# 2020 Gastrointestinal Cancers Symposium

## Guide to Abstracts

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1 Oral Abstract Session, Sat, 10:45 AM-12:15 PM
Pembrolizumab for advanced anal squamous cell carcinoma (ASCc): Results from the multicohort, phase II KEYNOTE-158 study. First Author: Aurelien Marabelle, Gustave Roussy, INSERM U0105, Villejuif, France
Background: For patients (pts) with ASCc, second-line or later treatment options have been limited. Pembrolizumab (pembro), an anti-PD-1 monoclonal antibody, has demonstrated antitumor activity in several tumor types (including ASCc) in the multicohort phase Ib KEYNOTE-028 study, KEYNOTE-158 (NCT02628067) is an open-label, phase 2, multicohort study that evaluates antitumor activity and safety of pembro in pts with previously treated advanced cancer. Results from the ASCc cohort are presented. Methods: Eligible pts were ≥18 y with histologically/cytologically documented metastatic and/or unresectable ASCc with prior treatment failure on or intolerance to standard first-line therapy, measurable disease per RECIST v1.1, ECOG PS of ≤1, and evaluable tissue sample for PD-L1 and biomarker analysis. PD-L1 expression was assessed by the PD-L1 IHC 22C3 pharmDX assay (Agilent Technologies). Pts received pembro 200 mg Q3W until disease progression, unacceptable AE, or completion of 35 cycles. The primary endpoint was ORR per RECIST v11 (assessed every 9 wk for 12 mo, then every 12 wk thereafter) by independent central review. Secondary endpoints were DO, OS, PFS and safety. Results: 112 pts with ASCc were enrolled (813% women; median age, 61 y [range 32-79]; ≥2 prior therapies, 73.2%). At database cutoff (Dec 6, 2018) 10 pts (8.9%) had completed 35 cycles and 102 discontinued; median follow-up was 12.0 mo (range, 0.8-33.0) Five pts had CR and 8 had PR; ORR was 11.6% (95% CI, 6.3-19.9%). Median DO was not reached (range, 6.0+ to 29.1+ mo). Responses occurred in 11/75 (14.7%) pts with PD-L1 combined positive score (CPS) ≥1 and 2/30 pts (6.7%) with PD-L1 CPS < 1. Among all pts, median OS was 12.0 mo (95% CI, 9.1-15.4), and median PFS was 2.0 mo (95% CI, 2.0-3.1). 68 (60.7%) pts had treatment-related AEs, including 21 (18.8%) who had grade 3-5 events; there were no treatment-related deaths. 4 pts (3.6%) discontinued due to treatment-related AEs. 27 pts (24.1%) had immune-mediated AEs/infusion reactions. Conclusions: Pembrolizumab demonstrated antitumor activity and manageable toxicity in pts with heavily pretreated advanced ASCc, regardless of PD-L1 status. Clinical trial information: NCT02628067. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

2 Poster Session (Board #A5), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM
Allele frequencies of two dihydropyrimidine dehydrogenase (DPYD) risk variants, c.1905+1G>A (2A) and c.2846A>T (D949V), in a direct-to-consumer genetic database. First Author: Cindy Kosinski, 23andMe, Sunnyvale, CA
Background: Pharmacogenetic (PGt) testing holds great potential for supporting clinical decision making and optimizing medication outcomes for cancer patients. Genetic variants in the DPYD gene are associated with reduced dihydropyrimidine dehydrogenase enzyme activity, and can cause severe fluoropyrimidine-related toxicity. However, the clinical uptake of PGt testing has been slow. Recent FDA authorization for a direct-to-consumer (DTC) PGt test will improve access to PGt testing. This study assessed the overall allele frequencies of DPYD c.1905+1G>A and c.2846A>T (D949V), in a generally unselected group of genotyped individuals who have used DTC genetic testing (23andMe, Inc. Sunnyvale, CA). Methods: Study participants were genotyped using Illumina genotyping arrays that included the DPYD c.1905+1G>A and c.2846A>T variants. Eligible subjects were >50 years of age and consented to participate in research. IRB approval was obtained from Ethical & Independent Review Services. Results: Out of approximately 6.4 million eligible participants included in this analysis, the overall allele frequencies of DPYD c.1905+1G>A and c.2846A>T were 0.42% and 0.47%, respectively. People of Ashkenazi Jewish, South Asian, and Eastern descent had the highest frequencies (0.56%, 0.56%, and 0.47%, respectively) for the DPYD c.1905+1G>A variant, and people of European and Hispanic/Latino descent had the highest frequencies (0.55% and 0.43%, respectively) for the DPYD c.2846A>T variant. Conclusions: This is the first description of an unselected cohort of individuals with DPYD c.1905+1G>A and c.2846A>T variants identified through DTC genetic testing. Preemptive DTC PGt testing can help disseminate potentially clinically useful information to a large number of consumers. Research Sponsor: 23andMe.

3 Poster Session (Board #A6), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM
Chemoradiation-related lymphopenia and its association with survival in patients with anal cancer. First Author: Grace Lee, Harvard Medical School, Boston, MA
Background: While treatment-related lymphopenia (TRL) is common and associated with poorer survival in multiple solid malignancies, little data exists for anal cancer. We evaluated TRL and its relationship with survival in anal cancer patients, addressing the gap of available clinical data (CDT). Methods: A retrospective analysis of 140 patients with non-metastatic anal squamous cell carcinoma (SCC) treated with definitive CRT was performed. Total lymphocyte counts (TLC) at baseline and monthly intervals up to 12 months after initiating CRT were evaluated. Cox regression analysis was performed to evaluate the association between overall survival (OS) and TRL, dichotomized by g TRL (< 0.2k/μl) two months after initiating CRT. Kaplan-Meier and log-rank tests were used to compare OS between patients with versus without g TRL. Results: Median time of follow-up was 55 months. Prior to CRT, 95% of patients had a normal TLC (> 1k/μl). Two months after initiating CRT, there was a median of 71% reduction in TLC from baseline and 84% of patients had TRL: 1% G, 31% G2, 34% G3, and 8% G4. On multivariable Cox model, g TRL at two months was associated with a 3.7-fold increased risk of death (p = 0.013). On log-rank test, the 5-year OS rate was shorter in the cohort with versus without g TRL at two months (32% vs. 86%, p < 0.001). Conclusions: TRL is common and may be another prognostic marker of OS in anal cancer patients treated with CRT. The association between TRL and OS supports the hypothesis that host immunity plays an important role in survival among patients with anal cancer. These results support ongoing efforts of randomized trials underway to evaluate the potential role of immunotherapy in localized anal cancer. Research Sponsor: None.

4 Poster Session (Board #A7), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM and Poster Walks, Sat, 12:30 PM-11:15 PM
Enhanced microbial diversity and chemoradiation response in HPV+ anal cancer. First Author: Ramez Kouzy, University of Texas MD Anderson Cancer Center, Houston, TX
Background: Anal cancer is a rare, but treatable, malignancy caused by the human papilloma virus (HPV). Because anal cancer is uncommon and carries a significant social stigma, this disease has rarely been studied in a prospective fashion, creating a large gap of which is white (<1% of CRT). Methods: A retrospective analysis of 140 patients with non-metastatic anal squamous cell carcinoma (SCC) treated with definitive CRT was performed. Total lymphocyte counts (TLC) at baseline and monthly intervals up to 12 months after initiating CRT were evaluated. Cox regression analysis was performed to evaluate the association between overall survival (OS) and TRL, dichotomized by g TRL (< 0.2k/μl) two months after initiating CRT. Kaplan-Meier and log-rank tests were used to compare OS between patients with versus without g TRL. Results: Median time of follow-up was 55 months. Prior to CRT, 95% of patients had a normal TLC (> 1k/μl). Two months after initiating CRT, there was a median of 71% reduction in TLC from baseline and 84% of patients had TRL: 1% G, 31% G2, 34% G3, and 8% G4. On multivariable Cox model, g TRL at two months was associated with a 3.7-fold increased risk of death (p = 0.013). On log-rank test, the 5-year OS rate was shorter in the cohort with versus without g TRL at two months (32% vs. 86%, p < 0.001). Conclusions: TRL is common and may be another prognostic marker of OS in anal cancer patients treated with CRT. The association between TRL and OS supports the hypothesis that host immunity plays an important role in survival among patients with anal cancer. These results support ongoing efforts of randomized trials underway to evaluate the potential role of immunotherapy in localized anal cancer. Research Sponsor: None.
Utility of circulating tumor DNA (ctDNA) versus tumor tissue clinical sequencing for enrolling patients (Pts) with advanced gastrointestinal (GI) cancer to matched clinical trials: SCRUM-Japan GI-SCREEN and GOZILA Combined Analysis. First Author: Yoshiaki Nakamura, National Cancer Center Hospital East, Kashiiwa, Japan

Background: Blood-based genomic profiling by ctDNA analysis has a promise to potentially identify actionable genomic alterations. However, utility of clinical sequencing with ctDNA compared with that with tumor tissue for enrolling cancer pts to matched clinical trials remains unclear. Herein we investigated the utility of ctDNA clinical sequencing by the SCRUM-Japan GI-SCREEN and GOZILA Combined Analysis. Methods: In the GI-SCREEN, tumor tissue samples of pts with advanced GI cancer were analyzed by a next generation sequencing (NGS)-based assay, Oncomine Comprehensive Assay since Feb 2015. In the GOZILA, plasma samples of pts with advanced GI cancer were analyzed by an NGS-based ctDNA assay, Guardant360 since Feb 2018. Tests were performed centrally by CLIA-certified and CAP-accredited laboratories. Pts with actionable alterations were enrolled to matched company-sponsored or investigator-initiated clinical trials. Results: As of Apr 2019, test results were generated in 5,029 out of 5,743 pts (88%) in GI-SCREEN and 1,089 out of 1,133 pts (99%) in GOZILA (P < 0.0001). Median turnaround time (TAT) was 35 days in GI-SCREEN and 12 days in GOZILA (P < 0.0001). There were no differences in other baseline characteristics between GI-SCREEN and GOZILA. Proportion of enrolled matching clinical trials in GOZILA was significantly higher than that in GI-SCREEN (12% vs 3% respectively, ORR: 17.5 vs. 16.7%, median PFS: 1.00 vs. 1.00, each P = 0.24). Conclusions: Clinical sequencing with ctDNA having the advantage of the shorter TAT enrolled more pts with advanced GI cancer to matched clinical trials than those with tumor tissue, while compromising neither efficacy. Clinical trial information: UMIN000029315.

Reception and survival outcomes by age following second-line therapy for metastatic CRC (mCRC): Analysis of 5,289 patients from the ARCAD Clinical Trials Program. First Author: Nadine Jackson McCleary, Dana-Farber Cancer Institute, Boston, MA

Background: Rates and survival outcomes for second-line therapy for mCRC for OA vs. YA are poorly understood. Methods: Pts with available subsequent treatment data after progression from first-line therapy were included. Associations between key clinical/disease characteristics, time to initial progression (TTiP) and rate of receipt of second-line therapy were evaluated. Time to progression (TTP) and overall survival (OS) were compared between OA and YA who were enrolled on second-line trials by categorizing adjusting for age, sex, ECOG PS, number of metastatic sites, presence of metastatic liver/ peritoneum. Results: OA comprised 16.4% of first-line trials. OA and EOCG PS >0 were less likely to receive second-line therapy than YA. Odds of receiving second-line therapy decreased by 11% for each additional decade of life in multivariate analysis (p=0.017). OA enrolled in second-line trials experience similar mTTP and mOS as YA (5.1 v. 5.2mos; 11.6 vs 12.4mos, respectively). Conclusions: OA are less likely to receive 2nd line therapy for mCRC. We did not observe a statistical difference in survival outcomes for OA vs. YA following second-line therapy. Further study is needed to examine unmeasured factors, including comorbidity and functional status given observed inferior outcomes among adults with EOCG PS >0, and consideration given to inclusion of geriatric assessment to select OA likely to benefit from 2nd line therapy for mCRC. Research Sponsor: NIH/NCI Gastrointestinal Spore Dana-Farber/Harvard Cancer Center.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Background: In stage III colon cancer patients treated with CAPOX, 3 months of therapy was as effective as 6 months. It was not the case for those receiving mFOLFOX6. We assessed the prognostic and predictive value of the Immunoscore (IS) in the mFOLFOX6 subgroup (90% of patients enrolled) of the IDEA France cohort study (PRODIGE-GERCOR). Methods: 1200 patients randomly assigned to 3 months (n = 593) or 6 months (n = 607) of mFOLFOX6, with available tumor sample, were included. Densities of CD3+ and cytotoxic CD8+ T-cells in the tumor and invasive margin were determined by immunohistochemistry, quantified by digital pathology, and converted to IS using the pre-defined cut-off.

The IS performance to predict disease-free survival (DFS) was assessed in each arm and adjusted in multivariate Cox models.

Results: In a two-category IS analysis, Low and (Int+High) IS were observed in 423 (43.5%) and 550 (56.5%) patients, respectively. Low IS was associated with ORR (P = 0.0007) when compared with T/N stage. A statistically significant interaction was observed for the IS predictive value for treatment duration (3 vs 6 months) in term of DFS in the whole population (P = 0.0566) and TN subgroups (Low-risk T1, N1 vs High-risk T4 and/or N2; P = 0.05). In patients with (Int+High) IS in the 3-month arm, the 3-year DFS was 71.5% (95% CI 65.7–76.6) versus 83.8% (95% CI 78.8–87.8) in the 6-month arm (HR = 0.528; 95% CI 0.372–0.750; log-rank P = 0.0004); the benefit retained in low-risk and high-risk patients (all P < 0.01). 6-month mFOLFOX6 showed no significant benefit for patients with Low IS (HR = 0.836, log-rank P = 0.269). Conclusion: The IS prognostic value in patients treated with mFOLFOX6 was confirmed. Its predictive value for benefit of longer duration treatment, despite a strong statistical signal, needs to be confirmed in an external validation cohort. Clinical trial information: NCT03422601. Research Sponsor: GERCOR.

11 Rapid Abstract Session, Sat, 7:00 AM-7:45 AM and Poster Session (Board #A2), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Nivolumab plus low-dose ipilimumab as first-line therapy in microsatellite instability-high/DNA mismatch repair deficient metastatic colorectal cancer: Clinical update. First Author: Heinz-Josef Lenz, University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA

Background: In the phase 2 CheckMate 142 trial, nivolumab plus low-dose ipilimumab demonstrated durable and clinically meaningful benefit. Results: Patients with mCRC from the CheckMate 142 trial were assigned to nivolumab plus low-dose ipilimumab or nivolumab alone. Treatment was switched to nivolumab monotherapy for mCRC after disease progression or discontinuation. The primary endpoint was investigator-assessed objective response rate (ORR). Results: For all patients (n = 455), median progression-free survival (PFS) was 7.7 months (95% CI 6.0–11.6) and OS was 24.0 months (95% CI 20.9–27.1). In the 6-month arm, median PFS was 7.2 months (95% CI 6.1–11.6) and OS was 24.0 months (95% CI 19.6–27.1). The 2-year OS rate was 44.1% (95% CI 35.6–52.1) and was 33.8% in the 3-month arm (95% CI 24.9–42.6). Conclusion: Nivolumab plus low-dose ipilimumab may represent a new first-line treatment option for patients with mCRC. Clinical trial information: NCT02060188. Research Sponsor: Bristol-Myers Squibb.

1ORR** in Overall Patients and Subgroups.

Nivolumab plus low-dose ipilimumab

<table>
<thead>
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<th>ORR (%)</th>
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<td>14/22 (64)</td>
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<tr>
<td>12/27 (46)</td>
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Prior adjuvant/neoadjuvant therapy

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<td>0.729 (63)</td>
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Mutation status

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KRAS mutation

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Extended response, duration, and safety data are still pending. Updated survival data will be presented. Previous ORR (median 12.9 months) was confirmed in all patients. Updated data will be presented. Updated survival data will be presented.

1Median follow-up defined as time on study from first dose to data cutoff, which was 13.8 months (range 9–19).

2Previously reported.

1ORR defined as the objective response rate (complete response + partial response) according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. (NCT02060188).

2Median follow-up defined as time on study from first dose to data cutoff, which was 13.8 months (range 9–19).

3Previously reported.
A computed tomography-based nomogram for preoperative prediction of synchronous peritoneal carcinomatosis in colorectal cancer. First Author: Zixu Yuan, The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Background: Peritoneal carcinomatosis (PC) of colorectal cancer remains one of the most aggressive and treatment-resistant forms of cancer. Early detection of PC can bring survival benefit for patients with synchronous PC both in the training set and test set. A nomogram based on five preoperative predictors of PC was created. This CT-based nomogram showed good diagnostic performance by calibration curve. The decision curve analysis suggested that this CT-based nomogram was clinically useful.

Conclusions: The CT-based nomogram has shown great potential in the detection and diagnosis of synchronous peritoneal metastasis in colorectal cancer. Research Sponsor: Natural Science Foundation of China (NSFC) grant (No. 8157120115, 81803163), Natural Science Foundation of Guangdong Province (2018A030310320 and 2018A030310319) and Key Grant (No. 2016A03031021).

14 Poster Session (Board #A8), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

15 Poster Session (Board #A9), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Clinical utility of comprehensive circulating tumor DNA (ctDNA) testing compared to standard-of-care (SoC) tissue testing in first-line (IL) metastatic colorectal cancer (mCRC) patients (pts). First Author: Manuel Benavides, Hospital Universitario Regional y Virgen de la Victoria, Malaga, Spain

Background: Accurate genotyping is mandatory for the management of mCRC pts. Tissue-based genotyping is still the SoC; however, it is not available for all pts. and may be exhausted by serial testing, resulting in incomplete genotyping. We aimed to establish the validity of comprehensive non-invasive ctDNA testing in IL mCRC pts for whom SoC tissue genotyping was available.

Methods: IL mCRC pts were tested with a comprehensive ctDNA test (Guardant360), a RAS ctDNA test (OncoBeam), and SoC tissue testing at the time of diagnosis. The primary endpoint was NCCN guideline biomarker discovery rate (KRAS, NRAS, and BRAF mutations, ERBB2 amplification, and microsatellite instability). Results: In 91 evaluable pts, the biomarker discovery rate was 54.9% (53/94) for SoC tissue testing, 59.3% (54/91) for comprehensive ctDNA testing (p = 0.0318 for non-inferiority vs. SoC), and 42.9% (39/91) for RAS ctDNA testing (inferiority not rejected vs. SoC). Both comprehensive and RAS ctDNA testing showed high positive agreement (85%, 44/52, and 86%, 37/43) and negative predictive agreement (96%, 268/279, and 93%, 93/100) relative to SoC tissue testing at the gene level. Expanding genotyping beyond KRAS codon 12/13 mutations increased biomarker discovery rate by 4% for tissue testing (50/91 vs. 32/42, McNemar’s p = 0.0001) and by 64% for comprehensive ctDNA (34/91 vs. 33/91, McNemar’s p = 0.0001). Turnaround time was significantly shorter for comprehensive ctDNA testing vs. SoC tissue testing (mean 11.7 days vs. 23.0 days, paired t-test p = 0.0002). On retrospective analysis, 92% of biomarker-positive pts would have been identified at 2 weeks using the comprehensive ctDNA test for initial genotyping with reflex to tissue for biomarker-negative pts, whereas initial use of SoC tissue testing would have identified only 85% of positive pts at 4 weeks (Fisher’s exact p = 0.0000). Conclusions: As previously reported for lung cancers, comprehensive ctDNA testing in IL mCRC identifies many biomarker-positive pts as SoC tissue genotyping with high concordance to tissue and in half the turnaround time. Research Sponsor: Guardant Health.

16 Poster Session (Board #A10), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

The impact of mismatch repair status to the preoperative staging of local colon cancer: Implications for clinical management. First Author: Torben Hansen, Danish Colorectal Cancer Center South, Vejle Hospital, Vejle, Denmark

Background: Colorectal cancer (CRC) is the third most common cancer and the second most common cause of death from cancer worldwide. Early detection of CRC can bring survival benefit for patients.

Methods: Data from the Danish Colorectal Cancer Group national clinical database addressing a cohort of patients operated for stage I-III colon cancer (n = 296) with a higher degree of over-staging assessed by CT-scan, compared to a reference cohort. A retrospective study of 296 patients operated at a specialised cancer centre were available for analyses. A dMMR was determined with a recently developed targeted DNA sequencing panel (Guardant360), a comprehensive ctDNA test (OncoBeam), and SoC tissue testing at the gene level.

Results: The dMMR status was significantly associated with the ease of genotyping. The accuracy of preoperative CT lymph node staging of colon cancer. Tumours with a deficient mismatch repair (dMMR) status had a higher degree of over-staging assessed by CT-scan, compared to a reference cohort. A retrospective study of 296 patients operated at a specialised cancer centre were available for analyses. A dMMR was determined with a recently developed targeted DNA sequencing panel (Guardant360), a comprehensive ctDNA test (OncoBeam), and SoC tissue testing at the gene level.

Conclusions: The impact of dMMR status to the preoperative staging of local colon cancer is significant. Research Sponsor: mProbe.

17 Poster Session (Board #A11), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Expression of antibody-drug conjugates (ADC) biomarkers in colorectal cancer. First Author: Sheeno P. Thyparabimil, OncoPlex Diagnostics, Culver City, MD

Background: Multiple ADCs are in clinical trials for CRC and the optimal strategy for selecting patients who may benefit from the treatment is evolving. Due to the unique mechanism of ADCs, patient selection should include testing for the expression of ADC-specific markers of resistance or response to the payload. We have built a multiplexed ADC biomarker panel in FFPE tumor tissue that simultaneously quantifies the protein levels of the antibody targets and also the payload markers.

Methods: FFPE tumor tissues from 363 CRC patients were microdissected and solubilized for mass spectrometry-based targeted proteomic analysis in our CLIA certified laboratory. We quantified protein levels of EGFR, HER2, HER3, Axin, Mesothelin, FRalpha, Trop2 (antibody targets), tubulin-beta3 and TOP1 (payload resistance and response markers, respectively) simultaneously. The multiplexed assay also quantified additional 22 clinically relevant proteins.

