was 77.7 years, with a median ASA class of 3. Twelve patients presented with lesions in the head and

neck, three in the perianal region, and the remainder on the extremities. Patients received an average of 10 IL2 treatments over a mean duration of 7 months. The complete response rate was 78.9%, and the overall response rate was 89.5%. All patients remain alive at the time of this report. **CONCLUSIONS:** In this small, nonrandomized cohort, intralesional IL2 with or without imiquimod demonstrated a durable overall response rate of 89.5%, suggesting potential utility in elderly, comorbid, or recurrent cSCC patients. Further research is warranted to validate these findings.

GP29. Axillary Lymph Node Management of Clinically N0 Male Breast Cancer: A Systematic Review

Georgia Nelson[1]; Nouf AlMarzooqi[2]; Shaila Merchant, MD, MSc[3]; Sean Bennett, MD, MSc[4]

[1]Queen's University, Kingston, Ontario, Canada; [2]McGill University, Montreal, Quebec, Canada; [3]Queen's UniversityKingston, Ontario, Canada; [4]Queen's University, Kingston, Ontario, Canada

INTRODUCTION: Axillary management of clinically node negative (cN0) male breast cancer (MBC) can be achieved through either sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND). MBC is a rare disease lacking clinical trials, with most management extrapolated from data in female breast cancer. Our aim was to synthesize the available data regarding sentinel node detection rate, predictive value, morbidity, and recurrence following SLNB or ALND for cN0 MBC. **METHODS:** A systematic search was performed to identify studies of axillary management in cN0 MBC patients. Cancer related outcomes (recurrence, survival), morbidity, demographic/descriptive data (tumor size/grade/receptor status, SLN status, treatments, diagnostic technique), SLNB accuracy (PPV, NPV, identification rate) and SLNB technique were evaluated and described. Methodological quality was evaluated using the JBI Critical Appraisal tool. **RESULTS:** Eleven studies were identified, with a combined total of 2895 cN0 MBC patients: 1951 SLNB, 118 SLNB followed by ALND, and 826 ALND. Majority of included patients (n=2646) came from one NCDB study. Of the 157 patients who underwent SLNB and have reported pathology results, 70 had a positive SLN (44.6%). SLN identification rate was 98%. The reported mean number of SLNs sampled ranged from 1.5 to 3.5. In patients undergoing both SLNB and ALND, the positive predictive value of SLNB to predict further positive nodes at ALND was 56%, while the negative predictive value was 100%. The recurrence of breast cancer following SLNB was below 3%. Two studies reported comparable overall survival between SLNB and ALND groups. In ALND patients there was a 12% incidence of post-operative morbidity – including lymphedema, paresthesias and pain – compared to a 4% incidence in SLNB alone. **CONCLUSIONS:** In cN0 MBC patients, SLNB has comparable survival to ALND, a high negative predictive value, high identification rates, low recurrence, and lower morbidity. These data support SLNB as standard of care for clinically node negative male breast cancer patients.

GP30. Evaluating the efficacy of curcumin and mastic gum enclosed in phospholipid-based lipid nanoparticles on Helicobacter pylori treatment using urea breath test delta values: A single-arm prospective pilot study

Ji-Hyeon Park[1]; Jun-Young Yang[2]; Youngbae Jeon[3]; Jung Ho Kim[4]; Woon Kee Lee[5]; Jeong-Heum Baek[6]

[1]Department of Surgery, Gil Medical Center, Gachon University College of Medicine, Incheon, Republic of Korea; [2]Department of Surgery, Gil Medical Center, Gachon University College of Medicine, Incheon, Republic of Korea; [3]Department of Surgery, Gil Medical Center, Gachon University College of Medicine, Incheon, Republic of Korea; [4]Department of Internal Medicine, Gil Medical Center, Gachon University College of Medicine, Incheon, Republic of Korea; [5]Department of Surgery, Gil Medical Center, Gachon University College of Medicine, Incheon, Republic of Korea; [6]Department of Surgery, Gil Medical Center, Gachon University College of Medicine, Incheon, Republic of Korea

