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Abstract Presentations: PSM Clinical Outcomes

1. Productivity Analysis of Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) Operative Procedures: Implications for Surgeons and Practice Planning

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INTRODUCTION: CRS+HIPEC operations can be long, involve multiple visceral resections, and are relatively infrequent within surgical oncology. Therefore, measures of physician work effort used for reimbursement such as work relative value units (wRVUs) may not fully capture CRS+HIPEC case complexity or surgeon time as a single data point. The purpose of this study was to evaluate multiple wRVU productivity and efficiency measures based on CRS+HIPEC data from a high-volume peritoneal surface malignancy practice.
METHODS: A retrospective cohort study of wRVUs for consecutive HIPEC cases at a single institution from January 2020 to February 2023 was performed. Laparoscopic HIPEC and CRS without HIPEC cases were excluded. Descriptive statistics were used to analyze productivity: total wRVU per case and efficiency: wRVU per visceral resection, per hour (based on operative case length), and per LOS.
RESULTS: In total 108 CRS+HIPEC operations were performed. It was the second CRS+HIPEC for 14 (13%) cases, and the third for 1 (0.9%). Median PCI score was 13 (IQR 7-22). 67 (62%) patients had a CC score of 0, 26 (24.1%) CC1, 13 (12%) CC2, and 2 (1.9%) with CC3 resection. Median number of claim procedure codes per operation, representing visceral resections, was 7 (IQR 5-9). Modifier 22, a measure of increased case complexity, was used in 63 (58%) cases. Excluding HIPEC codes, the most common codes were "Excision or destruction of open intraabdominal tumor" in 53 (49.1%), "Colectomy removal of ileum with ileocolostomy" in 45 (41.7%), and Cystourethroscopy with ureteral catheterization in 41 (38%). Codes with the highest wRVUs were "Hepatectomy total left lobectomy" with 53.04 wRVUs in one case, "Gastrectomy with Roux en Y reconstruction" with 39.53 wRVUs in 3 cases (2.8%), and "Hepatectomy resection liver partial lobectomy" with 39.01 wRVUs in 5 cases (4.6%). Median wRVU per case was 84 (IQR 55.4-111.3), and median case length was 10.6 hours (IQR 9.2-13.1). Median wRVU/hr of operative time was 7.7 (IQR 5.9-9.5). Median hospital length of stay was 8 days (IQR 7-10.8), and median wRVU per day of length of stay was 9.3 (6.1-13.1). Given these results, Table 1 estimates number of CRS+HIPEC cases needed to reach common annual RVU targets based on proportion of practice as CRS+HIPEC.
CONCLUSIONS: CRS+HIPEC procedures may have unique wRVU productivity and efficiency compared to other complex cancer procedures. Given the long duration, it is important to consider not only total wRVUs but assess multiple wRVU measures per unit time. Providing a more nuanced and comprehensive picture of work effort may benefit surgeons, divisions planning these operations, block time allocation, and operating room staff scheduling.

Table 1. Estimated number of CRS+HIPEC cases per year needed to meet common annual RVU targets based on the proportion of practice (in wRVUs) from CRS+HIPEC procedures. Conversion rate of median 84 wRVUs per CRS/HIPEC procedure.

RVU Target (per year)	75%	50%	25%
6000	53.6	35.7	17.9
7000	62.5	41.7	20.8
8000	71.4	47.6	23.8
9000	80.4	53.6	26.8
10000	89.3	59.5	29.8

2. Development of Peritoneal Complications in Patients with Peritoneal Metastases Who are Not Candidates for Cytoreductive Surgery

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INTRODUCTION: Peritoneal metastases (PM) from gastrointestinal cancers (GI) harbors poor overall survival. Although cytoreductive surgery (CRS) with or without hyperthermic intraperitoneal chemotherapy (HIPEC) may improve survival in select patient groups, many patients with peritoneal disease may never make it to surgical resection. We thus aimed to evaluate the natural history of patients with PM who are not candidates for surgery.
METHODS: Retrospective review was performed to identify patients with primary GI malignancy and PM, who were

evaluated by surgical oncology at a single tertiary institution (2020-2023). Patients were stratified by whether they were offered CRS or no-surgery. The no-surgery cohort was followed for development of peritoneal complications, defined as symptomatic ascites, malignant bowel obstruction, or bowel perforation.
RESULTS: A total of 300 patients with GI cancer and PM were included. 185 (62%) underwent surgical resection: 72% underwent complete CRS (+/- HIPEC) and 28% had incomplete CRS. The remaining 115 (38%) were evaluated but no CRS was offered, often due to high peritoneal disease burden (62%) and aggressive primary histology (19%). Most common primary cancer sites were colorectal (33%), appendiceal (18%), pancreatic (16%) and gastric (15%). Almost a quarter (22%) exhibited high-risk histology including signet ring and goblet cell features. In the no-surgery group, 83% restarted systemic chemotherapy and 80% developed relatively quick disease progression. At a median time of 7 months, 63 patients (55%) in the no-surgery cohort had developed peritoneal complications: 56% developed symptomatic ascites requiring admission for paracentesis or peritoneal drain; 48% developed malignant bowel obstruction from PM requiring admission and palliative intervention (palliative bowel resection, diverting ostomy, venting gastrostomy tube, or stent), and 5% presented with bowel perforation requiring emergent surgery. Overall, 53% of patients who were deemed not surgical candidates transitioned to hospice and died within a year.
CONCLUSIONS: GI malignancies with PM represent advanced disease with high symptom burden and poor prognosis. Our study shows that in patients who are not candidates for CRS, more than 50% will progress and develop peritoneal complications within a year, leading to high burden of hospital admissions. Therefore, continued follow up and earlier consideration of palliative procedures may benefit this patient population.

3. Anastomotic Leaks and the Role of Diverting Stomas in Low Anterior Resection with HIPEC
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INTRODUCTION: Anastomotic leak after low anterior resection (LAR) is a notable complication, with an incidence of ~15% in average-risk patients. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is an extensive surgical procedure in which LAR may be included, but typically the anastomosis is not low and preoperative pelvic radiation is rarely employed. Therefore, the decision to divert relies on consideration of various risk factors. The incidence and impact of diverting loop ileostomy (DLI) following CRS/HIPEC with LAR are not well described.
METHODS: We conducted a single institution retrospective review of patients who underwent CRS/HIPEC with LAR from 2018-2024. Demographic and surgical data including indications for surgery, peritoneal carcinomatosis index (PCI), completeness of cytoreduction (CC), HIPEC regimen, factors influencing decision for DLI, and patient outcomes were recorded. Data was analyzed using t-test and chi-squared analysis.
RESULTS: Thirty-five patients met inclusion criteria. 51% (n=18) had appendiceal primaries, 34% (n=12) had colon primaries, 2 had mesothelioma, 1 had small bowel adenocarcinoma, and 2 had peritoneal carcinomatosis of unknown primary. The average PCI was 18 (5-34). Most patients (91%, n=32) achieved optimal cytoreduction (CC0/CC1). All but one received intraperitoneal mitomycin C (40 mg for 90 minutes); the remaining patient received cisplatin (345mg for 60 minutes). 54% of patients (n=19) were diverted. Operative characteristics are summarized in Table 1. Reasons for diversion included tumor burden (n=2), low anastomosis (n=3), thin donut (n=1), prior operative field (n=6), positive leak (n=1), patient co-morbidities (n=1), need for complex closure (n=2), or unclear (n=3). Postoperatively, no diverted patients experienced clinically significant leaks, while 18% (n=3) of non-diverted patients had leaks requiring operation, including two washout/diversion procedures and one wide drainage. Neither of the patients with diversion at this time had continuity restored. Among primarily diverted patients, 63% (n=12) had bowel continuity restored. Post-DLI reversal complications included reoperation for anastomotic leak and bowel obstruction in 17% (n=2). At discharge, 10% (n=2) of diverted patients went to SNF or rehab, while all nondiverted went home.
CONCLUSIONS: LAR with CRS/HIPEC presents inherent complications. In our dataset, DLI prevented significant leak; however one-third of diverted patients did not undergo reversal, and reversal had its own complications. This emphasizes the need for careful consideration of when to create DLI in this cohort.

4. Leveraging Machine Learning to Predict Completeness of Cytoreduction after CRS-HIPEC
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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.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.

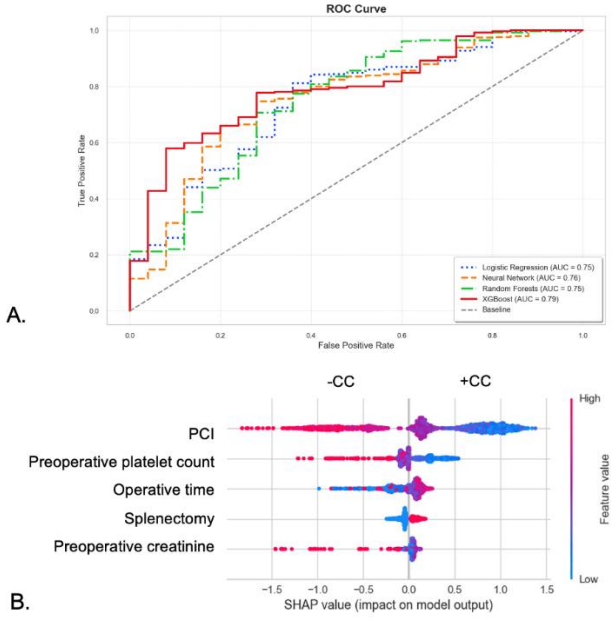

Figure 1. Receiver operating characteristic curves for logistic regression, neural network, random forest, and XGBoost models (A); SHAP values of the XGBoost model for predicting completeness of cytoreduction (B).

AUC, area under the curve; CC, completeness of cytoreduction; PCI, peritoneal carcinomatosis index; ROC, receiver operating characteristic; SHAP, shapley additive explanations.

5. A Cost Analysis of Acute Pain Management after Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy

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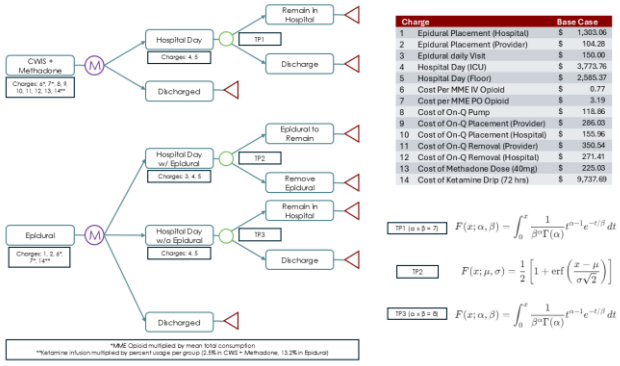
INTRODUCTION: Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is a major procedure that can lead to significant post-operative pain. Pain management with a continuous wound irrigation system (CWIS) plus intraoperative methadone has been shown to be superior to neuraxial analgesia with an epidural. This study used a Markov decision tree analysis to investigate the cost of CWIS plus intraoperative methadone compared with epidural analgesia after CRS/HIPEC.
METHODS: Patient data, including ketamine and opiate usage, length of stay and epidural duration, was extracted from hospital admission data from all patients undergoing open CRS/HIPEC at our institution from 2018 to 2021 and used to build the model. A Markov decision tree analysis was created for the two pain management strategies. Transition probabilities were calculated for each model using a cumulative distribution function centered around mean hospital length of stay and mean and standard deviation of epidural duration. Cost data, including base case, maximum and minimum charges, was obtained from publicly available hospital charge data from five NCI designated comprehensive cancer centers. After performing the Markov analysis for a sample of 1000 patients for each management strategy using our base case values, a probabilistic sensitivity analysis was performed using a Monte Carlo simulation with 5000 iterations.
RESULTS: For the 157 patients on which our cost model was based, length of stay was significantly shorter with the CWIS + Methadone group (7 vs. 8 days, p<0.01). Total opioid exposure was also significantly lower in the CWIS + Methadone group (252.8 ± 17.7 MME vs. 486.8 ± 86.6 MME; odds ratio [OR] 0.72, 95% CI 0.52–0.98, p = 0.04). Ketamine infusion was used for 13.2% of epidural patients compared to only 2.5% of CWIS + Methadone patients. In our base case analysis, we found savings of $7,357,831 over 1000 simulated patients (Total charges CWIS + Methadone: $21,823,030 vs. Epidural $29,180,861). This translates to a savings of $7,358 per patient. When dividing the cost parameters into provider (surgeon and anesthesia) charges and resource (facility and medication) charges, we found savings in both categories for the CWIS + Methadone group (Provider charges- $438 less per patient; resource charges- $6920 less per patient). In our probabilistic sensitivity analysis, CWIS + Methadone incurred fewer total charges in 92.9 % of simulations with an average charge of $19,332,069 (SD: $3,050,989) compared to $27,241,214 (SD: $4,038,017) for an epidural for an average savings of $7,760 per patient. The provider charges were lower in 90.4% of simulations for an average savings of $690.89 per patient. The resource charges were lower in 91.1% of simulations for an average savings of $7,069 per patient.
CONCLUSIONS: Previous research has demonstrated a shorter length of stay and decreased opiate use for patients managed with CWIS and intraoperative methadone when compared to epidural analgesia after open CRS/HIPEC. This study demonstrates that this management strategy is also the most cost-effective

strategy in most cases using publicly available charge data from 5 NCI designated comprehensive cancer centers. It is also important to note that the savings demonstrated is greater than the maximum daily charge for a hospital day indicating that the savings is due in part to both the shorter length of stay and well as lower labor and resources charges.



6. Perioperative and oncologic outcomes following combined peritoneal and liver resection/ablation for metastatic colorectal cancer

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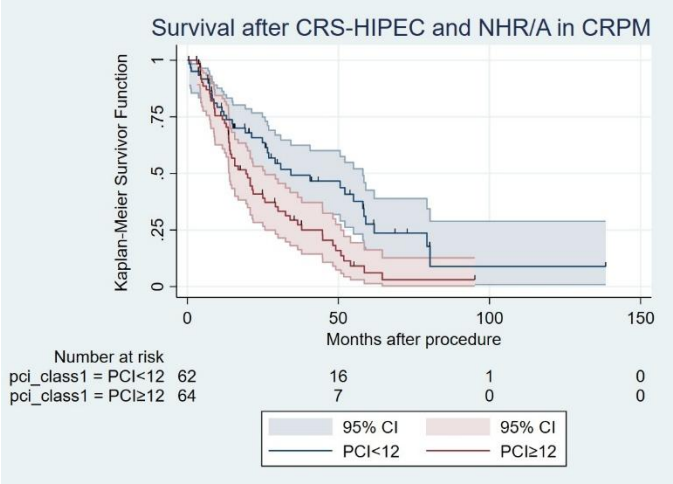
INTRODUCTION: Cytoreductive surgery (CRS), with or without hyperthermic intraperitoneal chemotherapy (HIPEC), offers a survival benefit in select patients with isolated peritoneal metastases from colorectal cancer (CRPM). We investigated perioperative and oncologic outcomes in a subset of such patients who received non-anatomic hepatic resections/ablations (NHR/A) during CRS-HIPEC.
METHODS: We conducted a retrospective cohort study of all patients undergoing combined CRS-HIPEC and NHR/A for mCRC at a high-volume center between 2001-2022. Multivariable Cox regression identified variables associated with overall survival (OS).
RESULTS: All 126 patients included in the study underwent CRS-HIPEC and NHR/A with complete cytoreduction (CC-0) in a synchronous fashion. The median age-adjusted Charlson comorbidity index (AACCI) was 9 (IQR 8-10), median peritoneal carcinomatosis index (PCI) was 12 (IQR 8-17), and 67% of patients received preoperative systemic chemotherapy. The median follow-up duration and OS (95% CI) after surgery were 62 months (43-80) and 26 months (19-34), respectively. On multivariable Cox analysis, PCI ≥12 (HR 1.7, p=0.02) and higher AACCI (HR 1.2 for each point, p=0.03) were associated with worse OS. The median OS was 34 months (25-58) for PCI <12 and 19 months (13-26) for PCI ≥12 (p=0.004) (Figure 1). The rate of major postoperative complications (Clavien-Dindo grade ≥ 3) was significantly lower for PCI <12 than PCI ≥12 (39% vs. 61%, p=0.046), including lower gastrointestinal (30% vs. 70%, p=0.02) and pulmonary (31% vs 69%, p=0.04) complications.
CONCLUSIONS: Our study shows that patients with limited CRPM (PCI<12) who undergo CRS-HIPEC combined with NHR/A have superior post-operative complication rates and long-term survival compared with those who have higher PCI. We suggest that eligibility for combined CRS-HIPEC and NHR/A in CRPM patients be restricted to those with PCI<12.



7. Decision Regret and Quality of Life in Caregivers of Patients with Appendiceal Cancer Undergoing Hyperthermic Intraperitoneal Chemotherapy

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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 the inclusion criteria. As overall DRS scores were very low (mean 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%), were 97.5% 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 their loved one to undergo HIPEC. No patient demographic, tumor or surgical outcomes were significantly associated 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 was not significantly correlated with regret (mean FACT-COST 25.9 ± 11.4 p=0.221). Regret

was significantly associated with worse QOL in all categories (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 reported 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.

8. Validation of Nomograms Predicting Survival in Patients undergoing CRS-HIPEC for Peritoneal Dissemination of Appendiceal Cancer

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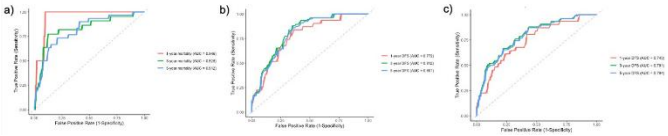
INTRODUCTION: Appendiceal cancers have a high rate of peritoneal dissemination. Optimal treatment involves cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC), although survival is dependent on a variety of factors. Three nomograms from the UK and Spain have been developed to predict overall survival (OS) and disease-free survival (DFS) in patients with PMP of appendiceal origin, and this study aims to validate these nomograms across a multicenter setting in the United States.
METHODS: This was a retrospective cohort study of patients with peritoneal dissemination from appendiceal cancer who underwent CRS-HIPEC at two tertiary centers in the US from 2007-2024. Receiver operating characteristic (ROC) curves and their respective area under the curve (AUC) were used to assess the UK and Spanish nomograms' predictive capabilities for OS (UK) and DFS (UK and Spain) in the entire cohort as well as subsets of patients with low grade or high grade tumors.
RESULTS: Overall, there were 532 patients included in the analysis with the following histologies: acellular mucin (n=82, 15.4%), low grade (n=252, 47.4%), high grade (n=117, 22.0%), and high grade with signet cell features (n=67, 12.6%). AUCs of the UK nomogram for 3- and 5-year mortality were 0.828 and 0.812, respectively. Among patients with low grade tumors, the AUCs for 3- and 5-year mortality were 0.610 and 0.696, respectively, while those for patients with high grade tumors were 0.820 and 0.727, respectively. In regards to DFS, the UK nomogram (AUC at 1-year: 0.727, 3-year: 0.831, and 5-year: 0.801) was slightly more accurate than the Spanish nomogram (AUC at 1-year: 0.740, 3-year: 0.791, and 5-year: 0.784) when predicting longer term outcomes. Among sub-analyses of patients with either low or high grade histology, the UK and Spanish nomograms performed worse when predicting DFS among high grade tumors (maximum AUC of 0.655 for 1-year DFS from UK nomogram) compared to low grade tumors (minimum AUC 0.689 for 1-year DFS from Spanish nomogram).
CONCLUSIONS: All three nomograms were relatively accurate at predicting OS and DFS in patients with peritoneal dissemination from appendiceal cancer. Sub-analyses among patients with either low or high grade tumors yielded varying performances. This suggests that there may be opportunities to develop improved nomograms based on tumor histology.

Figure 1. ROC curves for predicting **a)** OS from the UK nomogram, **b)** DFS from the UK nomogram, and **c)** DFS from the Spanish nomogram



9. Racial and Geographic Disparities in Utilization of CRS-HIPEC for Metastatic Mucinous Appendiceal Tumors: A National Analysis

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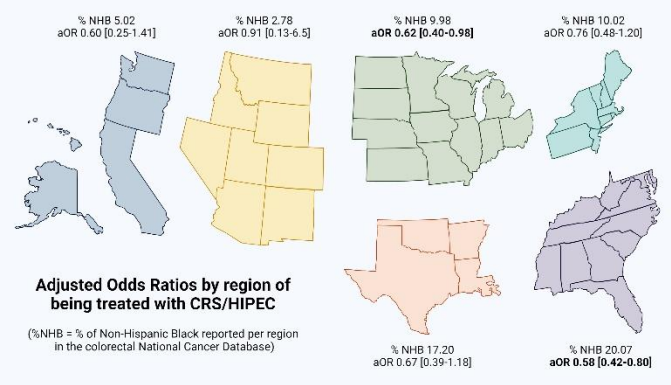
INTRODUCTION: Single-center studies have indicated significant disparities in the care of patients with appendiceal cancer and peritoneal metastasis. However, limited adjustments in these settings have hindered a comprehensive exploration of differences in advanced cancer therapy patterns. This study aims to investigate disparities in the utilization of CRS-HIPEC for metastatic mucinous appendiceal tumors.
METHODS: We analyzed data from the National Cancer Database (2004–2021) to identify patients diagnosed with Stage IV mucinous appendiceal tumors (histology codes 8470, 8480, 8481, 8490) located at the appendix (C18.1). Logistic regression models were employed to calculate the adjusted odds of receiving CRS-HIPEC based on demographic factors, disease characteristics, and facility attributes, including surgical volumes.
RESULTS: Out of 16,845 patients, 13% underwent CRS-HIPEC. Among those treated, 80% were Non-Hispanic White (NHW), 8.4% Non-Hispanic Black (NHB), 6.1% Hispanic, and 5.1% Asian/Pacific Islander/Other races. In contrast, among patients who did not receive CRS-HIPEC, a significantly higher proportion were NHB (12.6%, p?<?0.001). Following this line, adjusted analyses revealed persistent racial differences. NHB patients had 36% reduced odds of receiving CRS/HIPEC (aOR=0.64, 95% CI: 0.54-0.77) compared to NHW. Further exploration of factors associated with higher probability of receiving CRS-HIPEC showed that the reduced odds for NHB patients remained consistent across subgroups: patients under 60 years (aOR?=?0.75, 95% CI: 0.59–0.94), those with private insurance (aOR?=?0.58, 95% CI: 0.45–0.74), and those treated at academic facilities (aOR?=?0.63, 95% CI: 0.51–0.78) compared to NHW in the same category. Notably, stratified geographic analysis indicated that in regions with high proportions of NHB patients, such as the North Central and South Atlantic regions, these disparities persisted (aOR?=?0.62, 95% CI: 0.40–0.98; aOR?=?0.58, 95% CI: 0.42–0.80, respectively). Regional adjusted analyses are illustrated in Figure 1.

CONCLUSIONS: Significant racial disparities exist in the utilization of CRS-HIPEC for metastatic mucinous appendiceal tumors, disproportionately affecting Non-Hispanic Black patients. These disparities persist even after adjusting for demographic, socioeconomic, and facility-level factors, and are further pronounced in specific geographic regions. Addressing these inequities is crucial to ensure equitable access to advanced cancer treatments and improve outcomes for all patient populations.



10. Tailored Surveillance for Mucinous Appendix Cancer after Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy

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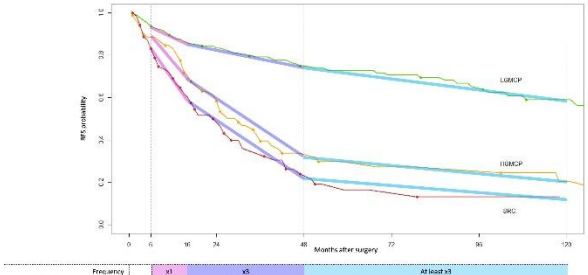
INTRODUCTION: In mucinous appendix cancer (MAC), despite varying recurrence rates across histologic subtypes, the surveillance schedule following cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) remains uniform – typically, every 6 months for 5 years followed by annual 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 (IQR: 8-12) days. Grade III/IV Clavien-Dindo complications occurred in 14.5% (n=56) of patients. Median FU was 92 (95% confidence interval [CI]: 83, 98) months . Median RFS was not reached (NR) (95% CI: 109, NR) for LGMCP , 30 (95% CI: 23, 39) months for HGMCP, and 23 (95% CI: 15, 31) months 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. RFS-driven surveillance for mucinous appendix cancer subtypes



Each dot on the survival curves represents a 5% drop in RFS. Vertical dashed lines mark the knots at 6 months (end of the early postoperative period), 16 and 48 months (statistically defined points dividing the RFS functions), and 120 months (end of the study observation period). The slope lines in pink, purple, and light blue correspond to the time frames between the knots, where the probability of recurrence is assumed to be constant. The table below the plot, color-coded to match the slope lines, indicates the minimum number of follow-up visits (n) and the intervals between visits (Δ) for each time frame. The risk of an event—either recurrence or death—is calculated for patients who enter each corresponding period recurrence free. The risk of event is cumulative throughout the corresponding period.

HGMCP, high-grade mucinous carcinoma peritonei; FU, follow up; LGMCP, low-grade mucinous carcinoma peritonei; mo, months; RFS, recurrence-free survival; SRC, signet ring cell.

Abstract Presentations: HPB

11. ctDNA as a novel biomarker of treatment efficacy in patients with unresectable colorectal liver metastases treated with hepatic arterial infusion

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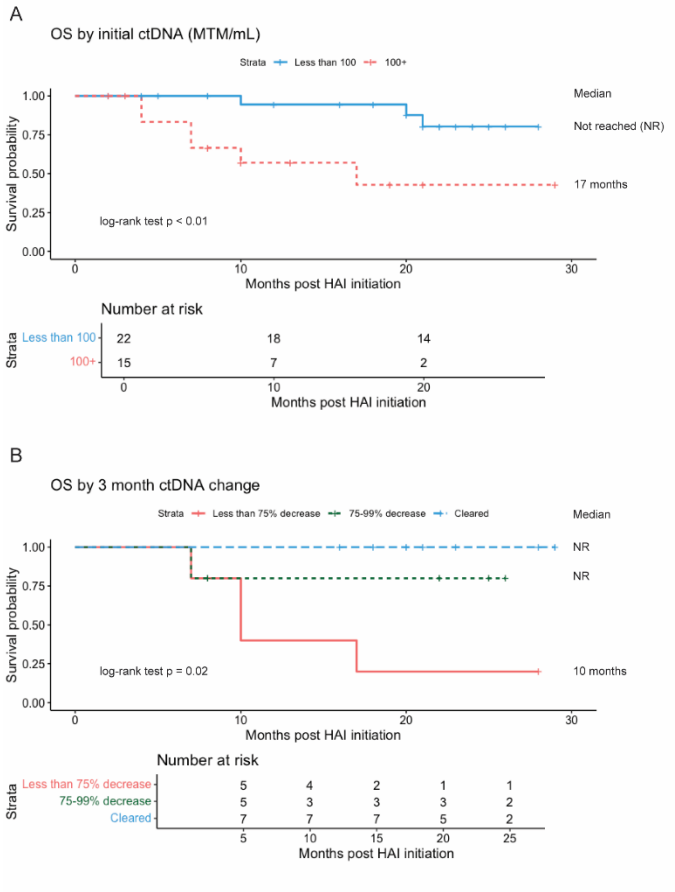
INTRODUCTION: Hepatic arterial infusion (HAI) pump chemotherapy is an expanding treatment for patients with unresectable colorectal liver metastases (uCRLM). While the role of HAI in this patient population remains the focus of several randomized trials in the United States and Europe, there is an unmet 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.