Results: Expression of EGFR(83%), HER2(52%), HER3(21.5%), Axin(14.7%), Mesothelin(26.5%), FRalpha(3.7%), and Trop2(59.8%) may indicate likely response to ADCs. Expression of TUBB3 (+) and TOP1 (≥1350a/mg/μL) in antibody target-positive subset may suggest resistance or response to payloads, such as taxanes and irinotecan, respectively (Table). Previously, we identified that HER2 expression >750a/mg/μL correlated with HER2 positivity. Accordingly, 1.4% (5/355) of CRC patients were HER2 positive, of which 40% (2/5) had TOP1 expression >1350a/mg/μL (75th percentile) suggesting that these 2 patients may receive benefit from a HER2/TOP1 ADC. (+) indicates expression ≥LOQ; (-) indicates expression <LOQ. Conclusions: In patients with CRC, quantitative proteomics identified both antibody targets and markers of resistance or response to payloads for multiple approved and investigational ADC therapies. Research Sponsor: mProbe.
A 13-ene colorectal cancer liquid biopsy with greater than 90 percent accuracy in diagnosis and assessment of disease status. 

**Background:** There are a paucity of blood-based biomarkers with clinical utility for colorectal cancer (CRC) We report here a 13-ene colon cancer circulating-free mRNA to diagnose CRC and identify disease burden and status. Clinical utility of the assay was assessed in surgical and chemotherapy patients.

**Methods:** Gene identification and validation: Publicly available colon cancer transcriptomes (TTs) (E-MTAB-57); gene expression in 3 CRC cell-lines (Lovo, IEC and DLD-1) (n=32) and validated in CRC tissue (n=42) . Tumor TT analysis: co-expression network generation and differential expression analysis compared with normal blood-based TT to identify candidate markers. Blood gene expression: CRC set (controls, n=312, controls n=117) and a CRC artificial intelligence model constructed. Normalized gene expression algo- rithmically scored (0-100). Matched tumor/ blood samples were available in 33 patients. RECIST criteria Clinical score assessment: Score utility was assessed in surgical and treated cohorts: Surgical: n=37, follow-up =7 days. Treated chem- otherapy: n=75; stable disease (SD): n=20, progressive disease (PD): n=55.

The relationship to CA and CA-19-9 were assessed. Statistics: Non-parametric (Mann-Whitney), Pearson-correlation, Fisher’s and AUROC analyses (Mean ±SEM). Results: Transcriptomic analysis identified a3 genes blood signature for CRC. Expression levels were significantly elevated (p<0.001, 20±100-fold) in cell lines and CRC tumors. The matched tissue/blood correlation r: 0.795 (p=0.002). In CRC, levels were 54.4±15 (p=0.0001) compared to controls (9.5±17); AUROC: 0.91±0.02, accuracy 90.5%, sensitivity 91.3%, specificity 81.2%. Surgical cohort: CRC assay accuracy 100% vs CEA (35%) or CA-19-9 (3%); paired germline and matched deep whole transcriptomic sequencing (RNA- Seq) (~20×106 reads per tumor) data from NantHealth was performed. Best Cancer Intrinsic Subtypes based on RNAseq was used to classify CRC into 5 BC subtypes. CRC classifier: 15.0% as Luminal B, 13.1% as Luminal A, and 1.8% as Basal-like. Surprisingly, there were no differences in HER2 (HER-E), 15/16 (9.0%) had over-expression of ERBB2 by RNAseq as CN gain, which is con- sistent with published data of HER2+ CRC. ERBB2 is very significantly up-regulated compared with HER2- subtype CRC (p<0.001), more than ERBB2 CN gain, suggesting that HER2-E may be more HER2 driven. Across subtypes APC and TP53 were the most commonly mutated genes at 65.3% and 52.6% respectively, however both were more enriched in HER2-E CRC (APC OR=3.3, p<0.001, TP53 OR=2.6, p=0.007). Other known drivers of CRC such as PIK3CA, KRAS, and BRAF, were not differentially mutated in HER2-E CRC, however NRTAS were significantly more enriched in non-HR-E CRC (OR=4.6, p=0.02). Additionally, over expressed TP53 over-expression and CN gain, PAM50-like gene classifier identifies a high rate of significantly elevated HER2-E CRC (99.67% ± 59%) which may represent an under appreciated population for HER2 directed therapy and clinical trials. Research Sponsor: NantHealth.

Rate of conversion from unresectable to resectable metastatic colorectal cancer (mCRC) in real-world patients (RWP) treated with FOLFIRI ± bevacizumab: A population-based retrospective cohort study. First Author: Tayyaba Bhatti, College of Medicine, University of Saskatchewan, Saskatoon, SK, Canada

**Background:** Recent evidence from randomized trials suggests that FOLFIRI (S5U, oxaliplatin, and irinotecan) ± bevacizumab is associated with higher re- sponse rates with a potential for conversion of unresectable to resectable disease in mCRC. Yet limited evidence is available about efficacy and safety of this regimen in RWP with mCRC. The current study aims to evaluate conversion rate and safety of FOLFIRI ± bevacizumab in RWP with unresectable mCRC.

**Methods:** Each year about 175 patients are diagnosed with mCRC in Saskatchewan. Based on FISH or IHC. Intrinsic molecular subtype is used to classify cancers into distinct biologic subtypes (eg. CMS 1-4 in CRC). A 50-gene cancer classifier: 15.0% as Luminal B, 13.1% as Luminal A, and 1.8% as Basal-like. Surprisingly, there were no differences in HER2 (HER-E), 15/16 (9.0%) had over-expression of ERBB2 by RNAseq as CN gain, which is con- sistent with published data of HER2+ CRC. ERBB2 is very significantly up-regulated compared with HER2- subtype CRC (p<0.001), more than ERBB2 CN gain, suggesting that HER2-E may be more HER2 driven. Across subtypes APC and TP53 were the most commonly mutated genes at 65.3% and 52.6% respectively, however both were more enriched in HER2-E CRC (APC OR=3.3, p<0.001, TP53 OR=2.6, p=0.007). Other known drivers of CRC such as PIK3CA, KRAS, and BRAF, were not differentially mutated in HER2-E CRC, however NRTAS were significantly more enriched in non-HR-E CRC (OR=4.6, p=0.02). Additionally, over expressed TP53 over-expression and CN gain, PAM50-like gene classifier identifies a high rate of significantly elevated HER2-E CRC (99.67% ± 59%) which may represent an under appreciated population for HER2 directed therapy and clinical trials. Research Sponsor: NantHealth.

Real-world costs of cetuximab + chemotherapy administered every two weeks versus 4 weeks of metastatic colorectal cancer. First Author: Chris Pescott, Global Evidence and Value Department, Merck KGaA, Darmstadt, Germany

**Background:** Cetuximab (CET) 250 mg/m2 weekly (q1w) after an initial dose of 400 mg/m2 added to chemotherapy (CT) is licensed for treatment of KRAS wild-type metastatic colorectal cancer (mCRC). In the real-world administration of CET+CT, costs associated with treatment regimens (TPT) were compared averaging 2 weeks (q2w) is common. We compared healthcare costs between q2w and q4w in a US claims database study. Methods: A cohort of 2,943 mCRC patients CET-treated between 2010 and 2016, identified in IBM MarketScan, was analyzed for costs associated with CET+CT q2w vs q4w. All-category costs (ACC), stratified by overall outpatient (OO), inpatient (OI), and pharmacy (OP) costs during the exposure period, were compared between groups. Additionally, subcategories of CRC- and skin toxicity (CT)-related claims were explored, and imputation of capitated claim costs was performed. Patients were weighted by the stabilized inverse probability of treatment (IPTW) based on a high- dimensional propensity score to control for confounding. Generalized linear models (GLMs) with gamma distributions were used to compare regimens. Inflation-adjusted costs (2016 US dollars) are presented per patient per month ($PPPM) with 95% CIs.

<table>
<thead>
<tr>
<th>Mean SPPM (D)</th>
<th>GLM ratio q2w vs Clw (CI)</th>
<th>p valuea</th>
</tr>
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<tbody>
<tr>
<td>Cost category</td>
<td>q2w</td>
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<tr>
<td>ACC112,289</td>
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a Two-sided test for difference in mean IPTW costs from the GLM with a 5% type I error rate.

Visit qicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Overall survival of cetuximab administered every two weeks versus weekly in real-world data of U.S. patients with metastatic colorectal cancer. First Author: Chris Pescott, Global Evidence and Value Department, Merck KGaA, Darmstadt, Germany

Background: Cetuximab (CET) administered weekly (q1w) at 250 mg/m², after an initial dose of 400 mg/m², is approved in combination with the mohypophyseal (CT) for the treatment of (K)RAS wild-type metastatic colorectal cancer (mCRC). The use of CET 500 mg/m² administered with CT every 2 weeks (q2w) is according to US clinical practice guidelines and observed routine. In this study, we compared q2w vs q1w regimens on overall survival (OS) in a presumed first-line (TL) treatment cohort and present updated data on the noninferiority of q2w vs q1w in line-agnostic (IL) + treatment using US real-world data. Methods: Using IBM MarketScan, a large US insurance claims database, we classified a cohort of mCRC patients treated between 07/2010 and 12/2016 with CET q1w or q2w based on observed infusion patterns. Absence of mCRC-related treatment claims preceeding CET initiation date (defined as the index date) qualified as CET treated in IL. A validated algorithm was used to determine patient death. Confounding was accounted for using high-dimensional propensity scoring (hdPS) with inverse probability of treatment weights. OS was compared using Cox proportional hazards re-gression. Imbalanced confounders under hdPS were added to the Cox model. In IL +, noninferiority of the q2w regimen was tested with a margin hazard ratio (HR) of 1.25. However, noninferiority could not be tested in IL due to the small sample size; a test for difference was instead used. Results: Of 2,730 CET exposed mCRC patients (updated, 1,779 (62.5%) and 951 (34.8%) were classified in q1w and q2w groups, respectively, among which 557 (33.1%) and 316 (33.2%) received CET in IL. The HR (95% CI) for OS of q2w vs q1w in IL was 1.10 (0.92-1.31), crude, and 1.05 (0.86-1.29; adjusted; p for difference: 0.625). In IL +, crude and adjusted HRs were 1.05 (95% CI 1.04-1.18) and 0.94 (0.85-1.03), re- spectively, rejecting the noninferiority hypothesis at p < 0.001. Conclusions: Only a third of patients received CET in IL in this study. OS was statistically noninferior in q2w vs q1w in IL, and adjusted results in IL suggest no differences between both treatment schedules. However, more data would be needed to formally test the noninferiority hypothesis in IL. Research Sponsor: Merck KGaA.

Exploreatory analysis of trifluridine/tipiracil in late-stage metastatic colorectal cancer (mCRC): Prognostic factors. First Author: Meinolf Karthaus, Hematology, Oncology, and Palliative Medicine, Klinikum Neuperlach and Harlaching, Munich, Germany

Background: Trifluridine/Tipiracil (FTD/TPI) is effective in pts with refractory metastatic colorectal cancer (mCRC) treatment by prognostic factors in the real world setting. Methods: This cohort included mCRC pts who were treated with FTD/TPI from 01/2016 until 08/2019 at two large volume CRC centers in Germany. Pts were classified with good prognosis characteristics (GPC) according to Tabernero et al. (abstract 677, ASCO-GI 2019) defined by 1 or 2 metastatic sites and time since diagnosis of first metastases > 18 mo. Results: A total of 44 mCRC pts (31 GPC and 13 PPC) were included in this analysis and treated with FTD/TPI. Six pts had a normal BMI (18-24.9), 17 pts had an overweight BMI (25–29.9) and obese BMI (≥ 30) pts had a trend towards improved mortality (HR 0.67, 95% CI 0.46-0.98) (HR 0.75, 95% CI 0.53-1.07) respectively. The p-value was 0.0675. We also found that pre-existing diabetes mellitus is associated with increased all-cause mortality (HR 1.43, CI 1.03 to 1.98, p < 0.05), as well as the use of aspirin at diagnosis (HR 1.60, CI 1.16 to 2.21, p < 0.05). Conclusions: Our results are similar to previous findings that patients with overweight status have worse mortality outcome, suggesting the importance of nutritional status prior to starting treatment. We also found that overweight and obese patients have trends towards improved survival compared to normal weight patients. Future focus can be directed to see whether overweight or obesity status past diagnosis affect survival trends. Aspirin use at diagnosis in our study population is associated with worse mortality outcome; literature is conflicting with outcomes and pre-diagnosis aspirin use. Our findings are similar for both locoregional colon cancers as well as metastatic disease. Research should be directed at seeing what kind of interventions such as nutrition or rehabilitation can be used to ameliorate the increased mortality trend in the overweight status group of patients. Research Sponsor: None.
Hyperthermic intraperitoneal chemotherapy post cytoreductive surgery in management of peritoneal carcinomatosis of colorectal primaries: Tertiary center experience. First Author: Ahmed Badran Sobh, Ain Shams University Hospital, Cairo, Egypt

Background: Hyperthermic intraperitoneal chemotherapy (HIPEC) in addition to Cytoreductive surgery (CRS) has shown benefit in overall survival (OS) in management of Peritoneal Carcinomatosis (PC) from Colo-rectal cancer (CRC). We report the origin we the outcomes and prognostic factors of patients with CRC who presented with PC and underwent CRS and HIPEC at King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia. Methods: Patients presented with PC from CRC origin and underwent CRS and HIPEC; from February 2009 to September 2015 were recruited. Results: 52 patients identified. A total of 55 CRS procedures were performed, where 3 patients underwent repeated CRS and HIPEC for tumor recurrence. All except 3 used mitomycin-C for HIPEC, the remaining received either melphalan (2 patients) or cisplatin plus mitomycin-C regimen (1 patient). Melphalan used for patients who underwent repeated HIPEC as 2nd line chemotherapy agent. Intraoperative Radiation therapy performed in 5 patients with tumor invading the surrounding structures, where performing a safe or complete resection was either technically difficult or carried high risk. Complication assessment by Clavien-Dindo score, 62% grade (I-II), while 31% had grade (III). Two patients (3.6%) died postoperatively; both from sepsis. Respiratory complications were the most commonly encountered morbidities. The 5-year overall survival (OS) was 50% with disease free survival (DFS) 29.5%. Univariate analysis showed poor OS and DFS encountered in; Signet-ring tumors (p < 0.0001) for both, peritoneal cancer index (PCI) (p = 0.003) for both, completeness of cytoreduction (CC) score >1 (p < 0.0001) for both, and 3-month post-operative carcinoembryonic antigen value (p < 0.0001) for both. In multivariate analysis; DFS was significant for (PCI) (p = 0.013) and (CC) score >1 (p < 0.003) while PCI > 6 was the only significant factor (p < 0.003) for OS. Conclusions: Addition of HIPEC to CRS was safe, and improved survival in patient with peritoneal Carcinomatosis of colo-rectal origin. PCI and CC score are prognostic factors of survival, signet-ring subtype may not benefit of this procedure. Research Sponsor: None.

Conditional survival of patients with rectal cancer undergoing Watch and Wait: The risk of recurrence over time. First Author: Laura Melina Fernandez, Champalimaud Foundation, Lisbon, Portugal

Background: Patients with rectal cancer and complete clinical response (cCR) after neoadjuvant chemoradiation (nCRT) have been offered non-operative management (W&W). Risk factors for local regrowth (RG) include baseline cT stage ≥3, and the influence of other factors for RG over time is unknown. Objective: Analyze the risk of recurrence over time through conditional survival (cDFS/cLRFS) estimates for rectal cancer patients after W&W. Methods: Retrospective analysis of all patients from the largest multicenter database of patients managed non-operatively (International Watch and Wait Database-IWWD). Only patients with cCR after nCRT and W&W with a median of 3 years of follow-up were included. cDFS was used to investigate the evolution of recurrence-odds, as patients remained disease-free after nCRT, 2-year cDFS was estimated at “x” years after nCRT based on the formula cDFSx = DFSx+2/DFSx. Results: 768 patients treated between 1991-2015 were included. Using cDFS estimates, the probability of remaining disease-free for 2 additional years once cCR was achieved and sustained for 1, 5, and 8 years, were 85%, 97%, and 95%, respectively. These contrast with the actuarial DFS for similar intervals of 70%, 68% and 65% respectively. Baseline cT was associated with the risk of RG at 1 year after a cCR (cT2 aLRFS 89% vs. cT3 82%; p=0.004). However, after sustaining a cCR for 1 year, baseline cT becomes irrelevant at 2 years (cLRFS: 94% vs. 90%; p = 0.14). Also, total dose of RT (≥50 vs <50 Gy) was associated with the risk of RG (aLRFS 76% vs 85%; p=0.03) at 1 year. Dose of RT becomes irrelevant at (2 years; cLRFS 93% vs. 90%; p = 0.10) once patients sustained a cCR for 1 year. Conclusions: Conditional survival estimates suggests that patients have significantly lower risks (~5%) of developing late RG at 5 years after sustaining cCR for 3 years. A sustained cCR over time may be more relevant for conditional survival than RT dose. The present data can have significant consequences for the recommendation of intensive surveillance, after sustaining 3ys of cCR. Research Sponsor: Champalimaud Foundation, Eureca (European Registration of Cancer Care).

Prognostic value of circulating tumor DNA (ctDNA) detection during adjuvant chemotherapy in patients with stage III colorectal cancer: The interim report of a prospective, observational study. First Author: Junjie Peng, Fudan University Shanghai Cancer Center, Shanghai, China

Background: Adjuvant chemotherapy (ACT) is the standard treatment for stage III colorectal cancers (CRC). However, optimal biomarker were still needed for individualized adjuvant strategies. Here, we conducted a prospective study in patients with stage III CRCs with combined ACT, to explore the prognostic effect of circulating tumor DNA (ctDNA) before and after ACT. Methods: The study enrolled 130 patients with stage III colon and rectal cancer ≥10cm from anal who received curative resection without neo-adjuvant therapy at Fudan University Shanghai Cancer Center. All patients received 3 or 6 months of ACT. The Roche AVENIO Surveillance Kit was used to assess somatic mutations by next-generation sequencing (NGS) in tissue, pre- and post-chemo plasma samples. The plasma were collected 3-5 weeks after surgery and after last cycle of ACT, respectively. Patients were classified as ctDNA (+) or (-) based on the detection of SNVs identified in tumor tissue at an AF of at least 5%. Results: In the interim analysis, 116 samples, 123 tissue, 92 pre-chemo and 98 post-chemo plasma samples were prospectively collected and detected, and a total of 86 matched samples were analyzed with a median follow-up of 12.0 months. ctDNA was detectable in 14 of 86 patients (16.3%) before ACT, and in 10 (11.6%) patients after ACT. After 1-year follow-up, long-term cDFS analysis identified 6 of 12 early relapses (4 patients had ctDNA (+) in pre- and post-chemo samples had early relapse. Before ACT, ctDNA (+) patients were 7 times more likely to relapse early than ctDNA (-) patients (HR, 7.37; 95% CI, 1.54-35.22; p = 0.03). Similarly, after ACT, ctDNA (+) patients were 13 times (HR, 13.37; 95% CI, 2.06-88.23; P = 0.007) more likely to relapse. Monitoring after ACT indicated that 7 of the 14 ctDNA (+) patients (50.0%) were cleared, and the early relapse rate decreased from 43.9% (3/7) to 28.6% (2/7) if ctDNA turned negative. Also, ctDNA analysis can potentially use the post-operative management and surveillance strategies for stage III CRC by enabling risk stratification, monitoring ACT efficacy, and detecting early relapse. Clinical trial information: ChiCTRIB00018754. Research Sponsor: Roche Diagnostics.

Construction and validation of a simple-to-use nomogram incorporating clinicopathological parameters into the TNM staging system to predict prognosis for stage II colorectal cancer. First Author: Shaobo Mo, Fudan University Shanghai Cancer Center, Shanghai, China

Background: Survival outcomes are significant different in stage II colorectal cancer (CRC) patients with diverse clinicopathological features. Objective of this study is to establish a credible prognostic nomogram incorporating easily available parameters for stage II CRC patients. Methods: A total of 708 stage II CRC patients at Fudan University Shanghai Cancer Center (FUSCC) during 2008 to 2013 were retrospectively analyzed in this study. Cases were randomly separated into training set (n = 1084) and validation set (n = 624). Results: cDFS analysis can potentially use the post-operative management and surveillance strategies for stage II CRC by enabling risk stratification, monitoring ACT efficacy, and detecting early relapse. Clinical trial information: ChiCTRIB00018754. Research Sponsor: Roche Diagnostics.

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Outcomes of elderly patients with resectable liver metastases from colorectal cancer (CRLM): Single center experience. First Author: Laura Mansour, Université de Montréal, Montreal, QC, Canada

Background: Half of patients with colorectal cancer develop liver metastases during the course of their disease. Surgery is the only potentially curative option for CRLM if resectable. Treatment of patients over 70 years old is challenging mainly by virtue of comorbidity and geriatric syndromes. Thus, we intended to report our experience with elderly patients with resectable CRLM. Methods: After approval by the Institutional Review Board (IRB), all records from a prospectively collected database at Centre Hospitalier de l’Université de Montréal (CHUM) were reviewed. RFS and OS in patients aged 70+ were calculated using the Kaplan-Meier survival curves. Results: From 2010 to 2016, 101 patients older than 70 years were identified. Safety and surgical complications were previously reported. Median age was 75 years. CRLM were synchronous in 46.5% and metachronous in 53.5%. Relapse free survival (RFS) of patients aged >70 years was 33.7 months. Overall survival (OS) of patients aged >70 years was comparable to those of less than 65 years old (median OS: 56 vs 62 months; p = 0.15, respectively). Hepatic relapse showed worse survival when compared to extra-hepatic recurrence, median OS: 44 vs 33.2 vs 29.3 months for non-hepatic, hepatic only and with other sites respectively (p = 0.034). Although non-significant, Patients with metachronous CRLM had superior mOS compared to those with synchronous disease (58.7 y vs 44.7 months; p = 0.22). Conclusions: Survival Outcomes of patients with an age >70 years were comparable to those of younger patients and what is reported in literature. Age should not be a limiting factor in the management of elderly patients with resectable CRLM. However, metastases in elderly patients should be offered with curative intents. Research Sponsor: None.
Background: Studies have demonstrated disparities in health care driven by socioeconomic factors. Patients with metastatic cancer represent the most vulnerable group of cancer patients. We hypothesized that these factors impact timeliness to chemotherapy in patients with metastatic colon cancer and their treatment outcomes. Methods: We queried the National Cancer Database (NCDB) for patients with metastatic colon cancer (AJCC pathology stage IV) diagnosed from 2004-2016. We selected patients treated with chemotherapy as first line treatment within 90 days of diagnosis. Time to initiation (TTI) was defined as time in days (d) from diagnosis to initiation of systemic chemotherapy and survival was measured in terms of months (m) from the day of diagnosis. Stepwise negative binomial regression and Cox proportional hazard models were used for analysis. Results: We identified 11,764 patients meeting the eligibility criteria. Median age was 62 (range 18-90) years and included 51% males. Median TTI was 9d (range 1-99) and median overall survival was 24.3m. TTI was significantly associated with race: Caucasian 26.6d (95% CI 25.6-27.7) vs. African American 28.9d (26.9-31.0) p-value=0.021, Median income: $63,000 23.5d (95% CI 22.4 - 24.5) vs. <$36,000 29.2d (27.3 - 31.0) p-value < 0.0001, Facility type: Community cancer center 23.6d (95% CI 21.6-25.6) vs. Academic/research program 26.5d (95% CI 25.5 - 27.4) p-value=0.004. Factors impacting survival in a multivariate model included time to chemotherapy initiation > 24.7m with TTI > 9d vs. 23.8m with TTI < 9d (p-value < 0.0001), type of facility - Academic/research program 26.4m vs. community cancer center 23.1m (p-value < 0.0001), age (p-value <0.001), comorbidities (p-value <0.0001) and site of primary. Conclusions: Patients with metastatic cancer are not free from disparities driven by social determinants of health that impact their outcomes. The findings suggest that further studies to identify barriers to healthcare access and continued efforts to improve them are warranted. Research Sponsor: None.