INTRODUCTION: Helicobacter pylori (H. pylori) infection remains a persistent health problem in Korea, where the prevalence of peptic ulcers and gastric cancer is high. This study aimed to determine whether phospholipid-based lipid nanoparticles containing curcumin and mastic gum are beneficial in the treatment of H. pylori infection. **METHODS:** This was a prospective single-arm pilot study. Patients with confirmed H. pylori infection (delta >8.5) according to a 13C-urea breath test (UBT) were included in this study. The study*s primary endpoint was to determine the change in the delta UBT values after consuming curcumin-mastic concentrate powder three times a day for 10 days. The rates of H. pylori eradication with standard H. pylori eradication regimens, clarithromycin-based triple therapy, and bismuth quadruple therapy were evaluated. **RESULTS:** A total of 25 patients participated in the study, with a mean age of 64.44±10.03 years, including 16 male (64.0%) and nine female (36.0%). After 10 days of consuming curcumin-mastic concentrate, the mean delta value of the UBT significantly decreased from 31.85±21.54 to 21.36±21.47 (mean difference=-10.49, P=0.018). Six (24.0%) patients achieved H. pylori eradication after ingesting a curcumin-mastic concentrate (delta value <2.5). The H. pylori eradication rate increased to 56.5% after clarithromycin-based triple therapy and to 85.0% after additional bismuth quadruple therapy. No adverse events related to curcumin-mastic concentrate intake were reported during the study period **CONCLUSIONS:** Curcumin-mastic concentrate has been demonstrated to reduce H. pylori activity safely in humans. This study suggests that administering curcumin-mastic concentrate before H. pylori eradication treatment may improve eradication rates; however, further large randomized controlled trials are needed to confirm this finding.

GP31. The use and clinical-oncological outcome after Total mesopancreatic excision and extended para-aortic lymphadenectomy in pancreatic head adenocarcinoma

Ahmed S. Alsibaie[1]; Anthony N. ghalioum[2]; Fouad S. Abdel[3]; Ahmed F. Elkhatib[4]; Ahmed O. Touny[5]; Haitham F. Othman[6]

[1]Department of Surgical Oncology, National Cancer Institute, Cairo University, 11796, Cairo, Egypt; [2]Department of Surgical Oncology, National Cancer Institute, Cairo University, 11796, Cairo, Egypt; [3]Department of Surgical Oncology, National Cancer Institute, Cairo University, 11796, Cairo, Egypt; [4]Department of Surgical Oncology, National Cancer Institute, Cairo University, 11796, Cairo, Egypt; [5]Department of Surgical Oncology, National Cancer Institute, Cairo University, 11796, Cairo, Egypt; [6]Department of Surgical Oncology, National Cancer Institute, Cairo University, 11796, Cairo, Egypt

INTRODUCTION: Recently, many studies suggested that the frequent recurrence of pancreatic head carcinoma locally, within the resection bed, may be due to inadequate clearance of the peripancreatic retroperitoneal margin, the so called mesopancreas, and is also considered a predictor of poor patient survival. The debate is still ongoing about the impact of total mesopancreatic excision and extended lymphadenectomy on early postoperative outcome and improving the rates of pathological R0 resection. **METHODS:** This study was a prospective interventional study during the period from January 2018 to January 2022. A total of one hundred and sixty two (162) patients underwent pancreaticoduodenectomy with total mesopancreatic excision and extended lymphadenectomy for pancreatic head adenocarcinoma. Marking of the mesopancreatic margin for pathological assessment was done, with dissection of perineural plexus and lymph nodes along the celiac axis, superior mesenteric artery and para-aortic lymph nodes in addition to the standard nodal stations excised. **RESULTS:** The mesopancreatic margin was positive in 8 patients (4.9%) and close (1-3mm) in 28 patients (17.2%). Paraaortic lymph nodes excision together with nodal tissues at the mesopancreatic triangle affected the staging of 39% of the patients. Regarding postoperative outcomes, Average hospital stay ranged from 7 days to 35 days, Hospital mortality occurred in six cases. Forty three (43) suffered post-operative pancreatic fistula, 23 patients had grade A fistula, 13 patients had grade B and 7 patients suffered grade C fistula. Biliary fistula occurred in 16 patients. All of them suffered from simultaneous pancreatic fistula. Post-operative diarrhea was significant in 111 patients (68.5%). **CONCLUSIONS:** the mesopancreatic excision and extended lymphadenectomy technique is safe and feasible, and especially useful in increasing pathological R0 resection and may become a more preferred method for pancreatic head carcinoma resection.