12. Surgical stress promotes development of colorectal liver metastases via modulation of hepatic regulatory T cells

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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 (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 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 (5x10^5) expressing firefly luciferase were injected into wild type (C57BL/6) mice via the portal vein. 70% hepatic I/R (60 minutes ischemic time) was performed 15 minutes 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 (% of Foxp3+/CD4+). Tumor growth was quantified by bioluminescence, tumor to body weight ratio, 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 ischemia/reperfusion 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.

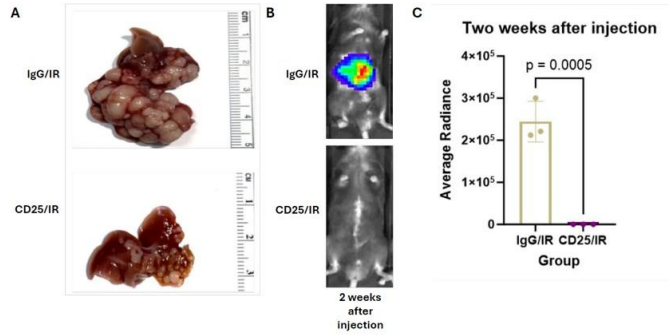

Figure. Treg depletion via CD25 neutralizing antibody reduces tumor growth after I/R injury. **A)** Representative photographs of macroscopic nodules and tumor volume. **B, C)** MC38-luciferase cells allowed in vivo tracking of tumor growth, measured in average radiance.

13. Reduced hepatotoxicity and equivalent survival with a lower hepatic arterial floxuridine starting dose in the adjuvant treatment of colorectal cancer liver metastases

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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.

14. Perceived Challenges and Strategies in Managing Biliary Sclerosis: A Qualitative Study of Hepatic Arterial Infusion Pump Chemotherapy Providers

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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. This qualitative study's objective 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.

15. 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

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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.

16. Histotripsy for the Treatment of Liver Tumors: A review of patients treated at a single institution

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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 intraoperative 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.

Abstract Presentations: PSM Appendix and CRC Translational Science

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

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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. PTO DNA was then 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.
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). 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.

Patient One (Tumor Site for PTO)	Chemotherapy Treatment	EZH1 + PANK4 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 + SIX4 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

Selected Cases to Model Intra- and Inter-Patient Tumor Heterogeneity in Regard to Chemotherapy Sensitivity or Resistance using a Patient Tumor Organoid Platform. Patient 1 presents with four peritoneal surface tumors, two of which contain co-occurring EZH1 and PANK4 mutations. After FOLFIRI treatment, the residual cells in the PTOs had a statistically significant depletion in cells containing mutations in pathways that regulate stem cell differentiation (EZH1) and fatty acid metabolism (PANK4). Patient 2 also presents with four peritoneal surface tumors, two of which contain co-occurring SLC22A5 and SIX4 mutations. In patient 2's liver stripping, treatment of FOLFIRI enriched for SLC22A5 and SIX4 mutant clones to increase in their PTOs, 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 and SIX4 mutant cells after FOLFOX treatment. Co-occurring mutations that regulate cation transport (SLC22A5) and cancer cell differentiation (SIX4) only appear after FOLFOX/ FIRI PTO treatment. Further analyses will integrate multiple gene mutations for the identification of potentially druggable cancer driver pathways and for the prediction of peritoneal surface disease clinical drug response.

18. Next generation sequencing identifies key targetable mutations in the treatment of appendiceal neoplasms

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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.

Figure 1. Simultaneous Mutation Rates of KRAS with other Targetable Genes

	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%

19. Tissue-based biomarkers of response to immune checkpoint blockade (ICB) in metastatic appendiceal adenocarcinoma (AA): validating spatial transcriptomics and proteomics of trial participants' surgical specimens.

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INTRODUCTION: We recently reported a clinical trial (NCT03074513) demonstrated survival benefit of atezolizumab-bevacizumab (AtezoBev) in unresectable metastatic AA patients (pts). This was intriguing considering low tumor mutational burden and low rates of mismatch repair deficiency in AA previously described. Being the first trial of ICB in metastatic AA, we aimed to understand the potential biomarkers of response amongst these pts using spatial transcriptomics.

METHODS: FFPE tissue from four trial pts was processed for spatial transcriptomics and proteomics using nanoString's GeoMX Digital Spatial Profiling (DSP) and CosMX Spatial Molecular Imaging (SMI) platforms, respectively. Sequential slides were stained with H&E or fluorescent markers for DNA (SYTO 13), epithelium (PanCK), bacteria (16s) and immune cells (CD45) for DSP or DNA (DAPI), membrane (CD298/B2M), immune cells (CD45) and CD8 T cells (CD8a) for SMI to aid in region selection. Immune deconvolution was performed with CIBERSORTx (RNA) or CELESTA (Protein). Differential cell abundance and proportion were evaluated using a linear mix model or Fisher's exact test.

RESULTS: Two pts continued to have an ongoing response while two pts are deceased. The longest OS among this subset of pts was 96 months from index operation and 84 months from trial therapy initiation. DSP transcriptomic analysis detected 78% (14,000/18,000) genes above the limit of quantification. Small tumor islands (10-200 cells) were noted within pools of mucin. Immune aggregates potentially representing two molecularly distinct subtypes of Tertiary Lymphoid Structures (TLSs) were noted peri-tumorally, with TLS1 containing more plasma cells (p=0.015) and a trend towards higher M2 macrophages (p=0.060). TLS2 aggregates had higher clonality (Gini coefficient p<0.001) and lower diversity (Shannon H p<0.001). Spatial proteomic analysis defined 10 niches. Niche 2 was compromised of lymphoid aggregates (CD4+ T cells) and TLSs (B cells and CD4+ T cells) (Figure 1).

CONCLUSIONS: Along with clinical outcomes showing efficacy in pts with metastatic AA following AtezoBev treatment, spatial proteomics and transcriptomics is a potential path to identify tissue-based biomarkers of future response to ICB therapy with VEGF inhibition in this difficult to sequence malignancy. Work is ongoing on additional tissues to define distinct niches and TLS structures preliminarily associated with response in this pilot data set.

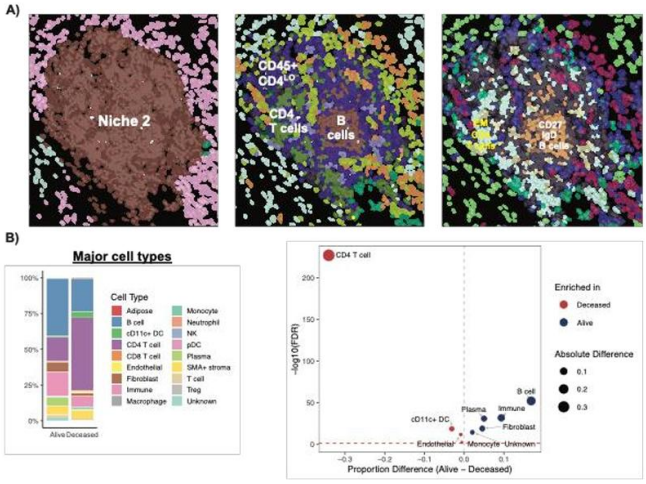

Figure 1. A) CosMx proteomic analysis of a patient with an ongoing response to atezolizumab with bevacizumab demonstrating the interaction of B cells and CD4+ T cells. B) Bulk analysis of the proteome of alive (n=2) versus deceased (n=2 processed; 1 passed quality control for further analysis) trial patients noted differential abundances of CD4+ T cells and B cells within immune aggregates. TLSs were noted to be less prevalent in the pt with progressive disease, with overall lower proportion of B cells and a higher proportion of CD4+ T cells within Niche 2.

20. Novel patient-derived tumor slice culture for appendiceal and colorectal peritoneal metastases

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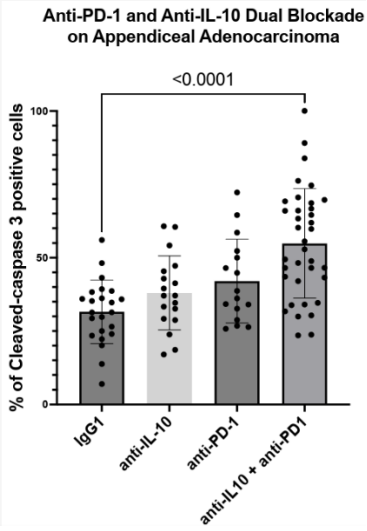
INTRODUCTION: Although a common site of metastases for abdominal cancers, peritoneal metastases lack a preclinical model that accurately recapitulates the tumor immune microenvironment. Tumor slice culture (TSC) provides an intact in vitro model that accounts for patient

heterogeneity and the multiple immune populations in complex solid tumors. We demonstrate the feasibility to produce viable peritoneal TSC and utilize TSC to display the efficacy of novel drug assays in peritoneal metastases.
METHODS: Peritoneal metastases were sterilely collected at the time of diagnostic laparoscopy or cytoreductive surgery. Specimens were trimmed into pieces of appropriate size and placed on a permeable PTFE membrane atop RPMI 1640 media on day 0 and incubated for 5-8 days at 37°C. H&E slides were evaluated by a trained pathologist for the presence of adenocarcinoma and confirmed by IHC staining of pan cytokeratin. The day following resection, TSCs were treated with either 20 ug/mL of IgG isotype control, 20 ug/mL of anti-PD-1 antibody, 20 ug/mL of anti-IL-10 antibody, or a combination treatment of 20 ug/mL anti-PD-1 antibody and 20 ug/mL anti-IL-10 antibody. Cell death was quantified via DAB IHC staining of cleaved-caspase 3 (CC3). Data points represent individual 20x fields manually assessed for CC3+ cells in QuPath digital pathology software. Data were compared using one-way ANOVA.
RESULTS: Peritoneal metastases TSC for appendiceal and colorectal primaries were developed for 24 patients. Of 11 cases with viability data, 3 were excluded due to low cell viability at time of resection (>60% CC3+ cells). TSC samples had a mean CC3+ value of 37.80% ± 17.54% at the time of resection. After 5-8 days in culture, there was a non-significant ($P > 0.05$) 5.22% increase in CC3 staining of untreated slices. A preliminary drug assay was performed on a case of metastatic appendiceal adenocarcinoma, which displayed a response ($P < 0.05$) to antibody treatment groups. Both anti-IL-10 and anti-PD-1 monotherapies were associated with modest increases in cell death (p=0.4770 and 0.1098 respectively). However, dual checkpoint blockade led to a significant response in appendiceal TSC with a mean increase of 21.89% ($p < 0.0001$, Figure).
CONCLUSIONS: Organotypic tumor slice culture from peritoneal metastases is a robust model to study the tumor microenvironment and response to therapeutics in appendix and colorectal cancers. Future work with peritoneal TSCs to understand the impact of IL-10 and PD-1 blockade on the peritoneal tumor microenvironment is warranted.



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

Christopher Sherry, DO; Hyun Park; Neda Dadgar; Chelsea Knotts, MD; Erin Grayhack; Rosie Blodgett; Ali Zaidi; Kunhong Xiao; Ashten Omstead; Vera Donnenberg; Albert Donnenberg; David Bartlett, MD; Patrick Wagner, MD
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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 associated 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.

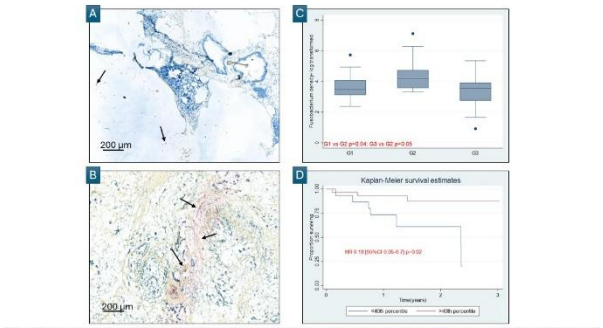

Figure 1: Fusobacterium nucleatum (Fn) infiltration of a low-grade tumor and associated mucin (panel A), and an infiltrative high-grade tumor with adjacent inflamed stroma (panel B) visualized with RNA in-situ with arrows indicating Fn infiltration. Fn density was associated with intermediate grade (panel 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).

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

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

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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 categorial 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.

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

Christopher Sherry, DO[1]; Kunhong Xiao[1]; Hyun Park[1]; Neda Dadgar[2]; Chelsea Knotts, MD[1]; Rosie Blodgett[1]; Erin Grayhack[1]; Ashten Omstead[1]; Ali Zaidi[1]; Vera Donnenberg[1]; Albert Donnenberg[1]; David Bartlett, MD[1]; Patrick Wagner, MD[1]
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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: Formalin-fixed, 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 x 10-13), regulation of hydrolase activity (n=14, p~1 x 10-10), and innate immunity as a broad reactome category (n=22, p=2.6 x 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.

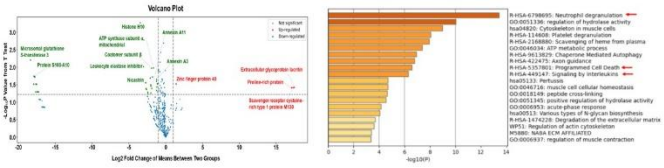

Figure: Proteomic comparison of carcinomatosis-related vs. benign peritoneal tissue illuminates neutrophil biology as a central element of the peritoneal immune microenvironment. Left panel, volcano plot identifying differentially expressed proteins with >50% change in carcinomatosis and p<0.05. Right 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.

24. Neutrophil Infiltration in the Peritoneal Tissue Microenvironment in Carcinomatosis

Christopher Sherry, DO[1]; Neda Dadgar[2]; Hyun Park[1]; Chelsea Knotts, MD[1]; Rosie Blodgett[1]; Erin Grayhack[1]; Ashten Omstead[1]; Ali Zaidi[1]; Kunhong Xiao[1]; Vera Donnenberg[1]; Albert Donnenberg[1]; David Bartlett, MD[1]; Patrick Wagner[1]
[1]Allegheny Health Network, Pittsburgh, PA, US; [2]Cleveland Clinic Foundation, Cleveland, OH, 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.

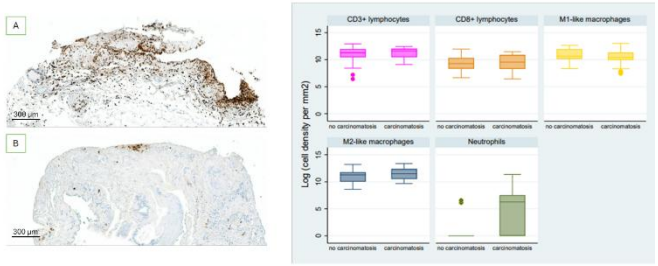

Figure 1: Left side depicts neutrophil infiltrate densities. Part A demonstrates high infiltration, part B demonstrates low infiltration, using immunohistochemistry techniques. The right side shows various cellular densities in obtained tissue samples from patient with and without carcinomatosis.

25. Apoptotic Markers in HIPEC Effluent as Predictors of Peritoneal Recurrence: A Novel Biomarker Approach

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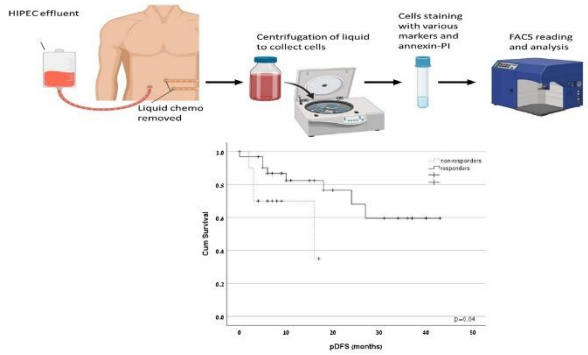
[1]Tel-Aviv Sourasky Medical Center, Tel-Aviv, IL; [2]Chaim Sheba Medical Center, Ramat-Gan, IL; [3]St. Raanana, IL; [4]Sheba Medical Center, Ramat Gan, Tel Aviv, IL; [5]Tel Aviv, IL

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.



26. Tumor-Associated Macrophage Subsets in Appendiceal Cancer

Christopher Sherry, DO[1]; Hyun Park[1]; Neda Dadga[2]; Chelsea Knotts, MD[1]; Rosie Blodgett[1]; Erin Grayhack [1]; Ashten Omstead[1]; Ali Zaidi[1]; Kunhong Xiao[1]; Vera Donnenberg[1]; Albert Donnenberg[1]; David Bartlett, MD[1]; Patrick Wagner, MD[1]
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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 macrophages (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.

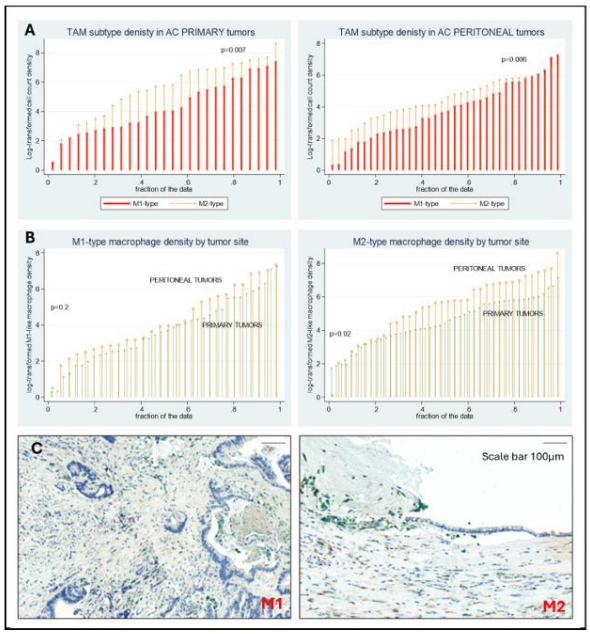

Figure 1: TAM density and distribution in appendiceal cancer. (A) M2-like TAMs are more abundant than M1-like TAMs in primary and peritoneal tumors, with significant differences in metastases (p=0.006). (B) M2-like TAM density is higher in peritoneal metastases (p=0.02), while M1-like TAMs show no significant site difference (p=0.2). (C) Immunohistochemical images of M1-like (left) and M2-like (right) TAMs. Scale bar: 100 µm.

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

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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 cm3 [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.

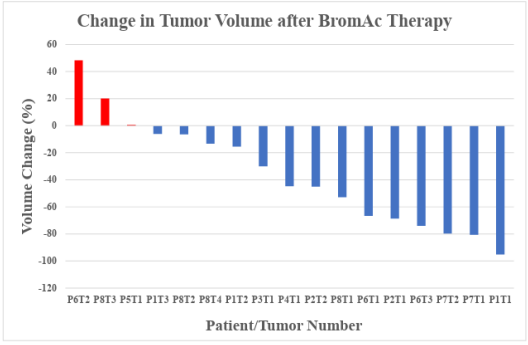

Figure 1: Change in tumor volume following BromAc therapy. Change in tumor volume was calculated for each individual tumor (T) in each individual patient (P). Tumor volume was calculated using the formula (4/3*Pi) * (x/2) * (y/2) * (z/2), where x, y, and z represent the largest measurement (cm) in the 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.

28. Surgical Intervention for Malignant Bowel Obstruction May Offer Improved Survival: Secondary Analysis of SWOG S1316

Jaewon Lee[1]; Kristen Dougherty[1]; Robert Krouse, MD, MS[2]; Virginia Sun, PhD, RN[3]; Gary B Deutsch[4]; Angeles Alvarez Secord[5]; Garnet L Anderson[6]; Kathryn B Arnold[6]; Elizabeth Gleeson, MD, MPH[1]; Jeremiah L Deneve[1]
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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 a subsequent encounter. Lysis of adhesions (69%), small bowel resection (41%), loop ileostomy (22%), gastrostomy placement (22%), and intestinal bypass (19%) were the most common palliative procedures. Surgery was associated with overall 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 initial hospitalization had lower rate 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. 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.

29. Prospective study of adjuvant oxaliplatin-based PIPAC with concurrent intravenous 5-fluorouracil and folinic acid after curative surgery for pT4a/b colon cancer (Clinicaltrials.gov NCT06091683)
Dario Baratti; Shigeki. Kusamura; Alessandro Gronchi; Marcello Guaglio; Gaia Colletti; Tommaso Cavalleri; Francesca Laura Nava; Marcello Deraco
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INTRODUCTION: We conducted a prospective single center pilot study to assess feasibility and safety of adjuvant oxaliplatin-based Pressurized Intra-Peritoneal Aerosolized Chemotherapy (PIPAC) after curative surgery for pT4a/b colon cancer. This strategy takes advantage of pathological examination to optimize patient selection, and better drug diffusion and penetration to overcome the (potential) limitations of the postoperative time setting. We also hypothesized that concurrent intravenous 5-fluorouracil and folinic acid (FU/FA) could increase oxaliplatin effect without harm
METHODS: Ten patients with pT4a/b, N0-2, M0, R0 colon cancer were enrolled. PIPAC was performed within 4-8 weeks from primary surgery with oxaliplatin (92 mg/m2) and concurrent intravenous 5-FU/FA (400/20 mg/m2). Adjuvant PIPAC was considered feasible if the laparoscopic procedure can be completed in ≥9 patients, and postoperative stay will be ≤3 days in ≥6 patients. Adjuvant PIPAC was considered safe if maximunm one conversion to open surgery, one severe complication (NCI-CTCAE v.4 grade 3-5), and one readmission within 30 days occurred. The trial is registered with Clinicaltrials.gov.NCT06091683.
RESULTS: Median age was 59 years (range 41-80). Median interval between primary resection and PIPAC was 6 weeks (range 3-7). The procedure was completed in all patients. Postoperative stay was ≤3 days in all but one patient. One patient had mild (grade 2) transaminase increase. No conversion, severe complication, death, or readmission occurred in the remaining patients. Metachronous peritoneal metastases (undetected at primary surgery) were discovered during PIPAC in one patient. The remaining patients are free of disease after a median of 19 months (range 10-35). Adjuvant systemic chemotherapy was not indicated for two patients (including the one with metachoronous peritoneal metastases), and started within 12 week from primary surgery for the remaining patients.
CONCLUSIONS: Adjuvant oxaliplatin-based PIPAC with concurrent intravenous FU/FA after curative surgery for pT4a/b colon cancer is feasible and safe. Preliminary oncological results are promizing.

30. Impact of Peritoneal Carcinomatosis and Malignant Ascites on the Outcome of Malignant Bowel Obstruction: Secondary Analysis of SWOG S1316
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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.

31. 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

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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 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 these 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.

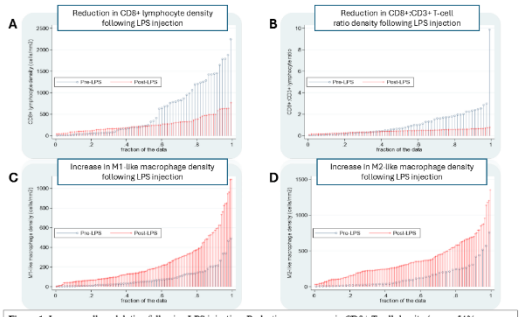

Figure 1: Immune cell modulation following LPS injection. Reductions were seen in CD8+ T-cell density (mean -54%, p<0.0001, panel A) and the CD8+/CD3+ T-cell ratio (mean -62%, p<0.0001, panel B). Macrophage densities, on the other hand, substantially increased following LPS injection for both M1-like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

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

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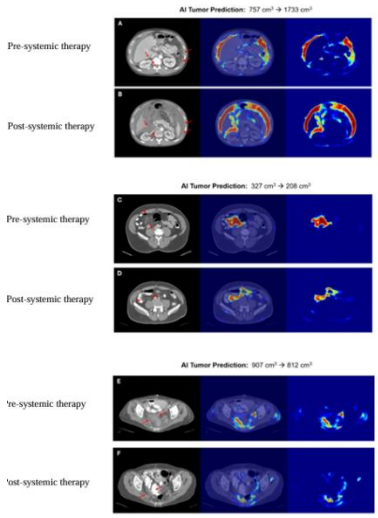
INTRODUCTION: Peritoneal carcinomatosis (PC) poses unique management challenges as current imaging techniques are limited in ability to quantitatively characterize disease burden and treatment response. Moreover, PC is not considered a measurable disease based on Response Evaluation Criteria in Solid 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 cm^3 to 1733 cm^3). Panels 1C and 1D demonstrate a patient with tumor response (327 cm^3 to 208 cm^3). 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 cm^3 to 812 cm^3).



33. DNA Damage in Live Injured Tumor Cells Enhances the Effectiveness of Immune Checkpoint Blockade: Is it Time for Combined HIPEC + Immunotherapy Trials?

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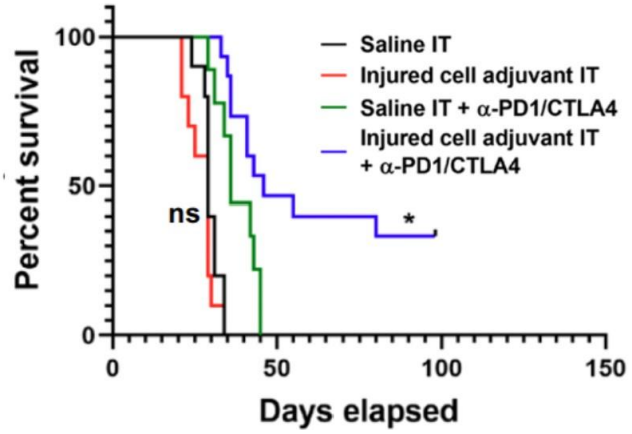
INTRODUCTION: Mechanisms by which heated intraperitoneal chemotherapy (HIPEC) enhances tumor responses are unclear, but may involve Immunogenic cell death (ICD), a process where dead cells expose damage-associated molecular patterns to stimulate the immune system. Although the ICD paradigm focuses on immunogenicity induced by cell death, we asked instead whether live but stressed/DNA-damaged tumor cells have the potential to engage and stimulate anti-tumor immunity.