Chemotherapy-induced neutropenia with FOLFOX in the adjuvant treatment of colorectal cancer. First Author: Joanna Gotfrit, Ottawa Hospital, Ottawa, ON, Canada

Background: Patients undergoing adjuvant treatment with FOLFOX for colorectal cancer (CRC) are at risk of developing chemotherapy-induced neutropenia (CIN). We performed a retrospective chart review of patients with CRC treated with FOLFOX at our institution from 2013 - 2015. Demographic and treatment data were collected. CIN was defined as ANC <1.5, and all episodes of neutropenia were assumed to be the result of chemotherapy administration to a total of 302 patients were included (baseline demographics in Table). In the overall cohort, 174 (58%) of patients had at least 1 episode of CIN. The risk CIN was 47% in stage II, 60% in low risk stage III (T1-3 and N1), and 58% in high risk stage III (T4 or N2). Among patients with at least 1 episode of CIN, the 1st CIN event occurred during the 1st 3 months of treatment in 76%, and the median cycle of 1st occurrence was 4 (95% CI 4-5), which did not differ by stage. Among patients who had at least 1 episode of CIN, 122 (44%) had a 2nd episode at a median cycle of 9 (95% CI 8-10). Among patients with at least 2 cycles of CIN, 79 (45%) received subsequent GCSF, initiated 1 cycle after the 1st CIN event 37% of the time. Among patients with at least 2 episodes of CIN (n=112), 52% (52) received GCSF after the 1st and 2nd event. Of these, 40 patients (69%) started GCSF newly after the 2nd CIN event. Among patients starting GCSF after the 2nd CIN event, 47% initiated GCSF 1 cycle later. The median cycle at which the relative dose intensity of FOLFOX decreased to <85% was cycle 6 (95% CI 5-8) in those with no CIN events, cycle 3 (95% CI 2-4) in those with at least 1 CIN event treated with GCSF, and cycle 5 (95% CI 4-6) in those with at least 1 CIN event treated without GCSF. Conclusions: CIN is a frequent occurrence during the adjuvant treatment of CRC with FOLFOX and most often occurs in the first 3 months of treatment. While oncologists may treat some patients with 3 months of FOLFOX rather than 6, physicians should be aware of CIN regardless of the planned duration of treatment. Early initiation of GCSF may be a consideration. Research Sponsor: Apo-Biologix.
Implications of postoperative complications on survival after cytoreductive surgery and HIPEC: A multi-institutional analysis of the United States HIPEC Collaborative. First Author: Adriana C. Gamboa, Winship Cancer Institute, Division of Surgical Oncology, Department of Surgery, Emory University, Atlanta, GA

Background: Postoperative complications (POCs) are associated with worse oncologic outcomes in various cancer histologies. The impact of POCs on the survival of patients with appendiceal or colorectal cancer after cytoreductive surgery/heated intraperitoneal chemotherapy (CRS/HiPEC) is unknown. Methods: US HIPEC Collaborative (2000-17) was reviewed for patients who underwent CRS/HiPEC for appendiceal/colorectal cancer. Analysis was stratified by non-invasive appendiceal neoplasm vs invasive appendiceal/colorectal adenocarcinoma. POCs were grouped into infectious, cardiopulmonary, thromboembolic, and intestinal dysmotility. Primary outcomes were 5-yr overall survival (OS) and recurrence-free survival (RFS). Results: Of 1304 pts, median age was 55 yrs, 41% were male (n = 537), 33% had non-invasive appendiceal (n = 426) and 67% had invasive appendiceal/colorectal adenocarcinoma (n = 878). In the non-invasive appendiceal cohort, POCs were identified in 55% (n = 233) and OS and RFS did not differ between patients who experienced a complication and those who did not (OS 94 vs 94% p = 0.26; RFS 68 vs 60% p = 0.15). In the invasive appendiceal/colorectal adenocarcinoma cohort, however, POCs (63%; n = 555) were associated with decreased OS (59 vs 74% p < 0.001) and RFS (72 vs 24% p < 0.001). Infectious POCs were most common (35%; n = 196). On multivariate analysis, according to gender, PCI and incomplete resection (CCR1), infectious POCs in particular were associated with decreased OS compared to no complication (HR 2.08 95%CI:1.48-2.91, p < 0.01) or OS of complications of any type (HR 1.75 95%CI:1.2, p < 0.01). This association persisted for infectious POCs and reduced RFS (HR 1.65 95%CI: 1.23-2.10 p < 0.01). Conclusions: Postoperative complications are associated with decreased OS and RFS after CRS/HiPEC for invasive histology, but not for an indolent disease like non-invasive appendiceal neoplasm. Infectious POC types, infectious complications are the main driver for this association. The exact mechanism is not known, but may be immunologic. Efforts must target best practices and standardized prevention strategies to minimize infectious POCs. Research Sponsor: Katz Foundation.

Outcomes of appendiceal adenocarcinomas compared to right and left-sided colorectal adenocarcinomas: An analysis from the National Cancer Database (NCDB). First Author: Manik Gupta Nair, Cleveland Clinic Foundation, Cleveland, OH

Background: Appendiceal carcinomas (AC) account for 2%-3% of colorectal cancers (CRC) and are generally treated like other CRC. However, there is limited data to guide treatment. While AC originates on the right side of the colon, there is no consensus on treatment like as right-sided CRC (R-CRC). The aim of this study is to learn how AC differ from right versus left-sided CRC (L-CRC). Methods: We identified historically confirmed cases of appendiceal and colorectal adenocarcinomas with information about stage and overall survival (OS) diagnosed between 2004 and 2015 from the National Cancer Database. Kaplan-Meier method and log-rank test were used to estimate and compare OS. Results: 833,939 patients met our inclusion criteria: 15,138 (1.8%) AC, 447,551 (53.7%) L-CRC, 308,794 (37.0%) R-CRC, and 62,456 (7.5%) transverse CRC (T-CRC). We excluded patients who have not been refractory or intolerant to standard chemotherapy. The survival outcomes were compared between pts from AC (n = 1142) and pts with CRC who sequentially received both of REG and FTD/TPI showed longest sOS (54.0 vs 40.0 months, p < 0.001). AC was lowest at 61 years for stage I-III disease and 58 years for stage IV disease. Stage IV AC was more common in females 3628/5739 (63.22%). AC had the best OS among site stages in stage I-III. Median OS for stage I-III AC was 128.8 months (95% CI: 117.9-139.0), with 5-year OS rate of 0.69 (95% CI: 0.67-0.70); L-CRC median OS was 111.6 months (95% CI: 110.9-112.4), with 5-year OS rate of 0.681 (95% CI: 0.680-0.683); R-CRC median OS was 88.5 months (95% CI: 87.8-89.9), with 5-year OS rate of 0.613 (95% CI: 0.601-0.635); and T-CRC median OS was 86.2 months (95% CI: 84.7-87.6), with 5-year OS rate of 0.608 (95% CI: 0.604-0.613) (p < 0.001). Table. Similar difference was observed in stage IV patients (Table). Conclusions: Patients with AC had significantly better OS for stages I-III and stage IV compared to patients with L-CRC, R-CRC, and T-CRC, though outcomes were more similar to L-CRC. The difference is more evidence for patients with stage IV disease. T-CRC had similar OS to R-CRC, as anticipated. Research Sponsor: None.

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<th>R-CRC</th>
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<td>(95% CI: 36.2-39.2)</td>
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</tbody>
</table>

Impact of postoperative complications on oncologic outcomes after rectal cancer surgery: An analysis of the United States Rectal Cancer Consortium. First Author: Adriana C. Gamboa, Winship Cancer Institute, Division of Surgical Oncology, Department of Surgery, Emory University, Atlanta, GA

Background: Postoperative complications (POCs) are associated with worse oncologic outcomes in several cancer types. The implications of complications after rectal cancer surgery are not known. Methods: The US Rectal Cancer Consortium (2007-17) was reviewed for patients with primary rectal adenocarcinoma who underwent R0/R1 low anterior resection (LAR) or abdominopelvic resection (APR). POCs were categorized as major or minor and grouped into infectious, cardiopulmonary (CP), thromboembolic (TE), renal, or intestinal dysmotility. Primary outcomes were 5-yr overall survival (OS) and recurrence-free survival (RFS). Results: Of 1136 pts, median age was 59 yrs (IQR 51-67), 61% were male (n = 693), median f/u was 31 mos (IQR 12-54), 70% underwent LAR (n = 799) and 30% APR (n = 337). Complication rate was 46% (n = 527), with 63% minor (n = 330) and 32% major (n = 170). Of all POCs, infectious complications comprised 20% (n = 105), cardiopulmonary 3% (n = 14), thromboembolic 5% (n = 52), renal 9% (n = 46) and intestinal excluded pts who have not been refractory or intolerant to standard chemotherapy. Outcomes of appendiceal adenocarcinomas compared to right and left-sided colorectal adenocarcinomas: An analysis from the National Cancer Database (NCDB). First Author: Manik Gupta Nair, Cleveland Clinic Foundation, Cleveland, OH

Background: Appendiceal carcinomas (AC) account for 2%-3% of colorectal cancers (CRC) and are generally treated like other CRC. However, there is limited data to guide treatment. While AC originates on the right side of the colon, there is no consensus on treatment like as right-sided CRC (R-CRC). The aim of this study is to learn how AC differ from right versus left-sided CRC (L-CRC). Methods: We identified historically confirmed cases of appendiceal and colorectal adenocarcinomas with information about stage and overall survival (OS) diagnosed between 2004 and 2015 from the National Cancer Database. Kaplan-Meier method and log-rank test were used to estimate and compare OS. Results: 833,939 patients met our inclusion criteria: 15,138 (1.8%) AC, 447,551 (53.7%) L-CRC, 308,794 (37.0%) R-CRC, and 62,456 (7.5%) transverse CRC (T-CRC). We excluded patients who have not been refractory or intolerant to standard chemotherapy. The survival outcomes were compared between pts from AC (n = 1142) and pts with CRC who sequentially received both of REG and FTD/TPI showed longest sOS (54.0 vs 40.0 months, p < 0.001). AC was lowest at 61 years for stage I-III disease and 58 years for stage IV disease. Stage IV AC was more common in females 3628/5739 (63.22%). AC had the best OS among site stages in stage I-III. Median OS for stage I-III AC was 128.8 months (95% CI: 117.9-139.0), with 5-year OS rate of 0.69 (95% CI: 0.67-0.70); L-CRC median OS was 111.6 months (95% CI: 110.9-112.4), with 5-year OS rate of 0.681 (95% CI: 0.680-0.683); R-CRC median OS was 88.5 months (95% CI: 87.8-89.9), with 5-year OS rate of 0.613 (95% CI: 0.601-0.635); and T-CRC median OS was 86.2 months (95% CI: 84.7-87.6), with 5-year OS rate of 0.608 (95% CI: 0.604-0.613) (p < 0.001). Table. Similar difference was observed in stage IV patients (Table). Conclusions: Patients with AC had significantly better OS for stages I-III and stage IV compared to patients with L-CRC, R-CRC, and T-CRC, though outcomes were more similar to L-CRC. The difference is more evidence for patients with stage IV disease. T-CRC had similar OS to R-CRC, as anticipated. Research Sponsor: Katz Foundation.
Background: Although potentially associated with increased infections, introperative pelvic drains are often placed during low anterior resection (LAR) to evacuate postoperative fluid collections and identify/curtail potential anastomotic leaks. Our aim was to assess the validity of this practice in a large dataset of patients undergoing LAR for rectal cancer.

Methods: Patients from the US Rectal Cancer Consortium database who underwent curative-intent LAR for a primary rectal cancer were included. Patients were categorized as receiving a closed suction drain intraoperatively or not. Primary outcomes were superficial surgical site infection (SSI), deep SSI, intraabdominal abscess, anastomotic leak, and need for secondary drain placement. Three subgroup analyses were conducted in patients who received neoadjuvant chemoradiation, had a diverting loop ileostomy (DLI), and had low tumors (<6cm from the anal verge).

Results: Of 996 pts, average age was 58 yrs, 61% were male, and 67% (n=551) received a drain. Drain patients were more likely to be male (64vs55%, p=0.041), have a smoking history (25vs19%, p=0.021), have received neoadjuvant chemoradiation (73vs61%, p<0.001), have low tumors within 6cm of the anal verge (56vs36%, p=0.001), and have received a DLI (80vs71%, all p<0.05). Drains were associated with an increased anastomotic leak rate (14vs8%, p=0.001), although there was no difference in the need for a secondary drainage procedure to control the leak (82vs88%, p=0.924). These findings persisted in all subset analyses. Drains were not associated with increased superficial SSI, deep SSI, or intraabdominal abscess in the entire cohort or each subset analysis. Reoperation (12vs10%, p=0.478) and readmission rates (28vs31%, p=0.511) were similar.

Conclusions: Although not associated with increased infectious complications, intraoperatively-placed pelvic drains after low anterior resection for rectal cancer are associated with an increase in anastomotic leak rate and no reduction in the need for secondary drain placement or reoperation. Routine drainage should be abandoned. Research Sponsor: None.

Visit QicaSym.org to search by abstract for the full list of abstract authors and their disclosure information.
A real-world application of liquid biopsy (LB) in metastatic colorectal cancer (mCRC). First Author: Letizia Procozzi, Department of Clinical and Experimental Oncology, Medical Oncology Unit, Istituto Oncologico Veneto IOV-IRCCS, Padua, Italy

Background: First-line decision making is the key to the successful management of mCRC patients (pts). RAS/BRAF status is essential to choose the best targeted agent. In hub centers, a not negligible proportion of pts referred from elsewhere may not have standard tissue-based (STB) molecular results available at the time of first oncologic visit (T0). LB may help circumvent these hurdles. Methods: A monoinstitutional prospective head-to-head comparison of LB versus (vs) STB testing was conducted in a real-world setting. Selection criteria included: mCRC with unknown RAS/BRAF status at T0, tissue from primary or metastases archived in external centers, no previous anti-EGFR agents. At T0, pts underwent plasma sampling for LB testing and procedure for tissue recovery. RAS/BRAF genotyping was carried out by droplet digital PCR on circulating-free (cf) DNA. Primary endpoint was the comparison of time to LB (T1) vs STB (T2) results. Secondary endpoints were the overall percent agreement (OPA), specificity, sensitivity, positive and negative predictive values (PPV and NPV) of LB. Urinary (u) cfDNA testing was also explored. Results: A total of 33 pts were included. Mean T1 was 7 (2-12) days (d) as compared to 22 (7-65) d mean T2. T1 included a mean time for tissue recovery of 17 d. The OPA between LB and STB was 83%. Compared to STB testing, LB specificity and sensitivity were 90% and 80%, respectively, with a PPV of 94% and NPV of 69%. In detail, at LB and STB testing, RAS mutation was found in 50% and 43% of pts; BRAF mutation in 17% and 13%, respectively. LB results included 1 false positive and 4 false negative (FN). FN showed a significantly (low tumor burden) i.e. total tumor volume) at basal CT scan. Concordance between STB and ucfDNA testing was 89%, with a sensitivity of 83% and specificity of 100% recorded for ucfDNA analysis. Conclusions: Faster turnaround time, high concordance and accuracy are 3 key-points supporting the adoption of LB in routine mCRC care, in particular when decision on first-line is urgent and tissue recovery from external centers may require a long time. Results should be interpreted with caution in LB wild-type cases with low tumor burden. Research Sponsor: None.

Treatment of metastatic colorectal cancer (mCRC) according to age. First Author: Laura Ortega, Hospital General Universitario Gregorio Marañón, Instituto De Investigacion Sanitaria Gregorio Marañon, Madrid, Spain

Background: Elderly patients with mCRC are underrepresented in clinical trials. For this reason, the optimal treatment in this population is uncertain. The aim of this study is to compare efficacy and safety outcomes in patients with mCRC treated in our institution according to age (<65 vs ≥65 years). Methods: We conducted a retrospective analysis of 482 patients with mCRC attended in the Hospital Gregorio Marañon (Spain) between January 2010 and 2018. Results: Patients characteristics table. First-line: chemotherapy (CT) 98.7% vs 97.3% respectively (p=0.324), biological agents (BA) 81.2% vs 79.0% (p=0.231), adjuvant chemotherapy (AC) 57.2% vs 63.9% (p=0.360). Overall survival more than ≥65 years-old patients XELOX (9.2% vs 17.5%) and capecitabine (2.0% vs 7.5%). Second-line: CT 64.9% vs 63.5% (p=0.764), BA 60.4% vs 51.1% (p=0.055). Significantly more ≥65 years-old patients received FOLFIRI (67.0% vs 54.5%) and more ≥65-years-old patients irinotecan (2.0% vs 8.6%). Third and subsequent lines: Significantly more young patients received a third-line (CT: 41.6% vs 31.0%; BA: 24% vs 21.6%), fourth-line (CT: 22% vs 11.9%; BA 36.6% vs 6.4%) and fifth-line of treatment (CT: 11.7% vs 5.8%; BA 4.5% vs 3.6%). More young patients underwent metastasis resection (74.0% vs 58.1%, p=0.000). There were no differences in rate of post-operative complications (p=0.840). There were no differences in overall survival (36.05m vs 28.06m, p=0.142), progression-free survival (first-line: 12.7m vs 11.78m, p=0.139; second-line: 8.7m vs 62.7m, p=0.254) or adverse event rate (73.4% vs 73.6%, p=0.967). Conclusions: Intensive treatment could be an effectiveness and safe option in selected elderly patients. Research Sponsor: None.

Eligibility of real-world patients with stage II/III colorectal cancer (CRC) in adjuvant chemotherapy (AC) trials. First Author: Atul Batra, Tom Baker Cancer Center, Calgary, AB, Canada

Background: The results of AC trials in stage II/III CRC are often generalized to real-world patients. However, clinical trials have stringent inclusion and exclusion criteria, which can potentially lead to poor generalizability of results and subsequent research. The aim of this study was to determine the proportion of real-world patients with stage II/III CRC who would be eligible for AC trials based on common eligibility criteria and to compare the outcomes in eligible and ineligible patients. Methods: We identified all patients diagnosed with stage II/III CRC in Alberta from 2015 to the Alberta Cancer Registry. Patients meeting any one of the following criteria were considered ineligible: age >75 years, anaemia, comorbidity conditions (heart disease, uncontrolled diabetes, kidney disease, liver disease) and history of a prior malignancy or immunosuppression. Logistic regression was used to describe the likelihood of receiving AC and Cox regression models were constructed to determine overall survival (OS). Results: A total of 7841 patients with stage II/III CRC were identified, of whom 52% were men and median age at diagnosis was 71 years (IQR: 61-79 years). Approximately 59% patients were deemed trial-ineligible in particular when decision on first-line is urgent and tissue recovery from external centers may require a long time. Results should be interpreted with caution in LB wild-type cases with low tumor burden. Research Sponsor: None.

The comparison of mFOLFOXIRI with CAOX/SOX as neoadjuvant chemotherapy for locally advanced rectal cancer. First Author: Tetsuji Terazawa, Department of Cancer Chemotherapy Center, Osaka Medical Collage Hospital, Osaka, Japan

Background: The standard therapy for the locally advanced rectal cancer (LARC) (Ra or Rb, 12Npstage, T3/4Nany) is chemoradiotherapy (CRT) followed by surgery. The CRT prevents local recurrence, but high grade complications or the improvement of distant recurrence still remain. Several studies about the neoadjuvant chemotherapy (NAC) without radiation showed favorable R0 resection rate and outcome, however the best regimen of NAC is unclear. The aim of this study is to investigate the efficacy and safety of mFOLFOXIRI and CAOX/SAOX as NAC. Methods: We identified all patients with LARC who were planned to receive mFOLFOXIRI (SFU 2400mg/m²/day2, leucovorin 200mg/m², oxaliplatin 85mg/m², irinotecan 150mg/m², every 2 weeks) or CAOX/SAOX (capcitabine 2000mg/m² or S1 mg/m² oxaliplatin 130mg/m², every 4 weeks) for 8-12 weeks as NAC, retrospectively. Results: Forty-nine pts received mFOLFOXIRI and thirty-two pts received XELOX/SOX between Jan 2015 and Mar 2019. The characteristics of mFOLFOXIRI and XELOX/SOX were as follows: median age, 64 (37-80) and 65 (33-68); PS 0/1, 46/4(94%)/36% and 16/44%(18/56%); Ra/Rb-P, 45(92%) and 1/32; clinical T2/3/4, 47(7%)/27(55%)/19(39%) and 13(3%)/26(53%)/20(42%) and 7(22%)/71(53%)/8(25%). The pathological response rate which was defined as tumor affected area over one-third were 61.2% in mFOLFOXIRI and 65.6% in CAOX/SAOX including complete remission of 4.1% and 12.5%, respectively. Six of 49 pts withdrew from mFOLFOXIRI due to toxicities, whereas one of 32 pts from CAOX/SAOX. One pt received CRT after SOX because of lack of efficacy. The major grade 3/4 toxicities of mFOLFOXIRI were neutropenia (n = 22, 45%), thrombocytopenia and febrile neutropenia (n = 4, 8%), and anemia (n = 3, 6%), whereas CAOX/SAOX neutropenia (n = 3, 9%), thrombocytopenia (n = 1, 3%) and hand-foot syndrome (n = 1, 3%). The one year of relapse free survival rate were 85.4% in mFOLFOXIRI and 79.2% in CAOX/SAOX. Conclusion: The pathological response of mFOLFOXIRI was comparable with CAOX/SAOX, CAOX/ SOX was less toxic. The further investigation including 5 year overall survival rate was needed. Research Sponsor: None.