GP32. Survival Benefit of Concurrent Chemoradiotherapy for Advanced Ampulla of Vater Cancer

Chae Hwa Kwon[1]; Hyung Il Seo[2]; Young Mok Park[3]; Byeong Gwan Noh[4]; Dong Uk Kim[5]; Sung Yong Han[6]; Suk Kim[7]; Nam Kyung Lee[8]; Seung Baek Hong[9]; Ji Hyun Ahn[10]

[1]BioMedical Research Institute, Pusan National University Hospital, Busan 49241, South Korea; [2]Department of Surgery, Pusan National University School of Medicine and Biomedical Research Institute, Pusan National University Hospital, Busan 49241, South Korea; [3]Department of Surgery, Pusan National University School of Medicine and Biomedical Research Institute, Pusan National University Hospital, Busan 49241, South Korea; [4]Department of Surgery, Pusan National University School of Medicine and Biomedical Research Institute, Pusan National University Hospital, Busan 49241, South Korea; [5]Department of Internal Medicine, Pusan National University School

of Medicine and Biomedical Research Institute, Pusan National University Hospital, Busan 49241, South Korea; [6]Department of Internal Medicine, Pusan National University School of Medicine and Biomedical Research Institute, Pusan National University Hospital, Busan 49241, South Korea; [7]Department of Radiology, Pusan National University School of Medicine and Biomedical Research Institute, Pusan National University Hospital, Busan 49241, South Korea; [8]Department of Radiology, Pusan National University School of Medicine and Biomedical Research Institute, Pusan National University Hospital, Busan 49241, South Korea; [9]Department of Radiology, Pusan National University School of Medicine and Biomedical Research Institute, Pusan National University Hospital, Busan 49241, South Korea; [10]Department of Pathology and Biomedical Research Institute, Pusan National University Hospital, Busan 49241, South Korea

INTRODUCTION: Currently, there is no standard adjuvant therapy for patients with resected ampulla of Vater (AoV) cancer. To evaluate the effectiveness of adjuvant concurrent chemoradiotherapy (CCRT) in patients with advanced AoV cancer who underwent curative resection. **METHODS:** This single-centered, retrospective study included 29 patients with advanced AoV cancer who underwent pancreaticoduodenectomy between 2006 and 2018. The impact of CCRT on advanced AoV cancer was analyzed. **RESULTS:** The 1-, 3-, and 5-yr recurrence-free survival (RFS) rates for patients with advanced AoV cancer were 82.8%, 48.3%, and 40.8%, respectively, and the overall survival (OS) rates were 89.7%, 62.1%, and 51.7%, respectively. Lymphovas cular invasion was found to be a significant risk factor for RFS and OS in patients with advanced AoV cancer in the univariate analysis, whereas T stage and lymph node metastasis were significantly associated with OS in the multivariate analysis. Compared to the patients who did not receive adjuvant CCRT, those who received adjuvant CCRT did not show statistically significant improvements in the RFS and OS, although they had a significantly lower average age and significantly higher platelet-to-lymphocyte ratio. **CONCLUSIONS:** Adjuvant CCRT did not improve survival outcomes in patients with advanced AoV cancer. These findings contribute to existing knowledge on the effectiveness of CCRT in this patient population and provide important insights for clinical decision-making.

GP33. Accuracy of Four Guidelines in Predicting Malignancy in Intraductal Papillary Mucinous Neoplasm (IPMN)

Seiko Hirono[1]; Masaharu Tada[2]; Kenjiro Iida[3]; Hideaki Sueoka[4]; Ami Kurimoto[5]; Koji Nogaki[6]; Daisuke Shirai[7]; Kazu Harada[8]; Ikuo Nakamura[9]

[1]Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Hyogo Medical University, Nishinomiya, Hyogo, Japan; [2]Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Hyogo Medical University, Nishinomiya, Hyogo, Japan; [3]Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Hyogo Medical University, Nishinomiya, Hyogo, Japan; [4]Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Hyogo Medical University, Nishinomiya, Hyogo, Japan; [5]Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Hyogo Medical University, Nishinomiya, Hyogo, Japan; [6]Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Hyogo Medical University, Nishinomiya, Hyogo, Japan; [7]Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Hyogo Medical University, Nishinomiya, Hyogo, Japan; [8]Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Hyogo Medical University, Nishinomiya, Hyogo, Japan; [9]Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Hyogo Medical University, Nishinomiya, Hyogo, Japan