METHODS: DNA damage-induced anti-tumor immunity was investigated using in vitro assays and in vivo murine tumor models

RESULTS: Treatment with the topoisomerase II inhibitors etoposide, doxorubicin, or mitoxantrone was found to potently induce T-cell activation and anti-tumor immunogenicity, particularly at early times after damage. Remarkably, T-cell activation was only induced by the live cell fraction , while minimal immunogenic activity was conferred by DC- and/or T-cell co-incubation with dead tumor cells, culture supernatants, or fractionated cell lysates. In vivo mouse models of B16F10 tumors demonstrated that intratumoral injection of live DNA damaged cells increased the efficacy of systemic immune checkpoint blockade causing tumor elimination and cure in 40% of the animals, increased overall survival, and created anti-tumor immune memory in survivors. Transwell assays verified that contact between tumor cells and T cells was necessary for immune activation. DC-priming of T cells could be bypassed by administration of IFNγ to the tumor cells after DNA damage. Live IFNγ-treated DNA-damaged tumor cells showed increased expression of positive co-stimulatory ligands and induced Granzyme B production in T cells, indicating that both Signals 2 and 3 required for T cell activation are generated in live DNA-damaged cells.

CONCLUSIONS: Live DNA-damaged tumor cells promote T cell killing through DC-dependent and -independent pathways, potently increasing the efficacy of immunotherapy. These findings demonstrate an alternative mechanism for HIPEC-induced anti-tumor activity that can be significantly enhanced when combined with immune checkpoint blockade.



34. Leading Consensus from the Ground Up: Leveraging Trainee Collaboration to Create the 2024 Peritoneal Surface Malignancies Consortium Guidelines

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INTRODUCTION: The 2024 Consensus Guidelines for the Management of Peritoneal Surface Malignancies (PSM), endorsed by the Society of Surgical Oncology sought consensus on management of six PSM “disease sites” by leveraging an adaptive, multicenter trainee-led team. Successful strategies for trainee-led generation of major

clinical management guidelines have rarely been previously described.

METHODS: The core steering committee comprised nine trainees under the supervision of three faculty, across three institutions (Figure 1a). Guidelines were created via two rounds of web-based modified Delphi consensus voting with iterative revision by multidisciplinary disease site working groups (DSWGs) ranging in size from 9 (neuroendocrine) to 16 (appendix). Current evidence addressing controversial topics was synthesized via rapid systematic reviews using the PICO (population, intervention, control, outcome) framework.

RESULTS: Each core trainee member was assigned a disease site, with two assigned as overarching project managers. Each core trainee directed reviews and coordinated revisions of their site guidelines with the associated DSWG. The nine core trainees supervised 50 multi-institutional trainee members; 3 to 15 trainees were assigned to each disease site at a given time and redistributed on a rolling basis, based on availability and project need (Figure 1b). Weekly steering committee meetings and extensive project management platform utilization enabled rapid iteration, prioritization and inclusion of review questions and pathways, and team reassignment. Asynchronous communication was heavily utilized, with 362 emails sent by the core leadership team for the appendix pathways alone. Review teams screened a total of 13,595 abstracts (range: 191 for the narrowest key question, to 2,632 for the broadest) and 1,513 full texts (range: 23 to 374), ultimately synthesizing data from 183 studies across eleven key questions. Nine pathways achieved Delphi consensus across the six PSM disease sites, integrating the feedback of over 250 total voters (101 to 145 per disease site). Each disease site core trainee(s) composed companion documents, producing a total of 388 pages of guideline figures, tables, and supporting text across all sites within one year of consortium formation.

CONCLUSIONS: The 2024 Consensus Guidelines for the Management of Peritoneal Surface Malignancies represent a large-scale effort to achieve national consensus in PSM management within a year of its launch. Future consortia may benefit from leveraging similar trainee-led networks to coordinate group decision-making.

Figure 1a. Steering Committee Network

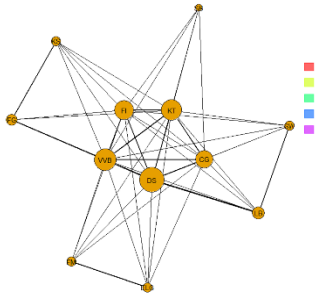
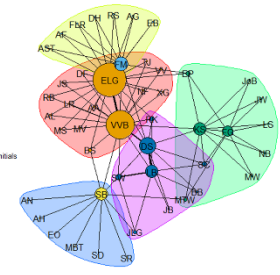


Figure 1b. Trainee Review Team Networks



35. Impact of Systematic Discontinuation of Mitomycin C HIPEC for Colorectal Peritoneal Metastasis on Oncologic Outcomes at an NCI Cancer Center

Muhammad Talha Waheed, MD; Isaac B Paz, MD; Thinzar Lwin, MD; Alessio Pigazzi, MD; Laleh Melstrom, MD; Yuman Fong, MD; Gagandeep Brar, MD; Dani Castillo, MD; Pashtoon M Kasi, MD; Marwan Fakih, MD; Mustafa Raoof, MD
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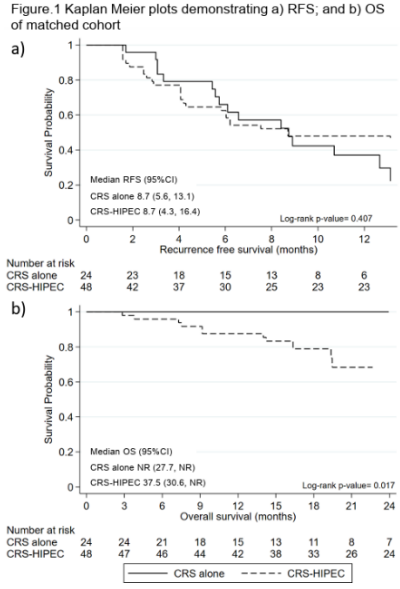
INTRODUCTION: PRODIGE7 demonstrated a lack of effectiveness of Oxaliplatin HIPEC after cytoreductive surgery (CRS) for colorectal peritoneal metastasis (CRCPM). Many centers switched to Mitomycin C (MMC) HIPEC. However, the oncologic benefit of MMC-HIPEC remains unclear.

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



36. Optimal duration of neoadjuvant chemotherapy prior to CRS±HIPEC for colorectal cancer: An assessment of survival and postoperative outcomes

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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.

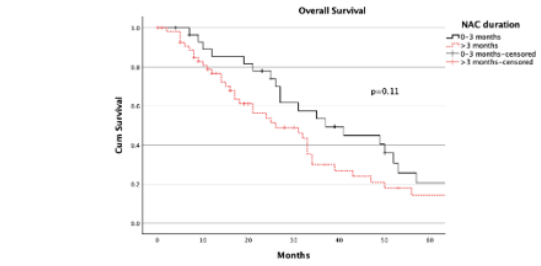
METHODS: A single institution database (2009-2024) of colorectal cancer (CRC) patients that underwent CRS±HIPEC was reviewed. CRC patients undergoing CRS±HIPEC for curative intent (completeness of cytoreduction 0 or 1) with known NAC duration were included. Analysis was stratified by NAC duration of 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.

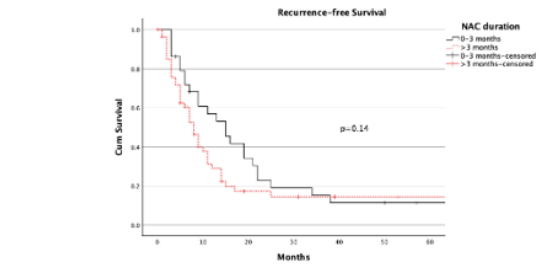
FIGURE 1.

A



Number at risk							
0-3 months NAC	29	18	11	6	4	3	2
>3 months NAC	54	18	7	6	4	4	3

B



Number at risk							
0-3 months NAC	29	25	23	17	12	9	5
>3 months NAC	54	41	26	19	10	7	5

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 (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.

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

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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.

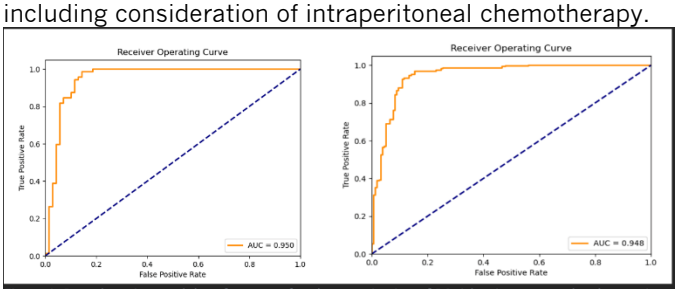

Figure 1: Deep learning model performance for characterization of PC risk using area under the receiver operating curve (AUC) demonstrating overall similar performance for (A) single local institutional cohort, and (B) aggregate multi-institutional international cohort.

38. Intraperitoneal Paclitaxel Induces Recruitment of Activated Eosinophils to the Peritoneal Cavity, Potentially Contributing to Anti-Tumor Effects Against Peritoneal Metastasis in Gastric Cancer

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INTRODUCTION: Recent studies highlight the significant influence of the tumor immune microenvironment on the efficacy of chemotherapy. The peritoneal cavity is home to numerous immune cell populations; however, the relationship between immune responses within the peritoneal cavity and response of peritoneal tumor remains poorly understood.
METHODS: This is a retrospective observational study. Single-cell suspensions were obtained from ascites or peritoneal lavages from 41 patients with peritoneal metastasis (PM) from gastric cancer (GC) who were treated with S1+oxaliplatin and intraperitoneal Paclitaxel (IP-PTX). In 28 patients, cells were collected both before and after 1-3 courses of IP chemotherapy. These samples were stained with monoclonal antibodies targeting specific lymphoid or myeloid subsets, and their proportions within CD45(+) leukocytes were analyzed via flow cytometry. Eosinophils were purified using magnetic cell sorting for subsequent RNA-Seq analysis.
RESULTS: Among the 41 patients with PM, the tumor-to-leukocyte ratio (TLR), defined as CD326(+) tumor cells divided by CD45(+) leukocytes, ranged from 0.002% to 58.1%. TLR did not correlate with the ratios of immune cells; however, the proportions of macrophages, B cells and neutrophils increased while CD8(+) T cells and NK cells tended to decrease as TLR increased. In the 28 patients, the proportions of lymphocytes in peritoneal cavity generally decreased with significant reductions observed in CD4(+) T cells and CD19(+) B cells after IP treatment. In contrast, the proportion of CD11b(+) myeloid cells increased post-treatment. Among the myeloid cells, the proportion of CD16(-) CD193(+) eosinophils markedly increased, particularly in patients with post-treatment negative peritoneal lavage cytology (CY0) (median 0.47% vs. 10.0%, p<0.0001). However, the change was not significant in patients with post-treatment positive peritoneal lavage cytology (CY1) (median 0.93% vs. 0.97%, p=0.84). Notably, patients with eosinophil ratios ≥2% following IP chemotherapy had significantly longer overall survival compared to those with lower

eosinophil ratios (17.3 months vs. 26.7 months, p=0.034; HR = 0.23 [0.06–0.89]). The peritoneal eosinophils displayed elevated CD11b and CD63 expression levels compared to circulating eosinophils (p<0.01), though SSC-A levels were lower. Gene ontology analysis revealed significant enrichment in pathways related to cytokine-mediated signaling, extracellular matrix organization, and response to interferon-gamma in peritoneal eosinophils (p<0.0001).
CONCLUSIONS: IP-PTX induces recruitment of activated eosinophils to the peritoneal cavity along with modulating other immune cell populations. These immune alterations may contribute to the anti-tumor response of PM to intraperitoneal chemotherapy

39. Bidirectional laparoscopic HIPEC for palliative and curative intent in gastric cancer peritoneal metastasis
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INTRODUCTION: Peritoneal metastasis from gastric cancer (GCPM) continues to pose diagnostic and therapeutic dilemmas, with ultimately near 100% mortality. Repeat laparoscopic HIPEC has been shown to be safe, well-tolerated and have possible therapeutic and palliative benefit in certain populations. However, appropriate patient selection remains difficult to ascertain and survival benefit of peritoneal directed therapy remains controversial. Herein we describe our initial experience with iterative laparoscopic HIPEC in GCPM for conversion gastrectomy and palliation of synchronous and metachronous disease.
METHODS: This is a single-center, retrospective review of GC patients with oligometastatic PM who underwent palliative or “curative” intent laparoscopic HIPEC from 2018-2024. Demographic, pathologic, genetic, and therapeutic data were obtained. After initiating chemoimmunotherapy, patients were considered for laparoscopic HIPEC if no disease progression was seen in the primary tumor or peritoneum. HIPEC was performed with the two-cannula technique with doublet or triplet regimens for 90 minutes. Patients who cleared the peritoneum both on cytology and biopsies were identified as candidates for conversion gastrectomy.
RESULTS: Laparoscopic HIPEC was performed 64 times across 33 patients. Eleven patients had extensive synchronous carcinomatosis, 11 patients were treated for disease recurrence after gastrectomy, and 11 patients were treated on the “conversion surgery” pathway. Iterative HIPEC was performed in 17 patients (median 2 cycles, IQR 1-8). The median PCI was 6 for all patients (IQR 1.75-11.25). PCI decreased in 9 patients, remained stable in 9 patients, and progressed in 12 patients. The median operative time was 160 minutes, with most patients discharging POD1. The most common pathologic mutations were TP53 (n=15), CDH1 (12), ARID1A (7), PIK3CA(4), KRAS (3), HER2/neu (2). Median CPS was 3. Six perioperative complications occurred, and 5 procedures were aborted due to disease progression. Eight conversion candidates (median PCI 4.1) cleared the peritoneum after HIPEC (median 1 cycle) and received gastrectomy (7 robotic, 1 open). All patients received chemoimmunotherapy prior to HIPEC (mean 6.6 cycles), and conversion gastrectomy (mean 9.4 cycles). After resection patients had a median RFS of 115 days and OS of 363 days.
CONCLUSIONS: Patients with low peritoneal disease burden, neoadjuvant chemoimmunotherapy, and iterative laparoscopic HIPEC achieving peritoneal clearance may be good candidates for conversion gastrectomy. Additional studies are warranted to predict tumor biology responsive to HIPEC, and durability of response following conversion gastrectomy.

40. Patient Selection for Cytoreductive Surgery and HIPEC for Gastric Cancer with Peritoneal Metastasis
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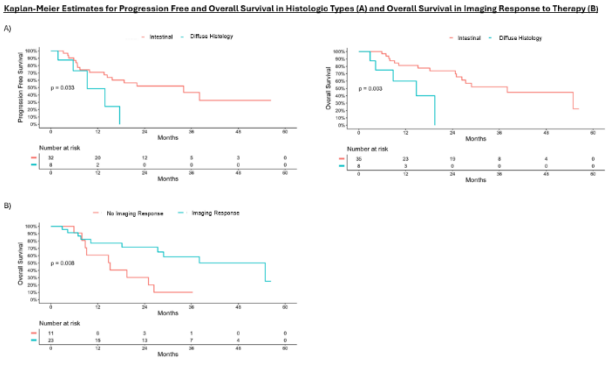
Mayo Clinic, Rochester, MN, US

INTRODUCTION: Peritoneal metastasis (PM) is the most common site of dissemination of gastric cancer (GC) and is associated with a poor prognosis. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) for GC with PM remains controversial due to modest survival and significant morbidity.
METHODS: Retrospective analysis of consecutive patients with GC and PM treated with CRS and HIPEC at a single institution from June 2019 to June 2024.
RESULTS: During the 5-year study period, 44 patients were identified. The median age was 56 (IQR 46-64) and all patients had an ECOG status of 0-1. All patients received total neoadjuvant therapy with either 8 cycles of systemic chemotherapy (78%) or 4 cycles of chemotherapy followed by chemoradiation (18%). The median peritoneal carcinomatosis index (PCI) at time of diagnostic laparoscopy was 2 (IQR 0-7) and 42 patients (95%) underwent complete cytoreduction (CC-0). An R0 resection was achieved in 38 (86%) patients. The median length of stay was 7 (IQR 4-10) days. There were 17 (39%) 90-day major complications (Clavien-Dindo grade ≥3), two (5%) CTCAE grade 4 cytopenia, and two (5%) acute kidney injury. The rate of anastomotic leak (all grades) was 16%. The 30-day readmission rate was 31%; the 90-day mortality rate was 2%. At a median follow-up of 31 months, the median progression-free survival (PFS) and overall survival (OS) were 22 and 29 months, respectively. One, two, and three-year PFS were 68%, 48%, and 42%, respectively; and the one, and three-year OS were 78%, 65%, and 48%, respectively. The peritoneum was the most common site of first relapse and occurred at a median of 7 (IQR 6-8) months. Non-peritoneal recurrences occurred at a median of 20 (IQR 7-15) months. Diffuse histology was associated with worse PFS and OS (PFS HR=4.96, 95%CI 1.51-16.29, p<0.033; OS HR=8.14 95%CI 2.17-30.5, p<0.003). Objective imaging response to systemic therapy was associated with improved OS (HR=0.24, 95%CI 0.08-0.68, p<0.008), but not PFS.
CONCLUSIONS: Strict patient selection, including; young age, excellent functional status, total neoadjuvant therapy with objective imaging response to therapy and intestinal histology resulted in reasonable morbidity, low perioperative mortality and promising 3-year PFS and OS.



41. Inter-rater Reliability of Laparoscopic Peritoneal Carcinomatosis Index Assessment after PIPAC

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INTRODUCTION: Change in peritoneal carcinomatosis index (PCI) has been proposed as a metric to evaluate response to intraperitoneal therapy. However, treatment related changes in the tumor-bearing and normal peritoneum make PCI assessment challenging. Here, we evaluate the inter-rater reliability of laparoscopic PCI in patients undergoing pressurized intra-peritoneal aerosol chemotherapy.
METHODS: This is a retrospective analysis of laparoscopic videos recorded from patients undergoing pressurized intra-peritoneal aerosolized chemotherapy (PIPAC) at an NCI-designated cancer center. All the videos were rated by 4 experienced surgeons. Videos were deidentified and raters were blinded to any patient characteristics The inter-rater reliability of PCI was assessed using Cohen kappa statistic (κ).
RESULTS: A total of 28 laparoscopic patient videos from 15 patients (median age 61 years; 50% female; primary cancer: 5 appendix, 5 colorectal, and 5 biliary tract) undergoing PIPAC were evaluated. PIPAC regimens were as follows: Oxaliplatin (6 patients), Mitomycin C (4 patients), and Nab-Paclitaxel (5 patients). Of the 28 videos, eleven were evaluated before PIPAC, whereas 17 were evaluated after PIPAC. When analyzing all patients, the overall inter-rater agreement was moderate (κ 0.45; p<0.001); and this agreement was lower when comparing patients that had been treated with PIPAC (Before vs. After; 0.51 vs 0.41). Before PIPAC, highest inter-rater agreement was recorded for right lower quadrant (κ 0.72; p <0.001) followed by left lower quadrant (κ 0.71;0.001). Whereas after PIPAC, the inter-rater agreement decreased for all regions except central (κ 0.57 vs. 0.37), right upper quadrant (κ 0.44 vs. 0.33), right flank (κ 0.46 vs. 0.35), and ileum (κ 0.39 vs. 0.29). No differences were noted in the agreement pattern depending on the regimen used.
CONCLUSIONS: Inter-rater reliability of laparoscopic PCI assessment in this study was moderate. Importantly, the reliability of PCI assessment decreases in PIPAC treated patients. Therefore, better and more objective methods are needed to quantify the burden of carcinomatosis in patients treated with intraperitoneal therapies.

42. Application of Pressurized IntraPeritoneal Aerosolised Chemotherapy in a tertiary academic center- a first real world US case series.

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Renaissance School of Medicine at Stony Brook University, Stony Brook, NY, US

INTRODUCTION: Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) is an innovative, minimally invasive approach to deliver chemotherapy directly into the peritoneal cavity, enhancing drug penetration while minimizing systemic toxicity. Emerging evidence highlights PIPAC's potential to improve outcomes in patients with advanced-stage malignancies, offering a new avenue where traditional systemic therapies have limited efficacy. Although there are clinical trials conducted at this moment in the US, to date there is no real world data from US institutions.
METHODS: A retrospective review of the first 22 procedures from 9/22/2023 to 10/11/2024 in 15 patients. One patient received 3 PIPACs, five received 2, and the rest one each. Five were females. Patient median age was 64 years (37-84), histology was appendiceal (9), Mesothelioma (2), stomach, biliary, gastric and colon. Six patients had previous surgery, whereas two of them had previous HIPEC. The median Karnofsky Performance Status was 90 (100-70), and the median PCI score was 26 (12-39). Indication in all patients was palliative treatment. Eleven patients (73.3%) had ascites. All of the patients were currently, or previously and could not currently tolerate, chemotherapy, and 4 patients were on FOLFOX-Bevacizumab, which did not stop for the procedure. Of the 22 procedures, 2 were performed with Doxorubicin (2.1mg/m2) and Cisplatin (10.5mg/m2) for the mesothelioma patients, whereas the rest were performed with Oxaliplatin 120mg/m2.
RESULTS: Twenty two PIPAC procedures were performed in total. The median duration of each procedure was 112 min (86-163). There were no Grade 2 or above adverse effects at the index admission. Lab values were collected and no abnormalities were observed. Particularly for the patients with mesothelioma treated with cisplatin, renal protection with sodium thiosulfate was applied, and there was no adverse effect in the renal function. All patients tolerated diet on POD#1, and the median hospital stay was 33.6 hours (9.6-106.6). Two patients reported readmission to their local hospital due to bowel obstruction within 30 days, and one was readmitted for failure to thrive due to progression of disease. From the patients with ascites, there as symptomatic improvement of the ascites. From the patients who had repeat PIPAC, improvement was observed in the volume of ascites (patient with mesothelioma) and in the patient who had 3 procedures, there was observed biologic regression of the tumor.
CONCLUSIONS: Our data in this first real world case series in the US are indicative that PIPAC has a role in the treatment of peritoneal surface disease. More experience from more centers is warranted, in order to be able to

perform clinical trials that will give this modality the opportunity to show its efficacy and potential.

43. Consensus Molecular Subtype Specific Drug Sensitivities in Colorectal Cancer: New Insights for Personalized HIPEC Strategies

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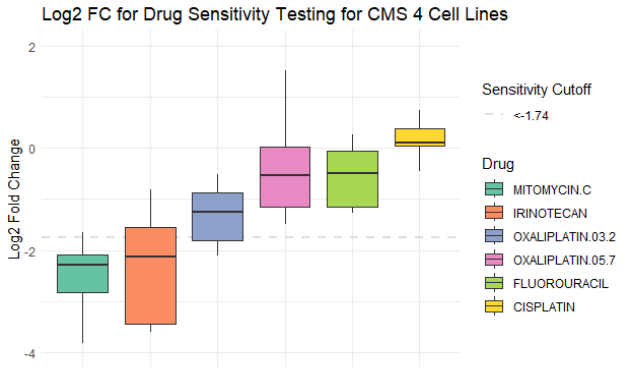
INTRODUCTION: While cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) has emerged as a promising approach for colorectal cancer (CRC) patients with peritoneal metastases (PM), its effectiveness remains variable. Given the predominance of Consensus Molecular Subtype 4 (CMS4) in CRC-PM, characterized by prominent transforming growth factor β activation, stromal invasion, and angiogenesis, we hypothesized that CMS4 exhibits distinct drug sensitivities compared to other subtypes.
METHODS: Drug sensitivity data from the DepMap PRISM Repurposing Dataset for 34 CRC cell lines, classified into CMS subtypes, was analyzed. Five drugs were selected for analysis: mitomycin-C, oxaliplatin, irinotecan, 5-fluorouracil and cisplatin. Differential drug response among CMS subtypes was assessed using log2 fold change (log2FC) in cell viability, with values less than -1.74 indicating sensitivity, based on the sensitivity threshold established in a prior study.
RESULTS: The 34 CRC cell lines were classified as 29% CMS1, 18% CMS2, 26% CMS3, and 26% CMS4. CMS4 cell lines demonstrated higher sensitivity than CMS2 lines to mitomycin-C (mean log2FC = -2.77 vs -0.66, p = 0.019) and irinotecan (mean log2FC = -2.26 vs -1.00, p = 0.03). Among the drugs tested in CMS4, only mitomycin-C and irinotecan met the sensitivity threshold (log2FC < -1.74), while oxaliplatin did not show sensitivity in this subtype (Figure).
CONCLUSIONS: CMS4 exhibits distinct drug sensitivity patterns, which may explain the success of mitomycin-C and limited efficacy of oxaliplatin in HIPEC trials. Future clinical trials should consider genomic subtyping and drug sensitivity testing to guide personalized HIPEC strategies for patients with CRC-PM.



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

Hannah McDonald, MD[1]; Anna Reagan, MD[2]; Charles Bailey[2]; Breanna Knicely[2]; Eva Goellner, PhD[2]; Joseph Kim, MD[2]
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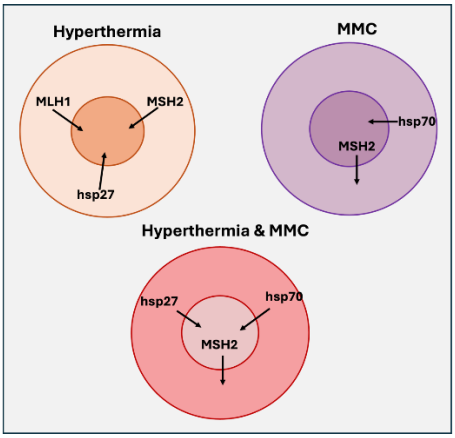
INTRODUCTION: The efficacy of heated intraperitoneal chemotherapy (HIPEC) is dependent on both hyperthermia and chemotherapy, which result in DNA damage. Mismatch repair (MMR) proteins and heat shock proteins (Hsps) are required for DNA repair. Given prior studies showing dysregulated MMR expression with exposure to hyperthermia and chemotherapy, we sought to characterize how HIPEC may impact MMR and Hsps proteins.
METHODS: The HT29 MMR-proficient (pMMR) colon cancer cell line was utilized for all assays. The dose for 50% cytotoxicity (IC50) 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 IC50 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 IC50 was significantly higher at 42°C compared to 37°C (p=0.007). Additionally, expression levels of 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 led to nuclear localization of MLH1, MSH2, and hsp27 (Figure 1). MMC exposure led to 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 IC50 in pMMR colon cancer cells, suggesting decreased the cytotoxic efficacy of MMC when heated. Of great clinical interest, the combined exposure to hyperthermia and MMC resulted in cytoplasmic localization of MSH2, a condition that has been clinically linked with MMR deficiency in colon cancer. Additional studies are examining whether this combined therapy may lead to microsatellite instability.



45. Is there value in repeat CRS±HIPEC for colorectal cancer peritoneal metastases?

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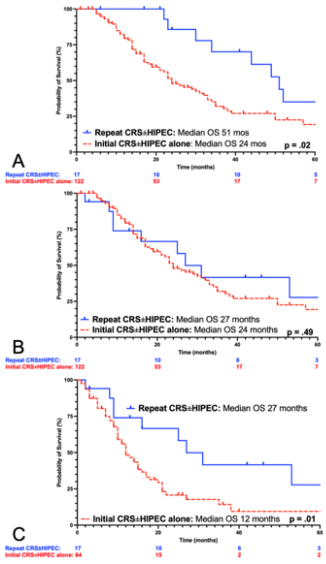
INTRODUCTION: Although cytoreductive surgery ± hyperthermic intraperitoneal chemotherapy (CRS±HIPEC) is a treatment strategy for pts with colorectal cancer peritoneal metastases (CRC-PM), the majority recur within one year. We assessed the oncologic value and perioperative safety of repeat CRS±HIPEC 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.