Survival of eligible and ineligible patients.

<table>
<thead>
<tr>
<th>Group</th>
<th>5-year OS %</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ineligible and received AC</td>
<td>56.3%</td>
<td>0.8</td>
<td>0.42-0.54</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ineligible and did not receive AC</td>
<td>74.4%</td>
<td>0.48</td>
<td>0.42-0.54</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Eligible</td>
<td>83%</td>
<td></td>
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</table>

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
The Prospective Dutch Colorectal Cancer (PLCRC) Cohort: Towards a unique patient-reported outcome enriched “real-world” data cohort. First Author: Jeroen W.G. Derksen, Department of Medical Oncology, University Medical Center Utrecht, Utrecht University, Utrecht, Netherlands

Background: The initiation of high-quality pan-population cohort studies is a major research need for the improvement of colorectal cancer outcomes as advocated by regulators and the research community. In 2013, the PLCRC cohort of the Dutch Colorectal Cancer Group was initiated in which longitudinal clinical data and patient-reported outcomes (PRO) are collected, along with pathologic data and biospecimens, to serve as an infrastructure for a broad body of observational and (randomized) interventional research. Here we report on the cohort’s progress and investigate whether it develops in the direction of a nation-wide cohort of “real-world” nature. Methods: Clinical and demographic data of all PLCRC participants, as prospectively collected in the Netherlands Cancer Registry by qualified data managers, were compared with the total Dutch CRC population with incidence between 2013-2017 (ref. population) which was also obtained from the Netherlands Cancer Registry. Variable distributions are compared using t-tests and χ²-tests, whereas cohort characteristics are descriptive. Results: In June 2019, 5,746 patients were enrolled in 52 / 75 Dutch hospitals, and 81% consented to receive repeated PROs. Compared to patients enrolled between 2013-16 (N = 1,093, 1-7 recruiting hospitals), we found a small shift towards the Dutch ref. population (N = 7,635) for patients enrolled between 2017-19 (N = 4,653, 17-52 hospitals) in terms of age at diagnosis (mean 64.6±10.2 years in 2013-15, 65.2±10.8 in 2017-19), and 69.5±10.9 in the ref. group, sex (65% males in 2013-16, 61% in 2017-19, and 56% in the ref. population), location of primary tumor (56% rectum in 2013-16, 40% in 2017-19, and 31% in the ref. population), N-stage (TNM N1/N2/N3 in 35% stage III cohort in 2013-16, 41% in 2017-19, and 48% in the population). Conclusions: Over the past years, the number of PLCRC recruiting centers and participating patients, with high consent rates for PROs, steeply increased. Further improvements in recruitment methodologies and increased enrolment of patients will continue to enhance PLCRC’s representation of the “real-world” and its ability to supplement trial-based evidence. Research Sponsor: Dutch Cancer Society, Other Foundation, Other Government Agency, Pharmaceutical/Biotech Company.

Adjuvant chemotherapy (AC) for stage III colorectal cancer (CRC) in the elderly: An Irish experience. First Author: Emily Harrold, Mater Misericordiae University Hospital, Dublin, Ireland

Background: Since 2004 6 months of adjuvant Oxaliplatin containing regimens consist of standard care for Stage III CRC despite cumulative neurotoxicity. The IDEA collaboration evaluated 3 versus 6 months of OXRT in high risk patients with adjuvant chemotherapy who had a median age of 64; individual studies included pts 685. Methods: This study is part of a retrospective review of the clinico-pathological records of consecutive CRC pts referred to the multi-disciplinary CRC team at an Irish tertiary referral centre from 2002-2018. We recorded characteristics, received and outcomes. Overall Survival (OS) was assessed using Kaplan-Meier analysis. Results: 869 pts were identified; 37% (328) female. 63% (551/869) < 70 and 37% (318/869) ≥ 70. Median OS for < 70 cohort was 31.5 months versus 19 months in ≥ 70 cohort (p < 0.0001). Stadie distribution in < 70 ≥ 70 cohorts was Stage II 14% (95/551);20% (63/318), Stage III 47% (260/551);46% (142/318) and Stage IV 38% (207/551);34% (31/318). In < 70 Stage III cohort 7% (37/551) pts received no AC, 42% (230/551) received FOLFOX, 39%;(651) received FOLFOX or XELOX, 7% (38/551) received FU/LEU, 32% (78/246) of pts < 70 developed PN with persistence at 6 months in 198(44/256). In ≥ 70 Stage III cohort 58% (83/142) did not receive AC. 23% (32/142) received an OXRT and 16% (23/142) received FU/LEU; there was a statistically significant survival difference with an OXRT 47% (15/32) of pts ≥ 70 receiving OXRT developed PN which persisted at 6 months in 28% (9/32). In < 70 cohort there was no significant survival difference in the IDEA-trial-defined low risk group between 12 versus < 12 FOLFOX. There was a numerical survival difference in the < 70 high risk group between 12 versus < 12 FOLFOX; this was not statistically significant. In the ≥ 70 age group there was no survival difference in either IDEA risk groups for 12 versus < 12 FOLFOX. Conclusions: > 50% of Stage III CRC patients ≥ 70 did not receive AC. OXRT was associated with a significant OS improvement in the < 70 age group in > 70 cohort and higher persistence at 6 months. Irrespective of IDEA-defined risk groups, there was no statistically significant survival difference for Stage III CRC ≥ 70 receiving 12 versus < 12 FOLFOX. Research Sponsor: None.
Do socioeconomic factors really have an impact on early detection of hepatocellular carcinoma and colorectal cancer? First Author: Anas Albawaliz, University of Missouri at Kansas City, Kansas City, MO

Background: Improving surveillance in hepatocellular carcinoma (HCC) and colorectal cancer (CRC) is an important topic in the field of gastroenterology and oncology due to significant benefit associated with early detection and better outcomes. Multiple studies have been undertaken to assess the association between the socioeconomic status of the population and adherence to HCC/CRC screening. Most of these studies used self-reporting surveys and faced limitations due to reporting bias. We aimed to assess the relevance of socioeconomic factors in the diagnosis of HCC and CRC in Jackson County, Missouri by means of a census-based study. Methods: We retrospectively studied 190 HCC and 690 CRC cases at our institution using a census-based analysis, which consisted of geocoding home addresses of patients and then attaching block level census variables for household occupancy, education level and household income. Statistical analysis was performed using Cox proportional hazard model and ordinal logistic regressions. Results: We did not find a statistically significant association between socioeconomic factors and adherence to surveillance guidelines for HCC and CRC. USPSTF-2019 guidelines for CRC and AASLD-2018 guidelines for HCC screening were taken into account. Variables that were analyzed included high school education or income less than 25 thousand dollars (p = 0.58). Study results were risk adjusted for age, race, and gender. Separate ordinal logistic regression analysis was done to also adjust for the stage at the time of eventual cancer diagnosis, no statistically significant result was obtained. Conclusions: Our study showed no association between demographic variables and participation in HCC or CRC surveillance. The study is limited by a relatively small sample size confined to local patients seen at our institution. Multicenter census-based surveys and meta-analyses need to be conducted to determine whether socioeconomic factors really have an appreciable impact on early screening and detection of HCC and CRC. Research Sponsor: None.

Colorectal cancer prevalence and risk factors among the uninsured of Tampa Bay: A free clinic study. First Author: Ethan Song, USF Health Morsani College of Medicine, Tampa, FL

Background: Uninsured patients with low socioeconomic status are at higher risk for developing colorectal cancer. There is limited quantifiable data regarding risk factors and prevalence of colorectal cancer in this vulnerable population. The purpose of this study is to assess the risk factors for colorectal cancer in the low income and uninsured patient population across nine free clinics around Tampa Bay, Florida. Methods: An IRB-approved manually extracted retrospective query of several medical record systems from nine government-approved free clinics in the Tampa Bay area in 2017 revealed 1,836 (36.1%) of 5,076 total patients who are over 50 years old. Patient demographics, weight, smoking status, alcohol use, type 2 diabetes status, inflammatory bowel disease and colorectal cancer prevalence were also extracted and analyzed. Results: Among patients over 50, the majority of patients were female (n = 1,073, 58.4%) and of Hispanic ethnicity (n = 752, 41.0%). Of the 1,349 patients who reported their smoking status, 213 (15.8%) were active smokers and 218 (16.2%) were past smokers, with a mean 16.3 (SD = 15.5) pack year history. Of the 1,224 patients who reported their history of alcohol consumption, 217 (19.3%) were current consumers and 40 (3.6%) were past consumers. The average BMI of patients over 50 years was 30.2 (SD = 6.9), with 558 (30.4%) cases of diabetes. Eleven patients (0.6%) had a history of inflammatory bowel disease. The prevalence of documented colorectal cancer in this sample was 0.6% (n = 11) in our sample population. Conclusions: There is a high prevalence of risk factors for colorectal cancer in this sample of uninsured patients but a lower reported prevalence of colorectal cancer compared to the general population. Additionally, many known risk factors for colorectal cancer, such as diet, physical activity, or family history, are not routinely documented by free clinics. As these clinics provide opportune points of primary care, this baseline data should prompt more attention to colorectal screening and risk factor modification in this vulnerable population. Research Sponsor: None.
Impact of race on incidence and survival from colorectal cancer in young adults in the United States. First Author: Dhruvika Mukhija, Northwestern University, Chicago, IL

Background: Multiple studies have reported an increasing incidence of colorectal cancer (CRC) in young (<45 years) adults. However, the impact of race on the burden of CRC in the United States has not been fully explored.

Methods: Using Surveillance, Epidemiology and End Results database, we identified patients with CRC and abstracted data on patient demographics, tumor location, and survival between 1973-2014, and compared these variables in patients 18-44 years with those >45 years. Cases where CRC was not the first/only malignancy were excluded. Categorical variables were compared using the Chi-square test and overall survival was analyzed using the Kaplan-Meier method. Results: Overall, 453,019 patients were included (27,352 <45, and 425,667 >45 years). 81.7% among those >45 years were caucasian, as compared to 74.3% < 45 years. Among those <45, 14.3% were black, 10.3% were Asian/Pacific Islander (API) and 11% were American/Alaska Native (compared to 10.1%, 7.5% and 6.0% respectively in adults >45) (p < 0.0001). Survival was poorer for non-white patients (black, API and AI) (94 months, 95%CI 90-100) as compared to white patients (153 months, 95%CI 145-156) overall, and individually for the <45 and >45 years subgroups as well. Conclusions: Racial distribution in patients with CRC differs significantly among patients <45 as compared to older adults, with incidence in American/Alaskan Natives approaching 2 times that of older adults, and 1.5 times in young Blacks and Asian/Pacific Islanders. Non-white patients have poorer survival across all age groups. With rates of CRC rising sharply in young adults, underlying reasons for these differences require further investigation to better channelize efforts for education and screening. Research Sponsor: None.

Racial distribution of CRC among subgroups.

<table>
<thead>
<tr>
<th>Race</th>
<th>American Indian/Alaska Native</th>
<th>Asian or Pacific Islander</th>
<th>Black</th>
<th>White</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 45</td>
<td>295(108)</td>
<td>282(103)</td>
<td>3694</td>
<td>1463</td>
<td>4560</td>
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<tr>
<td>Age ≥ 45</td>
<td>249(57)</td>
<td>379(53)</td>
<td>4339</td>
<td>1456</td>
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</tr>
<tr>
<td>Total</td>
<td>2703</td>
<td>4274</td>
<td>8033</td>
<td>2919</td>
<td>19659</td>
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</tbody>
</table>

| Percentage (N) | 4.02%                      | 0.55%                   | 17.8%  | 13.8%  | 29.1%  |

Poster Session (Board C14), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Metachronous colorectal pathology among survivors of young-onset colorectal cancer: Implications for postresection colonoscopic surveillance. First Author: Oliver Peacock, Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Patients with sporadic young-onset colorectal cancer (CRC) are postulated to have a more biologically active colorectal polyp to malignant transformation example in life. It is unknown whether rates elevated risk for metachronous colorectal pathology after the index cancer. We aimed to define this risk, to inform their post-resection endoscopic surveillance.

Methods: Consecutive CRC patients (aged 18-50, n = 728) were prospectively followed after surgical resection between 2009 and 2017. Patients presenting with hereditary CRC, recurrent disease, or without endoscopy follow-up were excluded. All endoscopy records were subjected to natural language processing and further reviewed. Metachronous colorectal pathology of interest included: high-risk adenoma, in number, or tubulovillous/high-grade dysplasia histology, second CRC, and endoscopically detectable local recurrence. Results: During a 48-month (median) follow-up, 457 patients underwent 1,952 person-years of colonoscopic follow-up. The median age at CRC diagnosis was 44 years. Disease arose from the proximal colon in 59.6%, distal colon in 23.0% and rectum in 67.6%, and was stages I/II in 191 (41.8%), III in 185 (40.4%), and IV in 81 (17.7%). The majority (95.8%) underwent segmental colectomy. The two most common variants among people of Northern European descent are MUTYH Y179C (rs34612342) and G396D (rs36053993), with a carrier frequency of 2%. However, understanding the frequency of these variants in other populations can better inform population health approaches for CRC screening and prevention. This study assessed the frequency of these two variants in a generally unselected group of genotyped individuals who have used direct-to-consumer (DTC) genetic testing. While these two variants were most common among people of European descent, they were also observed at relatively high frequency among people of Hispanic/Latino descent. These results may help guide CRC screening and prevention strategies in different ethnicities. Research Sponsor: 23andMe.

Allele frequencies of two MUTYH variants, Y179C, and G396D, in a direct-to-consumer genetic database. First Author: Hoang Nhan, 23andMe, Sunnyvale, CA

Background: MUTYH-associated polyposis (MAP) is an autosomal recessive condition that accounts for about 0.3-0.7% of all colorectal cancer (CRC) cases. The two most common variants among people of Northern European descent are MUTYH Y179C (rs34612342) and G396D (rs36053993), with a carrier frequency of 2%. However, understanding the frequency of these variants in other populations can better inform population health approaches for CRC screening and prevention. This study assessed the frequency of these two variants in a generally unselected group of genotyped individuals who have used direct-to-consumer (DTC) genetic testing (23andMe, Inc, Sunnyvale, CA). Methods: Study participants were genotyped on Illumina genotyping arrays, which included the Y179C and G396D variants. Eligible subjects were 23andMe customers who were at least 18 years of age and who consented to participate in research. IRB approval was obtained from Ethical and Independent Review Services. Results: Out of the 3,617,279 eligible participants included in this study, the overall allele frequencies of Y179C and G396D were 0.18% and 0.51%, respectively. People of European descent had the highest frequencies (0.22% and 0.59%), while people of Ashkenazi, Jewish, East Asian, and South Asian descent had the lowest frequencies (<0.015% for both variants). The allele frequencies for people of Hispanic/Latino descent were 0.15% and 0.51%. Conclusions: This is the first description of an unselected cohort of individuals with MUTYH Y179C and G396D variants identified through DTC genetic testing. While these two variants were most common among people of European descent, they were also observed at relatively high frequency among people of Hispanic/Latino descent. These results may help guide CRC screening and prevention strategies in different ethnicities. Research Sponsor: 23andMe.
Background: Despite population screening efforts, screening rates for colorectal cancer (CRC) remain suboptimal. A non-invasive, blood-based screening test for CRC has shown sensitivity and specificity in early-stage disease should improve adherence and ultimately reduce mortality; however, tests based on tumor-derived biomarkers have limited sensitivity. Here we used a multomic, machine learning platform to discover, refine, and combine tumor- and immune-derived signals to develop a blood test for the detection of early-stage CRC. Methods: Samples from 591 participants enrolled in a prospective study including average-risk screening and case-control cohorts (NCT03688906) were included in this analysis. CRC: n = 43; colonoscopy-confirmed CRC-negative controls: n = 548). Participants with CRC were 60% male with a mean age of 63, and controls were 55% male with a mean age of 60. Stage distribution was 54% early (I/II) and 34% late (III/IV) with 11% unknown. Plasma was analyzed by whole-genome sequencing, bisulfite sequencing, and protein quantification methods. Computational methods were used to assess and infer the performance of individual and combined assays.

Results: For colorectal adenocarcinoma, which represents ~95% of all CRCs, our multomic test achieved a mean sensitivity of 92% in early stage (n = 17) and 84% in late stage (n = 11) at a specificity of 90%. Across all CRC pathological subtypes, our test achieved a mean sensitivity of 80% in early stage (n = 19) and 83% in late stage (n = 12) at a specificity of 90%; the test detected the single squamous cell carcinoma but missed both neuroendocrine tumors. Individual assays achieved a mean sensitivity of 50% in early stage and 66% in late stage at a specificity of 90%. Conclusions: In a prospective cohort, we demonstrated high sensitivity and specificity for early-stage adenocarcinoma by combining tumor- and immune-derived signals from ctDNA, epigenetic, and protein biomarkers. While most CRCs are adenocarcinomas, detection of all pathological subtypes is required to maximize sensitivity in a screening population. Further analysis of molecular and pathological subtypes, as well as the entire ~3000 patient cohort, is underway. Clinical trial information: NCT03688906. Research Sponsor: None.
Does nutritional status affect treatment tolerability, response, and survival in metastatic colorectal cancer patients? Results of prospective multicenter study, First Author: Senem Karabulut, Istanbul University Onkology Institute, Istanbul, Turkey

Background: The efficacy and tolerability of modern cytotoxic chemotherapy regimens is closely related to the overall survival in mCRC patients. Methods: In this multicenter study, demographic, oncologic and nutritional data were collected prospectively from mCRC patients. Nutritional status was determined using the Malnutrition Universal Screening Tool (MUST). Results: Patients with nutritional risk (MUST > 2) had a lower median OS than those with normal nutritional status (MUST < 2) (9.2 months vs. 11.9 months, P = 0.001). Multivariate analysis revealed that patients with nutritional risk were more likely to have a significant complication related to the primary tumor (OR 1.84, 95% CI 1.47-2.31, P = 0.001), have poorly differentiated tumors (OR 1.24, 95% CI 1.10-1.34, P = 0.001), and were more likely to have a complication related to chemotherapy (OR 1.20, 95% CI 1.01-1.42, P = 0.025) compared to patients with normal nutritional status. Conclusions: Our study showed that moderate/severe malnutrition in mCRC patients was associated with decreased overall survival and increased chemotherapy toxicity.

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Clinical and pathologic characteristics of early-onset colorectal cancer (EoCRC). First Author: Arif Ahmad Arif, University of British Columbia, Vancouver, BC, Canada

Background: Although CRC incidence continues to fall in patients over 50 due to adoption of screening programs, there has been an increasing incidence in patients < 50 where screening does not occur. We investigated the clinical and pathologic characteristics of EoCRC in BC. Patients < 50 years were analyzed. Results: The cumulative incidence of CRC was 3.7% (95% CI 3.1-4.2) per 100,000 person-years. Of those aged 18-49 years, 2762 patients diagnosed with CRC and referred to BC Cancer between 1990-2016. Patients < 50 were classified as early onset CRC and analyzed for baseline and disease characteristics. Results: In the 2540/27612 (9.2%) of patients < 50 patients were more likely to be female (OR 1.33, 95% CI 1.12-1.58, P = 0.001) compared to patients ≥ 50. At diagnosis, patients < 50 were more likely to have a significant complication related to the primary tumor (OR 1.18, 95% CI 1.06-1.32, P = 0.001), specifically, greater rates of perforation (OR 1.84, 95% CI 1.47-2.31, P < 0.001). Although high risk features used to guide adjuvant therapy decisions in patients < 50 with stage II CRC were not higher, with similar T4 prevalence, poor differentiation, lymph node metastases (OR 1.84, 95% CI 1.47-2.31, P = 0.001), have poorly differentiated tumors (OR 1.24, 95% CI 1.10-1.34, P = 0.001), and were more likely to have a complication related to chemotherapy (OR 1.20, 95% CI 1.01-1.42, P = 0.025) compared to patients with normal nutritional status. Conclusions: Our study showed that moderate/severe malnutrition in mCRC patients was associated with decreased overall survival and increased chemotherapy toxicity.

The incidence of peritoneal carcinomatosis and impact on outcomes in relapsed early T4 colorectal cancer, First Author: Rosemary Habib, The University of Sydney, Sydney, NSW, Australia

Background: There is limited data regarding the association between peritoneal carcinomatosis (PC) and clinical outcomes in colorectal cancer (CRC). We examined the incidence of PC and explored the relationship to survival (RFS & OS) in 129 patients with early stage T4 colorectal cancer. Methods: We retrospectively analyzed 129 patients with stage II/III CRC referred to a tertiary centre in Western Sydney between 2009-2016 were obtained. Associations between clinical outcomes and baseline prognostic factors were investigated using proportional hazards regression models. The effect of prognostic factors on outcome were examined by tumour stage. Results: 495 patients were identified, 281 (57%) with stage II and 214 (43%) with stage III. Median follow-up was 38 months. 330 (67%) had T3 and 165 (33%) had T4 disease. Median age at diagnosis was 72 years (95% CI 64-80). Younger patients (OR per 10 years = 1.39, P = 0.01), N stage II (OR 1.51; P = 0.001) was more likely to develop PC. Younger patients (< 50 years) were more likely to develop PC compared with 35% (n = 19) with T4 disease (P = 0.02). Compared with non-PC, PC was associated with poorer median OS (28 vs 46 months; P = 0.03). Median RFS for T3 was 16 months, T4, 14 months (NS). Median OS for T3 was 34 months Vs T4 28 months (P = 0.45). Of those with PC relapse, the diagnosis of PC was highest in the first two years post-operatively (88%), 9 patients (38%) with PC died due to bowel obstruction Vs 4 (5%) patients with non-PC relapse (P < 0.01). Poorer OS was associated with PC (HR 1.74; P = 0.03), right sided primary (HR 1.60; P = 0.05), T stage (HR 1.69; P = 0.03), LVI (HR 1.95; P < 0.01), N stage (HR 1.51; P < 0.01), and number of metastases at baseline (HR 1.25; P = 0.04). On multivariable analysis right sided primary and T4 stage remained significant.

Conclusions: Patients with PC relapse have an 18 month shorter median OS than those with non-PC relapse. Further, PC recurrence is more common in patients with T4 compared with T3 CRC and was the only site of metastatic disease in 7% of relapsed patients with T4 CRC. Consideration for peritoneal cytoreduction and/or HIPEC should be given for patients with PC metastases. For patients with resected early stage T4 CRC, consideration should be given for surveillance laparoscopy.