INTRODUCTION: Surgical indications for intraductal papillary mucinous neoplasm (IPMN) have been proposed in four major guidelines: the American Gastroenterological Association (AGA), the 2017 International Consensus Guidelines (ICG), the European Guidelines (EG), and the American College of Gastroenterology (ACG). This study aimed to evaluate the accuracy of these guidelines in determining surgical indications for IPMN. **METHODS:** A retrospective analysis was conducted on 76 IPMN cases that underwent surgical resection between 2018 and 2023. The surgical indication factors proposed by AGA, ICG, EG, and ACG were analyzed in relation to pathological findings. The utility of each guideline was assessed. **RESULTS:** Of the 76 IPMN cases, 40 were low-grade dysplasia (LGD), 16 were high-grade dysplasia (HGD), and 20 were invasive intraductal papillary mucinous carcinoma (IPMC). The diagnostic accuracy for HGD/invasive IPMC cases was as follows: AGA: 67/76 (88.2%), 2017 ICG high-risk stigmata (HRS): 59/76 (77.6%), ICG worrisome features (WF): 40/76 (52.6%), ICG HRS + WF: 38/56 (50.0%), EG absolute criteria (AC): 57/76 (75.0%), EG relative criteria (RC): 41/76 (53.9%), EG AC + RC: 40/76 (52.6%). Missed HGD/invasive IPMC rates and overtreatment rates were: AGA: Missed HGD/invasive IPMC: 7/45 (15.6%), Overtreatment: 2/31 (6.4%), ICG HRS: Missed: 0/23 (0%), Overtreatment: 17/53 (32.1%), ICG WF: Missed: 1/6 (16.7%), Overtreatment: 35/70 (50%), ICG HRS + WF: Missed: 0/2 (0%), Overtreatment: 38/74 (51.4%), EG AC: Missed: 0/21 (0%), Overtreatment: 19/55 (34.5%), EG RC: Missed: 8/21 (38.1%), Overtreatment: 27/55 (49.1%), EG AC + RC: Missed: 0/4 (0%), Overtreatment: 36/72 (50%), ACG: Missed: 0/1 (0%), Overtreatment: 39/75 (52%), The number of surgical indication factors was significantly higher in HGD/invasive IPMC cases than in LGD cases across all guidelines (median values: AGA: 1 vs. 0, P<0.001; ICG HRS: 1 vs. 0, P<0.001; ICG WF: 4 vs. 1, P<0.001; ICG HRS + WF: 6 vs. 2, P<0.001; EG AC: 2 vs. 0, P<0.001; EG RC: 2 vs. 1, P=0.006; EG AC + RC: 4 vs. 1, P<0.001; ACG: 4 vs. 2, P<0.001). **CONCLUSIONS:** Among the four guidelines, AGA demonstrated the lowest overtreatment rate but had the highest missed HGD/invasive IPMC rate. ICG HRS, EG AC, and ACG had zero missed HGD/invasive IPMC rates but showed higher overtreatment rates compared to AGA. Further studies are necessary to identify factors that can reduce both missed malignancies and overtreatment rates.

GP34. Axillary Surgery after Neoadjuvant Chemotherapy: Population-Based Trends over Time

Ekaterina Kouzmina[1]; Matthew Castelo[2]; Nicole J Hook Long[3]; Julie Hallet[4]; Natalie Coburn[5]; Frances C Wright[6]; Lena Nguyen[7]; Sonal Gandhi[8]; Katarzyna Jerzak[9]; Andrea Eisen[10]; Amanda Roberts[11]

[1]Department of Surgery, University of Toronto, Toronto, Ontario, Canada;; [2]Department of Surgery, University of Toronto, Toronto, Ontario, Canada; [3]Department of Surgery, Sunnybrook Health Sciences Centre, Canada; [4]Department of Surgery, Sunnybrook Health Sciences Centre, Canada; [5]Department of Surgery, University of Toronto, Toronto, Ontario, Canada; [6]Department of Surgery, Sunnybrook Health Sciences Centre, Canada; [7]ICES, Toronto, ON, Canada; [8]Department of Medical Oncology, Sunnybrook Health Sciences Centre, Canada; [9]Department of Medical Oncology, Sunnybrook Health Sciences Centre, Canada; [10]Department of Medical Oncology, Sunnybrook Health Sciences Centre, Canada; [11]Department of Surgery, Sunnybrook Health Sciences Centre, Canada