46. NF2 and Downstream Genes are Potential Targets for Treatment in Peritoneal Mesothelioma

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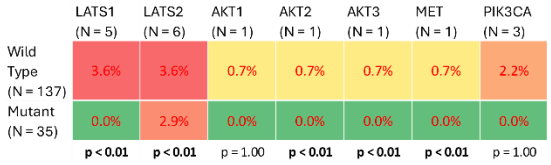
INTRODUCTION: Mesothelioma is a group of rare neoplasms arising from serosal tissue. Those of peritoneal origin account for only 30% of cases. Historically, even with next-generation sequencing (NGS), targetable therapy is limited. Recently, NF2 and downstream targets of the Hippo-YAP and PI3K-AKT-mTOR 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.

Figure 1. Simultaneous Mutation Rates of NF2 with other Targetable Genes



47. Outcomes of Clinically Detected Stage III Melanoma Through Individualized Neoadjuvant (PRADO) Approach At a Single Institution

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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%) 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.

48. Real-World Experience of Neoadjuvant Immunotherapy for Melanoma

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INTRODUCTION: Randomized trial data supports neoadjuvant immune checkpoint inhibition (ICI) for high-risk resectable melanoma. The optimal peri-operative strategy, including ICI regimen and surgical approach, remains undetermined.
METHODS: Using an IRB-approved protocol, we retrospectively reviewed 54 patients (pts) treated with neoadjuvant intent for stage II-IV melanoma between 2020 and 2024. Data pertaining to treatment type, anti-tumor outcomes and safety was collected.
RESULTS: Fifty-four pts received neoadjuvant ICI; the majority (81%) had a cutaneous primary and macroscopic stage III disease (93%). 52% (28/54) were treated with anti-CTLA4/anti-PD1 (Ipi/Nivo), 43% (23/54) anti-PD1 monotherapy (PD1) and 5% (3/54) anti-PD1/anti-LAG3 (Nivo/Rela). Compared to the PD1 cohort, pts treated with Ipi/Nivo tended to be younger, BRAF-mutant, with a lower ECOG performance status at baseline. During the neoadjuvant course, there were 11 dose-limiting toxicities (n=7 Ipi/Nivo; n=4 PD1). Eight pts (15%) did not complete surgical resection (3 Ipi/Nivo, 3 PD1, 2 Nivo/Rela). Twelve pts treated with Ipi/Nivo underwent complete lymph node dissections (CLND) and 13 underwent index node excisions (INE) only. Eleven pts treated with PD1 underwent CLND and 9 underwent INE only. Of the pts who underwent CLND, 29% (8/28) required physical therapy referral for lymphedema, 14% (4/28) required IV antibiotics, and 57% (16/28) had a drain in place for more than 2 weeks. Pts in the INE-only cohort had 0 such complications. Of evaluable pts, 52% (13/25) treated with Ipi/Nivo and 65% (13/20) with PD1 had a major pathologic response (MPR). Of the 6 patients who underwent INE without MPR, only 3 underwent subsequent CLND. Twenty-one pts received adjuvant therapy, 15 ICI and 6 BRAF/MEK inhibitors. Mean RFS for pts who completed surgery was 399 days with a median follow-up of 294-days. Five pts have recurred: 1 on Nivo/Rela (mucosal, CLND/pNR/adjuvant radiation), 1 on Ipi/Nivo (INE/pPR/no adjuvant), and 3 on PD1 (1 CLND/pNR/no adjuvant; 2 INE/pCR/no adjuvant). Three deaths occurred after surgery: 1 related to disease progression and 2 unrelated to melanoma.
CONCLUSIONS: Real-world neoadjuvant immunotherapy selection may be influenced by age, BRAF status and performance status. Pathologic response rates were similar between immunotherapy regimens and aligned with randomized trial outcomes.Our data demonstrates a real-world ability to personalize surgical approach and adjuvant strategy based on pathologic response.

Real-World Neoadjuvant Immunotherapy for Melanoma						
Treatment	**Ipi/Nivo (28)**		**Anti-PD1 Monotherapy (23)**		**Nivo/Rela (3)**	
Baseline Characteristics						
Age (Average, range)	59 (21-82)		72 (30-89)		65 (49-80)	
Sex	22M		18M		3F	
Race/ethnicity (white, non-Hispanic)	25		20		3	
ECOG 0 at baseline	23		14		2	
ECOG 1 at baseline	4		8		1	
Prior adjuvant BRAF/MEKi	4		0		0	
Toxicity that limited dose or delayed surger	7		4		0	
BRAF Mutation (V600E/K/R)	16		4		2	
BRAF V600 WT	10		6		1	
Unknown BRAF status	2		10		0	
Surgery						
Did not complete surgery	3		3		2	
due to fatal toxicity	1		0		0	
due to unrelated AE	0		1		0	
due to PD	1		1		1	
due to response	1		1		1	
Completed Surgery	25		20		1	
Avg days from C1D1 to surgery (avg, range)	60 (36-156)		80 (52-141)		59	
CLND	12		11		1	
INE Only	13		9		0	
INE with subsequent CLND	4		0		0	
Response						
Pathologic complete response (pCR)	8		13		0	
Major pathological response (MPR)	5		0		0	
Pathologic partial response (pPR)	2		0		0	
Pathologic non-response (pNR)	9		7		1	
Mixed (1 lesion MPR, 1 lesion pNR)	1		0		0	
Adjuvant Therapy						
Response	**MPR (13)**	**non-MPR (12)**	**MPR (13)**	**non-MPR (7)**	**MPR (0)**	**non-MPR (1)**
Adjuvant immunotherapy	3	5	6	1	0	0
Adjuvant BRAF/MEKi	0	4	0	2	0	0
Adjuvant radiation only	0	0	0	0	0	1
No adjuvant treatment	10	2	7	3	0	0
Unknown adjuvant	0	1	0	1	0	0
Surgical Complications						
Surgery Type	**CLND (28)**			**INE (18)**		
PT Referral for lymphedema	8			0		
IV antibiotics	4			0		
Drain in place > 2 weeks	16			0		

49. T-VEC Shifts CD8 Phenotype to Reverse Anti-PD1 Resistance

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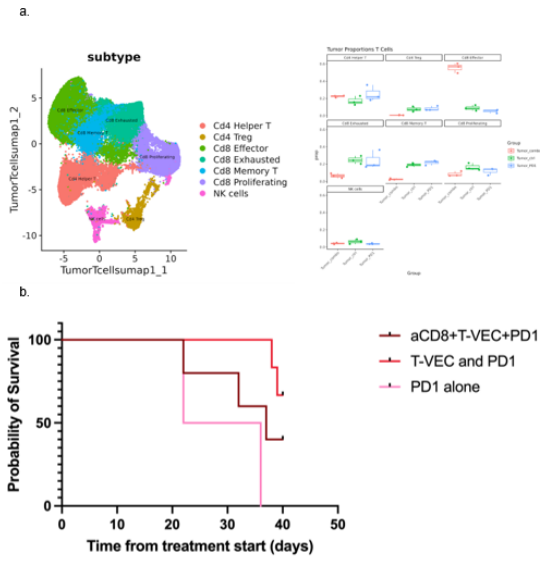
INTRODUCTION: Though immune checkpoint inhibitor (ICI) therapy has revolutionized melanoma treatment, a significant percentage of patients continue to experience disease progression on ICI. We have shown previously that T-VEC, an oncolytic virus, synergizes with anti-PD1 to significantly enhance tumor 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. Single 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.

Figure 1:
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 100mm³. Median survival was 37 days, 29 days, and not reached for CD8 depletion, anti-PD1, and T-VEC+anti PD1 groups respectively.



50. Digital Spatial Proteomics Reveals Immune Microenvironment Dynamics in Melanoma Brain Metastases and Correlates with Treatment Response and Survival

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INTRODUCTION: Melanoma brain metastases (MBM) develop in approximately 60% of patients with metastatic melanoma and present distinct molecular features compared to primary melanoma and extracranial metastases (ECM). MBM are characterized by a unique immune microenvironment, including a higher density of CD8+ T cells than ECM and macrophages with a pro-tumorigenic phenotype. However, the precise cellular composition and spatial architecture of the MBM ecosystem remain incompletely understood, necessitating further investigation.

METHODS: A tissue microarray slide was constructed,

comprising 353 cores extracted from matched tumor and normal adjacent tissue specimens from MBM or ECM. High-plex proteomic analysis was performed using the Nanostring GeoMx platform with spatial resolution. Digital counts from a 68-plex panel of oligo-linked protein probes were quantified simultaneously in three tissue compartments defined by fluorescence colocalization [tumor (S100+/MART1+/SOX10+), leukocytes (CD45+), and macrophages (CD68+)]. Barcodes were normalized with internal spike-in controls to account for system variation.
RESULTS: Of 52 patients with melanoma brain metastases, 60% were female (31/52) and the median age was 56. 67% (35/52) received immunotherapy (IT), and majority were located on either the trunk (35%) or lower extremities (21%). 65% of cases (34/52) yielded ECM cores. 42% had either a complete (CR) or partial (PR) response to IT, 21% had stable disease (SD), and 36% had progressive disease (PD). MBM samples differentially expressed CD56+ in all three compartments and CD66b in CD45 and tumor compartments. In PD-1-treated MBM samples, granzyme A, CD27, and CD95 were differentially expressed in patients with a CR or PR. MBM samples overexpressing CD3+, CD4+, and CD8+ in the CD45+ compartment correlated with higher overall survival (OS) (p = 0.027, p = 0.0053, p = 0.016). Higher expression of CD14 in CD68+ macrophages was associated with improved OS (p = 0.0025).
CONCLUSIONS: Our proteomic analysis identified differential expression of immune-related proteins associated with treatment response and overall survival. These findings provide insight into the distinct immune microenvironment of MBM and highlight potential targets for improving therapeutic strategies.

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

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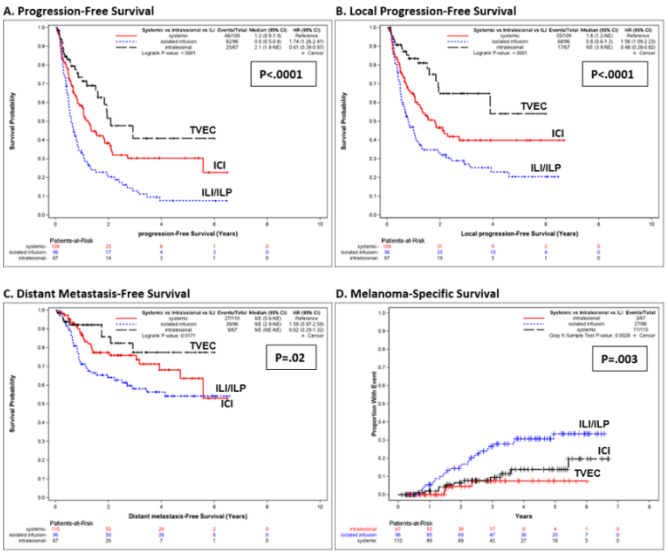
INTRODUCTION: Isolated limb infusion and perfusion (ILI/ILP) has been mainstay treatment for unresectable melanoma in-transit metastases (ITM), but use of immune checkpoint inhibitors (ICI) and intralesional therapies (talimogene laherparepvec (TVEC)) has increased management options. This study compares 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.

Figure 1.
Survival outcomes after first-line isolated limb infusion/perfusion (ILI/ILP), immune checkpoint inhibitors (ICI), or intralesional therapy with talimogene laherparepvec (TVEC) for melanoma in-transit metastases.



52. Relationship of Mitochondrial Complex I Activity and Response to Immunotherapy Treatment in Melanoma

Patients

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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.

53. Isolated limb infusion/perfusion for unresectable acral versus non-acral melanoma in-transit metastases

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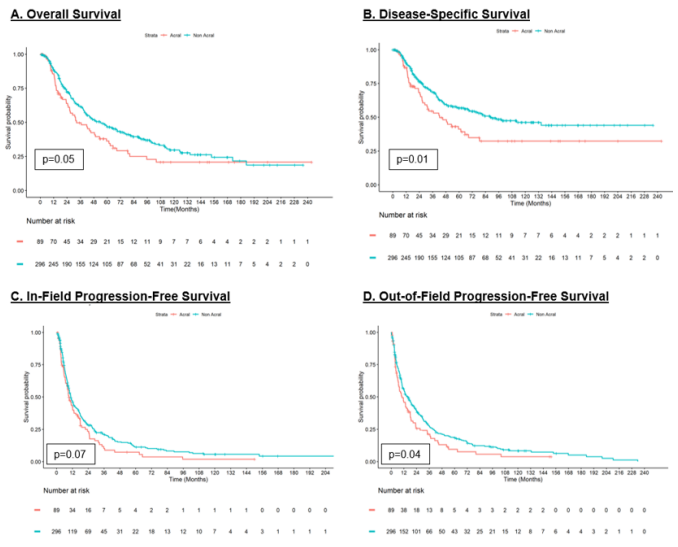
INTRODUCTION: Acral lentiginous melanoma (ALM) has a worse prognosis compared to non-ALM cutaneous melanoma and a poorly understood tumor genetic profile, limiting therapy options. This is the first study to directly compare outcomes of isolated limb infusion or perfusion (ILI/ILP) for unresectable in-transit 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 melanoma (ALM) versus non-ALM unresectable in-transit metastases.



ALM: Acral lentiginous melanoma

54. Impact of sentinel lymph node biopsy on recurrence and survival for Merkel cell carcinoma

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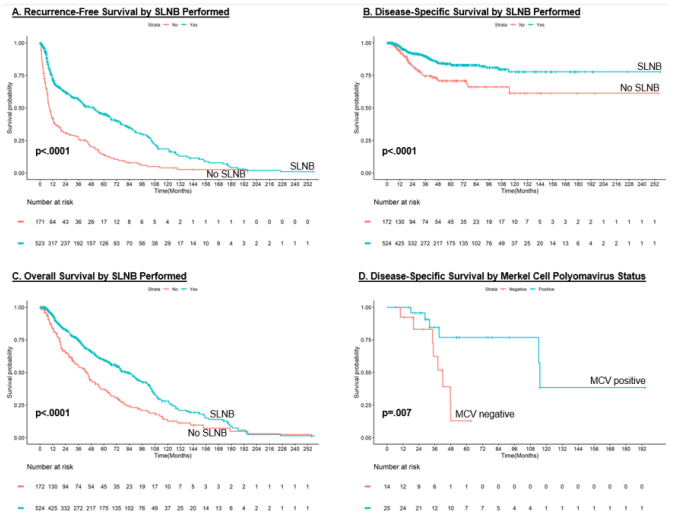
INTRODUCTION: Merkel cell carcinoma (MCC) is a rare disease that carries a poor prognosis in advanced stages. Sentinel lymph node biopsy (SLNB) at the time of excision is standard of care, but the impact of SLNB on survival is unclear. This study examines the impact of SLNB on recurrence and overall 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% of patients who did not have a SLNB developed regional recurrence, compared to 20% of those who had a SLNB. On Kaplan-Meier (KM) analysis, median recurrence-free survival (RFS) (median 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).



SLNB: Sentinel lymph node biopsy, MCV: Merkel cell polyomavirus

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

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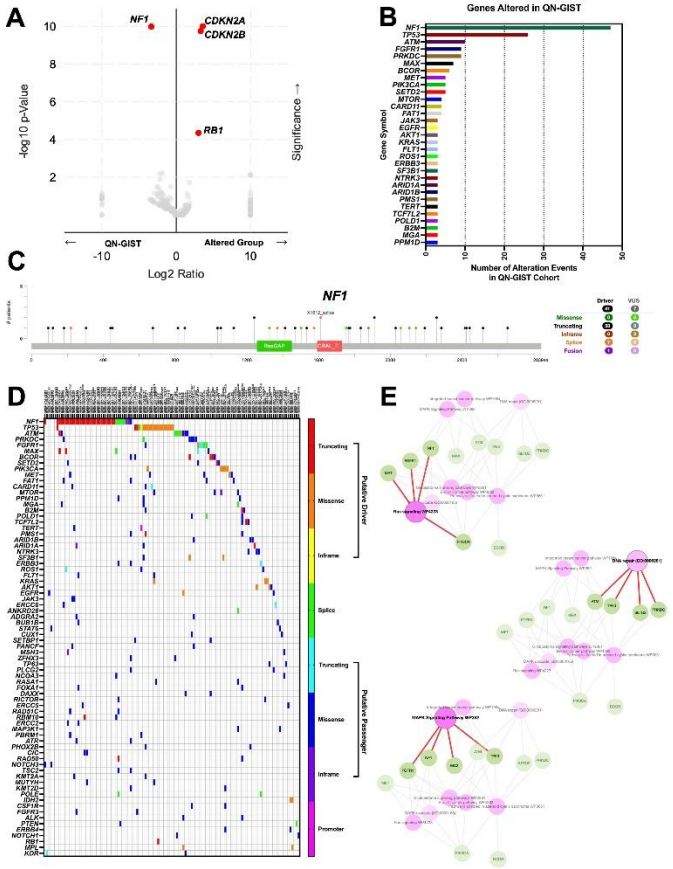
INTRODUCTION: Gastrointestinal stromal tumors (GIST) lacking hallmark KIT, PDGFRA, BRAF, and/or SDHA-D driver mutations—so called “quadruple negative” GISTs (QN-GIST)—respond poorly to conventional therapy. This analysis identifies candidate therapeutic targets for patients with QN-GIST using the world’s 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.



56. Outcomes of In-Transit Melanoma (ITM) Treated with Checkpoint Inhibitors (CPI) In The Modern Era
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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	59.3	63.7	60.2
Median Overall Survival (months)	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%)

57. 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

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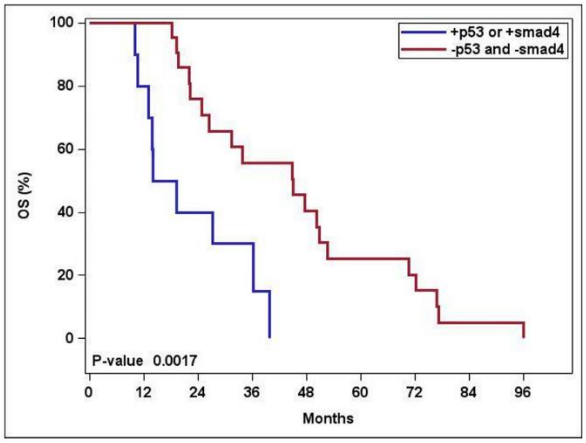
INTRODUCTION: Expanded mutation profiling has been utilized to guide clinical decision making in multiple cancer types but has not yet been adopted in the treatment of high-grade appendiceal peritoneal metastasis (HG-APM). There is currently a paucity of data for mutation profile impact on outcomes and also rates of actionable mutations in HG-APM.
METHODS: A single-institution retrospective study was performed on 42 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 (17 vs. 45 months, p = 0.002, Fig. 1) as well as PFS (5 vs.9 months, p = 0.030). Twelve out of 33 (36%) wildtype vs. 0/9 (0%) p53/SMAD4 patients underwent iterative CRS (p = 0.04) which might contribute to their prolonged survival.
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.



58. Efficacy and toxicity of Bevacizumab in the treatment of metastatic Appendiceal Adenocarcinoma

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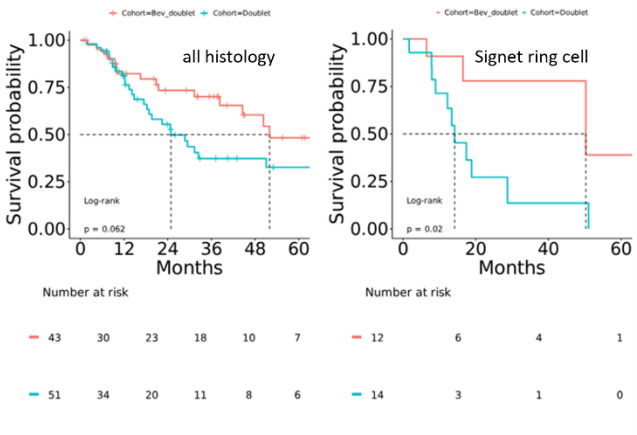
INTRODUCTION: Systemic treatment of metastatic appendiceal adenocarcinoma (AA) has been challenging due to the lack of an evidence-based AA chemotherapy regimen and historical reliance on colorectal cancer data. In the United States, but less commonly in Europe, bevacizumab is frequently incorporated in treatment of AA given its approved use for CRC. However, previously there have been no studies evaluating if there is a survival benefit attributable to bevacizumab in patients with AA.
METHODS: The Palantir Foundry system was used to extract data from the MD Anderson Cancer Center (MDA) electronic medical record for patients with biopsy-proven, metastatic AA who received chemotherapy at MDA from 2015 to 2024. Only patients with complete staging and histopathology data were included in the analysis.
RESULTS: A total of 238 patients with metastatic AA were identified, of these, 41% (n=98) received bevacizumab at some point in their treatment. Patients who received bevacizumab were demographically similar to patients who received non-bevacizumab chemotherapy in terms of age at diagnosis, race, and sex; mucinous histology was more frequent in the bevacizumab cohort (56%, n=55 vs. 40%, n=56 in non-bevacizumab cohort). The 98 patients who received bevacizumab were treated with 1-6 lines of therapy per patient (mean = 1.57). The most frequently used bevacizumab-containing regimens were FOLFOX + bevacizumab (33%, n=51), FOLRIRI + bevacizumab (33%, 5-FU + bevacizumab (15%, n=23), and atezolizumab + bevacizumab (10%, n=16). Only three regimens containing bevacizumab were discontinued due to complications: one instance of hand-foot syndrome attributed to capecitabine, one instance of cardiomyopathy attributed to immunotherapy, and one bowel perforation attributed to bevacizumab. To determine if bevacizumab was associated with overall survival (OS) benefit we performed Kaplan-Meier analysis with OS calculated from start of first line chemotherapy to death, in patients with metastatic AA who received either 5-FU doublet therapy alone or 5-FU doublet therapy with bevacizumab. Patients who received bevacizumab had double the OS of those that did not (median 52 vs 25 months for doublet therapy alone, HR: 0.56, p= 0.066). The effect of bevacizumab was particularly notable in patients with signet ring cell tumors (median OS 50 vs 14 months for doublet therapy alone, HR: 0.24, p= 0.03).
CONCLUSIONS: Bevacizumab is frequently added to cytotoxic chemotherapy in the treatment of AA. These retrospective data suggest limited toxicity and an OS benefit to adding bevacizumab to doublet chemotherapy, particularly in the case of signet ring cell histology.



59. Histology of Recurrent Mucinous Appendiceal Cancer after CRS-HIPEC for Low Grade Peritoneal Metastases

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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.

Table 1

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

60. Appendiceal cancers display immunosuppressed microenvironment and mucin infiltration on multiplex immunofluorescence analysis

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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).

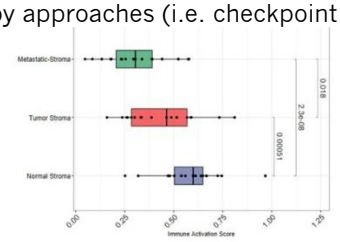

Figure 1: Immune activation scores are significantly lower in the metastatic and primary tumor microenvironment compared to the stroma in the normal appendix (A).

61. Clinical outcomes of high-grade appendiceal mucinous neoplasms
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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.

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

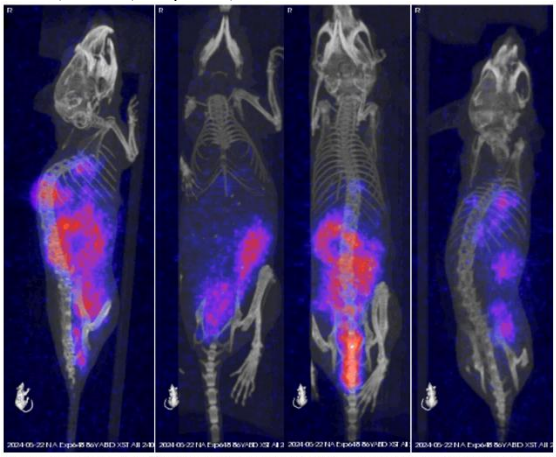

Figure 1: PET CT with [^{86}Y]Pr exhibiting widespread peritoneal metastasis in an IP model of AC.

63. True Incidence of Appendiceal Neoplasms in Patients Presenting with Complicated Appendicitis: A Call for a Revised Management Algorithm

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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. Multivariable 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%). Multivariable 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.

ePoster: Applied Research

P1. A System-Wide Clinical Data and Biobank Repository Initiative Across an Integrated Health Network: Insights from the "Moonshot" Program

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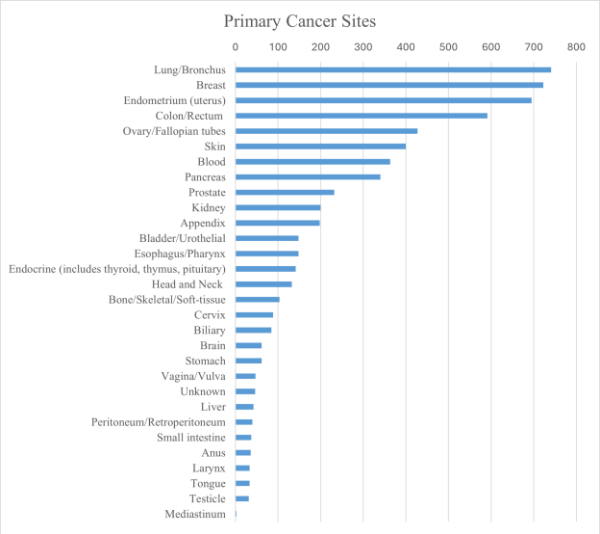
INTRODUCTION: Advances in cancer treatment depend on the rapid translation of new scientific discoveries into patient care. To facilitate this, Allegheny Health Network launched the "Moonshot" program in 2021, aimed at prospectively collecting patient clinical data and integrating it with cancer genomics 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.