Research Sponsor: None.

Research Sponsor: None.
Gray areas and evidence gaps in the management of rectal cancer as revealed by the comparison of recommendations from national and international clinical guidelines. First Author: Giacomo Bregni, Institut Jules Bordet-Université Libre de Bruxelles (ULB), Brussels, Belgium

**Background:** While the management of nonmetastatic and oligometastatic rectal cancer has rapidly evolved over the last few decades, many gray areas and highly debated topics remain that foster significant variation in clinical practice. We aimed to identify controversial points and evidence gaps in this disease setting by systematically comparing recommendations from national and international clinical guidelines.

**Methods:** Twenty-six clinical questions reflecting practical challenges in the routine management of nonmetastatic and oligometastatic rectal cancer patients were selected. Recommendations from the ESMO, NCCN, JSCCR, Australian and Ontario guidelines were extrapolated and compared using a 4-tier classification system (i.e., identical/very similar, similar, slightly different, different). Overall agreement between guidelines (i.e., substantial/complete disagreement, partial disagreement, partial agreement, substantial/complete agreement) was assessed for each clinical question and compared against the highest level of available evidence according to the Oxford CEBM Levels of Evidence guidelines by using the y² statistical test.

**Results:** Guidelines were in substantial/complete agreement, partial agreement, partial disagreement, and substantial/complete disagreement for 8 (30.8%), 2 (7.7%), 7 (26.9%), and 9 (34.6%) clinical questions, respectively. High level of evidence supported clinical recommendations in 2/10 cases (20%) where guidelines were in agreement and in 10/16 cases (62.5%) where guidelines were in disagreement (φ² = 4.4726, p = 0.034). Agreement was frequently reached for questions regarding diagnosis, staging, and radiology/pathology pro-forma reporting, while disagreement characterized most of the treatment-related topics.

**Conclusions:** Substantial variation exists across national and international clinical guidelines in the recommendations for the management of nonmetastatic and oligometastatic rectal cancer. This variation is only partly explained by the lack of supporting, high-level evidence. Research Sponsor: None.

77 Poster Session (Board #D7), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Provider perspective: The clinical value of a novel digital medicine program in gastrointestinal oncology. First Author: Cathy Cao, Dana-Farber Cancer Institute, Boston, MA

**Background:** There is an increased use of oral anti-cancer therapies (OACTs) for treatment of gastrointestinal (GI) cancers. While OACTs provide convenience compared to IV agents, they carry similar risks for drug-drug interactions (DDI), toxicities, and unique challenges like adherence and drug access. Patients on OACTs have fewer touch-points with clinicians, requiring more patient ownership of treatment. Pharmacist co-management of pts has been shown to be successful in teaching and monitoring of IV therapy. We sought to assess feasibility of pharmacist co-management for pts prescribed OACTs for treatment of GI cancers. Methods: In 2019, the Dana-Farber GI Cancer Center (GCC) had an embedded pharmacist 8 hrs/week to help with co-management of pts on OACTs. The pharmacist provided (1) in-person and telephone teaching; (2) comprehensive medication reconciliation; (3) DDI review; and (4) supportive care recommendations. Patients were identified by reviewing provider schedules and through provider referrals. The initial teach visit was one-on-one with each patient before initiation, with joint visits with providers thereafter for monitoring and adherence checks. Data were collected to quantify the types of support/recommendation provided by pharmacist and the impact on clinical workflow.

**Results:** After 4 months in the GCC clinic, the pharmacist has co-managed 26 new pts, 67% seen in-person. In initial visits, the pharmacist identified 3 DDI, updated 15 medication lists, and assisted 11 pts/providers with drug access and drug information. The pharmacist saw 10 of 26 pts for follow up, totaling 21 encounters. The pharmacist assisted in 17 of the 21 encounters with drug access and drug information. Pharmacists spent 20 min/pt on teaching. For follow-up visits, the pharmacist did not additional in-visit clinical resources as patients were seen with providers.

**Conclusions:** Pharmacist co-management of patients on OACTs is feasible and offers an added safety resource to pts and providers from initial teaching to focused and frequent drug monitoring. This co-management approach has potential to impact clinical outcomes, such as the use of emergency/hospital visits, the duration of therapy, and adherence. Research Sponsor: None.
Nonoperative management (NOM) in rectal cancer: Physician perspectives on offering NOM as standard of care. First Author: Andrea Marie Covelli, Mount Sinai Hospital, Toronto, ON, Canada

Background: 20% of rectal cancer patients will have a complete response (cCR) following neoadjuvant chemoradiotherapy. Non-operative management (NOM) with close surveillance can spare patients proctectomy and avoid the sequelae of surgery. Patients are interested in and advocate for NOM, whereas oncologists appear to be reluctant to offer this option. We wished to identify the perceptions and barriers that oncologists face when considering NOM. Methods: This qualitative study explored oncologists’ experiences treating rectal cancer and identified their perceptions and values around NOM. Purposive and snowball sampling identified medical, radiation and surgical oncologists who treat a high volume of rectal cancer across Canada. Colon/carcinologists varied in length of practice and gender. Data were collected via semi-structured interviews. Constant comparative analysis identified key concepts. Results: Data saturation was achieved after 40 interviews: 20 surgeons, 12 radiation and 8 medical oncologists. The dominant theme was “NOM is not ready for prime time.” Most oncologists felt that there is insufficient long-term data around NOM and single center studies appear ‘too good to be true’. Physicians voiced concerns about worsening oncologic outcomes in the setting of regrowth, the challenges in defining a cCR and apprehension around patient compliance to surveillance. Some oncologists felt that NOM is limited to a very select population and voiced reluctance in offering it to younger patients or patients with more advanced disease. There was little consideration to improved functional outcomes with NOM. Overall, the majority of participants felt that NOM is ‘trading the benefit of saving the rectum for the uncertainty of an inferior oncologic outcome’. Conclusions: Oncologists felt that NOM should not be offered as a standard of care option following a cCR. Most felt that there is insufficient data supporting NOM and are concerned around worse oncologic outcomes. Patient views of NOM are critical to assess if patients value the same outcomes. Additional research is needed to address barriers should patients wish to consider NOM as a treatment option in the setting of a cCR. Research Sponsor: ARCC – Canadian Centre for Applied Research in Cancer Control.

Clinical outcomes of patient migration in locally advanced rectal cancer from community cancer centers: An analysis of the National Cancer Database. First Author: Rohit Kumar, University of Louisville School of Medicine, Division of Hematology and Medical Oncology, James Brown Graham Cancer Center, Louisville, KY

Background: With cancer care changing at a rapid pace, patients are becoming increasingly involved with their management and oftentimes migrating to a different facility for their treatment at other institutions (adjusted HR 0.80, 95% CI 0.74-0.86, p = 0.001). The majority of patients who were excluded from chemotherapy. We analyzed 2 populations; chemotherapy regained were younger (63 vs 65 years, p = 0.006), as did patients without private insurance (OR 1.17, 95% CI 1.06-1.29), Charlson/Deyo comorbid score (p = 0.006). Blacks presented at later stages (71.4% at stage 3 or 4 vs 66.3% for whites 61 yrs. Stage distribution at diagnosis: stage 1: 100, stage 2: 275, stage 3: 615, stage 4: 376. All treatment at the CCC and 56% had part or all of their care elsewhere. Patients who migrated were younger (63 vs 65 years, p = 0.001) and had got insurance (43.5 vs 35.8%, p<0.001). On multivariate analysis, age =65 years (OR 1.12, 95% CI 1.02-1.24), gov’t insurance (OR 1.17, 95% CI 1.06-1.29), Charlson/Deyo comorbidity score =2 (OR 1.29, 95% CI 1.11-1.49), higher income (OR 1.29, 95% CI 1.16-1.27) and Stage III (OR 1.15, 95% CI 1.07-1.24) were associated with higher probability of migration. The treatment characteristics and outcomes are shown in Table 5. The 5-year OS rate was better in patients who received part or all of their treatment at the CCC versus those who received part or all of their treatments elsewhere were compared using rank sum and X² tests where appropriate. Cox model was used for survival analysis. Results: Of the total population, 51% were stage II and 49% were stage III. Ethnic and economic distributions were similar between the groups. Approximately 44% of patients received all their treatment at the CCC and 56% had part or all of their care elsewhere. Patients who migrated were younger (63 vs 65 years, p<0.001) and had got insurance (43.5 vs 35.8%, p<0.001). On multivariate analysis, age =65 years (OR 1.12, 95% CI 1.02-1.24), gov’t insurance (OR 1.17, 95% CI 1.06-1.29), Charlson/Deyo comorbidity score =2 (OR 1.29, 95% CI 1.11-1.49), higher income (OR 1.29, 95% CI 1.16-1.27) and Stage III (OR 1.15, 95% CI 1.07-1.24) were associated with higher probability of migration. The treatment characteristics and outcomes are shown in Table 5. The 5-year OS rate was better in patients who received part or all of their treatment at other institutions (adjusted HR 0.80, 95% CI 0.74-0.86, p<0.001). Conclusions: Further studies are needed to provide direction for future strategies to reduce the apparent survival disparities in patients who migrate from CCC. Research Sponsor: None.

Racial and socioeconomic disparities in overall survival in colorectal cancer (CRC) at West Cancer Center (WCC), Memphis, TN, First Author: Vanessa Woekey, West Cancer Center and Research Institute/University of Tennessee Health Science Center, Germantown, TN

Background: WCC, a comprehensive regional community oncology center in Memphis, Tennessee and the Mid-South region, serves a racially, geographically and socioeconomically diverse patient cohort. We sought to evaluate disparity of outcomes in survival by race and socioeconomic status, in addition to patient and tumor characteristics. Methods: All consecutive patients referred to and treated at WCC with colorectal adenocarcinoma from 2007-2013 were included. Individual chart review was performed to verify diagnosis, stage, and date of cause of death. Kaplan-Meier Overall Survival curves were generated for the entire cohort and by race, sex, tumor location and income derived from zip code. WCC survival data were compared to SEER data. Results: From 2007-2013, 1,176 patients were included in the analysis: 405 blacks, 757 whites, 14 others. Median age at diagnosis: Blacks 58 yrs, whites 61 yrs. Stage at diagnosis: stage I: 100, stage 2: 275, stage 3: 425, stage 4: 376. All stages combined, blacks trended towards shorter OS vs whites (5-year OS: 52.8% vs 58.3%; median survival 71.0 mos vs 98.6 mos; p = 0.095). Blacks presented at later stages (71.4% at stage 3 or 4 vs 66.3% for whites) but no statistically significant OS differences were seen when compared by stage. Patients at or below the median income of $39,590 for WCC had worse 5-year OS (51.6% vs. 61.1%; p = 0.006), as did patients without private insurance (48.0% uninsured, 50.0% privately insured, 50.0% publicly insured, 62.0%; p<0.001). Adjusted for stage, 5-year OS was statistically significant for stage 4 (private: 18.0%, Medicaid/Medicare: 9.4%, uninsured: 8.3%; p=0.020). A higher proportion of blacks were below the median income (65% vs 29%) but no statistically significant differences were found when adjusted by race. Overall, cancer survival outcomes were similar to SEER results. Conclusions: At WCC, black patients with CRC presented at a later stage than whites, however, adjusted for stage, no significant racial difference in OS was found. Income and insurance status affected survival outcomes. Overall, our results reveal racial and socioeconomic disparities in colorectal cancer in a diverse US population. Research Sponsor: None.

Quality of timely adjutant chemotherapy for veterans with colorectal cancer. First Author: Richard Lewis Martin, Vanderbilt Hematology Oncology, Nashville, TN

Background: National Comprehensive Cancer Network (NCCN) recommends adjuvant chemotherapy for patients with high risk stage II or stage III colorectal cancer (CRC). Treatment within 8 weeks of surgery improves disease free survival and decreases recurrence. National Veterans Health Adminis- tration (VHA) CRC data demonstrated adherence to this standard; however, there was regional variation. We sought to describe time to treatment at a Southeast Regional VHA facility to determine local targets for quality improvement initiatives. Methods: We retrospectively reviewed 705 electronic medical records of patients who underwent colorectal surgery from January 1, 2000 to December 31, 2015 at VHA Tennessee Valley Healthcare System. Two trained clinician abstractors reviewed standard elements (k = 0.79-0.92). The population included patients with pathological stage high risk II or III CRC and excluded those with metastatic disease or documented NCCN defined exclusion from chemotherapy. We analyzed 2 populations; chemotherapy received and a sensitivity analysis population of patients who were eligible for, but did not receive, chemotherapy (no documentation of NCCN ineligibility or declined). The primary outcome was chemotherapy within 8 weeks of surgery, evaluated during three time periods due to changes in NCCN guidelines. Results: Of 705 colorectal surgeries, we excluded 262 for non-cancers, 220 for stage I or low-risk stage II cancers, and 46 for NCCN defined exclusion, yielding 177 cases: 120 colon and 57 rectal cancers. Patients were 98% male, 85% white, and median age 64 years [Interquartile Range 60, 70]. Among those receiving chemotherapy (123/177 [69.5%]), median time to treatment was 50.5 days [40, 64]; with 63% receiving chemotherapy within 8 weeks. Results varied over time. Between 2000-2004 75% received within 8 weeks; 2005-2009, 62%; 2010-2015, 41%. Including all eligible patients, the proportion receiving timely treatment declined: overall 44%; 2000-2004, 57%; 2005-2009, 45%; 2010-2015, 25%. Conclusions: Improving care processes for patients with CRC can improve timely treatment. Exploring barriers such as prolonged hospitalization, wound healing, and port placement may reveal areas for quality improvement. Research Sponsor: None.

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Gaps in caregiving for young-onset colorectal cancer patients. First Author: Kim Lynn Newcomer, Colorectal Cancer Alliance, Washington, DC

Background: The rise of young-onset colorectal cancer (YO-CRC) is an alarming public health issue. Interestingly, the proportion of new cases diagnosed in young people (20-49) had increased from 6% in 1990 to 11% in 2013 and coincides with the declining CRC cases in older people. YO-CRC patients face unique clinical challenges as many are diagnosed at advanced stages of the disease and subjected to aggressive treatments. In addition, diagnosis often disrupts early family and career developmental tasks and goals, suggesting the need for additional psychosocial support. Caregivers are an important part of the patient journey. Caregivers serve as liaisons with the medical community and the patient’s social network. The goal of this study is to cast light and explore the experience of caregivers who were caring for YO-CRC patients.

Methods: The online survey was completed by 208 caregivers, diverse in age, gender, and race/ethnicity. Participants indicated their relationship as either: spouse/partner, parents, siblings, children, and non-family members.

Results: Caregivers self-report they do not understand the important aspects of patients’ medical needs despite 79% of caregivers are college graduates and 43% had an advanced degree. Most of the respondents (76%) lack understanding about treatment options and 56% did not feel confident they understood healthcare decisions. Overall, caregivers needed more information and guidance for managing the side-effects of treatment. A majority of caregivers (93%) reported fatigue due to lack of sleep and 63% reporting they missed eight hours or more of work each month. Participants (73%) reported they needed help for panic and anxiety and employed different coping mechanisms to deal with the toll of caregiving.

Conclusions: Our survey indicates we must recognize caregivers as the patient’s healthcare partners and engage them in the entire plan of care. A growing population of YO-CRC patients means a growing population of caregivers who are navigating work, parenthood, impacts on sexual health, and role changes right along with that patient. Such understanding could help in developing appropriate interventions for caregivers aimed at reducing their burden and stress in caring for patients with YO-CRC.

Research Sponsor: None.

84 Poster Session (Board #D14), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Travel distance and time to adjuvant chemotherapy in veterans with colorectal cancer. First Author: Richard Lewis Martin, Vanderbilt Hematology Oncology, Nashville, TN

Background: Patients from rural areas have well described disparities in quality cancer care. We hypothesized that longer travel distance is associated with less chemotherapy acceptance and less timely treatment. Methods: We reviewed 705 electronic medical records of patients with colorectal surgeries from January 1, 2000 to December 31, 2015 at the Veterans Health Administration Tennessee Valley Healthcare System. Two trained abstractors reviewed standard elements (k = 0.79 - 0.92). The study sample included patients with pathological stage high risk II or III CRC and excluded those with metastatic disease or documented National Comprehensive Cancer Network (NCCN) defined medical exclusions from chemotherapy. Primary exposure was distance to care calculated from central zip code of residence to Nashville infusion center. Primary outcomes were receipt of any chemotherapy, and days from surgery to first treatment (truncated at 120 days). We analyzed 2 populations; chemotherapy received and a second sensitivity population who were eligible for, but did not receive, chemotherapy (no documentation of NCCN ineligibility or declined). Results: Of 705 colorectal resections, we excluded 262 for non-cancer, 220 for stage I or low risk stage II, and 46 for NCCN exclusion criteria, yielding 177 cases: 120 colon and 57 rectal. Most patients were male (98%) and white (85%); median age was 64 (Interquartile Range 60, 70). Distribution by travel distance was 60/177 (33.9%) < 50 miles, 61/177 (34.5%) 50-99 miles, and 56/177 (31.6%) > 100 miles. Of all eligible patients, 123/177 (69.5%) patients received chemotherapy and 54/177 (30.5%) did not receive chemotherapy. Among receivers, median times to treatment were 52 days [40, 61] < 50 miles; 48.5 [40,61] 50-99 miles; and 54 [43,77] > 100 miles, p = 0.3. Patients not receiving chemotherapy varied by distance: 15/60 (25%) < 50 miles; 18/61 (30%) 50-99 miles; 2/56 (38%) > 100 miles. p = 0.3. Including non-receivers, median times to treatment were 58 days [43,120] < 50 miles; 58.5 [46.5,120] 50-99 miles; and 80 [48.5,120] > 100 miles, p = 0.1. Conclusions: Distance to care may influence acceptability of chemotherapy. Understanding patient/provider reasons for omission merits exploration. Research Sponsor: None.

86 Poster Session (Board #D16), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

An intersectional investigation of race and sex on receipt of adjuvant chemotherapy in stage III colon cancer. First Author: Benjamin Powers, University of Maryland Capital Region Medical Center, Washington, DC

Background: Race and sex disparities exist for receipt of adjuvant chemotherapy (AC) for stage III colon cancer. However, most studies have not used an intersectional approach, which assesses the cumulative effects of different identities (e.g., Black women) and their distinct, intersecting variables. Using this approach, we assessed the summative impact of these identities on receipt of AC for stage III colon cancer. Methods: The National Cancer Database was queried from 2004 to 2015 for patients who underwent surgery for stage III colon cancer and were healthy enough for AC. Receipt of AC was assessed chi-squared and multivariable logistic regression analyses. Results: 92,696 patients were identified. White patients had higher rates of care at community cancer centers. Black patients had higher rates of treatment at academic cancer programs (p < 0.001). Overall 83.5% received AC. Black males and females had higher rates of AC (86.5% and 86.2%, respectively) compared to White males and females (85.3% and 80.5%), respectively (p < 0.001). In adjusted analysis, Black males had the lowest odds of AC (OR 0.73), followed by Black females (OR 0.89) and White females (OR 0.91). When evaluated by age < 65 years and adjusting for potential confounders, Black males remained the least likely group to receive AC (OR 0.70). Black females had similar odds of receipt of AC (OR 0.99) and White females had increased odds (OR 1.22) relative to White males. Conclusions: Despite higher rates of treatment at academic centers, Black males and females had lower odds of receipt of AC after adjusting for confounders. Younger Black males persisted with the lowest odds of AC, although younger Black females had odds similar to younger White males. Additional research is necessary to identify drivers of these disparities and interventions to ameliorate them. Research Sponsor: None.

Relative odds of AC (Adjusted OR [95% CI])

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<tr>
<th>Overall Cohort</th>
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<td>Intersectional Group</td>
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<td>White Females</td>
<td>0.91 [0.87-0.95]</td>
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<td>Black Males</td>
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*Adjusted for pathologic stage, age, comorbidities, grade, margin, hospital surgical volume, and facility type.
87 Poster Session (Board #D17), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Effect of weight loss in patients with metastatic colorectal cancer treated within the randomized phase III FIRE-3 trial (AIO KKR 0306). First Author: Lian Liu, Comprehensive Cancer Center, University Hospital, LMU Munich, Munich, Germany

Background: A subgroup of RAS wild-type metastatic colorectal cancer patients within the FIRE-3 study consisted of 400 patients. Gaining insight into frequency and effects of weight change among patients treated with FOLFIRI plus either cetuximab or bevacizumab was aim of this analysis. Methods: A subgroup of 400 RAS wild-type metastatic colorectal cancer (mCRC) patients of the FIRE-3 trial were evaluated. A linear mixed model was used to explore the mean evolution of weight over time. The presence of a breakpoint at month 1 was investigated by the addition of an adequate parameter into the model. A linear evolution was supposed from month 1. In this exploratory analysis, patients were grouped into cohorts according to weight change using the cut off % ≥ 5%. Kaplan-Meier estimates and median survival times were analyzed using log-rank testing. Hazard ratios and corresponding 95% confidence interval from univariate Cox proportional hazards were followed by a multivariate analysis. Results: Patients lost in average 0.75 kg during the first month of treatment, whereas body weight increased hereafter 0.43 kg per month. Of note, patients older than 65 years lost most body weight at month one (1.35kg) and gained least hereafter (0.20kg per month). Within this population a weight loss of ≥ 5% was observed to be an independent prognostic factor for both PFS after 3 months (HR 1.72, 95% CI 1.26-2.34, P < 0.001) and OS after 3 months (HR 1.75, 95% CI 1.29-2.39, P < 0.001). This remained significant when adjusted for age, sex, ECOG score, primary tumor side and treatment arm. Conclusions: In the overall RAS wild-type population, weight loss is an independent prognostic factor for survival in patients with RAS wild-type metastatic colorectal cancer patients and may predict the frequency of adverse events. Therefore, we assume that early preventative measures targeted at weight maintenance might contribute to improved outcomes among this population. Research Sponsor: None.

88 Poster Session (Board #D18), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Splenomegaly during oxaliplatin-based chemotherapy in colon cancer. First Author: Ruoyu Ji, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Background: Splenic enlargement has been reported in patients treated with oxaliplatin. However, the characteristics of oxaliplatin-induced splenomegaly were not well studied. Here we evaluated the change of splenic volume and its clinical significance in patients treated by oxaliplatin-based regimen.