INTRODUCTION: Sentinel lymph node biopsy (SLNB) after neoadjuvant chemotherapy (NAC) has recently become the standard of care for patients with cN1 disease converted to cN0. We aimed to describe real-world population-level trends of axillary surgery de-escalation NAC over an 8-year period.
METHODS: A population-based cohort study of women aged 18 years or older with cT1-3N1 breast cancer in Ontario who underwent NAC and subsequent surgery between April 2012- January 2020 was performed. Axillary surgery (SLNB, axillary lymph node dissection (ALND), SLNB followed by ALND) and trends over time were evaluated using Cochran Armitage test and grouped by procedure type and receptor subtype. **RESULTS:** Between 2012-2020 (n = 2,692), SLNB and SLNB + ALND increased by 24.1% ($p < 0.01$) and by 2.9% ($p < 0.01$) respectively. ALND decreased by 26.9% ($p < 0.01$). SLNB use increased by 12.6% ($p < 0.01$) for hormone receptors positive (HR+) cancers, 33% ($p < 0.01$) for HER2+ cancers, and 29.6% ($p < 0.01$) for triple negative (TN) cancers. HR+ cancers had a decrease in ALND of 18.7% ($p < 0.01$), HER2+ cancers - of 35.6% ($p < 0.01$), and TN cancers - of 28.4% ($p < 0.01$). HR+ cancers had an increase in SLNB + ALND of 6.1% ($p < 0.01$), HER2+ cancers of 2.6% ($p < 0.01$), and TN cancers of 4% by 2017, then a decrease of 5% by 2020 ($p <0.01$). **CONCLUSIONS:** De-escalation of axillary surgery to SLNB has increased over time for appropriately selected cN1 patients post NAC.

GP35. Learning curves for minimally-invasive intersphincteric resection using risk-adjusted cumulative sum curves

Sanjay Singh, MS, MCh[1]; Mufaddal Kazi, MS, MCh[2]; Ashwin Desouza, MS, MCh[3]; Avanish Saklani, MS, FRCS[4]

[1]Asian Cancer Institute Cumballa Hill Hospital, Maharashtra, IN; [2]Tata Memorial Hospital, Maharashtra, IN; [3]Tata Memorial Hospital, Mumbai, IN; [4]Tata Memorial Hospital, Mumbai, IN

INTRODUCTION: Achieving competency is crucial to ensure optimal outcomes in minimally invasive intersphincteric resection. This study documents the learning curves for minimally invasive intersphincteric resection using risk-adjusted cumulative sum curves with the surgical failure as a composite endpoint, providing a dynamic assessment of performance and competency attainment. **METHODS:** All consecutive minimally invasive intersphincteric resections performed by a single team of surgeons at a tertiary referral colorectal

cancer unit were audited. Surgical failure was defined as any of the following: positive resection margin, local recurrence, or unreversed ostomy at one year. Risk-adjusted cumulative sum and Bernoulli cumulative sum curves were used for sequential assessment of performance. **RESULTS:** Amongst 310 intersphincteric resections, surgical failure was observed in 66 patients (21%). A positive margin was seen in 11 patients (3.5%), unreversed stoma at one year in 53 (17%), and local recurrence in 18 patients (5.8%). The risk-adjusted cumulative sum identified the first inflexion point corresponding to the achievement of competency after the 40th case. Further, other instances of higher-than-predicted surgical failures were observed and explained. While laparoscopic intersphincteric resection risk-adjusted cumulative sum curves mirrored the curves for entire cohort, the robotic curves could not identify any discernible inflexion. **CONCLUSIONS:** The learning curve for intersphincteric resection by minimally invasive technique was achieved after the 40th case for a team that was trained in minimally invasive colorectal surgery. The broader applicability of cumulative sum curves for early detection of deterioration in outcomes highlights the need for their wider use in procedural monitoring.