P2. Difficult Conversations with Cancer Patients: An Oncologist's Perspective

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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, surgical oncologists 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

P3. Employer Sponsored Insurance Mediates Receipt of Neoadjuvant Treatment in Locally Advanced Rectal Cancer

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INTRODUCTION: Insurance is a known mediator of multidisciplinary oncologic care. In the United States, employer sponsored insurance (ESI) is the most common form of private insurance yet is understudied. We hypothesize state level ESI characteristics influence treatment and survival outcomes in locally advanced rectal cancer, specifically in receipt of neoadjuvant chemotherapy and radiation (NACR)
METHODS: Patients aged 40-80 years old, diagnosed with stage II/III rectal adenocarcinoma 2005-2019 were identified in the National Cancer Database. Unique combinations of region and Medicaid expansion variables were used to pair NCDB data with publicly available state level employment and insurer data. 21,712 cases were included in our analysis. Multivariate logistic regression analysis was performed with treatment strategy as a dependent variable and relevant clinical, social, and economic patient factors as independent variables. Primary endpoints of the study were receipt of NACR and 5 year overall survival (OS)
RESULTS: Overall, 47% of patients were privately insured, of which 44% received NACR. State level analysis revealed that in areas dominated by retail employers, those with private insurance were less likely to receive NACR, as opposed to states with healthcare sector as largest employer: (42.5% versus 45.38% p<0.0001). Additionally, multivariate analysis revealed private insurance associated with an increased risk of mortality HR 1.27 [95% CI (1.048-1.553)] as was Medicaid insurance HR 1.51 [95% CI (1.232-1.867)]. There was no survival difference for Medicare insured patients. A more pronounced effect was observed for black patients, who had the lowest overall rates of NACR as an initial treatment strategy (38.7% , p < 0.0001) . Privately insured black patients were more likely to have ESI from retail/sales (19.2% versus 14.6% , p < 0.0001) and less likely from healthcare sector (25.% versus 34.2 %, p < 0.0001), as compared to non-black patients. Indexing of state level average copays, deductible, co-insurance rates, as well as median income revealed significantly higher ESI costs for black patients (0.39 versus 0.32, p < 0.0001). Consistent with cost mediated insurance choices, black patients were more likely to be Medicaid (18.8% versus 8.2%, p <0.0001) or uninsured (4.5% versus 2.3 %
CONCLUSIONS: NACR is associated with improved overall survival in LARC. Despite similar cancer burden, black patients had worse survival outcomes mediated, in part, by ESI. Efforts to address treatment disparities should focus specifically on the quality of ESI plans offered by employers.

P4. Histotripsy for Treatment of Liver Tumors: A Novel Transthoracic Approach

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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

P5. Incidence and associated factors of neoplastic diagnosis following appendectomy for a clinically abnormal appendix

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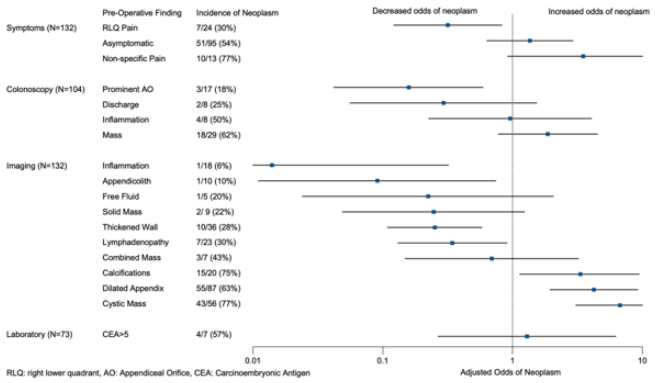
INTRODUCTION: Appendiceal abnormalities, beyond those typical of acute appendicitis, are occasionally detected on imaging or endoscopy, leading to surgical evaluation for a diagnostic appendectomy. How often these reflect an underlying neoplasm, however, remains unclear. This study aimed to determine 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.



P6. Incidence of and Risk Factors for Radiographically Occult Nodal Metastases in Colon Cancer: Is It Time for a New Lymphadenectomy Standard?

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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, odds of pathologic upgrade increased by 1.2%. Nodal harvest also correlated with increased odds of pathologic upgrade at a rate of 0.6% per node excised; patients with ³18 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 large, 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

P7. Interpreter Utilization for Patients with Limited English Proficiency in a Peritoneal Surface Malignancy Clinic

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INTRODUCTION: Limited English proficiency (LEP) has been correlated with significant disparities including reduced access to health care, longer surgical hospitalizations, and lower quality of care. Despite attempts to mitigate language barriers in clinical care, linguistic disparities persist, impacting patient experiences and cancer outcomes. In this study, we evaluated professional medical interpreter (PMI) usage for patients with LEP seen for peritoneal surface malignancies in the outpatient setting.

METHODS: In this retrospective cohort study, patients evaluated at a Peritoneal Surface Malignancy (PSM) clinic in an academic institution over a 14-month period during 2023-2024 were identified. Of note, in early 2024, an electronic consent form was implemented, requiring documentation of PMI usage prior to submission. Patient demographics including age, sex, race, ethnicity, primary language, diagnosis, and PMI usage were analyzed for patients with LEP.

RESULTS: Of 752 clinic visits identified, 160 (21.3%) were for patients who spoke a primary language other than English (Table). In this cohort, the most common primary languages were Spanish (57.6%) and Vietnamese (18.8%). Median age was 61.4 years (IQR 53.7, 72.6). Seventy (43.8%) of these visits documented the use of a PMI. A PMI was used in the majority of visits (88.6%). When declining an interpreter despite being offered one, patients opted for a family member to translate instead. There were 18 preoperative visits for LEP patients during which informed consent was signed. PMI use was documented on paper consent forms 63.6% of the time. This improved to 100% following implementation of the electronic consent method midway through the study.

CONCLUSIONS: Documentation of PMI during PSM clinic visits for LEP patients occurred in less than 50% of visits and in less than two-thirds of procedural consents, although PMI documentation in consents improved following the implementation of a new electronic consent method. Standardized electronic medical record templates requiring documentation of PMI utilization or declination can better inform not only PSM clinics, but institutional cancer care practices as a whole.

Table. Patient Characteristics and Interpreter Use

Clinic Visits by Primary Language	**No.**	**(%)**
Total Number of Visits	n=752	
English	588	(78.2)
Other	160	(21.3)
Unreported	4	(0.5)
Type of Visit		
New / Consultation	174	(23.1)
Return	578	(76.9)
Documentation of PMI for Patients with LEP	n=160	
Absent	90	(56.3)
Present	70	(43.8)
Patient used Interpreter	62	(88.6)
Patient declined Interpreter	8	(11.4)
Characteristics of Patients with LEP	n=66	
Age, *years*, median (IQR)	61.4	(53.7, 72.6)
	No.	**(%)**
Sex		
Male	31	(47.0)
Female	35	(53.0)
Race		
White	13	(19.7)
Asian	23	(34.9)
Other / Mixed	30	(45.5)
Ethnicity		
Other Hispanic/Latino(a) or Spanish Origin	37	(56.1)
Non-Hispanic/Latino(a)	29	(43.9)
Primary Language		
Spanish	38	(57.6)
Vietnamese	12	(18.2)
Korean	6	(9.1)
Mandarin	3	(4.6)
Cantonese	2	(3.0)
Farsi	4	(6.1)
Dari	1	(1.5)
Diagnosis		
Appendiceal neoplasm	17	(25.8)
Colon adenocarcinoma	13	(19.7)
Rectal cancer	3	(4.6)
Gastric adenocarcinoma	11	(16.7)
GIST	8	(12.1)
Other	14	(21.2)

ePoster: HPB

P8. CTNNB1 exon 3 hotspot mutations in early-onset hepatocellular carcinoma

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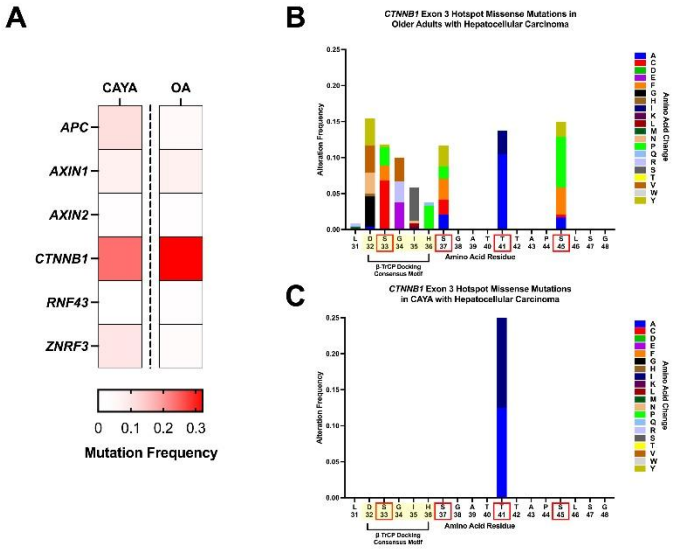
INTRODUCTION: Hepatocellular carcinoma (HCC) frequently exhibits overactivation of WNT–β-catenin signaling. Children, adolescents, and young adults (CAYA) (NCI definition: age ≤ 39 years) with HCC demonstrate distinct clinicopathologic features despite similar rates of CTNNB1 alterations. The current 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 CTNNB1mutations 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.



P9. Chromosome 9p deletions are associated with higher rates of R1 resection across GI cancers

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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 R0 vs R1 resection across GI cancers

P10. Intratumoral lymphangiogenesis does not correlate with outcomes in Hepatocellular Carcinoma

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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.

P11. Liver Metastasectomy in Ovarian Cancer: Is There a Survival Benefit?

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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 it 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.

P12. Patient-Specific Variations in Hepatic Arterial Infusion Pump Flow Rates at High Altitude

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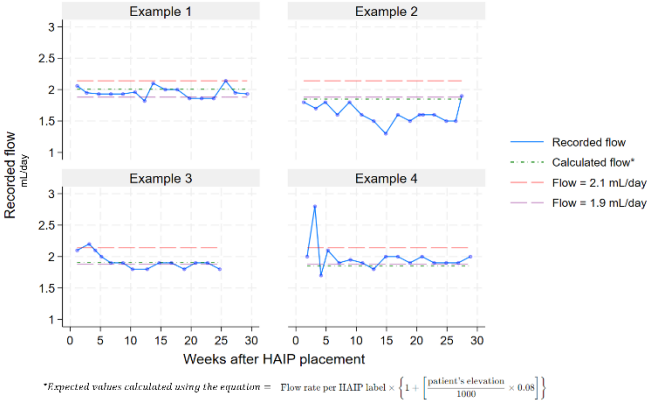
INTRODUCTION: Previously, we reported patients' altitude as a significant determinant in HAIP flow variation rates;however, the combined effects of other factors, such as heat exposure, fever, surgical stress, and trips to varying altitudes, on flow variability remain poorly described.
METHODS: Utilizing our prospectively maintained HAIP program database, we analyzed flow rate variations in patients with an Intera® pump. Flow variability was compared relative to three reference points: (1) the expected baseline flow calculated using the manufacturer's equation; (2) a flow rate of 1.9?mL/day; and (3) a flow rate of 2.1?mL/day. We assessed how factors such as heat exposure, fever, surgical stress, and travel to different altitudes influenced deviations from these reference flow rates.
RESULTS: Clinical data from ten patients were evaluated over the first 30 weeks post-HAIP placement. Significant variability in flow rates was observed in all patients during FUDR/heparinized saline refills, particularly during the initial infusions compared to expected flow values. Notably, the expected baseline flow value for each patient was close to 1.9?mL/day in most cases. Despite this, 90% of patients exhibited flow rates exceeding this cutoff during their visits, raising concerns among treating clinicians that even a one-day delay in refill could result in a dry pump. Regarding the 2.1?mL/day cutoff, 40% of patients exceeded this flow rate at least once, necessitating earlier refills to prevent dry pump. Variations exceeding all proposed cutoffs were associated with a combination of heat exposure, fever, surgical stress, and altitude changes during travel, but did not follow a predictable pattern and were unique in each instance. When patients transitioned to a 50% glycerin solution, flow variations persisted in the presence of these factors but did not exceed a 10% change from steady values.
CONCLUSIONS: At high altitudes, HAIP flow rates are unpredictable and significantly influenced by a combination of environmental and physiological factors, resulting in patient-specific variations. Comparative studies at sea level are needed to better understand these effects and provide clearer guidance. Enhanced awareness and monitoring strategies are essential, especially when patients receiving FUDR treatment.



P13. Proteomic Profiling of Pancreatic Cancer Response to Novel Oncolytic Virotherapy

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INTRODUCTION: Vesicular Stomatitis Virus (VSV) is a promising candidate in the treatment of pancreatic adenocarcinoma (PDAC) in the context of novel oncolytic virotherapy. Unlike traditional chemotherapy, VSV

selectively targets cancers cells due to innate susceptibility of cancer biology while simultaneously stimulating an immune response. The aim of this study is to investigate the proteomic profiles of key pathways within PDAC in response to treatment with VSV.
METHODS: The study investigated the effects of a novel virus treatment (VMG) on MiaPaCa2 pancreatic ductal adenocarcinoma (PDAC) cells. VMG is a modified virus where the G protein of vesicular stomatitis virus (VSV) is replaced with that of the morreton virus. Mass spectrometry-based proteomic profiling was employed to identify differentially expressed proteins in treated cells. The resulting data underwent bioinformatics analysis, including Ingenuity Pathway Analysis (IPA), to interpret the proteomic findings and identify key affected pathways. ?The research focused on elucidating the main molecular pathways impacted by VMG treatment, particularly those relevant to PDAC biology and treatment response.
RESULTS: We have shown the dose-dependent cytotoxicity of VMG on different PDAC cell-lines. Proteomics analysis resulted in 4,151 identified proteins across treatment and control groups. Among those, 248 (5.97%; [$p < .05$]) proteins demonstrated a significant regulatory expression compared to control. Among these proteins, 123 and 125 proteins were uniquely up or down regulated respectively to either VMG or Control. 41 out of 123 up-regulated proteins were uniquely detected in the VMG group 52 out of 125 down-proteins were uniquely detected in control group. Pathway analysis revealed several significantly enriched pathways ($p < 0.05$) associated with the VMG treatment, including DNA replication, Cell cycle checkpoints, Ribosome biogenesis, p53 signaling, and Peroxisomal protein import.
CONCLUSIONS: The study demonstrates that the novel virus treatment (VMG) significantly alters the proteomic landscape of MiaPaCa2 pancreatic ductal adenocarcinoma (PDAC) cells.? The identification of 248 differentially expressed proteins, with distinct up- and down-regulation patterns, underscores the profound impact of VMG on cellular processes. Notably, the enrichment of pathways related to DNA replication, cell cycle checkpoints, ribosome biogenesis, p53 signaling, and peroxisomal protein import suggests that VMG targets critical cellular mechanisms involved in PDAC progression and survival. These findings not only provide insight into the molecular mechanisms of VMG's anti-tumor activity but also highlight potential biomarkers and therapeutic targets for PDAC treatment. Further investigation of these altered pathways may lead to improved strategies for combating this aggressive malignancy and offer new avenues for combination therapies in PDAC management.

P14. Safety and Feasibility of the Use of Transcutaneous Electrical Nerve Stimulation for Delayed Gastric Emptying after Pancreaticoduodenectomy: A Pilot Study
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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 wanted 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 were recorded.
RESULTS: Among 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 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. A low rate of DGE (10%) was observed, however, more questions on ideal treatment parameters remain that warrant further study.

ePoster: Peritoneal Metastases

P15. 900 patients later: outcomes of cytoreduction and heated intraperitoneal chemotherapy for appendiceal neoplasms
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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 (OR 1.2, CI 1.1-1.4, p <0.001) and EBL (OR 1.0, CI 1.000 – 1. 001, p-0.030) were associated with incomplete resection. 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 correlated with incomplete resection. Meaningful survival is observed in low grade primary appendiceal neoplasms even with incomplete cytoreduction.

P16. An incidence-based assessment of colorectal peritoneal metastasis in the United States: A SEER retrospective cohort study

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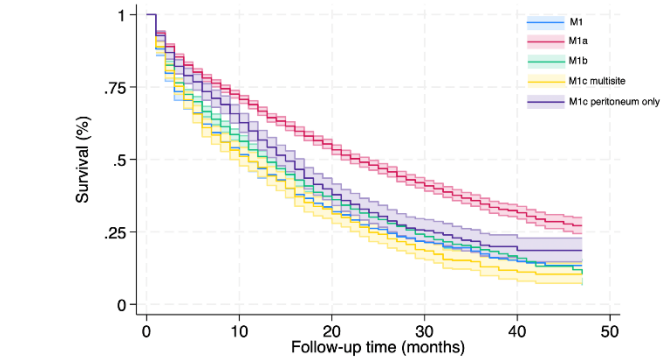
INTRODUCTION: Epidemiologic data of the incidence, distribution, and prognosis of colorectal peritoneal metastasis are limited. The 8th Edition AJCC Staging Manual introduced the M1c category for peritoneal carcinomatosis as a prognostic factor. We assessed the epidemiology and prognosis of M1c colorectal metastasis in the United States.
METHODS: The incidence-based SEER database was used to identify 12,117 patients with metastatic (M1) colorectal adenocarcinoma diagnosed from 2018-2021. Extent of disease and staging variables were used to determine sites of metastasis. Demographic and treatment variables were included as covariates. Descriptive statistics and survival analyses were conducted. The prevalence of M1 sub-categories and associated survival rates were analyzed.
RESULTS: Median age at diagnosis was 65 years (IQR 55-75) and females were 45% of the cohort. The distribution of M1 sub-categories was M1a (46%), M1b (26%), M1c (19%), and uncategorized (9%). Among patients with M1c disease, 46.7% had peritoneal-only metastasis, comprising 9% (1,092/12,117) of the entire cohort. By M1 sub-category, there were differences in age, sex, ethnicity, primary site, mucinous histology, and receipt of chemotherapy and surgery (p<0.05); M1c had a higher proportion of right-sided tumors (45.7%) and mucinous histology (10%) compared to M1a (33% and 2%, respectively) or M1b (30% and 2%, respectively). Median OS for M1 uncategorized was 16 months (IQR 5-37), whereas for M1a, M1b, and M1c it was 23 (IQR 8-not reached), 13 (IQR 4-29) and 13 (IQR 4-27) months, respectively (p<0.01). For the M1c sub-category, median OS was 15 months (IQR 6-31) for peritoneal-only metastasis and 11 months (IQR 4-24) for M1c with multisite metastasis (p<0.01). After adjustment for potential confounders, M1c multisite metastasis had the highest odds of mortality relative to M1a disease (HR 1.91; 95% CI, 0.57-0.71) with M1b (HR 1.57; 95% CI, 1.47-1.68) and M1c peritoneal-only disease (HR 1.21; 95% CI, 1.10-1.33) also having increased odds of mortality.
CONCLUSIONS: Colorectal peritoneal metastasis accounted for approximately 20% of incident cases of metastatic colorectal cancer, for which roughly half had peritoneal-only disease. There were significant survival differences among patients with peritoneal-only disease when compared to patients with peritoneal plus other (hematogenous) metastatic sites. These data demonstrate that colorectal peritoneal metastasis is not rare and that survival differences in the M1c subgroup suggest unique tumor biology.

Figure 1: Kaplan Meier Overall Survival Estimates of Metastatic Colorectal Cancer by AJCC 8th Edition Staging by M1c Peritoneum Only and M1c Multisite (Peritoneum + Other Distant Sites) Metastasis



P17. Challenging The Role of Neoadjuvant Therapy in Peritoneal Mesothelioma Before Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy

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INTRODUCTION: Peritoneal Mesothelioma (PM) is a rare malignant condition where the abdominal peritoneal lining is the site of primary tumor. Cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) remains the gold standard treatment for PM. We aim to evaluate outcomes between patients who received neoadjuvant therapy before CRS/HIPEC and patients who received surgical intervention without neoadjuvant therapy.
METHODS: A prospectively maintained database of patients who underwent CRS ± HIPEC was retrospectively reviewed and 20 patients with epithelioid PM were identified. 13 patients fitted the criteria for the two treatment groups. Median disease-free survival (DFS) and median overall survival (OS) were calculated.
RESULTS: In the neoadjuvant-to-surgery-cohort, 4 patients received cisplatin with pemetrexed, 1 patient received cisplatin with immunotherapy and 1 patient received immunotherapy alone. The median number of rounds prior to surgery was 4.5 (range, 3-8). The median PCI score for the neoadjuvant cohort was 14 (IQR, 9.5-18.5). For the direct-to-surgery-cohort, median PCI score was 26 (IQR, 18-34). The median DFS was 9 (IQR, 5-13) months and the median OS was 29 (IQR, 0 to NA) months for the neoadjuvant-to-surgery-cohort. Patients in the direct-to-surgery-cohort experienced a median DFS of 32.5 (IQR, 26.5-38.5) months and OS was not reached. Only one patient in this cohort passed 7 months after CRS and HIPEC. Despite the small size of the cohorts, there was a numeric advantage both on median DFS (9 months vs 32.5 months) and OS (29 months vs. OS was not reached) in the patients of the direct-to-surgery-cohort, despite having a higher tumor burden (PCI score, 26 vs 14).
CONCLUSIONS: Our findings suggest that the role of neoadjuvant chemotherapy before CRS and HIPEC in PM requires further investigation. The rarity of the disease poses challenges in conducting large-scale clinical trials. Careful patient selection for neoadjuvant chemotherapy is essential before surgical intervention and future studies should focus on patients with the potential to benefit most from neoadjuvant approaches.

P18. Characteristics and Outcomes of External Referral Patients Undergoing Cytoreductive Surgery at an International Peritoneal Surface Malignancy Program

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INTRODUCTION: Given the limited number of high-volume centers offering cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC), patients may seek care outside of their health system. To understand the implications to 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 who were treated at Allegheny Health Network from January 2022 to March 2024. We categorized patients into two groups: in-system (IS; patients referred from within our integrated network) and out of system (OOS; patients from outside our health system). Patient and disease characteristics, surgical outcomes, and institutional costs were compared.
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 carcinomatosis 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 either a 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 peritoneal 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

P19. Comparative Analysis of Patient Body Surface Area and Peritoneal Surface Area: Implications for HIPEC Dosing

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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.

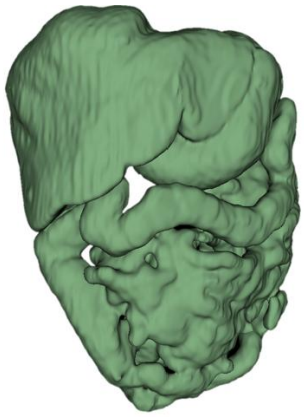

Figure. Example of intraperitoneal organ segmentation prior to wrapping

P20. Comparison of Outcomes after CRS-HIPEC Among Patients With Mucinous vs Non-Mucinous Neoplasms
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INTRODUCTION: While cytoreductive surgery (CRS) with the addition of hyperthermic intraperitoneal chemotherapy (HIPEC) has been well-studied and utilized in treating mucinous cancers with peritoneal dissemination, its use in non-mucinous neoplasms is less well defined. With different clinicopathologic features, these types of cancers may differ in their response to CRS-HIPEC. Here we aim to compare oncologic outcomes among patients with mucinous vs non-mucinous cancer with peritoneal carcinomatosis undergoing CRS-HIPEC, in order to better understand the therapeutic role in these two patient populations.
METHODS: A prospectively maintained database of patients undergoing CRS/HIPEC at an academic tertiary referral institution between 2011 and 2023 was retrospectively reviewed. Demographic, oncologic and outcomes data were compared. Recurrence free and overall survival were assessed via Kaplan Meier curves and multivariate Cox-proportional hazards models adjusted for age, sex, race, Charlson Comorbidity index, peritoneal cancer index (PCI) and post-operative complications.
RESULTS: Within a cohort of 180 total patients undergoing CRS-HIPEC, 60 (32%) had non-mucinous vs 129 with mucinous neoplasms (68%). Patients with non-mucinous neoplasms were more likely to be smokers (22% vs 7%, p=0.003) and have lower PCI (mean 10.4 vs 15.7, p=0.0002). Otherwise the two groups were demographically similar without significant comorbidity differences. Operative details such as surgical time (487 vs 518 min, p=0.11) and cytoreduction score (mean 0.12 vs 0.19, p=0.3) also did not differ between groups. After surgery, length of stay (9.6 vs 9.2 days, p=0.8), 60 day readmissions (25 vs 24%, p=0.9), and Clavien Dindo score (severity of post-operative complications) (mean 2.8 vs 2.9, p=0.65) were similar between groups. Patients with non-mucinous neoplasms were found to have worse recurrence-free survival on univariate (p=0.0075) and multivariate analyses (adjusted HR 2.08 for recurrence, p=0.036). However, there was no significant difference in overall survival between groups on univariate (p=0.73) or multivariate analyses (adjusted HR 1.12 of death,

p=0.83). Kaplan-Meier curves are demonstrated in Figure 1.
CONCLUSIONS: In this cohort, non-mucinous neoplasms were found to have poorer recurrence-free survival after CRS-HIPEC compared to mucinous cancers. Otherwise, non-mucinous cancers had similar post-operative outcomes and overall survival. These findings contribute to prognostication and risk-stratification for patients with differing cancer histopathologies undergoing CRS-HIPEC.

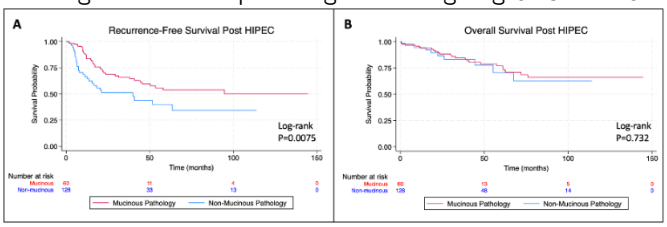

Figure 1: Kaplan-Meier curves for probability of A) disease recurrence and B) overall survival based on mucinous vs non-mucinous cancer pathology

P21. Cytoreductive Surgery Plus Hyperthermic Intraperitoneal Chemotherapy (CRS+HIPEC) Leads to Sustained Long-term Quality of Life in Patients with Peritoneal Surface Malignancies

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INTRODUCTION: Cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (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, Hispanic, female, had primary appendiceal malignancy, and Eastern Cooperative Oncology Group (ECOG) status of 0. Mean preoperative peritoneal cancer index (PCI) score was 15 (range 0-39). 47 (68%) patients had R0 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.

P22. Development of a Quantitative Method to Assess Peritoneal Sclerosis in Patients Undergoing PIPAC

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INTRODUCTION: Intra-peritoneal chemotherapy can result in peritoneal sclerosis which can be detrimental to quality of life. Here, we propose and develop a quantitative method for measuring the severity of peritoneal sclerosis – Peritoneal Sclerosis Index (PSI).
METHODS: This is a retrospective analysis of laparoscopic videos for patients undergoing pressurized intra-peritoneal aerosolized chemotherapy (PIPAC) at an NCI-designated cancer center. All the videos were deidentified and scored by 4 experienced surgical oncologists. Raters were blinded to any patient characteristics. PSI scoring ranged from 0-39 with regional contribution to score shown in Table 1. The inter-rater reliability of PSI was assessed using Cohen kappa statistic (κ)
RESULTS: A total of 28 laparoscopic patient videos from 15 patients (median age 61 years; 50% female; primary cancer: 5 appendix, 5 colorectal, and 5 biliary tract) undergoing PIPAC were evaluated. PIPAC regimens were as follows: Oxaliplatin (6 patients), Mitomycin C (4 patients), and Nab-Paclitaxel (5 patients). Of the 28 videos, 11 were evaluated before any PIPAC therapy, whereas 17 were evaluated after PIPAC. Overall, inter-rater reliability of PSI was the same as PCI - moderate 0.45 ($p<0.001$). There was variation in PSI agreement among raters by region: The highest agreement was seen in the small bowel (jejunum/ileum κ 0.51-54) region and lowest in the flanks (0.26-0.31). The overall agreement in PSI increased after treatment (before κ 0.36, after κ 0.46).
CONCLUSIONS: The study proposes a novel tool to quantify peritoneal sclerosis. Inter-rater reliability of laparoscopic PSI assessment is similar to that that of PCI: The reliability improves in patients treated with PIPAC. Future studies will evaluate the impact of PSI on quality of life and prognosis.