Methods: Patients with stage II-IV primary colon cancer treated with oxaliplatin and capecitabine in China National Cancer Center from January 2016 to December 2017 were screened for this retrospective study. Those with complete laboratory tests and computed tomographic data before and during and up to 1.5 years after the chemotherapy were selected. The splenic size was measured at AWVolumeshare5. Splenomegaly was defined as an over 30% increase of splenic size from baseline. Recovery of splenomegaly was defined as the splenic size fell back to a 0.9 to 1.1-fold range of baseline. Results: Out of a total of 144 patients, 102 (70.8%) had over 30% increase, 72 (50.0%) had over 50% increase, and 22 (15.3%) had over 100% increase in splenic size after oxaliplatin-based regimen. Among the 102 splenomegaly patients, 5 (4.9%) develop splenomegaly within 3 chemotherapy cycles, 53 (53.0%) within 6 cycles, 73 (71.6%) within 9 cycles, and 102 (100.0%) within 3 months after the last administration of oxaliplatin. Compared to the group without splenomegaly, patients with splenomegaly received more cycles of oxaliplatin administrations (median 8 vs 6, P < 0.001) and greater dose intensity (total dose per square meter) (median 822.8mg/m² vs 629.3mg/m², p < 0.001). Patients with splenomegaly had higher incidence of thrombocytopenia (61.7% vs 38.1%, p = 0.009) and are more likely to undergo oxaliplatin dose reduction due to thrombocytopenia (21.6% vs 7.1%, p = 0.038). The recovery rates of splenic size within 0.5, 1 and 1.5 years after the end of oxaliplatin treatment were 23.2%, 50.6% and 74.3%, respectively. Conclusions: Splenomegaly are common in patients treated with oxaliplatin-based chemotherapy, and most would recover in 1.5 years after completion of therapy. Patients with splenomegaly are prone to experience thrombocytopenia and oxaliplatin dose reduction. Further studies are needed to reveal the mechanism how oxaliplatin induce splenomegaly. Research Sponsor: None.

89 Poster Session (Board #D19), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

How to improve toxicity evaluation in clinical trials? Testing new metrics from irinotecan or oxaliplatin-based treatments in metastatic colorectal cancer (mCRC): A pooled analysis from 2,349 patients in ARCAD database. First Author: Christophe Tournigand, Hôpital Henri Mondor, Assistance Publique-Hôpitaux de Paris, Créteil, France

Background: Monitoring of adverse events (AE) is crucial in clinical trials. Maximum grade per patient (pt) is commonly used but better metrics are needed to aid describing and comparing AE profiles. Methods: We developed and evaluated 2 longitudinal AE summary metrics. 1) Onset time of max grade and evaluated 2 longitudinal AE summary metrics. 1) Onset time of max grade and evaluated 2 longitudinal AE summary metrics. 1) Onset time of max grade and evaluated 2 longitudinal AE summary metrics. 1) Onset time of max grade and evaluated 2 longitudinal AE summary metrics and effects of weight change among patients treated with TOLFIRI plus either cetuximab or bevacizumab was aim of this analysis. Methods: A subgroup of 400 RAS wild-type metastatic colorectal cancer (mCRC) patients of the FIRE-3 trial were evaluated. A linear mixed model was used to explore the mean evolution of weight over time. The presence of a breakpoint at month 1 was investigated by the addition of an adequate parameter into the model. A linear evolution was supposed from month 1. In this exploratory analysis, patients were grouped into cohorts according to weight change using the cut off % ≥ 5%. Kaplan-Meier estimates and median survival times were analyzed using log-rank testing. Hazard ratios and corresponding 95% confidence interval from univariate Cox proportional hazards were followed by a multivariate analysis. Results: Patients lost in average 0.75 kg during the first month of treatment, whereas body weight increased hereafter 0.43 kg per month. Of note, patients older than 65 years lost most body weight at month one (1.35kg) and gained least hereafter (0.20kg per month). Within this population a weight loss of ≥ 5% was observed to be an independent prognostic factor for both PFS after 3 months (HR 1.72, 95% CI 1.26-2.34, P < 0.001) and OS after 3 months (HR 1.75, 95% CI 1.29-2.39, P < 0.001). This remained significant when adjusted for age, sex, ECOG score, primary tumor side and treatment arm. Conclusions: In the overall RAS wild-type population, weight loss is an independent prognostic factor for survival in patients with RAS wild-type metastatic colorectal cancer patients and may predict the frequency of adverse events. Therefore, we assume that early preventative measures targeted at weight maintenance might contribute to improved outcomes among this population. Research Sponsor: None.

90 Poster Session (Board #D20), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

DPYD gene polymorphisms in patients with gastrointestinal tumors receiving chemotherapy with 5-fluourouracil. First Author: Oleg Ivanovich Kit, Rostov Research Institute of Oncology, Rostov-on-Don, Russian Federation

Background: Complete or partial deficiency of the DPD enzyme due to genetic polymorphisms of the DPYD gene causes acute toxicity of fluoropyrimidines, which are widely used in combination chemotherapy regimens for various malignant neoplasms. The purpose of the study: to identify polymorphisms of the DPYD gene significant for 5-fluorouracil-induced toxicity. Methods: Venous blood samples from Caucasian patients were used to identify alleles of *2A rs3918290, *5 rs1801159, *13 rs55886062 and rs67376798 DPYD by RT-PCR and direct sequencing. Inclusion criteria were: verified diagnosis of gastrointestinal tumors, age>18 years old, fluoropyrimidine-containing regimes of treatment. Results: 104 pts were included, 54% were female. Mean age-61 years. Colorectal cancer was found in 40.7% pts, non-colorectal in 19.3% pts. Hematological and non-hematological toxicity Gd-3-4 was found in 24% pts. Allele *5rs1801159, which causes enzyme deficiency was found in 28% of patients, (frequency 0.28) which is significantly higher than the population frequency of the allele charactering for Caucasoid population (p <0.05). Meanwhile genotyping did not reveal the *2A, *13 alleles and rs67376798 alleles in the DPYD gene. Conclusions: *5rs1801159 allele was found as the main DPYD polymorphism associated with fluoropyrimidine toxicity in Cauca- sian pts with gastrointestinal tumors. Research Sponsor: None.

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**Feasibility of using fitness tracker to assess activity level and toxicities in colorectal cancer (CRC) patients (Pts). First Author: Thomas Holden, Fox Chase Cancer Center, Temple Health, Philadelphia, PA**

**Background:** Performance status (PS) is used to predict tolerance and morbidity associated with CRC treatment. Monitoring activity level at the start of therapy using a wearable fitness tracker Fitbit (FB) may provide a more accurate estimate of a pt’s overall PS and help predict treatment related toxicity (T). **Methods:** With IRB approval, we prospectively enrolled CRC pts undergoing therapy into 2 cohorts, medical undergoing chemotherapy (M) and surgical undergoing definitive surgery (S). Our objective was to assess feasibility of using FB to track activity level and secondarily correlate with T. After documenting baseline ECOG PS, M and S pts wore FB for 4 days while receiving chemotherapy or prior to surgery, respectively. Pts’ mean steps per day (SPD) were calculated excluding days FB was worn (<12 hours). To stratify prediction of toxicity risk, a cutoff of 5000 SPD was selected and any post-operative complication (S pts) or hospitalization (M pts) was counted as T. The study met accrual of 80 pts. **Results:** On final analysis, 80 pts were evaluated for the primary aim. 68 pts had at least 3 days with ≥12 hours of FB usage, meeting the 75% feasibility endpoint. 76 pts had at least 1 day with ≥12 hours of FB usage with data for analysis. SPD correlated with PS and the SPD and active minutes (read by device) for PS 0 and PS 1 pts was 6332 steps and 122 mins and 2925 steps and 55 mins, respectively (p = 0.0033). Rate of T was 25% in pts with PS 0 and 33% in pts with PS 1. With SPD, rate of T was numerically lower in pts with >5000 SPD compared to pts with <5000 SPD (21% vs 32%, p = 0.15). **Conclusions:** We observed high rates of compliance with FB in CRC pts. SPD cutoff of 5000 correlated with ECOG PS 0 vs 1. We observed usefulness of SPD as an identifier for toxicities and suggestion that it may be more reliable compared to PS alone in a small sample of pts. These conclusions provide rationale to study SPD in conjunction with PS for risk stratification of pts undergoing therapy, and can possibly be incorporated into pre-habilitation selection in high risk groups. Research Sponsor: Colon Cancer Coalition, ACS IRG grant.

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**Prospective DPYD testing and dose adjustment in colorectal cancer patients prior to fluoropyrimidine-based chemotherapy: Experience in a regional cancer center. First Author: Janet Shirley Graham, Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom**

**Background:** The fluoropyrimidines (FP), 5-Fluorouracil (5-FU) and capecitabine are a mainstay of colorectal cancer (CRC) treatment. Dihydropyrimidine dehydrogenase (DPYD), an enzyme encoded by the DPYD gene, is the initial and rate-limiting step in pyrimidine catabolism, deactivating over 80% of 5-FU. Approximately 5% of the population are deficient in DPYD and can develop severe or fatal FP toxicities. Currently, few national guidelines recommend routine prospective DPYD testing. In July 2019, we commenced a 6 month prospective, single-arm, phase II study of CRC pts undergoing first FP treatment in a large regional cancer centre. **Methods:** All CRC patients eligible for first exposure to FP are tested using a rapid molecular assay screening for five SNPs (detects 70% of DPYD mutations) and we will present data on prevalence of each. We will use electronic chemotherapy prescribing records (July 19-Jan 20) to collect information on dose modifications and toxicities. Since the pilot is completed we will perform a cost-effectiveness analysis. **Results:** Data from the first 3 months of this pilot have been reviewed and 201 patients have been tested with 15 heterozygotes identified, of which 2 had more than one mutation. No homozygotes were found. All heterozygote patients are started with a dose reduction (or have alternative therapy). One patient treated at 50% dose was hospitalised with several grade 3 toxicities despite dose reduction. Two patients have had subsequent dose escalation by 25%. Nine patients have received one dose reduced cycle without complication. Three patients are due to start dose-reduced treatment. **Conclusions:** Routine prospective testing of DPYD status in a large regional cancer centre is feasible and with a sufficiently swift result turned up to permit up-front dose modification. Detailed toxicity analysis and cost-effectiveness data will be presented. Research Sponsor: Hospital funds.

**Evaluation of adjuvant chemotherapy-associated steatosis in colorectal cancer. First Author: Michelle (Chae Min) Lee, St. Michael’s Hospital, Toronto, ON, Canada**

**Background:** Chemotherapy-associated steatosis (CAS) is poorly understood in context of colorectal cancer (CRC). It has been anecdotally observed that CRC patients undergoing chemotherapy appeared to develop steatosis at a higher rate than expected, and that statin therapy may have protective effects against CAS. Here, we sought to evaluate 1) the frequency of CAS in Stage II-III CRC patients; and 2) whether patients on statin therapy develop CAS at a lower frequency. **Methods:** This study retrospectively examined medical records of 267 Stage II-III CRC patients who received adjuvant chemotherapy and were followed up at St. Michael’s Hospital, Toronto, Canada between January 1, 2006 and January 1, 2017. Patient information, relevant co-morbid conditions, statin use, and adjuvant chemotherapy were collected. Baseline and incident steatosis for up to one year from chemotherapy start date was assessed based on imaging reports (CT, ultrasound, MR). **Results:** Of 267 patients, 78 (29.2%) had steatosis at baseline radiology, prior to treatment with adjuvant chemotherapy. Of the remaining 189 cases, the incidence of steatosis within one year of adjuvant chemotherapy start date was significantly greater in patients who received adjuvant treatment (n = 132) compared to those who did not (n = 57), (39% vs. 23%, p = 0.03). Among patients who underwent chemotherapy, statin use for preexisting hyperlipidemia, a known risk factor for steatosis (n = 39), was associated with a lower incidence of steatosis compared to no statin administration (n = 93), although this result was not significant (31% vs. 42%, p = 0.243). Among statin users, 42.9% of patients treated using oxaliplatin-containing FOLFOX regimens (n = 21) developed steatosis, compared to 20% in patients on a capcitabine regimen (n = 15). There was a trend towards significance, with p = 0.151. **Conclusions:** Chemotherapeutic treatment of Stage II-III CRC is associated with an increased incidence of steatosis. Statins may protect against adjuvant chemotherapy-induced steatosis, which is of particular significance in CRC chemotherapy, particularly with single agent capcitabine. Prospective clinical trials should be considered to prioritize protective use of statin in this critical patient population. Research Sponsor: None.

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Randomized phase II trial of CAPOX with continuous versus intermittent use of oxaliplatin as an adjuvant chemotherapy after curative resection of stage II/III colon cancer (CCOG-1302 study). First Author: Masanori Nakamura, Department of Surgery, Konan Kosei Hospital, Konan, Japan

**Background:**
The aim of this study was to evaluate the efficacy and safety of CAPOX with intermittent use of oxaliplatin compared to continuous use of oxaliplatin as an adjuvant setting for colon cancer. **Methods:** Patients with curative resection of stage II or III colon cancer were randomly assigned to receive either CAPOX with continuous use of oxaliplatin (continuous arm: 2 cycles of CAPOX) or CAPOX with intermittent use of oxaliplatin (intermittent arm: 2 cycles of CAPOX—4 cycles of capecitabine)—2 cycles of CAPOX). The primary endpoints were frequency of disease-free survival (DFS) rate at 3-year after surgery and perioperative serious neuropathy (PSSN) at 1-year after surgery. The secondary endpoints included DFS, overall survival (OS), compliance and safety. **Results:** A total of 220 patients were enrolled. The intent-to-treat and safety population comprised 100 and 99 patients in the continuous arm, and 101 and 98 patients in the intermittent arm, respectively. After a median follow-up period of 39 months, disease recurrence and death occurred in 37 patients (19%) and 30 patients (15%) in the continuous arm and 37 patients (19%) and 28 patients (14%) in the intermittent arm, respectively. The 3-year DFS was 78% (95% CI, 70-87%) in the continuous arm and 82% (95% CI, 74-90%) in the intermittent arm (HR, 0.80; 95% CI, 0.42-1.52; p = 0.49). In the patients with stage III disease, the 3-year DFS was 74% (95% CI, 66-86%) in the continuous arm and 80% (95% CI, 71-88%) in the intermittent arm (HR, 0.75; 95% CI, 0.38-1.51; p = 0.43). The frequencies of PSSN at 1-year after surgery were 58% (95% CI, 48-68%) in the continuous arm and 19% (95% CI, 11-26%) in the intermittent arm (p < 0.01), and those at 3-year after surgery were 37% (95% CI, 27-47%) and 9% (3-16%), respectively (p < 0.01). **Conclusions:** CAPOX with planned intermittent use of oxaliplatin could be equally effective as an adjuvant setting for colon cancer, and substantially reduce long-term PSSN and potential improve patient quality of life. Clinical trial information: UMIN00002535. Research Sponsor: None.

**Poster Session (Board #E5), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM**
Comparing FOLFIRI plus bevacizumab with doublet chemotherapy plus anti-EGFR antibody: A systemic review and network meta-analysis. First Author: Jianwei Zhang, The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

**Background:** FOLFIRI plus bevacizumab (Triplet+Bev) improved survival benefit when compared with doublet chemotherapy plus Bev (doublet+Bev) as initial treatment in metastatic colorectal cancer (mCRC). Several previous studies have compared the efficacy of doublet plus EGFR antibody (doublet+EGFRi) with doublet+Bev. However, little is known about triplet+Bev comparing with doublet+Bev. **Methods:** We did a systematic review and network meta-analysis with a systematic literature search on PubMed, Embase, Web of Science, and other electronic databases. The primary endpoints were frequency of disease-free survival (DFS) rate at 3-year after surgery and perioperative serious neuropathy (PSSN) at 1-year after surgery. The secondary endpoints included DFS, overall survival (OS), compliance and safety. **Results:** A total of 43 pts were enrolled. Median age was 61 (range 29-82), 14 pts (33%) were female and 39 (91%) left sided. 30 pts (70%) had liver metastases and 40 (iver) liver metastases were included. 2 pts were MSI-H, one MSI-low and 45 MSS. Besides, 3 pts were KRAS wild type and 48 other mutations (14%). In the first-line treatment, disease control rate was well tolerated and bevacizumab was not associated with unexpected adverse events to standard FOLFOX/cteuximab. Central tissue review found 4 pts to be ineligible due to low frequent KRAS or BRAF mutation (15-31%). Thus, ITT included 39 pts. The ORR was 79.5%, including 6 complete (CR) and 25 partial responses (PR). Further 5 stable diseases were noted, thus disease control rate was 92.3%; 2 pts had progression and 1 was not evaluable. Early tumor shrinkage (E1S) rate (≥20% after 8 weeks) was 79.5% (1C, 27 PR and 3 SD with ≥20%-30% in MSI-H pts and 1P in the other group), respectively (p < 0.01). Panel sequencing was feasible with I53 mutations detected, showing an immediate ctDNA drop within 4 weeks of treatment, mirroring the high rate of early tumor response. Notably, the 4 pts with fever had a high T cell infiltration in the tumor. Final data including the potential endpoints and the primary end points will be presented at the meeting. **Conclusions:** The AVETUX regimen was feasible producing a high rate of responses in MSS pts mainly occurring within the first 8 weeks. The noted ORR/E1S of 79.5% warrants further evaluation in a randomized trial. Clinical trial information: NCT03174405. Research Sponsor: Merck KgA.
mFOLOXIRI with or without cetuximab as conversion therapy in patients with RAS/BRAF wild-type unresectable liver metastases colorectal cancer: The FOCUSM study. First Author: Huabin Hu, The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Background: Conversion therapy for unresectable colorectal liver metastases (LMD) may downsize tumours to create a situation where the patient has no evidence of disease (NED). We assessed the effectiveness of mFOLOXIRI plus mFOLOXIRI or mFOLOXIRI in this setting. Methods: FOCUSM was a prospective 2:1 controlled, multicenter, phase II trial. Given no free drugs offered and the patients' affordability for cetuximab, the study design has been amended from randomization to non-randomization since September, 2016. Patients with unresectable LM were assigned to receive cetuximab (500mg/m²) plus mFOLOXIRI (oxaliplatin 85 mg/m², irinotecan 165 mg/m², folinic acid 400 mg/m², 5-fluorouracil 2800mg/m² 46th infusion, every 2 weeks) (group A) or mFOLOXIRI (group B). Primary endpoint was the rate of NED achieved, secondary endpoints were ORR, the rate of local and ablative treatment (LAT), OS, PFS and DpR.

Results: From February 2014 to July 2019, 114 patients were enrolled at 6 centers in China and 101 patients were in the ITT population (67 group A, 34 group B). Treatment groups were generally well balanced, although more patients with >5 LM were in group A. The rate of NED achieved was 62.7% in group A and 38.2% in group B (P = 0.020). At a median follow-up of 19.4 months, patients in group A had significantly prolonged the mOS, mORR, mPFS, mOS ≥ 5 years and mOS ≥ 10 years compared with group B. Patients with NED achieved yielded a significant survival benefit, whether in group A (Not reached vs. 49.4 months; P = 0.001) or group B (Not reached vs. 25.1 months; P = 0.007).

Conclusions: The rate of NED achieved was 62.7% in group A and 38.2% in group B (P = 0.020). At a median follow-up of 19.4 months, patients in group A had significantly prolonged the mOS, mORR, mPFS, mOS ≥ 5 years and mOS ≥ 10 years compared with group B. Patients with NED achieved yielded a significant survival benefit, whether in group A (Not reached vs. 49.4 months; P = 0.001) or group B (Not reached vs. 25.1 months; P = 0.007).

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Poster Session (Board E47), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

VOLTAGEL-B study: Nivolumab monotherapy and subsequent curative surgery following preoperative chemoradiotherapy in patients with locally recurrent rectal cancer (LRRC) without previous radiotherapy. First Author: Takeshi Kato, Department of Surgery, National Hospital Organization Osaka National Hospital, Amagasaki, Japan

Background: Chemoradiotherapy (CRT) followed by curative resection in patients (pts) with local recurrence after radical surgery for primary rectal cancer is the preferred strategy if radiotherapy (RT) was not previously performed. In VOLTAGE-A study, nivolumab plus surgery following CRT showed a promising pathologic complete response (pCR) rate of 30% in pts with microsatellite-stable (MSS) advanced primary rectal cancer. The treatment sequence was prospectively investigated in pts with Locally Recurrent Rectal Cancer (LRRC) in VOLTAGE-B. Methods: Pts with pelvic LRRC without previous RT were included. Five cycles of nivolumab (240 mg q2 weeks) plus surgical curative following CRT (50.4 Gy with capecitabine 1,650 mg/m²) were performed. The pCR rate using AJCC tumor regression grading and curative resection rate were key endpoints. Planned sample size in VOLTAGE-B was set 10 pts in an exploratory manner. Results: From May to Oct 2018, 10 pts were included. Median age was 65 and 6 were male. Curative resection was performed in nine pts with MSS. One had a newly diagnosed supracaval lymnode metastasis before surgery. As one pt with AJCC grade 0, seven with grade 2, and one with grade 3, were observed, pCR rate was 10%. As of cut-off date of Apr-2019, three pts showing recurrence out of the nine pts were observed. Nivolumab-related adverse events (AEs) were only one pt with grade 1 hyperthyroidism and one with grade 1 erythema. Grade 3/4 surgery-related AEs were observed in six pts, including two pts with ileus and two with pelvic infection. No treatment-related mortality was observed. pCR rate of 10% with acceptable toxicity was shown in MSS LRRC pts treated with nivolumab plus curative surgery following CRT. Translational research exploring better predictors of efficacies of study treatment are ongoing. Clinical trial information: NCT02948348. Research Sponsor: ONO Pharmaceutical.

Poster Session (Board E10), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Irinotecan, cetuximab, and bevacizumab (CBI) versus irinotecan, cetuximab, and placebo (CI) in irinotecan-refractory metastatic colorectal cancer (mCRC): Results from an ACCRU network randomized phase II trial. First Author: Maria Lipsyc-Sharf, Department of Internal Medicine, Brigham and Women's Hospital, Boston, MA

Background: Combination irinotecan and cetuximab is approved for irinotecan-refractory mCRC, it is unknown if the addition of bevacizumab would improve outcomes. We studied the efficacy and safety of CBI compared with CI in patients (pts) with RAS wildtype, irinotecan-refractory mCRC. Methods: In this multicenter, randomized, double-blind, placebo-controlled phase II trial, pts with RAS wildtype mCRC and no prior anti-epidermal growth factor receptor therapy with at least 1 irinotecan-based chemotherapy regimen and received bevacizumab in at least 1 prior line of therapy were randomized 1:1 to irinotecan 180 mg/m² (or previously tolerated dose), cetuximab 500 mg/m² and bevacizumab 5 mg/kg vs CI every 2 weeks until disease progression, intolerable toxicity, or withdrawal of consent. The primary endpoint was progression-free survival (PFS). Multivariable Cox proportional hazard models stratified by number of prior lines of therapy and bevacizumab receipt in immediate prior line were performed. Secondary endpoints included overall survival (OS), objective response rate (ORR), and adverse events (AEs). The study was closed early in January 2018 for reasons related to accrual and funding after enrollment of 36 out of a planned 60 pts. Results: Between July 2015 and December 2017, 36 pts were randomized (19 to CBI, 17 to CI). 34 pts (94%) were treated with 2 or more prior chemotherapy regimens. Baseline characteristics were similar between arms. Median PFS was 9.7 vs 5.5 mo for CBI and CI arms, respectively (log-rank P = 0.76; multivariable HR = 0.64; 95% CI, 0.25-1.66). Median OS was 19.7 vs 10.2 mo for CBI and CI (log-rank P = 0.04; multivariable HR = 0.41; 95% CI, 0.15-1.09). ORR was 37% for CBI vs 12% for CI (P = 0.13). Grade 3 or higher AEs occurred in 47% of pts receiving CBI vs 35% for CI (P = 0.46). Conclusions: In this prematurely discontinued trial, there were non-significant increases in PFS and ORR and a statistically significant 9.5 mo increase in median OS in CBI compared to CI. Further investigation of CBI for treatment of irinotecan-refractory mCRC is warranted. Clinical trial information: NCT02292758. Research Sponsor: Genentech, Inc.
A phase II study investigating cabozantinib in patients with refractory metastatic colorectal cancer (AGICC 17CRC01). First Author: Aaron James Scott, Banner-University of Arizona Cancer Center, Division of Hematology and Oncology, Tucson, AZ

Background: Therapeutic resistance to antiangiogenics in metastatic colorectal cancer (mCRC) inevitably develops via multiple mechanisms. As including upregulation of the MET kinase pathway. Cabozantinib, an oral multityrosine kinase inhibitor targeting MET, AXL, and VEGF, demonstrated significant anti-tumor activity in CRC xenograft and cell line models. Methods: A single-arm, two-phase II study was conducted at 16 AGICC centers in Japan. All 44 patients (pts) with mCRC who had progressed on or were intolerant of standard of care agents were treated with cabozantinib 60 mg daily in q3 cycles. The primary endpoint was 12-wk PFS rate. Based on the control arm of phase III CORRECT study, the Kaplan-Meier 12-wk PFS rate estimate was 13% and served as the null hypothesis. This study was powered at 0.906 to detect the alternative hypothesis of 12-wk PFS rate of 33% with a type I error rate of 0.044. Secondary endpoints were safety, RR, OS, and retrospective analysis of PFS and RR based on RAS, BRAF, and PIK3CA mutation status. Results: 44 pts were enrolled and 34 pts were response-evaluable as having undergone at least the first 6-wk restaging scan. 10 pts discontinued treatment prior to the first 6-wk scan due to clinical disease progression. Median number of cycles was 4 and median follow-up was 2.5 months. As of data cutoff 8/23/2019, 55 Grade 3/4 AEs were reported with the most common being hypertension, fatigue, diarrhea, pain, rash, nausea, vomiting, and proteinuria. 32 AEs occurred in 18 pts. 5 Grade 5 AEs were reported: disease progression (3), disseminated intravascular coagulopathy, and bowel perforation. 15 pts (34%) achieved ≥ 12wk PFS and 8 patients remained on treatment. Best response was 1 PR and 31 SD with a DCR at 6 wks of 72.7%. Of the pts who achieved ≥ 12-wk PFS, 12 had left-sided primary tumors, 5 had a RAS mutation, had a PIK3CA mutation, and all pts were BRAF WT and MSI stable.

Conclusions: Cabozantinib was deemed safe and demonstrated encouraging efficacy in a heavily pretreated mCRC pt population. These results support further investigation of cabozantinib in mCRC. Clinical trial information: NCT03542877. Research Sponsor: Exelixis.

Clinical impact of primary tumor location in patients with metastatic colorectal cancer (mCRC) treated with regorafenib or trifluridine/tipiracil (TFTD) as later-line. First Author: Hiromichi Nakajima, Department of Gastroenterology and Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa, Japan

Background: In the recent years, primary tumor location (PTL) is considered as an important prognostic and predictive factor in first-line treatment of mCRC. Although regorafenib (REG) and trifluridine/tipiracil (TFTD) have been available recently, the prognostic value of PTL in later-line with these agents is not well understood. TFTD improved survival regardless of PTL in the CORRECT trial, while REG did not show survival benefit in the patients (pts) with rectal cancer in the REGOTAS study. We retrospectively evaluated pts with mCRC who were registered in a multicenter observational study (the REGOTAS study). The main inclusion criteria were ECOG PS of 0-1, resectable or nonresectable CRC, and no prior use of REG and TFTD. The impact of PTL on overall survival (OS) were evaluated using Cox proportional hazards models based on baseline characteristics and propensity score matching. Results: A total of 550 pts (223 pts in the REG group, 327 pts in the TFTD group; 122 pts in the right-sided, 428 pts in the left-sided) were included in this study. Although the right-sided pts was significantly shorter OS compared with the left-sided pts by univariate analysis (hazard ratio [HR] 0.79, 95% confidence interval [CI] 0.63-0.99, P = 0.04), multivariate analysis revealed that PTL was not an independent prognostic factor (HR 0.88, 95% CI 0.69-1.1, P = 0.26). The similar results were obtained in each treatment group. In subgroup analysis according to PTL, OS were comparable between REG and TFTD groups regardless of PTL (HR 0.93, 95% CI 0.62-1.39 in the right-sided; HR 1.08, 95% CI 0.83-1.39 in the left-sided [excluding rectum]); and HR 1.01, 95% CI 0.62-1.62 in the rectal cancer pts). These results were similar in sensitivity analysis using propensity score-matching. Conclusions: In the present study, PTL is not a prognostic factor in patient with mCRC treated with either REG or TFTD. No difference in OS was observed between REG and TFTD groups irrespective of PTL. Research Sponsor: Japanese Society for Cancer of the Colon and Rectum.

Pemetrexed plus erlotinib as a salvage treatment in high EGFR-expressing metastatic colorectal cancer patients following failure of standard chemotherapy: A phase II single-arm prospective study. First Author: Seonggyu Byeon, Samsung Medical Center, Seoul, South Korea

Background: We conducted a single-arm, phase II study to evaluate the combination of pemetrexed and erlotinib as a salvage treatment in high EGFR-expressing (≥ 3+ or over 8%) colorectal cancer (CRC) patients who failed to show a benefit after standard chemotherapy. Methods: We investigated pemetrexed and erlotinib (pemetrexed 500 mg/m² on Day 1 and erlotinib 100 mg/day on Days 1-21) as a salvage treatment, given every three weeks, until disease progression or intolerable toxicity. The primary outcome was overall response rate (RR). Results: From May 2017 to April 2018, 29 metastatic CRC patients with high EGFR expression who previously received the standard therapies were enrolled into this trial. The regimen was well tolerated. Skin rash, vomiting, fatigue, and anorexia were common toxic effects but were mostly manageable and controllable side effects of only grades 1 or 2. In intent-to-treat analysis, three partial responses (PRs) were observed in enrolled patients, revealing an overall RR of 10.3%. The response rate was 9.7% (95%CI, 0.62-1.62 in the rectal cancer pts). These results were similar in the left-sided 

Poster Session (Board #E11), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Poster Session (Board #E12), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Poster Session (Board #E13), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Poster Session (Board #E14), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

First Author: Katsuya Ohta, Higashiosaka City Medical Center, Higashiosaka, Osaka, Japan

Background: Single agent of panitumumab (Pmab) is expected to be well tolerated and to improve survival in first-line setting in patients (pts) who are not eligible or unsuitable for intensive chemotherapy. Here, we analyzed the efficacy and safety of Pmab for chemotherapy-naive or elderly Japanese pts with wild-type (wt) RAS unresectable colorectal cancer (CRC) that has not been yet studied. Methods: We conducted a multi-center phase II study. Pts aged over 76 years, unresectable colorectal cancer (CRC) have not been yet studied. RAS wt, unresectable CRC. The survival analysis including OS, PFS and TTF is awaiting. Clinical trial information: UMIN000024528. Research Sponsor: None.

Phase II study of panitumumab monotherapy in chemotherapy-naive frail or elderly patients with unresectable, RAS wild-type colorectal cancer: OGGSG 1602. First Author: Katsuya Ohta, Higashiosaka City Medical Center, Higashiosaka, Osaka, Japan

Background: Single agent of panitumumab (Pmab) is expected to be well tolerated and to improve survival in first-line setting in patients (pts) who are not eligible or unsuitable for intensive chemotherapy. Here, we analyzed the efficacy and safety of Pmab for chemotherapy-naive or elderly Japanese pts with wild-type (wt) RAS unresectable colorectal cancer (CRC) that has not been yet studied. Methods: We conducted a multi-center phase II study. Pts aged over 76 years, unresectable colorectal cancer (CRC) have not been yet studied. RAS wt, unresectable CRC. The survival analysis including OS, PFS and TTF is awaiting. Clinical trial information: UMIN000024528. Research Sponsor: None.
Background: The anti-PD-1 antibody pembrolizumab (P) provides response rates of 28–57% in patients (pts) with microsatellite-stable metastatic colorectal cancer (mCRC) vs 0% in those with non-MSI-H cancers. STAS3 has been previously reported as a potential key driver of immune evasion. This study investigates efficacy and safety for the combination of BBI608 (nabaplatinucasin), which blocks phosphorylated STAT3 and downstream platelet-activating factor (PAF), with P, in pts with mCRC. BBI608 480 mg Bid with P was determined as the recommended phase II dose in phase I. Methods: Phase II included Cohorts A (MSI-H) and B (non-MSI-H). Pts with mCRC not responding to or intolerant of standard chemotherapies were enrolled. The primary endpoint was immune-related objective response rate (irORR), according to irRECIST. The sample size for Cohort A (10 pts) was derived in an exploratory manner. In Cohort B, assuming null and alternative hypotheses of irORR = 5% and 20% led to an estimated required sample size of 40 pts, with a ‘sided alpha of 5% and power of 90%. Genomic profiles and the consensus molecular subtypes (CMS) of colorectal cancer sample size of 40 pts, with a 1-sided alpha of 5% and power of 90%. Genomic

Conclusions: BBI608 with P showed encouraging anti-tumor activity with acceptable toxicity for non-MSI-H mCRC pts as well as MSI-H mCRC pts. Impact of CMS on the efficacies of this combination warrants further investigation in the additional cohort of this study. Clinical trial registration: NCT02851004. Research Sponsor: Sumitomo Dainippon Pharma Co., Ltd.
Background: Msi-h/dmmr and pol-e mutation had been proven to have a potential of achieving better outcome in mCRC patients with the use of mbev as the first-line chemotherapy. However, reported response rates are often < 50%. Several preclinical studies reported COX inhibitor improve antigen presentation and T-cell infiltration in tumors. We investigated the efficacy of PD-1 blockade combined with COX inhibitor in colorectal cancer patients with Msi-h/dmmr or pol-e mutation. Methods: PD-1 blockade was a prospective, single arm, phase II study. Patients with Msi-h/dmmr or pol-e mutation advanced or metastatic colorectal cancer received PD-1 blockade (nivolumab 200mg q3w; or,Cetuximab 100mg q3w; or,Nivolumab 3mg per kilogram, q2w) plus COX inhibitor (celecoxib 400mg or aspirin 200mg, p.o. qd). The primary endpoint was ORR, secondary endpoints included PFS, OS and safety. Results: Totally 24 patients were enrolled. 18 (75.0%) patients had left first line chemotherapy failed and 6 (25.0%) patients had at least second lines chemotherapy failed. 22 patients were Msi-h/dmmr and 2 patients were with pol-e mutation. At a median follow-up of 14.5 months, the ORR was 83.3% (20/24), including 5 patients achieved CR (4.2%) and 15 patients achieved PR (62.5%). One-year survival rates was 91.3% (95%CI, 79.7%-99.7%). The reported treatment-related adverse events were listed in table below. Conclusions: The combination of PD-1 blockade plus COX inhibitor was associated with higher response rates in advanced or metastatic colorectal cancer patients with Msi-h/dmmr or pol-e mutation than PD-1 alone as historical controls. Clinical trial information: NCT03638297. Research Sponsor: None.

PD-1 blockade combined with COX inhibitor in patients with msi-h/dmmr or high TMB, advanced or metastatic colorectal cancer (PCOX study). First Author: Zehua Wu, Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Background: Msi-h/dmmr and pol-e mutation had been proven to have a potential of achieving better outcome in mCRC patients with the use of mbev as the first-line chemotherapy. However, reported response rates are often < 50%. Several preclinical studies reported COX inhibitor improve antigen presentation and T-cell infiltration in tumors. We investigated the efficacy of PD-1 blockade combined with COX inhibitor in colorectal cancer patients with Msi-h/dmmr or pol-e mutation. Methods: PD-1 blockade was a prospective, single arm, phase II study. Patients with Msi-h/dmmr or pol-e mutation advanced or metastatic colorectal cancer received PD-1 blockade (nivolumab 200mg q3w; or,Cetuximab 100mg q3w; or,Nivolumab 3mg per kilogram, q2w) plus COX inhibitor (celecoxib 400mg or aspirin 200mg, p.o. qd). The primary endpoint was ORR, secondary endpoints included PFS, OS and safety. Results: Totally 24 patients were enrolled. 18 (75.0%) patients had left first line chemotherapy failed and 6 (25.0%) patients had at least second lines chemotherapy failed. 22 patients were Msi-h/dmmr and 2 patients were with pol-e mutation. At a median follow-up of 14.5 months, the ORR was 83.3% (20/24), including 5 patients achieved CR (4.2%) and 15 patients achieved PR (62.5%). One-year survival rates was 91.3% (95%CI, 79.7%-99.7%). The reported treatment-related adverse events were listed in table below. Conclusions: The combination of PD-1 blockade plus COX inhibitor was associated with higher response rates in advanced or metastatic colorectal cancer patients with Msi-h/dmmr or pol-e mutation than PD-1 alone as historical controls. Clinical trial information: NCT03638297. Research Sponsor: None.

The treatment strategy of the second-line chemotherapy for metastatic colorectal cancer (mCRC) patients (pts) with early progression in the first-line chemotherapy with bevacizumab (BEV), BEV beyond progression (BBP), or non-BBP, First Author: Takeshi Kawakami, Division of Gastrointestinal Oncology, Shizuoka Cancer Center, Shizuoka, Japan

Background: BBP has been recognized as one of the standard 2nd-line treatment strategy for pts with mCRC based on the ML18147 trial. However, this trial excluded pts with disease progression ever, this trial excluded pts with disease progression within 100 days in the 1st-line BEV-containing chemotherapy between Apr 2010 and Dec 2016. This multi-institutional retrospective study compared the efficacy and safety between the 2nd-line chemotherapy with BEV (BBP) and without BEV (non-BBP), adjusting ECOG PS, WBC, ALP, number of metastatic sites, RAS status, and sidedness using Cox proportional hazard model.

Methods: The subjects were mCRC pts who received the 2nd-line chemotherapy after experiencing disease progression < 100 days in the 1st-line BEV-containing chemotherapy between Apr 2010 and Dec 2016. This multi-institutional retrospective study compared the efficacy and safety between the 2nd-line chemotherapy with BEV (BBP) and without BEV (non-BBP), adjusting ECOG PS, WBC, ALP, number of metastatic sites, RAS status, and sidedness using Cox proportional hazard model.

Results: 61 pts. were evaluated. Patients’ backgrounds are listed in table below. Comparing BBP and non-BBP, the 1st line chemotherapy regimen was oxaliplatin- or irinotecan-based (53/67 and 34/68), RAS status was wild (mutant/unknown: 28/36 and 76/16), sex (male/female: 53/47 and 32/68), tumor location (right/left:11/44 and 56/40), 60% disease status (stage IV/recurrence: 67/33 and 84/16), number of metastatic sites (1/2/3: 33/67 and 20/80), the 1st-line regimens (oxaliplatin-based/irinotecan-based: 83/17 and 96/4%) between two arms. The 2nd-line chemotherapy regimens with EGFR antibody-containing/cytotoxic alone were 64/36% in non-BBP, respectively. The response rates were 5.9 and 8.7% in BBP and non-BBP. Median PFS were 7.9 and 2.8 months (HR 0.39, 95%CI 0.21-0.73, P = 0.002). The reported treatment-related adverse events were listed in table below. Conclusions: The 2nd-line chemotherapy for pts with early progression in the 1st-line BEV-containing chemotherapy showed poor outcomes regardless of strategy. Research Sponsor: None.

Background:

- The treatment strategy of the second-line chemotherapy for metastatic colorectal cancer (mCRC) patients (pts) with early progression in the first-line chemotherapy with bevacizumab (BEV), BEV beyond progression (BBP), or non-BBP, First Author: Takeshi Kawakami, Division of Gastrointestinal Oncology, Shizuoka Cancer Center, Shizuoka, Japan

- Methods: The subjects were mCRC pts who received the 2nd-line chemotherapy after experiencing disease progression < 100 days in the 1st-line BEV-containing chemotherapy between Apr 2010 and Dec 2016. This multi-institutional retrospective study compared the efficacy and safety between the 2nd-line chemotherapy with BEV (BBP) and without BEV (non-BBP), adjusting ECOG PS, WBC, ALP, number of metastatic sites, RAS status, and sidedness using Cox proportional hazard model.

- Results: 61 pts. were evaluated. Patients’ backgrounds are listed in table below. Comparing BBP and non-BBP, the 1st line chemotherapy regimen was oxaliplatin- or irinotecan-based (53/67 and 34/68), RAS status was wild (mutant/unknown: 28/36 and 76/16), sex (male/female: 53/47 and 32/68), tumor location (right/left:11/44 and 56/40), 60% disease status (stage IV/recurrence: 67/33 and 84/16), number of metastatic sites (1/2/3: 33/67 and 20/80), the 1st-line regimens (oxaliplatin-based/irinotecan-based: 83/17 and 96/4%) between two arms. The 2nd-line chemotherapy regimens with EGFR antibody-containing/cytotoxic alone were 64/36% in non-BBP, respectively. The response rates were 5.9 and 8.7% in BBP and non-BBP. Median PFS were 7.9 and 2.8 months (HR 0.39, 95%CI 0.21-0.73, P = 0.002). The reported treatment-related adverse events were listed in table below. Conclusions: The 2nd-line chemotherapy for pts with early progression in the 1st-line BEV-containing chemotherapy showed poor outcomes regardless of strategy. Research Sponsor: None.
Efficacy and safety of regorafenib in combination with chemotherapy as second-line therapy in patients with metastatic colorectal cancer: A network meta-analysis. First Author: Xiaoyu Xie, The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Background: Recent studies have shown efficacy of chemotherapy (CTX) in combination with different biological agents including regorafenib (REG) in second-line treatment of metastatic colorectal cancer (mCRC). As there is no evidence on the relative efficacy and safety of REG as compared to other biological agents in combination with CTX, we evaluated the same in this network meta-analysis (NMA). Methods: Randomized controlled trials (RCTs) comparing efficacy and safety of biological agents + CTX against CTX alone as second-line treatment of mCRC were retrieved from PubMed, EMBASE and Cochrane databases. Progression free survival (PFS) was the primary outcome, while objective response rate (ORR), overall survival (OS) and safety were secondary outcomes. Outcomes were compared by random/mixed-effects NMA using Bayesian (R software, Gemtc package) and frequentist approaches. Results: Twelve RCTs comparing 9 different treatment regimens with a total of 6805 patients were included for analysis. Hazard ratios (HR)/ odds ratio (OR)/ relative risk (RR) and 95% confidence intervals (CI) for PFS, ORR and grade ≥ 3 adverse events (AE) of selected comparisons from the results of the NMA are shown in table. Conclusions: REG combined with CTX might be a potential alternative to conventional therapeutic options and could be considered as the best option for treating KRAS and BRAF mutated mCRC patients. Future RCTs are needed to confirm our results. Research Sponsor: None.

Analysis of efficacy and safety.

<table>
<thead>
<tr>
<th>Regorafenib + CTX vs other agents + CTX</th>
<th>PFS</th>
<th>ORR</th>
<th>Grade ≥ 3 AE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PFS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>vs Alimta + FOLFOX</td>
<td>0.96, 0.68-1.37</td>
<td>1.02, 0.84-1.24</td>
<td>117, 0.93-1.49</td>
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<tr>
<td>vs Bevacizumab + FOLFOX</td>
<td>0.97, 0.75-1.25</td>
<td>1.03, 0.73-1.43</td>
<td>117, 0.93-1.49</td>
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<tr>
<td>vs Cetuximab + FOLFOX</td>
<td>0.84, 0.64-1.12</td>
<td>1.04, 0.84-1.32</td>
<td>0.95, 0.68-1.33</td>
</tr>
<tr>
<td>vs Clofarabine + FOLFOX</td>
<td>0.96, 0.59-1.59</td>
<td>0.91, 0.69-1.24</td>
<td>0.97, 0.70-1.37</td>
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<tr>
<td>vs Sunitinib + FOLFOX</td>
<td>0.72, 0.45-1.16</td>
<td>0.63, 0.43-1.05</td>
<td>1.34, 0.81-1.59</td>
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<tr>
<td>vs Panitumumab + FOLFOX</td>
<td>0.96, 0.68-1.37</td>
<td>2.04, 0.45-33</td>
<td>0.44, 0.11-1.64</td>
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<tr>
<td>vs Ramucirumab + FOLFOX</td>
<td>0.90, 0.65-1.30</td>
<td>0.40, 0.19-0.81</td>
<td>0.96, 0.75-1.29</td>
</tr>
<tr>
<td><strong>ORR</strong></td>
<td></td>
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<tr>
<td>vs Alimta + FOLFOX</td>
<td>0.62, 0.46-0.84</td>
<td>2.28, 1.26-4.17</td>
<td>1.54, 1.01-2.34</td>
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<td>vs Bevacizumab + FOLFOX</td>
<td>0.54, 0.38-0.78</td>
<td>3.75, 2.26-6.20</td>
<td>1.14, 0.78-1.65</td>
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<td>vs Cetuximab + FOLFOX</td>
<td>0.45, 0.30-0.68</td>
<td>2.61, 1.39-4.90</td>
<td>1.25, 0.87-1.79</td>
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<tr>
<td>vs Clofarabine + FOLFOX</td>
<td>0.58, 0.37-0.93</td>
<td>2.06, 1.16-3.61</td>
<td>1.37, 0.93-2.00</td>
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<tr>
<td>vs Sunitinib + FOLFOX</td>
<td>0.57, 0.36-0.92</td>
<td>2.52, 1.45-4.38</td>
<td>1.48, 0.96-2.29</td>
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<tr>
<td>vs Panitumumab + FOLFOX</td>
<td>0.71, 0.49-1.02</td>
<td>2.26, 1.27-4.05</td>
<td>1.29, 0.83-2.01</td>
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<td>vs Ramucirumab + FOLFOX</td>
<td>0.70, 0.45-1.08</td>
<td>2.07, 1.23-3.45</td>
<td>1.29, 0.83-2.01</td>
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Poster Session (Board #F1), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Benefit of oxaliplatin in stage III colon cancer according to IDEA risk groups: Analysis of MOSAIC and C-07 trials. First Author: M. Cecilia Monge B., National Cancer Institute, National Institutes of Health, Bethesda, MD

Background: The IDEA pooled analysis compared 3 to 6 months of adjuvant chemotherapy for stage III colon cancer. The overarching goal was to reduce chemotherapy-related toxicity, mainly oxaliplatin-induced neuropathy. Patients were stratified into low-risk and high-risk, suggesting low-risk patients may be offered only 3 months of treatment. In our previously published analysis using retrospective data from the National Cancer Database (NCDB) we showed similar benefit for oxaliplatin in both low and high IDEA risk groups. No treatment-related deaths occurred. Conclusions: Regorafenib dose escalation was well tolerated with PFS similar to that reported in the CORRECT study, indicating that WDES may represent an option for regorafenib administration. Clinical trial information: UMIN000028933. Research Sponsor: None.