Table 1. Scoring criteria of PSI

Peritoneal Sclerosis Index (PSI)			
Parietal Peritoneum – 9* regions		Small Bowel – 2^ regions	
Score	Criteria	Score	Criteria
0	no sclerosis	0	no sclerosis
1	patchy opaque or translucent confluent	2	sclerosis without mesenteric shortening or inter-loop adhesions
2	opaque confluent but non-adhesive	4	inter-loop adhesions but no mesenteric shortening
3	adhesive or inaccessible	6	mesenteric shortening or inaccessible
*Central, right upper quadrant, epigastrium, left upper quadrant, left flank, left lower quadrant, pelvic, right lower quadrant, right flank ^Jejunum & ileum			

P23. Discordance between laparoscopic and open assessment of peritoneal disease burden

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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 1: Demographic and Oncologic Characteristics for Patients Undergoing Sta
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

P24. Distance from Treatment Facility and Socioeconomic Factors on Patient Outcomes Following Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (CRS-HIPEC): A Divide in Care?

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INTRODUCTION: Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) requires adequate resources for a successful recovery and research is limited for vulnerable populations. We hypothesized that racial minorities and distant-living patients would be underrepresented and show worse outcomes. This is the first study to investigate outcomes amongst distant-living CRS-HIPEC patients.
METHODS: A retrospective review of demographics, Clavien-Dindo classifications, readmissions, and death after surgery was performed on 271 patients who underwent CRS-HIPEC from 2018 through 2023 at a high-volume CRS-HIPEC academic institution serving patients from urban, near-rural, and far-rural populations. All patients independent of diagnoses were included, and patients under 18 years of age were excluded. Patients with a home address greater than 100 miles from the institution's address were considered "distant-living". Categorical associations were tested with Chi-square or Fisher's exact tests. All tests were two-tailed and were conducted in IBM SPSS Statistics, version 29.0.
RESULTS: Racial minorities were underrepresented (black=2.6%, Hispanic=2.6%). Approximately 71% of the study population were married while 29% were not. Travel

distance for CRS-HIPEC ranged from 2.7 to 543 miles (Median= 28.8) and about 26% were distant-living. Relationship status did not impact complication or readmission rates. Those with Medicare or Medicaid had a higher incidence of readmission within 90 days of discharge compared to those with Commercial insurance (p=0.05). However, insurance type did not impact complication or mortality rate. A significant difference was found in mortality status with near-living patients having a higher incidence of mortality following CRS-HIPEC compared to distant-living patients (p= 0.018). There was no significant difference between distant-living and near-living patients in their complications or readmission within 90 days of discharge when compared to those living <100 miles from the treatment facility.
CONCLUSIONS: Following CRS-HIPEC, socioeconomic factors such as insurance type and distance from treatment facility may impact patient outcomes and should be investigated further. Racial minorities were underrepresented. Reasons for access disparity among racial minorities should also be explored in future studies.

P25. Does Systemic Chemotherapy Benefit Patients with High-grade Mucinous Appendiceal Neoplasms Undergoing CRS-HIPEC? A National Database Analysis

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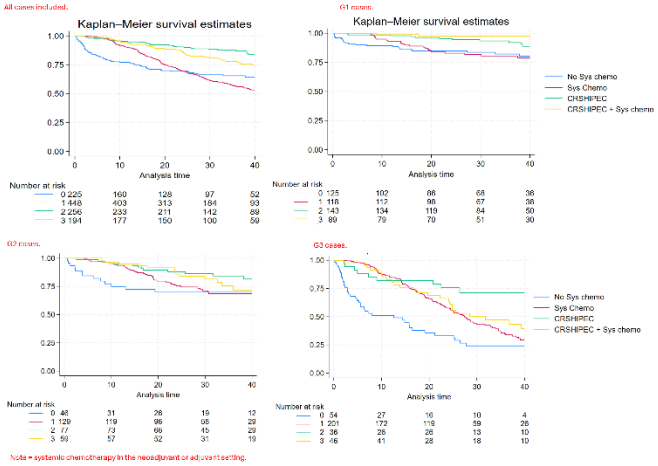
INTRODUCTION: The American Joint Committee on Cancer (AJCC) 8th edition introduced a three-tiered grading system (G1–G3) for mucinous appendiceal neoplasms (MAN). Optimal treatment for peritoneal involvement of MAN is cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC). 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.



P26. Early Onset Appendiceal Adenocarcinoma: Characteristics of a National Cohort

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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.

P27. Efficacy of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Appendiceal Goblet Cell Carcinoma with Peritoneal Disease

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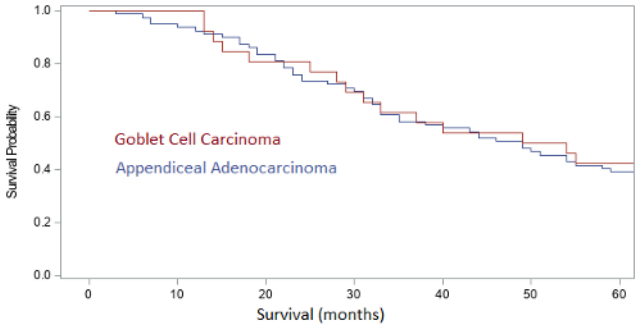
INTRODUCTION: Appendiceal Goblet cell carcinoma (GC) are rare malignancies regarded as aggressive tumors with proclivity to spread to the peritoneum. The literature regarding optimal treatment of GC with peritoneal disease is limited. Given the propensity for peritoneal spread, cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) may be a favorable treatment modality. This study compares patient with adenocarcinoma of the appendix (AA) with appendiceal GC with peritoneal disease treated with CRS/HIPEC.
METHODS: A single-institution, prospectively collected database of all patients undergoing CRS/HIPEC was retrospectively reviewed from 2003-2021 for all patients with a diagnosis of appendiceal peritoneal disease. Patients with peritoneal disease from appendiceal GC versus AA treated with CRS/HIPEC were compared. Bivariable comparison using Chi-square and survival analysis using Kaplan-Meijer were used to compare those with and without GC. Cure rate was defined as no recurrence of disease and survival greater than 5 years from CRS/HIPEC.
RESULTS: The study included 106 patients including 26 (24.5%) with GC. Patients with GC undergoing CRS/HIPEC were similar to those with AA in terms of sex, race, and age (p>0.05). Complete cytoreduction was achieved at similar rates when comparing those with GC and AA (61.5% vs 58.8%, p=0.46). Extent of surgical resection required was similar with no difference in rates of visceral resection (p=0.42), number of anastomoses (p=0.18), and rate of ostomy creation (p=0.26). The rate of postoperative complications was similar (GC 38.5%, AA 41.3%, p=0.80). Rate of recurrence was lower in patient with GC compared to AA (30.8% vs 63.8%, p=0.003). No patients with GC underwent repeat CRS/HIPEC while 6.3% (5) patients with AA had second CRS/HIPEC. Median overall survival (OS) was 51.5 months for those with GC and 49.0 months in those with AA (p=0.30) (Figure 1). The cure rate for patients with GC was 26.9% compared to 20% of patients with AA (p=0.46)
CONCLUSIONS: Despite the rarity and aggressive biology of GC, with careful patient selection and treatment with CRS/HIPEC, short-term and long-term survival outcomes can be similar to treatment of carcinomatosis from AA.



P28. Elevated Core Body Temperatures During Hyperthermia Intraperitoneal Chemotherapy Does Not Impact Postoperative Outcomes

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INTRODUCTION: The cytotoxic effects of hyperthermic intraperitoneal chemotherapy (HIPEC) after cytoreductive surgery (CRS) is shown to be most potent above 40oC. While high perfusate temperatures may theoretically risk systemic hyperthermia and resultant complications, current data are sparse. This study investigates associations between systemic hyperthermia during HIPEC and postoperative outcomes.
METHODS: A retrospective study was performed on a prospectively collected database of patients diagnosed with peritoneal surface malignancies who underwent CRS/HIPEC between 2007 and 2019 at a tertiary care center. HIPEC average inflow and outflow temperatures are targeted for 42-43oC. Core body temperature (CBT) was recorded by bladder temperature probe before and during HIPEC. Groups were defined by CBT < 38oC (normal CBT) or > 38oC (high CBT). Characteristics were compared between groups using chi-square, independent t-test and Mann-Whitney U-test.
RESULTS: 143 patients met inclusion criteria, with 99 (69.2%) patients identified to have elevated CBT during HIPEC (38.87oC + 0.65 vs 37.26 oC + 0.68, P<.001). There were no significant differences in demographics, baseline characteristics, age at surgery and pre-operative BMI between groups. The majority of tumors were appendix or colorectal origin (55.9% in elevated CBT vs 49.1%, P=0.471), with similar peritoneal cancer index (PCI) scores between groups (14.07 + 8.46 in elevated CBT vs 16.60 + 8.69, P=0.112). The majority of patients obtained CC 0-1 scores prior to HIPEC (85.8% vs 76.8%, P=0.237). There were similar median number of organs excised (4 [range 0-10] vs 4 [range 0-10], P=0.551) and

number of bowel anastomoses performed (1 [range 0-6] vs 1 [range 1-3], P=0.953). Mitomycin C was the most common HIPEC agent used (87.9% vs 90.9%, P=0.348). There were no significant differences in inflow or outflow temperatures, flow rate or average duration of HIPEC between groups. Those with elevated CBT during HIPEC started at an average higher baseline CBT (35.96oC + 1.15 vs 35.05oC + 1.00, P<.001), and had a greater change in temperature (2.91oC + 1.01 vs 2.21oC + 1.12, P<.001). However there were no significant differences in ICU or hospital lengths of stay, or time to resumption of bowel function. 30 day Clavien-Dindo complication rates were also similar between groups.

CONCLUSIONS: Some patients may be more susceptible to elevated CBT during HIPEC, despite controlled perfusate temperatures. However mild elevations in CBT did not significantly impact immediate or 30 day complication rates. While CBT still needs to be monitored consistently, mild elevations in CBT during HIPEC may not necessitate frequent interventions that may significantly impact operative time.

Table 1: Baseline Characteristics and Operative Outcomes After HIPEC

	Normal CBT N=44 (%)	Elevated CBT N=99 (%)	Entire Cohort N=143 (%)	P-value
Sex				
Female	25 (56.8)	61 (61.6)	86 (60.1)	0.712
Male	19 (43.2)	38 (38.4)	57 (39.9)	
ECOG Score				
0	14 (31.8)	33 (33.3)	47 (32.9)	0.539
1	19 (43.2)	41 (42.4)	61 (42.7)	
2	1 (2.3)	3 (3.0)	4 (2.8)	
Primary Tumor Origin				
Appendiceal cancer	16 (30.2)	27 (26.5)	43 (27.7)	0.471
Colorectal cancer	10 (18.9)	30 (29.4)	40 (25.8)	
Hepato-pancreato-biliary cancer	4 (7.5)	3 (2.9)	7 (4.5)	
Pseudomyxoma peritonei	7 (13.2)	15 (14.7)	22 (14.2)	
Other[^]	16 (30.2)	27 (26.5)	43 (27.7)	
Age at surgery (mean, SD)	55.16 ± 10.41	57.17 ± 10.95	56.55 ± 10.79	0.305
PCI score (mean, SD)	16.60 ± 8.69	14.07 ± 8.46	14.83 ± 8.58	0.112
CC score				
0	19 (44.2)	52 (53.1)	71 (50.4)	0.237
1	14 (32.6)	32 (32.7)	46 (32.6)	
2	6 (14.0)	12 (12.2)	18 (12.8)	
3	4 (9.3)	2 (2.0)	6 (4.3)	
HIPEC agent				
Carboplatin	1 (2.3)	6 (6.1)	7 (4.9)	0.348
Cisplatin	2 (4.5)	6 (6.1)	8 (5.6)	
Mitomycin C	40 (90.9)	87 (87.9)	127 (88.8)	
Mitoxantrazone	1 (2.3)	0 (0)	1 (0.7)	
Inflow temp (C, mean, SD)	43.05 ± 0.86	43.06 ± 0.74	43.06 ± 0.78	0.903
Outflow temp (C, mean, SD)	43.06 ± 1.28	41.31 ± 0.64	41.20 ± 0.90	0.078
Flow rate (lpm, mean, SD)	1.20 ± 0.26	1.16 ± 0.23	1.17 ± 0.24	0.420
Duration of HIPEC (min, mean, SD)	99.27 ± 15.32	97.11 ± 15.06	97.78 ± 15.12	0.432
Core body temperature pre-HIPEC (°C, mean, SD)	35.05 ± 1.00	35.96 ± 1.15	35.68 ± 1.18	**<.001**
Core body temperature during HIPEC (°C, mean, SD)	37.26 ± 0.68	38.87 ± 0.65	38.38 ± 0.99	**<.001**
Average change in temp (°C, mean, SD)	2.21 ± 1.12	2.91 ± 1.01	2.70 ± 1.01	**<.001**
ICU stay needed?	19 (43.2)	40 (40.4)	59 (41.3)	0.854
ICU length of stay (days, mean, SD)	5.39 ± 12.23	4.48 ± 12.93	4.76 ± 12.65	0.753
Hospital length of stay (days, mean, SD)	12.64 ± 19.75	10.33 ± 13.51	11.04 ± 15.66	0.419
Time to flatus (days, mean, SD)	4.25 ± 1.84	4.48 ± 1.97	4.42 ± 1.93	0.684
Time to bowel movement (days, mean, SD)	5.25 ± 1.49	5.27 ± 1.87	5.26 ± 1.78	0.975
30 Day Complications (Clavien-Dindo)				
1	9 (37.5)	21 (36.2)	30 (36.6)	0.207
2	3 (12.5)	18 (31.0)	21 (25.6)	
3	6 (25.0)	6 (10.3)	12 (14.6)	
4	6 (25.0)	11 (19.0)	17 (20.7)	
5	0 (0)	2 (3.4)	2 (2.4)	

[^] Other includes cancers of the small bowel, gynecologic system, melanoma, neuroendocrine tumors, primary peritoneal mesothelioma, and gastric cancer.

P29. Evaluation of Tumor Marker and Imaging Endpoints for Recurrence of Intraperitoneal Malignancies Following Cytoreductive Surgery & Hyperthermic Intraperitoneal Chemotherapy

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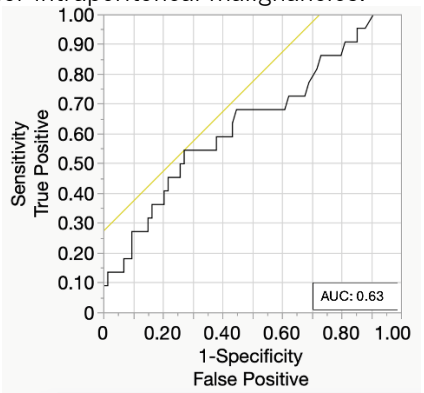
INTRODUCTION: Identifying recurrence following cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) for metastatic intraperitoneal-limited malignancies remains a challenge. Cross sectional imaging is primarily used to diagnose recurrence but is thought to be inaccurate for peritoneal diseases, as recurrences are believed to occur long before detection via imaging. The aims of this study were to identify a surrogate biochemical tumor marker that can detect recurrence and determine how much earlier it is recognized than imaging-based recurrence in patients undergoing CRS+HIPEC.

METHODS: All patients who underwent CRS+HIPEC for intraperitoneal colorectal and appendiceal malignancies between 2010-2022 and had evidence of disease recurrence were examined utilizing a prospectively maintained, single-institution database. Patients with a completeness of cytoreduction (CC) score of 0/1 and complete tumor marker data were retrospectively reviewed for preoperative and postoperative carcinoembryonic antigen (CEA) levels. Time of recurrence was defined as date of radiographic evidence of recurrent intraperitoneal disease. The first postoperative CEA level following CRS+HIPEC was considered the patient's new baseline. CEA levels preceding the last level drawn prior to date of recurrence were normalized by the patient's new baseline level and compared to the last documented normalized CEA level prior to recurrence. An ROC was generated for CEA levels in patients with a CC 0 and a minimum of three postoperative CEA levels prior to recurrence, and Youden's index was used to define a percent increase in CEA level from postoperative baseline indicative of recurrent disease.

RESULTS: A total of 43 patients were included in this study. The median age of the CC 0/1 score cohort was 56 [IQR 48-64] with most of the cohort identifying as White (90.7%). Majority of patients (63%) had an elevated CEA (> 2.5 ng/mL) prior to CRS+HIPEC. The median preoperative CEA was 4.1 [IQR 1.9-10.7]. The median time from date of surgery to date of radiographic disease recurrence was 14.5 months [IQR 8.0-23.0]. A total of 27 patients with CC 0 were included in the model (FIGURE). The optimal threshold for percent CEA increase was determined to be 1.83. The median percent increase in CEA from postoperative baseline to prior to radiographic recurrence detection was 2.0 [IQR 1.2-4.2, p=0.03]. When compared to recurrence identified by imaging, the last drawn CEA level occurred a median of 16 days [IQR 2-73] earlier. Median overall survival for CC 0 patients was 63.3 months.

CONCLUSIONS: In a single-institution cohort of complete cytoreduction patients who underwent CRS+HIPEC for intraperitoneal malignancy, a CEA increase of 1.83 times their postoperative baseline level was identified as an indicator of disease recurrence. While validation with a large cohort is warranted, this study indicates that tumor marker thresholds can be used with imaging to measure recurrence free survival and could serve as valuable tools if implemented in clinical trials evaluating treatment strategies for intraperitoneal malignancies.



P30. External Validation of Basingstoke Prognostic Nomogram in Patients with Mucinous Appendix Cancer Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy

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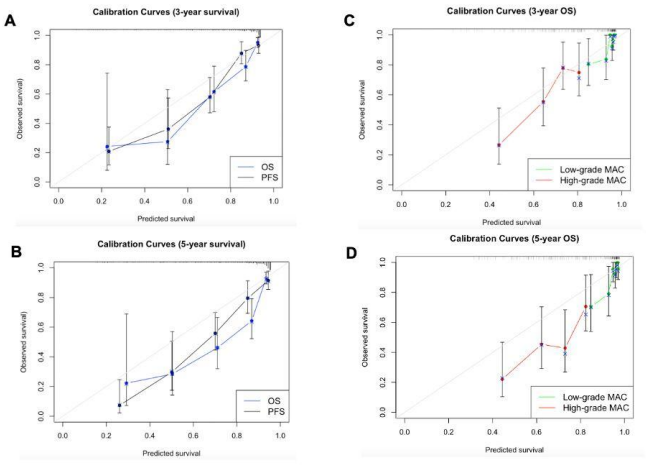
INTRODUCTION: Despite an existing consensus on cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) in mucinous appendix cancer (MAC), patient prognosis after the procedure remains variable. To address this, the Peritoneal Malignancy Institute Basingstoke (PMIB) developed a 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]: 46-65). 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).



MAC, mucinous appendix cancer; OS, overall survival; PFS, progression-free survival

P31. Hyperthermic intraperitoneal chemotherapy (HIPEC) with carboplatin vs. cisplatin-doxorubicin for stage III/IV ovarian cancer

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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.

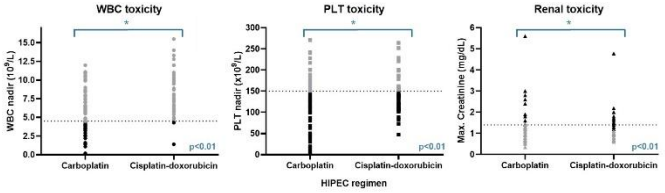

Figure 1. Hematologic and renal toxicities monitored for 30-days after CRS/HIPEC. Dashed lines denote cutoff values for toxicity based on the Common Terminology Criteria for Adverse Events. Black figures denote toxicity grade ≥1 and light gray figures depict absence of toxicity (grade 0). Asterisks denote statistical significance.
CRS: cytoreductive surgery, HIPEC: hyperthermic intraperitoneal chemotherapy, PLT: platelets, Max: maximum, WBC: white blood cells.

P32. Implementation of a Social Determinants of Health Screening Pilot in Patients with Peritoneal Malignancy
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INTRODUCTION: The updated 2022-2023 CMS Framework for Health Equity prioritizes collection of individual-level social determinants of health (SDOH) data to enhance access to equitable care for cancer patients. A pilot was launched in our cancer center's peritoneal surface multi-disciplinary clinic to assess feasibility of implementing standardized collection, reporting and analysis of SDOH data, with the goal of a system-wide rollout upon successful implementation.
METHODS: Between January and May of 2023, the EHR patient portal was leveraged to create and distribute a survey screening five SDOH domains (Figure). Operational workflow data were collected real-time and collated at the end of the study.
RESULTS: Overall survey completion rate was 62.9% (22/35) and 81.8% (18/22) were completed prior to the visit via the EHR portal. Median age was 54, and 57% identified as female. 51% (18/35) had appendiceal and 23% colorectal primary tumors. Three patients (8.6%) screened positive. 7.3 % (8/110) of unique responses across all five domains met scoring thresholds for referral to supportive care services (SCS). 100% of positive screens were connected to and received assistance from SCS within 7 days. The SDOH survey was incorporated into the Commission on Cancer-mandated Distress Screening questionnaire and implemented system-wide.
CONCLUSIONS: Incorporating SDOH questions into the EHR-portal and in-person workflow was feasible and led to successful screening and evaluation of patients with SDOH-related needs. Experience from the pilot enabled a cancer-center-wide rollout, which will improve the understanding and mitigation of disparities in healthcare access and delivery.

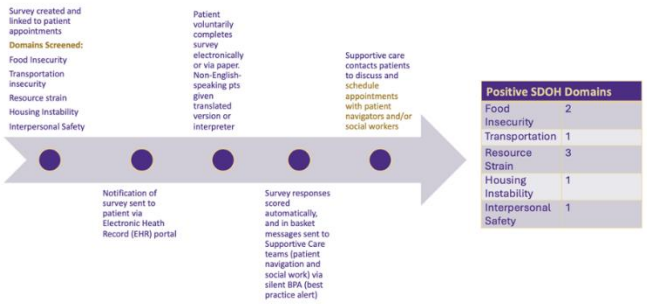

Figure: Workflow for implementation of the SDOH screening pilot

P33. Maintenance vs Adjuvant Systemic Therapy Following Cytoreductive Surgery and HIPEC for Peritoneal Carcinomatosis from Gastric Origin
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INTRODUCTION: Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) are increasingly investigated for peritoneal carcinomatosis (PC) from gastric adenocarcinoma (GAC). The role of adjuvant vs maintenance systemic therapy after CRS/HIPEC remains unknown.
METHODS: A retrospective review of a prospectively maintained database of patients who underwent CRS/HIPEC by a single surgeon was performed. Patients with PC from GAC were selected and divided into treatment groups based on the type of adjuvant therapy they received: no adjuvant therapy, adjuvant chemotherapy (AC), or maintenance chemotherapy (MC). Kaplan Meier analysis with log-rank test were performed to compare disease-free survival (DFS) and overall survival (OS) between the groups.
RESULTS: 13 patients met selection criteria, 10 (76.9%) were females, median age was 52, mean body mass index was 25.8±6.0, and median peritoneal carcinomatosis index (PCI) was 7. 11 (84.6%) had synchronous diagnoses of PC with the primary GAC in situ, whereas PC diagnosis was metachronous in 2 (15.4%). All patients received 6 months of neoadjuvant chemotherapy, had CC0/1 resection during their CRS/HIPEC, and none had a 30-day postoperative mortality. 5 patients (38.5%) received no adjuvant therapy following CRS/HIPEC, 4 (30.8%) had AC, and 4 (30.8%) had MC. Median PCI for the groups were 7, 5, and 4, respectively (Kruskal-Wallis, p=0.635). After a mean of 27.8 months of follow-up, median DFS was 6.0 vs. 5.9 vs. 54.3 months, respectively (p=0.008), and median OS was 8.1 vs. 13.0 vs. 67.0 months, respectively (p=0.006). One patient in the MC group had PCI 0 (positive peritoneal washing, no measurable disease) survived 96 disease with no evidence of disease after completing two years of MC. Multivariable backward conditional Cox regression analysis could not confirm the association of adjuvant therapy type with DFS or OS due to the small sample size.
CONCLUSIONS: Our limited data suggests that MC may have a role in improving DFS and OS in patients with PC from GAC primary compared to observation and possibly AC after neoadjuvant chemotherapy and complete CRS/HIPEC. Further investigation in trial setting is needed to confirm these findings.

P34. Optimizing Preoperative Evaluations for Patients with Colorectal Cancer with Peritoneal Metastases

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INTRODUCTION: The staging of colorectal cancer with peritoneal metastasis (CRCPM) presents a unique challenge for surgical oncologists. At presentation, a decision between palliative chemotherapy and neoadjuvant treatment with a plan for future metastasectomy is often required. This is especially difficult for CRCPM given the inherent difficulties of quantifying disease burden on cross sectional imaging. Currently, the definition of resectability requires a diagnostic laparoscopy (DL) or laparotomy. Given the morbidity associated with these procedures and associated delays in treatment initiation, we sought to identify factors associated with aborted or incomplete surgical resection in patients thought to be candidates for cytoreductive surgery (CRS).
METHODS: We performed a retrospective analysis of our institution's prospectively collected database of patients with CRCPM between 2017-2024. Patients with CRC and known or suspected PM who underwent pre-resection DL were included. Patient demographics, pre-operative evaluation including high-definition CT and/or MRI, CEA tumor marker, liquid biopsy/ctDNA, and peritoneal washings were collected. DL findings and surgical plans were examined. Univariate and multivariate analyses were performed to identify factors associated aborted CRS following DL.
RESULTS: We identified 124 patients with CRCPM who underwent staging DL between 2017-2024. Median age was 52, 62 were female (50%), and 94 had left sided colon or rectal adenocarcinoma (75.8%) and 62 had pre-operative liquid biopsy (50%). Among this cohort of patients considered for CRS, 25 (20%) had findings on DL not appreciated on preoperative workup. Of those, 22 did not ultimately undergo CRS or it was aborted (17.8%). On univariate analysis, patients with rectal cancer were more likely to be deemed unresectable following DL compared to those with left or right sided CRC (p=0.05). Patients with positive nodal metastases as seen on pre-operative imaging were also less likely to undergo resection following DL than those without nodal metastases (p=0.02). In addition, carrying mutations in TP53 and SMAD4 were associated with higher rates of aborted CRS (p=0.04 and P<0.01; respectively). On multivariable analysis, having nodal metastases seen on pre-operative imaging was associated with a significantly higher odds ratio for change in surgical plan and aborted CRS (OR 3.84, p=0.01).
CONCLUSIONS: CRCPM presents a major oncologic challenge. While preoperative high-definition imaging, detection of ctDNA and CEA may offer insight into a patient's disease course, they failed to predict an inability to resect in nearly 20% of patients. DL continues to offer a reliable and accurate tool for effective pre-operative planning and can help significantly minimize non-therapeutic laparotomy. DL should be considered in patients with high-risk features such as nodal metastases and TP53 or SMAD4 mutations.

P35. Outcomes Following "Failed" Diagnostic Laparoscopy in Patients with Peritoneal Carcinomatosis not Amenable to Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

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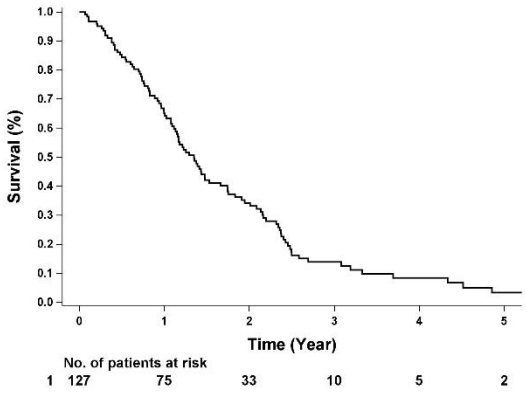
INTRODUCTION: Patients with peritoneal carcinomatosis have poor response to systemic therapy and poor prognosis. While cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) can improve survival, some patients are ineligible for CRS/HIPEC due to disease burden. This paper seeks to characterize the outcomes, including survival, treatment history, and cause of death, for patients who are evaluated by diagnostic laparoscopy (DL) but subsequently deemed ineligible for CRS/HIPEC based on burden and/or distribution of disease at one major referral center.
METHODS: Medical records were retrospectively reviewed for patients who were evaluated for CRS/HIPEC from 1/1/2009-1/1/2024. Those who underwent DL but were ultimately deemed ineligible for CRS/HIPEC due to burden of disease were included. Clinical data was extracted from chart review and date of death confirmed using publicly available obituaries. Treatment course and causes of death are summarized by descriptive statistics. Overall survival (OS) is characterized by Kaplan-Meier analysis.
RESULTS: One hundred and twenty-seven patients were included in the study cohort with a median age of 53.0 years. Median Peritoneal Cancer Index (PCI) score was 25 with 54 (42.5%) operative reports noting incomplete visualization/concern that PCI under-estimated disease burden. Forty-seven (37.0%) patients had washings for peritoneal cytology performed. Ninety-one patients (71.7%) underwent additional therapy. Median follow-up was 1.16 years (IQR 0.71 – 2.09). Median OS was 1.35 years. Sixty (47.2%) died of their malignancy while 43 (33.9%) had no cause of death documented. The most common causes of death were bowel obstruction (30, 23.6%), multifactorial/failure to thrive (22, 17.3%), and malignant ascites (15, 11.8%). Patients who underwent some form of additional therapy following their DL had prolonged OS compared to those who did not (1.48 versus 0.62 years, p<0.001) as did patients who enrolled in a clinical trial versus those who did not (1.91 versus 1.38 years, p=0.028). There was no significant OS difference based on primary pathology, PCI score, peritoneal cytology, or presence of hematogenous metastases.
CONCLUSIONS: OS for patients with peritoneal carcinomatosis from appendiceal or colorectal cancer who are assessed for CRS/HIPEC by DL but ultimately deemed ineligible is 1.35 years without significant variation based on primary pathology, PCI score, peritoneal cytology, or presence of hematogenous metastases. Those patients who can get some form of additional therapy following their DL have prolonged OS. The most common causes of death are bowel obstruction, failure to thrive, and malignant ascites.



P36. Overall and progression-free survival and treatment of recurrence after CRS-HIPEC for patients with malignant peritoneal mesothelioma

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INTRODUCTION: Background 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: 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: 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 not 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: Conclusion 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

P37. Pancreatic fistula after cytoreductive surgery and HIPEC: Incidence and risk factors at a high-volume center

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INTRODUCTION: Cytoreductive surgery and heated intraperitoneal chemotherapy (CRS/HIPEC) is an extensive surgical procedure with the potential for multiple postoperative complications. Postoperative pancreatic fistula (POPF) is a challenging complication in patients undergoing pancreatectomy. The incidence of POPF, and risk factors for its development, in patients undergoing CRS/HIPEC are not well understood. We sought to evaluate POPF incidence and risk factors in a cohort of patients undergoing CRS/HIPEC at an NCI-designated Cancer Center, with a goal of earlier POPF identification and management in at risk patients.
METHODS: We performed a single institution retrospective review over an 8-year period of patients undergoing CRS/HIPEC with distal pancreatectomy (DP)/splenectomy; splenectomy alone was used as a comparison group. Data were extracted for demographics, cancer diagnosis, and perioperative factors associated with extent of disease and completeness of cytoreduction (CC). POPF was defined as drain amylase >200U/L with continued drain requirement at discharge.
RESULTS: The cohort included 83 patients in total. We identified 50 patients who underwent CRS/HIPEC with DP/splenectomy and 33 undergoing splenectomy alone. Patients were 59% female, and median age was 56.8 (IQR 18.9). Most primary tumors were appendiceal in origin n=63 (75.9%). There were no differences in baseline demographics or perioperative factors between groups.

PCI values (20.5 vs 20.7, p=0.59), rates of CC-0/1 cytoreduction (80.0 vs 84.4%, p=0.62), and operative times (710 vs 772 mins, p=0.16) were also similar between the groups. The incidence of POPF in those undergoing DP/splenectomy was 60.0% vs 15.2% in those that had splenectomy alone (p<0.001). POPF were grade A (n=17, 48.6%) or B (n=17, 48.6%), with only one patient categorized as grade C. DP was associated with a 10-fold increase of POPF (OR 10.53, p<0.001). Patients with higher preoperative albumin (OR 0.88, p=0.044) and those who were transfused intraoperatively (OR 0.23, p=0.030) were less likely to have POPF. An elevated first postoperative drain amylase (median day 6) was associated with POPF (p=0.015), however, values of subsequent drain amylase levels were not. Additional drain placement was needed in 20 patients and was placed on POD day 15 (range 7-35).
CONCLUSIONS: Distal pancreatectomy is associated with a high risk of POPF in patients undergoing CRS/HIPEC. Lower preoperative albumin was associated with higher POPF. The first postop drain amylase may be helpful to guide subsequent drain management. This data supports making every effort possible to avoid pancreas resection during CRS/HIPEC.

P38. Partial Hepatectomy is Safe and Effective for Patients Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy
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INTRODUCTION: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) is traditionally 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 CRS-HIPEC on patient outcomes and survival remains unclear. This study aims to evaluate major morbidity and survival 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 from 2012-2023. Descriptive analysis using Chi-squared and t-test was performed to compare baseline characteristics between cohorts. Major morbidity 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 2415 patients were identified, of which 206 (8.5%) underwent concurrent hepatectomy while the majority (2,209, 91.5%) did not. 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 primary 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 cytoreductive surgery with or without hepatectomy as a component of their cytoreduction. These findings indicate that partial hepatectomy can be performed safely in conjunction with 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.

P39. Patient-Reported Financial Toxicity of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy
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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 it 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, pe<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.

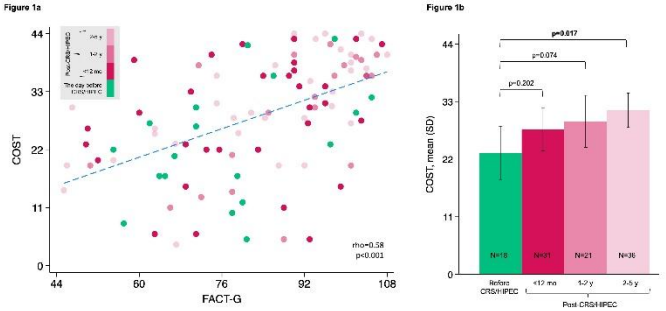

Figure 1a. The scatterplot illustrates individual data points for COST and FACT-G scores, representing financial toxicity and quality of life, respectively. The dashed line marks linear prediction. Spearman correlation analysis showed a significant moderate-to-strong correlation between COST and FACT-G (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.

BIPOC, black, indigenous, or people of color; CRS/HIPEC, cytoreductive surgery and hyperthermic intraperitoneal chemotherapy; mo, months; NACT, neoadjuvant chemotherapy; SD, standard deviation; y, years.

P40. Perioperative Chemotherapy in Stage IVA-B Appendiceal Cancer Undergoing Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy
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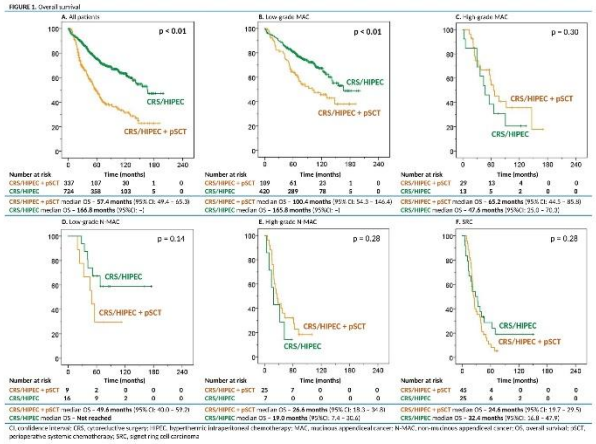
INTRODUCTION: Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is commonly accompanied by perioperative systemic chemotherapy (pSCT) to treat appendiceal cancer (AC) with peritoneal spread. However, the impact of pSCT on survival remains unclear with some small studies 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.



P41. Practice Setting Does Not Affect Survival in Patients Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Appendiceal Adenocarcinoma
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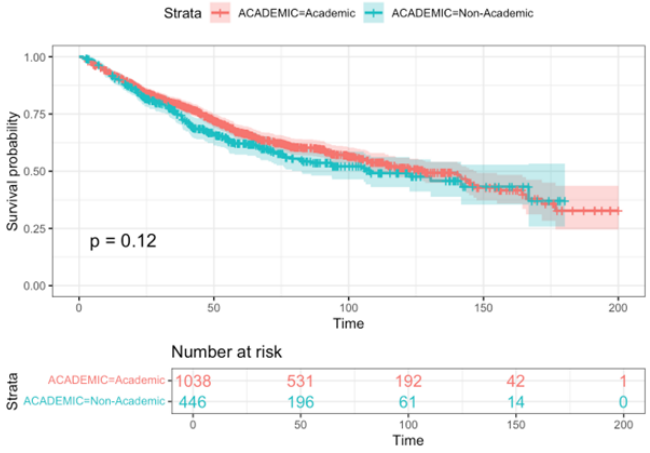
INTRODUCTION: The indications for, and volume of, cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) procedures continue to expand in the United States. This study examined the differences in outcomes of patients undergoing CRS-HIPEC for appendiceal adenocarcinoma based on practice setting type.
METHODS: Patients with appendiceal adenocarcinoma who underwent CRS-HIPEC were identified from the National Cancer Database (2006-2021). Patient demographics, tumor characteristics and postoperative outcomes were compared between academic vs. non-

academic facilities. The primary outcome was overall survival (OS). Multivariable Cox regression was used to determine the risk of mortality. Kaplan Meier curves compared OS between groups.
RESULTS: We identified 1,605 patients with appendiceal adenocarcinoma who underwent CRS-HIPEC (1,116 in academic setting and 489 in non-academic). The median age was 51 years, and the majority were female (53%), White (87%), and non-Hispanic (94%), with private insurance/managed care (62%). Academic centers had a higher proportion of patients traveling >50 miles (51% vs 21%; p<0.001) for treatment. Non-academic centers had a higher incidence of liver metastasis at diagnosis (14% vs 26%, p<0.001). Ninety-day mortality was higher in academic settings (3.9% vs 1.4%; p=0.013). There was no difference in 30-day mortality (0.5% vs 1.6%; p=0.075), readmission rate (7.0% vs 9.0%, p=0.30) or length of hospital stay (median 9 days for both groups; p=0.50). OS did not differ significantly (p=0.12). Including both types of centers, multivariate analysis demonstrated a higher risk of mortality among males (HR 1.51; 95% CI 1.21 – 1.88;0.001). Mortality risk was significantly lower in the highest income quartile (HR 0.56, 95% CI 0.38 – 0.81; p=0.009) vs lowest quartile, and mucinous histology had a better prognosis than non-mucinous (HR 0.31, 95% CI 0.23 – 0.40;0.001). Race (p=0.48), insurance status (p=0.39), academic settings (p=0.45), and urban-rural location (p=0.53) were not significant predictors of mortality.
CONCLUSIONS: No differences in OS were found based on practice setting type for patients undergoing CRS-HIPEC for appendiceal adenocarcinoma. Equivalent outcomes are likely related to surgeon experience and the presence of a comprehensive program in either practice setting type. The greater 90-day mortality observed in the academic cohort might be explained by higher complexity of cases.



P42. Prognostic factors and survival in peritoneal mesothelioma: contemporary outcomes from a high-volume institution

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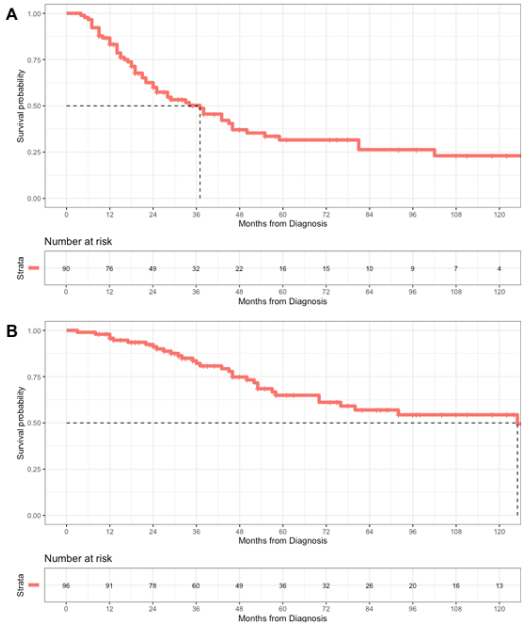
INTRODUCTION: Peritoneal mesothelioma (PeM) is a rare malignancy that has historically been associated with poor prognosis. In the appropriate patients, cytoreductive surgery (CRS) with intraperitoneal chemotherapy has been shown to improve survival. We evaluated survival outcomes and prognostic factors in a contemporary cohort of patients treated at our institution.
METHODS: Patients diagnosed with PeM between 2009 and 2023 and underwent curative-intent CRS with or without heated intraperitoneal chemotherapy (HIPEC) were identified. The peritoneal carcinomatosis index (PCI) and completeness of cytoreduction (CCR) score were determined at surgery. Recurrence-free survival (RFS), overall survival (OS), and associated factors were analyzed using standard statistical methods.
RESULTS: Of 96 patients, the median age was 52.5 (interquartile range [IQR] 42.5-62) years and 60 (62%) were female. The histologic subtype was predominantly epithelioid in 89 (93%) patients, while 7 (7%) patients had a biphasic subtype. Eight (8%) patients had a BAP1 germline mutation. Seven (7%) patients underwent CRS alone and 89 (93%) underwent CRS/HIPEC, most commonly with cisplatin monotherapy (n=85 [96%]). The median PCI was 20 (IQR 13-27). CCR-0 (no residual disease) was achieved in 48 (50%) and CCR-1 (residual disease <2.5 mm) in 42 (44%) patients. After a median follow-up time of 78 (95% CI 55-97) months, the median RFS time was 37 (95% CI 25-50) months, and the 5-year RFS rate was 31.6% (95% CI 22.1-45.1%). The median OS time was 125 (95% CI 76-not reached) months, and the 5-year OS rate was 65.0% (95% CI 54.7-77.2%). Increasing age and CCR score were associated with decreased RFS and OS. Male sex was associated with worse OS, but not RFS. PCI was not associated with survival outcomes.
CONCLUSIONS: Long-term survival can be achieved following CRS/HIPEC for PeM, and our findings reiterate the importance of complete cytoreduction. The differential outcomes by sex warrant further investigation. Future studies should focus on molecular characterization of PeM to improve prognostication and patient selection for curative-intent surgery.

Figure 1. Kaplan-Meier estimates of (A) recurrence-free survival and (B) overall survival in patients with peritoneal mesothelioma who underwent cytoreductive surgery +/- heated intraperitoneal chemotherapy



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P43. Reducing Disparities in Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: The Role of Enhanced Recovery After Surgery Protocols at a High-Volume Academic Institution

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INTRODUCTION: Enhanced recovery after surgery (ERAS) protocols have demonstrated significant benefits in reducing length of stay (LOS) and complications. Studies have demonstrated a reduction in disparities with perioperative care standardization. ERAS guidelines for cytoreductive surgery (CRS) +/- hyperthermic intraperitoneal chemotherapy (HIPEC) were published in 2020. Here we describe our experience with ERAS protocol implementation on minority patients undergoing CRS with or without HIPEC.
METHODS: ERAS order sets were developed by institutional multidisciplinary ERAS committee based on available best practice protocols for patients undergoing CRS with or without HIPEC for peritoneal surface malignancies. The order sets went live in the electronic health record (EHR) for these procedures on July 1, 2019. A Tableau dashboard using EHR data was developed to monitor utilization of order sets by service, with ability to drill down on individual providers and specific ERAS protocol components. A prospectively maintained retrospective database of patients undergoing CRS/HIPEC at a high-volume academic institution was queried from January 1, 2014, to June 1, 2024. Length of stay (LOS) and inpatient comorbidity were analyzed pre- and post-ERAS implementation by white and non-white patients.
RESULTS: A total of 779 patients queried from the institutional database with 387 in the pre-ERAS (prior to July 1, 2019) cohort and 392 in the post- eras cohort. Non-white patients accounted for 34.8% and 31.1% of the pre- and post-ERAS cohorts, respectively. Provider compliance was low in the first two fiscal quarters following initial implementation (<25%), but gradually increased to average monthly compliance >80% since May 2020. Prior to ERAS implementation, the median LOS was 9 days for both white and non-white groups and decreased to 8 (P <0.001). The inpatient comprehensive complication index (ICCI) for non-white patients was 13.5 in the pre-ERAS cohort and 10.9 in the post ERAS cohort (p = 0.16), while it remained relatively constant for white patients pre- and post- implementation (12.4 v. 12.2; p = 0.84).
CONCLUSIONS: These results demonstrate that ERAS implementation may modestly decrease relative disparities in postoperative morbidity observed between white and non-white patients undergoing CRS/HIPEC. More robust benefits may be limited due to the heterogeneity and complexity inherent with these procedures and existing experience of this high-volume institution.

P44. Robotic versus Open Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy: A Propensity Score-Matched Study

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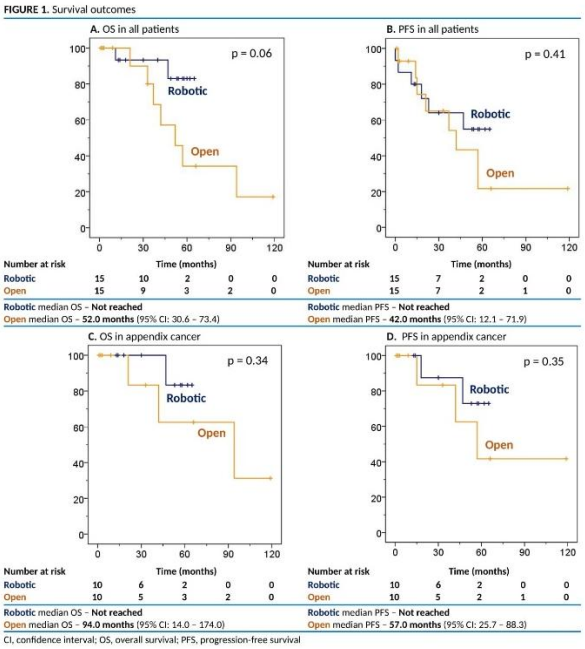
INTRODUCTION: Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is often associated with extensive surgical resection and has traditionally been performed via an open approach. However, in select patients with low tumor burden, a minimally invasive robotic approach can 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.



P45. Shaping surgical success: A qualitative analysis of attitudes towards prehabilitation for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy
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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 stake-holders, 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.

P46. The Atypical Presentation and Delayed Timing of Anastomotic Leak in Patients who Undergo Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy
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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.

P47. The Chatbot Will See You Now: Assessing the Quality of ChatGPT vs Google regarding Patient Centered Questions about HIPEC

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INTRODUCTION: Cytoreductive surgery and hyperthermic intraperitoneal chemoperfusion is an aggressive surgical procedure to treat peritoneal surface malignancies. Due to the complexity of the surgery, patients often turn to the internet for additional information. With the advent of AI, the resources available online have expanded, however, the quality of these may vary. This study aimed to assess the quality of ChatGPT compared to Google as a source of patient education by comparing answers to frequently asked questions regarding HIPEC.
METHODS: A Google search was conducted using the term "Hyperthermic Intraperitoneal Chemoperfusion (HIPEC)" to identify the 10 most common questions pertaining to this topic. Responses were recorded and references to each question were obtained from Google and ChatGPT. A survey-based approach was utilized to rate the quality of answers from both sources in a blinded manner and distributed to practicing surgical oncologists who perform HIPEC. Quality was scored from 1 (poor quality) to 5 (high quality), according to the Global Quality Scale (GQS). Differences in GQS for Google vs ChatGPT were compared using Wilcoxon matched pairs signed rank test.
RESULTS: All n=16 surgical oncologists who perform HIPEC operations who began the survey also completed it. The ten questions and the grades for each answer from Google and ChatGPT are shown in the attached Table. The average QPS for Google was 2.73, indicating that HIPEC surgeons assessed Google's answer as poor quality with important topics missing, and with limited use to patients. Alternatively, the average score for ChatGPT was 4.06, indicating good quality, that most important topics were covered, and that answers were useful to patients. All 16 (100%) respondents indicated ChatGPT as the source they would "recommend [their] patient to get healthcare information from." This final question offered the choice of either source as well as "none of the above.&rdquo
CONCLUSIONS: ChatGPT provided higher quality resources and information over Google to the most commonly asked questions regarding HIPEC. This study highlights the potential of AI platforms as a valuable source of information for patients and provides key insights to surgeons about the quality of sources patients may access while researching potential treatment.

Table: Questions and Global Quality Scores

	GQS (mean ± SD)		
Question	**Google**	**ChatGPT**	***p***
1. What is HIPEC?	3.50 ± 1.10	4.19 ± 0.75	0.0313
2. What is the survival rate for HIPEC surgery?	1.88 ± 0.72	3.94 ± 0.85	0.0001
3. How is HIPEC done?	2.50 ± 0.82	4.25 ± 0.77	0.0002
4. Is HIPEC risky?	2.25 ± 0.77	4.06 ± 0.93	0.0004
5. Is HIPEC surgery successful?	2.88 ± 0.81	3.56 ± 0.73	0.0566
6. Why is HIPEC controversial?	2.94 ± 0.77	4.19 ± 0.75	0.001
7. How long is the hospital stay after HIPEC?	3.19 ± 0.75	4.25 ± 0.58	0.0005
8. Why is HIPEC called the mother of all surgeries?	2.25 ± 1.06	4.00 ± 1.10	0.0002
9. Do you lose your hair with HIPEC?	3.19 ± 0.98	3.75 ± 0.68	0.1748
10. Who is not a candidate for HIPEC?	2.75 ± 0.86	4.44 ± 0.63	0.0001

GQS: global quality scores; SD: standard deviation

P48. The LOS-PCI Index: An exploratory benchmark metric for quality of care in cytoreductive surgery

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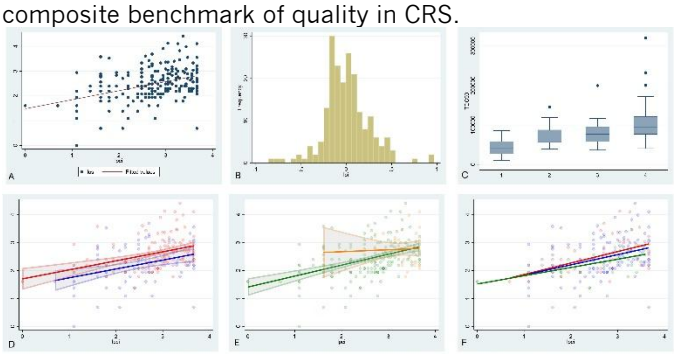
INTRODUCTION: Cytoreductive surgery (CRS) is a critical component in the comprehensive management of selected patients with peritoneal surface malignancies (PSM). Despite advancements in standardization and perioperative care pathways, the risk and cost associated with CRS remain high. Evaluating the quality of CRS across centers or within individual centers over time is limited by the complexity and heterogeneity of patients, as well as the lack of granular quality metrics. This study introduces an exploratory metric incorporating a ratio of length of stay (LOS) as an indicator reflecting perioperative outcomes to peritoneal carcinomatosis index (PCI) as a risk-adjustment measure of overall complexity.
METHODS: A total of 274 consecutive patients undergoing CRS for PSM at a single high-volume quaternary referral center between 2022 and 2024 were included. Patient demographic data, PCI, LOS, use of heated intraperitoneal chemotherapy (HIPEC), completeness of cytoreduction (CC) score, morbidity, mortality, and 90-day total direct cost (TDC) were collected 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, termed the "LOS-PCI Index" (LPI), was characterized and tested for association

with clinical and outcome variables using linear or logistic regression for continuous and 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-day 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<0.001); panel C. LPI varied by addition of HIPEC (p=0.001, Panel D), but not by completeness of cytoreduction (Panel E, p=0.9). Over the course of the three-year study, a trend toward stepwise improvement in LPI was observed (p=0.06, Panel F).
CONCLUSIONS: The LOS-PCI Index, an exploratory metric for programmatic evaluation in CRS, is easily calculated, closely correlates with morbidity, mortality and cost of care, and may be modifiable over time through perioperative care pathways and standardization. While no single performance indicator is likely to capture all facets of care for PSM patients, validation studies in independent series are planned to assess whether LPI has utility as a composite benchmark of quality in CRS.



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.

P49. Treatment Patterns for Patients with Non-Mucinous Appendix Cancer and Peritoneal Metastases: A National Cancer Database Study

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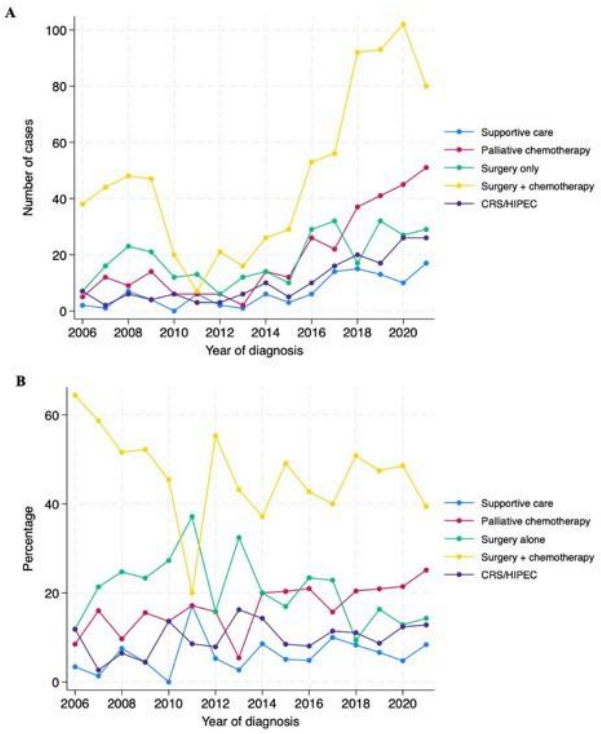
INTRODUCTION: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is the standard of care (SoC) for mucinous appendix cancer (MAC) with peritoneal metastases (PM). However, due to its rarity, the data on existing treatment patterns (TP) for non-mucinous appendix cancer (NMAC) 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 (61.5%) 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 (75.6%) 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 patterns in advanced NMAC by year of diagnosis.



CRS/HIPEC, Cytoreductive surgery and hyperthemic intraperitoneal chemotherapy; NMAC, non-mucinous appendix cancer

P50. Understanding the Quality of Life and Recovery of Patients Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy

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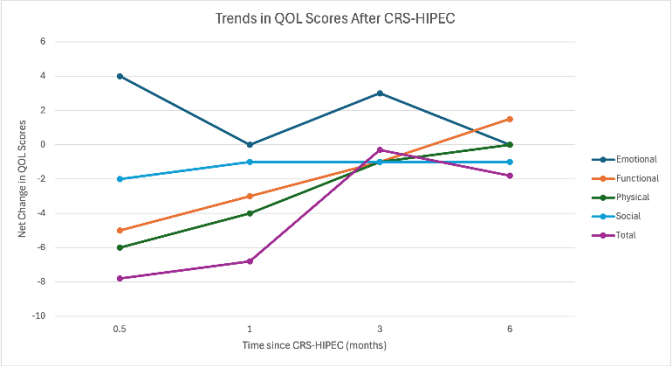
INTRODUCTION: Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) are complex, heterogeneous operations that can be difficult for patients to understand and prepare for. We aim to characterize patient experiences and quality of life (QOL) after CRS-HIPEC.
METHODS: A prospective, 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.&rdquo
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 go through it again. 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.



P51. Upfront Colectomy vs. Initial Appendectomy followed by Completion Colectomy for Appendiceal Cancer: Comparison of Outcomes

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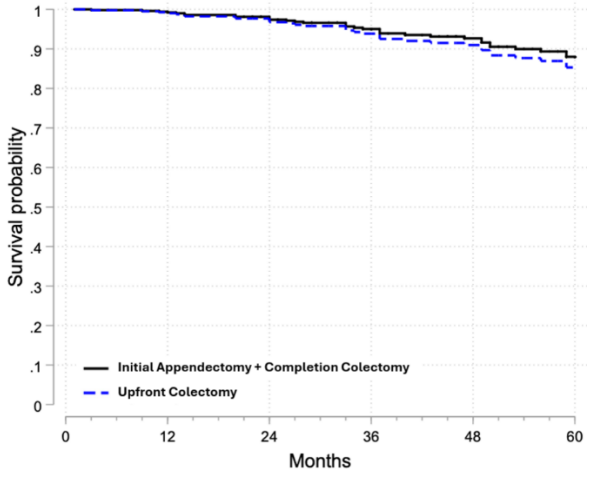
INTRODUCTION: The decision to perform right hemicolectomy for appendiceal tumors depends on histologic features of the primary tumor. A staged approach (initial appendectomy followed by completion colectomy - IA+CC) allows for histologic assessment of primary tumor and may avoid unnecessary right colectomy. 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.



P52. Whole genome sequencing reveals distinct mutational signatures in appendiceal cancer subtypes

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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. These differences may uncover tumor biology and guide therapy.
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 (SBS) and 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 SBS13 (cytidine deamination) and SBS18 (oxidative damage, possibly prognostic). GCAs showed contributions from SBS17a/b, linked to oxidative stress, 5-FU exposure, and genomic instability. These signatures have also been associated with worse prognosis and increased metastasis, particularly in GI cancers. MUCs had the highest mutational burden (23,156 variants/sample), with notable SBS88, associated with colibactin exposure from E. coli, potentially indicating microbiome-driven mutagenesis linked to colorectal cancer. 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 had a heterogeneous landscape, with some showing SBS3, suggesting homologous recombination deficiency. 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. ADs exhibit oxidative damage (SBS18), which may have important prognostic value. SBS17a/b in GCAs is linked to oxidative stress and chemotherapy exposure, suggesting a more aggressive disease course. MUCs may reflect microbiome-driven mutagenesis. SRCs exhibit genomic instability, with SBS3 indicating potential sensitivity to PARP inhibitors. 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.

ePoster: Sarcoma/Melanoma

P53. Adoption of Immunotherapy in Clinical Stage III Cutaneous Melanoma in the United States

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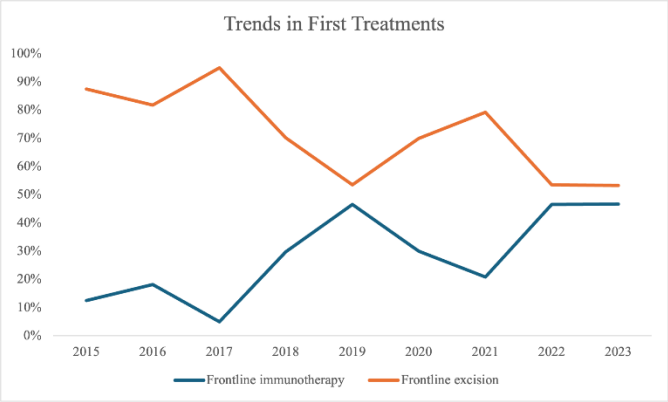
INTRODUCTION: Cutaneous melanoma has seen significant advancements in therapeutic options over the past decade, particularly with the advent of CTLA-4-, PD-1-, and PD-L1-directed immunotherapy. While surgical excision remains the cornerstone of treatment for early stage melanoma, recent studies suggest an oncologic benefit of immunotherapy for advanced disease in both the adjuvant and neoadjuvant settings. This study aimed to analyze trends in the transition from adjuvant immunotherapy to neoadjuvant immunotherapy in patients presenting with clinical stage III cutaneous melanoma.
METHODS: We queried the TriNetX database, a real-world database consisting of over 100 million patient records in the United States, for cases of cutaneous melanoma diagnosed after January 1, 2015. Cases were identified using ICD-10 codes identifying cutaneous melanoma and linked with CPT codes identifying excision and medication codes identifying immunotherapy. Patients with clinical stage III (Tany, N1+) disease were included in the study. Patients were excluded if they were diagnosed with N1c, N2c, N3c, or M1 disease to further identify the surgical cohort. Usage of neoadjuvant immunotherapy versus upfront excision was evaluated. The Chi-squared test for trend was used to compare proportions of neoadjuvant immunotherapy in 2015 and 2023.
RESULTS: A total of 471 patients met inclusion for the study. The mean age was 66 years, 555 (92%) were White, and 370 (61.4%) were male. Three hundred fifty patients (74.3%) underwent upfront excision while 121 (25.7%) received neoadjuvant immunotherapy. One hundred fifty-nine patients (33.8%) underwent excision first, with a

median time to treatment 35 days from diagnosis, followed by adjuvant immunotherapy. Twelve patients (2.5%) received immunotherapy followed by excision, while 85 (18.1%) received immunotherapy only. Of those who received neoadjuvant immunotherapy, 61 (13.0%) had first line pembrolizumab, 40 (8.5%) had first line nivolumab, and 15 (3.2%) had first line nivolumab and ipilimumab. In 2015, 12.5% of clinical stage III patients received neoadjuvant immunotherapy, with 46.7% of patients receiving neoadjuvant immunotherapy in 2023 ($p<0.001$).
CONCLUSIONS: This study highlights a significant shift in the management of clinical stage III cutaneous melanoma over the recent decade, with a notable increase in the adoption of neoadjuvant immunotherapy. While surgical resection remains the curative-intent treatment modality, the proportion of patients receiving immunotherapy as the first treatment has risen substantially, reflecting the ubiquitous role of immunotherapy in melanoma management. These findings underscore the evolving treatment landscape and the importance of continued research to optimize therapeutic strategies for patients with locally advanced cutaneous melanoma.



P54. Complete Metastasectomy of Skin or Soft Tissue Metastases for Recurrent Melanoma in the Modern Era of Immunotherapy
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INTRODUCTION: Historically, complete surgical expiration has been critical in the management of recurrent and advanced melanoma in the era that preceded effective systemic immunotherapy that exists today. Long-term survival has been reported in the range of 20 to 40% in those with resectable recurrent disease. Soft tissue and skin metastases are usually associated with improved survival compared to nodal or distant visceral, lung, or brain metastases. With the development of effective targeted and checkpoint blockade immunotherapy, the most aggressive systemic therapy boasts long-term survival up to 50%, raising the question of the importance of surgery in the management of resectable recurrent melanoma metastases in the era of modern immunotherapy. The objective of this study is to evaluate the role of complete metastasectomy of skin or soft tissue melanoma metastases in the era of modern immunotherapy.
METHODS: Patients treated at an academic center from 2011 to 2024 with melanoma recurrence were identified using a retrospective IRB-approved database. Demographics, recurrence site, tumor characteristics, immunotherapy use, and extent of surgery, and overall survival were analyzed. Descriptive statistics were performed, and Kaplan Meier method was used to estimate overall survival.
RESULTS: A total of 85 melanoma patients were found to have recurrence. The most common sites of recurrence include skin (n = 41, 48.2%), soft tissue (n = 16, 18.8%), and lymph nodes (n = 29, 34.1%). The majority of recurrences were unifocal (70.6%, n = 60) while 29.4% (n = 25) were multifocal. Among those with soft tissue/skin recurrences, 37 (43.5%) patients underwent curative-intent treatment. Surgery only was performed in 27 (73%) patients while 10 (27%) patients were treated with both surgery and immunotherapy. There were no differences in survival between those treated with surgery only and those treated with both surgery and immunotherapy (83% vs 53%, P=0.159).
CONCLUSIONS: In the era of effective modern checkpoint blockade and targeted therapy, surgery alone can confer similar outcomes as those treated with both surgery and immunotherapy for patients with resectable soft tissue or skin melanoma recurrences. Further investigation is warranted to understand the role of metastasectomy for other sites of melanoma recurrences. Surgery alone can be considered for those with resectable soft tissue or skin metastases who are poor candidates for systemic immunotherapy.

P55. Defining the Role of Systemic Immunotherapy for Clear Cell Sarcoma
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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

P56. Detection of Recurrence in Stage II and III Melanoma Patients Using Point of Care Ultrasound

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INTRODUCTION: Despite guidelines for nodal surveillance with ultrasound (US) in sentinel node positive stage III melanoma patients, the role of US is not clarified for Stage II patients nor for Stage III patients with in-transit or clinically positive melanoma. The aim of this study was to assess the diagnostic value of point-of-care (POC) US in detecting Stage II and III melanoma recurrences in comparison with clinical assessment and axial imaging.
METHODS: A single-institution retrospective review was conducted of patients presenting with Stage II and III melanoma from 03/2010 - 06/2024. Chart review identified patients with disease recurrence (classified as local, lymph node, in-transit, or distant); diagnostic method for recurrence detection (clinical assessment or imaging); imaging modality (US, PET or PET/CT, CT, or MRI). We defined detection by clinical assessment a finding on physical exam or a finding on imaging that was ordered based on an elicited patient symptom. We also assessed the rate of detection for each modality for locoregional recurrences and rate of concurrent distant metastases.
RESULTS: There were a total of 207 patients identified with Stage II melanoma of whom 39 recurred (18.8%) and a total of 202 patients identified with Stage III melanoma of whom 67 recurred (33.1%). In the overall cohort, 55.7% of recurrences were detected with clinical assessment (61.5% in Stage II and 52.2% in Stage III). POC US 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). Locoregional recurrence made up 62 (58.5%) of recurrences (64% Stage II and 55% Stage III) of which 41 (66.1%) were identified clinically, 15 (24.2%) were identified with US and 6 (9.7%) were identified with axial imaging (Figure 1). Of the locoregional recurrences detected via clinical assessment, 7 (17.0%) were associated with distant metastases on further work up and of the 6 locoregional recurrences identified on axial imaging, 2 (33%) also had distant metastases. Of the 15 locoregional recurrences discovered by POC US, 0 were found to have distant metastases upon further workup.
CONCLUSIONS: POC US identified 24% of locoregional recurrences, with axial imaging detecting fewer locoregional recurrences than clinical exam or US. In our cohort, POC US identified isolated locoregional recurrences without concurrent distant disease. The majority of recurrences were detected clinically highlighting the importance of clinical surveillance. Additional cost-benefit analysis may further inform the value of incorporating routine POC US with clinical evaluation in melanoma surveillance.

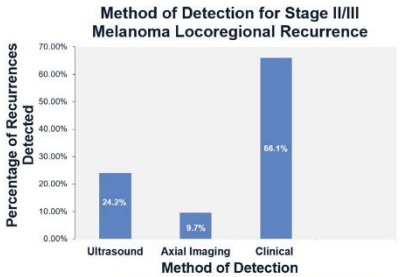

*Figure 1: **Method of detection of Stage II and III melanoma locoregional recurrence.** Clinical examination detected 66.1% of locoregional recurrences, while POC US detected 24.2% and axial imaging detected 9.7%.*

P57. Effect of Metastasectomy on survival in patients with metastatic Gastric Gastrointestinal Stromal Tumors

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INTRODUCTION: The survival benefit of surgery in metastatic Gastric Gastrointestinal Stromal Tumor (gGIST)

is still unclear. The objective of this study was to compare survival in primary site surgery and metastasectomy in gGIST patients.
METHODS: The NCDB (2004-2017) was evaluated for metastatic gastric GIST resections. Patients who had systemic therapy only were compared to those who had systemic therapy and primary site or primary and metastatic site resection. Patient demographics and treatment variables were compared. Kaplan-Meier and log rank analysis was implemented to compare survival across groups. Cox-proportional hazard model was used to determine predictors of survival in each group
RESULTS: Out of 1,203 patients with metastatic gGIST, 723 patients had systemic therapy only, 305 patients had systemic therapy and primary site surgery, and 175 patients had systemic therapy, primary site surgery, and metastasectomy. A larger portion of those who did not receive surgery were uninsured and underwent palliative care compared to those who did receive primary site surgery or metastasectomy. A larger portion of patients who received metastasectomy were younger than the age of 63, in contrast to other groups. There was no difference in distributions of sex, race, comorbidity index, median income, high school graduate status, geographical location, or radiation treatment between groups. There was a statistically significant decrease in survival in those who received systemic therapy alone compared to those who received systemic therapy and surgery (40.4 vs 104 months, HR = 2.51, p < 0.01) (Fig. 1A). There was no significant difference in survival for surgery at primary site alone compared to surgery for both primary site and metastases (90.7 vs 117 months, HR = 1.13, p = 0.47) (Fig. 1B). Factors associated with improved overall survival in patients who received surgery at the primary site alone include female sex (HR = 0.65), having private insurance (HR = 0.39), and a higher median income (HR = 0.77). For patients who also received metastasectomy, improved overall survival was associated with having private insurance (HR = 0.03), Medicare (HR = 0.06), or Medicaid (HR = 0.06). All mentioned variables met statistical significance on multivariate analysis (p < 0.05).
CONCLUSIONS: Surgery significantly improved survival in metastatic gGIST. Surgery for metastatic site may not have additional survival benefit. Further studies are needed to elaborate on surgery for specific metastatic sites to assess its value.

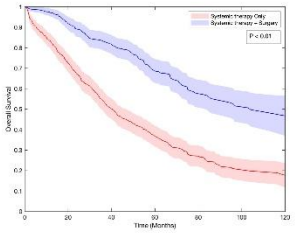

Figure 1A

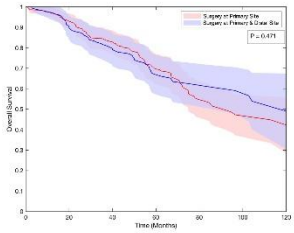

Figure 1B

P58. Impact of Insurance Patterns on Survival in Patients with Solitary Fibrous Tumors
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INTRODUCTION: Background: 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: 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: 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: Conclusion: 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.

P59. Laparoscopic assisted cryoablation of abdominal wall desmoid fibromatosis, case series and local experience.
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INTRODUCTION: Desmoid tumors (DTs) are rare, non-metastatic but locally aggressive connective tissue neoplasms. Standard treatments include surgery, radiation, and ablation, though current guidelines recommend active surveillance unless tumors progress or

symptoms worsen. Cryotherapy has shown potential in treating DTs, but its use in rectus abdominis tumors is limited due to proximity to critical structures. This study presents three cases where laparoscopic-assisted cryoablation was applied to rectus abdominis DTs, a technique not previously reported, and its clinical outcome.
METHODS: Three patients with progressing rectus abdominis DTs underwent laparoscopic-assisted cryoablation. Tumor visualization and safety were enhanced using laparoscopic guidance during percutaneous cryoablation. Data on patient demographics, procedure details, complications, and postoperative outcomes were collected, and tumor characteristics were analyzed with imaging before and after treatment.
RESULTS: The mean tumor size was 7.4 cm, and an average of 14 probes were used per case. Two patients experienced full symptom resolution postoperatively, while one had a complication requiring embolization due to an inferior epigastric artery injury. Follow-up imaging at three months showed significant tumor shrinkage and necrosis in two patients. The third case had increased tumor volume due to hematoma formation, though cryoablation was still radiologically successful.
CONCLUSIONS: Laparoscopic-assisted cryoablation appears to be a feasible and promising technique for rectus abdominis DTs, particularly when concerns about intra-abdominal injury exist. Early results suggest effective symptom control and tumor response, though further research is needed to confirm long-term outcomes.

P60. Minimal-invasive isolated limb perfusion
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INTRODUCTION: In patients diagnosed with melanoma, approximately 4-10% will develop in-transit metastasis (ITM). Surgical resection is an option if the number of tumors is limited, but if this is not feasible or the tumors are rapidly recurring, isolated limb perfusion (ILP) or isolated limb infusion (ILI) are established treatment options. This study presents the feasibility of a novel technique that combines the benefits of both methods: minimal-invasive ILP (MI-ILP).
METHODS: A prospective cohort study including 17 patients undergoing MI-ILP, 14 patients were diagnosed with melanoma ITM, one with squamous cell carcinoma, one with sarcoma and one with Merkel cell carcinoma. Percutaneous vascular access of the extremity vessels was performed, and the inserted catheters were then connected to a perfusion system and the extremity was perfused with melphalan. A detailed video presentation of the technique will be shown. Response was evaluated by modified RECIST 1.1 criteria for cutaneous metastases, and toxicity graded according to the Wieberdink classification.
RESULTS: The median age of patients was 69 years (range, 64 -76). Patients had on average three ITMs (range, 1 – 8) and the average size of their largest tumor was 15 mm (range, 4 -250). None of the patients had evidence of synchronous lymph node metastasis, but one patient had systemic metastases. All patients underwent the procedure without the need for conversion to an open procedure. In one of the 17 patients, perfusion was not possible due to a high leakage through the bone-marrow, and response was evaluable in 16 of 17 patients. Nine of 16 patients (56%) had a complete response, 5 of 16 (31%) a partial response and 2 of 16 (13%) showed progressive disease. Local toxicities were: grade I (6%), grade II (56%), grade III (32%), and grade IV (6%).
CONCLUSIONS: This series of 17 patients shows the feasibility of minimal-invasive ILP. One patient had a high leakage, and for the first time the exact route could be visualized. In this early report, MI-ILP gives the same treatment characteristics as open ILP, but with the advantage of a minimal invasive vascular access.

P61. Multimodality Management of Desmoplastic Small Round Cell Tumor Offers the Potential for Improved Outcome
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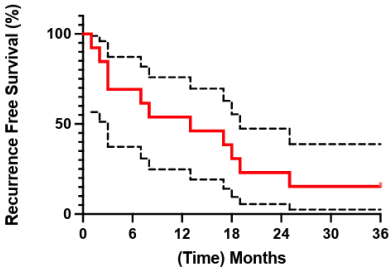
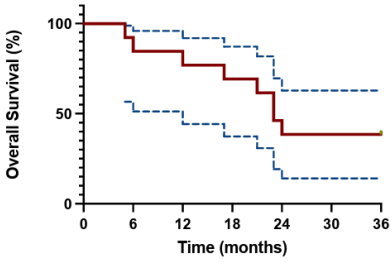
INTRODUCTION: Desmoplastic small round cell tumor (DSRCT) is a rare intra-abdominal sarcoma affecting adolescents and young adults. Neoadjuvant chemotherapy followed by cytoreduction and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) and adjuvant radiotherapy may offer improved local control. 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.



3 Year Recurrence Free Survival



3 Year Overall Survival

P62. Pharmacokinetics of intratumoral tigilanol tiglate in soft tissue sarcoma: data from a Phase IIa clinical trial

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INTRODUCTION: Tigilanol tiglate (TT) is an epoxytigliane diterpene small molecule being studied as an intralesional therapeutic given its effect on tumor cells, tumor vasculature and the immune environment with promising activity observed in multiple tumor types. Here we present the pharmacokinetic analyses of a Phase IIa study (NCT05755113) to assess the efficacy of intratumoral injections of TT in patients with advanced/metastatic soft tissue sarcoma (STS).
METHODS: We analyzed data from a single center, single arm, open label study which enrolled 11 patients with STS of the extremities and body wall. TT was dosed at 0.5 mg per 1.0 cm3 tumor, with maximum dose not to exceed 3.6 mg/m2 body surface area. Tumor volume was measured by ultrasound. Blood samples for pharmacokinetic studies were collected pre-treatment and at 5 timepoints in the 24 hours after the first TT injection. The area under the concentration-time curve (AUClast), defined from pre-dose to time of last quantifiable concentration and calculated using the linear-log trapezoidal rule, was studied for association with patient and tumor characteristics.
RESULTS: Pharmacokinetic data was analyzed from 9 evaluable patients, 3 with undifferentiated pleomorphic sarcoma, 3 with leiomyosarcoma, and the remainder with other histologies. Total tumor volume measured from 1.3 cm3 – 77.16 cm3. The mean volume of injected tumor was 8.8 cm3. Maximum TT concentration was achieved soon after dosing at a median of 5 minutes. The mean half-life of TT was 2h. The individual dose normalized Cmax ranged from 4.09 to 55.51 ng/mL, and the dose normalized AUClast ranged between 4.83 and 77.44 hr*ng/mL. For 6 out of 9 patients, more than 90% of the drug was eliminated by 4h; all the patients had 84% or more of the drug eliminated by 4h. The AUClast was significantly associated with the total dose of TT (p=0.05) and total size of the injected tumor(s) (p=0.05). Two reports of grade 1 and grade 2 flushing each were in the 6 patients with the highest AUClast. All reports of grade I fevers and flu-like symptoms were in 3 patients with the highest AUClast.
CONCLUSIONS: Patients with STS who underwent intratumoral injections of TT demonstrated rapid clearance of the drug. Measurable concentrations of TT in plasma were observable in all patient samples from 5 min until 4h post-dose, with four patients demonstrating small but observable concentrations at 24h post treatment. Flushing, fever and flu-like symptoms may be associated with higher systemic exposure of TT. Given the short half-life of TT, an expansion cohort to explore more frequent dosing is planned.

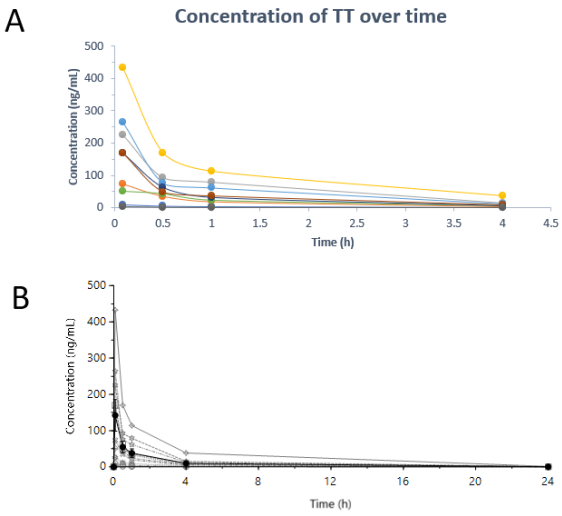

Figure 1: Plasma concentration of TT over time with individual curves representing each patient enrolled in trial. Concentration of TT was determined from blood samples collected at 5 minutes, 30 minutes, 1 hour, 4 hours (A) and 24 hours post treatment (B).

P63. Population-based experience of neoadjuvant treatment for patients with gastrointestinal stromal tumors (GIST)

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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%)

P64. The Impact of Talimogene Laherparepvec (T-VEC) on Survival in In-Transit Disease From Acral Lentiginous Melanoma

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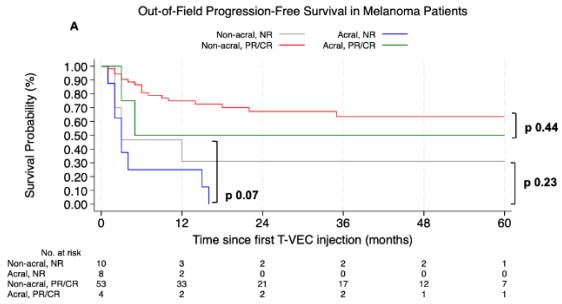
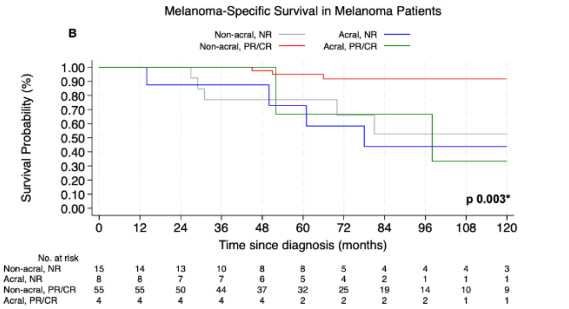
INTRODUCTION: Talimogene laherparepvec (T-VEC) is an intralesional oncolytic virus approved for treatment of metastatic melanoma to cutaneous, subcutaneous, and nodal sites. T-VEC is proven to result in high local response rates, but less is known about response to T-VEC injection in metastases from 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).

* denotes significance (p<0.05)





P65. The use of radar-guided localization to identify metastatic melanoma after neoadjuvant therapy

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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).