A phase I/II study of Pexa-Vec oncolytic virus in combination with immune checkpoint inhibition in refractory colorectal cancer. First Author: M. Cecilia Monge B., National Cancer Institute, National Institutes of Health, Bethesda, MD

Background: The benefit of immune checkpoint inhibition is limited to the small percentage of advanced colorectal cancer (CRC) patients whose tumors present mismatch repair (MMR) gene abnormalities; immunotherapy has not shown benefit in patients with MMR proficient CRC. Oncolytic immunotherapy represents a unique therapeutic platform. This phase I trial tests the safety of the combination of pexaclinimogene davacinc (Pexa-Vec) plus durvalumab (durva) in patients with locally advanced or metastatic CRC. Methods: Eligible patients with advanced proficient mismatch repair (pMMR) CRC received intravenous infusion of Pexa-Vec at dose level 3 x 10⁸ plaque forming units (pfu) (DL3) or at 10⁹ pfu (DL2) every 2 weeks for 4 doses and durva 1500 mg every 28 days. Response was assessed at CT every 4 weeks. Adverse events were recorded and managed. The primary (futility) endpoint is safety, tolerability and feasibility of this combination therapy. Samples of tumor and peripheral blood were collected for assessment of immune parameters. Results: Sixteen patients (6 males and 10 females) enrolled with a median age of 52.1 years (range 29-69) from Dec, 2017 to Oct, 2018. Four patients were treated with Pexa-Vec at DL2 and durva+velutamide patients were treated with Pexa-Vec at DL2 and durva. The most common treatment related adverse events (TRAES) included fever 15/16 (94%), hypertension 12/16 (75%), chills 12/16 (75%), fatigue 8/16 (50%), sinus tachycardia 1/6 (16%) and rash 6/16 (38%). Grade 3/4 TRAES were reported in 8/16 (50%) patients; the most common were fever 7/16 (44%), lymphopenia 2/6 (13%), neutropenia 1/6 (16%) and anemia 1/6 (16%). 14 patients were evaluable for response analysis; one patient 1/14 (7%) achieved a confirmed partial response (lasting 7.1 months) and continues to receive treatment, while 13 patients had progressive disease. The median progression free survival (PFS) was 2.2 months (95% CI 2.2-2.3 months) and the median overall survival (OS) was 7.5 months (CI: 4.9-10.1 months).

Efficacy and safety of regorafenib as third-line therapy in metastatic colorectal cancer: An indirect meta-analysis. First Author: Yinying WU, The First Affiliated Hospital of Xi’an Jiaotong University, Xi an, China

Background: The evidence base for optimum third-line therapy for metastatic colorectal cancer (mCRC) is not conclusive. Recent studies have demonstrated the efficacy of regorafenib as third-line therapy in mCRC. This indirect meta-analysis compared the efficacy and safety of regorafenib in comparison to other available third-line therapies in mCRC. Methods: Literature search for randomized controlled trials was conducted in PubMed, Embase, and Cochrane Library for studies evaluating the efficacy and safety of regorafenib, sorafenib, TAS-102 and nintedanib as third-line therapies in mCRC patients. The primary outcomes included overall survival (OS), progression-free survival (PFS) and objective response rate (ORR) as the secondary outcome. Hazard ratio (HR) and relative risk (RR) with their respective 95% confidence interval (CI) were used for analysis of survival, clinical response and safety data, respectively. An adjusted indirect meta-analysis with placebo as the common comparator was performed. Results: We identified 8 RCTs studying comparability of regorafenib (2 studies), sorafenib (2 studies), TAS-102 (3 studies) and nintedanib (1 study) against placebo. The OS with regorafenib was significantly better when compared to nintedanib (HR= 0.66, 95% CI 0.45, 0.95, p=0.02), but was similar to that of fluoruridine (HR=1.01, 95% CI 0.67, 1.52, p=0.94) and TAS-102 (HR= 0.97, 95% CI 0.68, 1.38, p=0.68). The PFS and ORR for regorafenib were slightly better than TAS-102 (PFS: HR= 0.86, 95% CI 0.54,1.37, p=0.5; ORR: RR= 1.13, 95% CI 0.11, 10.51, p=0.92) and nintedanib (PFS: HR= 0.68, 95% CI 0.42, 1.10, p=0.02; ORR not reported) but was lower than fluoruridine (PFS: HR= 1.53, 95% CI 0.93, 2.52, p=0.08; ORR: RR= 0.68, 95% CI 0.045, 10.32, p=0.79). Safety analysis showed that the relative risk of adverse events was lower in patients treated with regorafenib in comparison to fluoruridine but was similar to that of nintedanib and TAS-102. Conclusions: Regorafenib with its efficacy and safety profile combined with comprehensively continuously anti-angiogenic therapy, might be the first option in third-line mCRC. Head-on comparisons are required for further validation. Research Sponsor: None.

Optimizing FOLLIRINOX tolerability in patients with colorectal cancer through dosing irinotecan in the morning for men and in the afternoon for women. First Author: Francis Lei, Warwick University, Coventry, United Kingdom

Background: Irinotecan (IR) toxicity was worse in female (F) than in male (M) patients (pts) on FOLLIRI for metastatic colorectal cancer (MCC). This finding could reflect different optimal administration timing of IR in M and F pts along the 24 hours. IR pharmacology is regulated by the circadian clock, and its least toxic daily time (LTT) occurred ~6 hours later in F as compared to M mice. The relative timing of sex for the LTT of IR is addressed in this study using data from an international randomized trial, whose primary endpoint was not met for all the 193 pts with MCC (EORTC 05010). Methods: 130 M and 63 F were randomized to receive chronomodulated IR (180 mg/m² over 6-h, with peak delivery in the morning at 5:00 or 9:00), in the afternoon (at 13:00 or 17:00) or at night (at 21:00 or 02:00) on day (a), followed by fixed-time chronomodulated oxaliplatin-5-fluorouracil-leucovorin for 4 a. Triplet combination was given q3 weeks as 1st or 2nd line, without prophylactic G-CSF. The relevance of IR timing for male toxicity was determined separately in M and F, using Cosinor and Fisher Tests. Results: Baseline characteristics M or F pts did not differ significantly according to IR timing group. Main worse grade 3-4 toxicities per pt after 6 courses were diarrhea (M, 40.2%; F, 51.9%) neutropenia (M, 12.6%; F, 18.4%), fatigue (M, 13.4%; F, 17.3%) and anorexia (M, 8.2%; F, 9.6%). These toxicities were reduced following IR delivery in the morning for M, but in the afternoon for F, with statistically significant rhythms (p = 0.05 from cosinor) and sex×timing interactions (Fisher Exact, diarrhea, p = 0.023; neutropenia, p = 0.015; fatigue, p = 0.056; anorexia, p = 0.032). IR timing was most critical for F. Grade 3-4 toxicities ranging from 55% to the pts (morning) to 29.4% (afternoon) for diarrhea, and from 25.9% (morning) to 0% (afternoon) for neutropenia. IR timing did not significantly influence efficacy. Conclusions: The present study results supports the administration of irinotecan in the morning for M and afternoon for F to order to minimize IR toxicities of MCC therapy without impairing efficacy. Prospective trials testing sex specific timing issues are warranted. Clinical trial information: 05010. Research Sponsor: ARTBC International, Warwick University UK.

Cobimetinib plus vemurafenib (C/V) in patients (Pts) with colorectal cancer (CRC) with BRAF V600E mutations: Results from the TAPUR Study. First Author: Kelsey Klute, University of Nebraska Medical Center, Omaha, NE

Background: TAPUR is a phase II basket study evaluating anti-tumor activity of commercially available targeted agents in pts with advanced cancers with genomic alterations. Pts in a cohort of CRC pts treated with the BRAF V600E mutation targeted with C/V were selected. Methods: Eligible pts had advanced CRC, no standard treatment (tx) options, measurable disease, ECOG PS 0-2, and adequate organ function. Genomic Testing was performed in ELIA-certified, CAP-accredited site selected labs. Pts had BRAF V600E/KR/IR mutation and no MAP2K1/2, MEK1/2, NRAS mutations. Recommended dosing was C, 60 mg orally once daily for 21 days, 7 days off, followed by 960 mg orally twice daily. Simon two-stage design was used to test the null rate of 15% vs. 35% (power = 0.85, α = 0.10). If < 2 of 10 pts in stage 1 have disease control (DC) (objective response (OR) or stable disease at 16 weeks (wks) according to RECIST (SD16+) if ≥18 more pts enrolled. If ≤7 of 28 pts have DC, the tx is worthy of further study. Secondary endpoints are progression-free survival (PFS), overall survival (OS) and safety. Results: Thirty pts enrolled from August 2015 to August 2018; 2 were not evaluable for efficacy. Demographics and outcomes are summarized in Table. All pts had BRAF V600E mutations. Eight PR and 8 SDW were observed for DC and OR rates of 57% (95% CI, 43% to 67%) and 29% (95% CI,13% to 49%), respectively. Twelve pts had at least 1 grade 3 AE or SAE at least possibly related to C/V including elevated liver enzymes, decreased lymphocytes, dyspnea, diarrhea, fatigue, hypercalcemia, hypophosphatemia, rash, photosensitivity, upper GI hemorrhage, and vomiting. Conclusions: The combination of C/V showed anti-tumor activity in heavily pre-treated pts with BRAF V600E mutations. Further study is warranted to confirm the efficacy of C/V in this population. Clinical trial information: NCT02693535. Research Sponsor: Genentech.
Efficacy and safety of the combination of aflibercept with fluorouracil, leucovorin, and irinotecan in patients aged 70 years and older with metastatic colorectal cancer previously treated with an oxaliplatin-based regimen in Spain: A retrospective multicenter cohort study. First Author: Laura Gutierrez Sainz, Medical Oncology Department, Hospital Universitario La Paz, Madrid, Spain.

Background: Colorectal cancer is currently the third most common cancer in females and the second most common cancer in males. The results of the VELOUR study showed that the addition of aflibercept to fluorouracil, Leucovorin, and Irinotecan (FOLFIRI) produced an advantage in both progression-free and overall survival (PFS and OS) in patients with metastatic colorectal cancer (mCRC) previously treated with an oxaliplatin-based regimen. The purpose of this study was to evaluate the efficacy and safety of the combination of aflibercept with FOLFIRI in patients aged 70 years and older with mCRC. Methods: We conducted a retrospective multicenter study, which included all patients aged 70 years and older with mCRC treated with Aflibercept plus FOLFIRI between May 2013 and March 2019 in 5 centers in Spain. Data regarding clinical and pathological characteristics, treatment response and survival were collected. Results: We selected 69 patients, of whom the majority (n = 48, 69.6%) were males with a median age of 75 years (range 70-84 years). Patients received an average of nine courses of aflibercept with FOLFIRI overall. Regarding response rates, 17 patients (24.6%) achieved a partial response, 37 (53.6%) had stable disease and 15 (21.7%) had disease progression. The median PFS was 9.1 months (CI 95%: 6.8-11.4 months) and the median OS was 22.8 months (CI 95%: 18.1-27.5 months). Treatment adverse events grade 3 and 4 were reported in 42 patients (60.9%). The most frequently reported treatment adverse events grade 3 and 4 were: asthenia (18.8%), diarrhea (18.8%), stomatitis and ulceration (18.8%) and neutropenia (18.8%). In patients grade 3 and 4 events treated with anti-VEGF therapy were infrequent. Adverse events led to permanent discontinuation of treatment in 26.1% of patients. Conclusions: In our sample the combination of aflibercept with FOLFIRI in patients aged 70 years and older with mCRC was efficacious and safe. Aflibercept plus FOLFIRI is a good therapeutic option for the treatment of mCRC in patients aged 70 years and older previously treated with oxaliplatin. Research Sponsor: None.

Poster Session (Board #F12), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Negative impact of cachexia during chemotherapy on survival as first-line chemotherapy for metastatic colorectal cancer. First Author: Kazuki Nozawa, Department of Clinical Oncology, Aichi Cancer Center Hospital, Nagoya, Aichi, Japan.

Background: Sarcopenia and muscle loss during chemotherapy (Cx) has a poor prognosis in metastatic colorectal cancer (mCRC). It is unclear whether cachexia during Cx has a survival impact. Methods: mCRC patients (pts) receiving first-line Cx at a single institution between Jan 2015 and Jun 2018 were retrospectively evaluated. Pts receiving doublet Cx with bevacizumab or anti-EGFR agents, ECOG Performance Status (PS) 0-2, and abdominal computed tomography (CT) before and after initiating first-line Cx at least once were included and classified into those with (cachexia group) and without cachexia (non-cachexia group) cachexia. The skeletal muscle index (SMI) was calculated from the CT cross-section area at L3 divided by the length squared. Muscle loss was defined as a > 5% reduction in the SMI. The association between muscle loss and cachexia during Cx, time to treatment failure (TTF) and overall survival (OS) was determined by univariate and multivariate analysis including muscle loss, primary tumor location, ECOG PS, number of metastatic sites, ALP, WBC, LDH, KRAS status, and BRAF status as independent variables. Results: Of 562 included pts, 185 were eligible and 37% experienced cachexia. Differences in all patient characteristics such as muscle loss, ECOG PS 2, KRAS mutant, and BRAF mutant (28%, 8%, 32%, and 10% with cachexia group and 27%, 3%, 32%, and 8% without cachexia group) were not significant. Median follow-up was 26.8 months. Muscle loss was not associated with TTF (13.3 vs. 15.5 months, HR = 1.05; 95% CI: 0.76-1.45, p = 0.76). OS was shorter (24.4 vs. 29.9 months, HR = 1.23; 95% CI: 0.86-1.76, p = 0.25), but the difference was not significant in univariate and multivariate analysis. However, cachexia group presented significantly shorter TTF [median TTF 11.9 vs. 16.9; HR1.52, 95% CI: 1.22-2.07, p < 0.01; adjusted HR (aHR) 1.53, 95% CI: 1.21-2.11, p < 0.01] and shorter OS (median OS 21.4 vs. 34.1 months; HR 1.81, 95% CI: 1.29-2.55, p < 0.01; aHR 1.97, 95% CI: 1.38-2.81, p < 0.01) than non-cachexia group.

Conclusions: Cachexia during Cx has a well tolerated and can have a negative impact on survival in pts with mCRC. Research Sponsor: None.
Continued cetuximab in second-line treatment for patients with unresectable metastatic wild-type KRAS, NRAS, and BRAF colorectal cancer after disease progression during first-line cetuximab-based therapy. First Author: Ying Liu, Department of Oncology, Henan Cancer Hospital, Zhengzhou University Affiliated Cancer Hospital, Zhengzhou, China

Background: Cetuximab plus chemotherapy is a first-line treatment option for metastatic KRAS wild-type colorectal cancer patients. Currently, no data are available on continuing cetuximab or changing bevacizumab as second-line therapy beyond first-line cetuximab-based chemotherapy. Methods: Patients (aged ≥18 years) with metastatic, histologically and genetically confirmed wild-type KRAS, NRAS and BRAF colorectal cancer progressing after first-line cetuximab plus chemotherapy were randomly assigned (1:1 ratio) to second-line chemotherapy with cetuximab (arm A) or with bevacizumab (arm B) 5 mg/kg per week equivalently. The choice between oxaliplatin-based or irinotecan-based second-line chemotherapy depended on the first-line regimen (switch of chemotherapy). The primary endpoints were progression-free survival (PFS) and objective response rate (ORR). The second endpoint was overall survival (OS). Results: 77 Patients (from July 1, 2016 to Sept 20, 2019, 77) were randomized (41 in arm A and 36 in arm B). ORR was 29.3% and 19.4% in Arm A and Arm B (p = 0.33). PFS was 7.2 months (95% CI 5.2–9.2) for Arm A and 5.9 months (95% CI 5.1–7.6) for Arm B (p = 0.67). OS was 18.5 months (95% CI 15.1–21.8) for Arm A and 17.5 months (95% CI 15.4–19.7) for Arm B (p = 0.44). Patients with ECOG PS 0 had significantly longer PFS and OS than ECOG PS 1 in second-line therapy whether cetuximab or bevacizumab combined with chemotherapy. ECOG 0 group vs ECOG 1 group, PFS was 8.7 months vs 4.6 months (p = 0.00) and OS was 21.2 months vs 12.3 months (p = 0.00).

Most grade 3–4 adverse events in both arms were neutropenia (19.4% VS 16.7%), diarrhea (7.5% vs 11.1%), and nausea (10% vs 13.9%).

Conclusions: Continuing cetuximab or changing bevacizumab plus standard second-line chemotherapy in patients with metastatic wild-type KRAS, NRAS and BRAF colorectal cancer after first-line cetuximab plus chemotherapy have similar clinical benefits. ECOG score is an independent predictor of progression and second-line treatment efficacy for colorectal cancer. Research Sponsor: Health and Family Planning Commission of Henan Province, China.

Phase I with expansion cohorts in a study of NEO-201 in adults with chemo-resistant solid tumors. First Author: M. Pia Morelli, NCI, Bethesda, MD

Background: NEO-201 is a humanized IgG1 monoclonal antibody (mAb) generated against tumor-associated antigens (TAA) from colorectal cancer. Our preclinical data demonstrated that NEO-201 exerts anti-tumor activity by NK-mediated ADCC and CDC against several tumor types. We identified NEO-201 as a potential agent in a small cohort of CEACAM-5 and -6, which is expressed by tumor tissue but is not present in the surrounding healthy tissue.

Methods: This is a first-in-human phase 1 study to determine the maximum tolerated dose (MTD) and recommended phase II dose (RP2D) of NEO-201 in adults with advanced solid tumors that have high likelihood of expression NEO201 antigen and have progressed to standard of treatments. This is a classic 3+3 dose escalation, with cohort expansion at the MTD. NEO-201 is administered intravenously every two weeks, and at four dose levels (DL1 = 1mg/kg, DL2 = 2mg/kg, DL3 = 4mg/kg and DL4 = 8mg/kg). Patients are evaluated for safety according to CTCAEv5.0, and for response according to RECISTv1.1. Biological samples are collected to understand NEO-201 pharmacokinetics, the effects on immune profile and the correlation with treatment toxicity and response. Results: Here we report the safety data and pharmacokinetics from DL1 and 2. A total of 9 evaluable patients were enrolled. Prolonged neutropenia, defined as G2 neutropenia lasting for ≥7 days, was observed at DL2. The cohort was expanded to a total of 6 patients and no further DLs were observed. Seven out of nine of the patients enrolled had colon cancer, two had pancreatic cancer and one had hormone positive breast cancer. The most frequent treatment-related AEs were infusion reaction which was observed in all patients, and moderate fatigue (33%). Best response was SD observed in two patients (one on each of DL1 and DL2). Dose escalation continues on DL3 and DL4. NEO201 antigen expression in patient tumor tissue, circulating CECAM6/CEACAMS, and MICA will be evaluated to correlate with response and toxicity. Conclusions: NEO201 has shown some promising activity and has the potential to understand dosing and further toxicity profile and to identify biomarkers for patient selection. Clinical trial information: NCT03476681. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.
Pembrolizumab (P) in patients (Pts) with colorectal cancer (CRC) has demonstrated clinical benefit in patients with metastatic colorectal cancer (mCRC) harboring TMB-high tumors. Results from the TAPUR Study. First Author: Yael Meiri, Cancer Treatment Centers of America, Atlanta, GA

Background: TAPUR is a phase II basket study evaluating anti-tumor activity of commercially available targeted agents in pts with advanced cancers with genomic alterations. Results in a cohort of CRC pts with mCRC were reported. Methods: Patients had advanced CRC, no standard treatment (tx) options, measurable disease, ECOG PS 0-1, and adequate organ function. Genetic testing was performed in CLIA-certified, CAP-accredited sites or central labs. Pts had TMB measured by FoundationOne test (n=26) or other tests (n=2) approved by the Molecular Tumor Board. TMB >10 mutations/megabase (M/b) was defined as high TMB. Results: Twenty-eight pts enrolled from November 2016 to September 2018 were evaluable for efficacy and safety. Demographics and outcomes are summarized in Table 1. All pts had TMB >10 mutations/megabase. Clinical trial information: NCT02969352. Study Sponsor: Genentech.

<table>
<thead>
<tr>
<th>Median age, yrs (range)</th>
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<td>Male, %</td>
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<td>DC rate, % (OR or SD16+) (90% CI)</td>
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<td>OR rate, % (OR or PR) (90% CI)</td>
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<td>OR rate, % (SD16+) (95% CI)</td>
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<td>Median OS, months (95% CI)</td>
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Conclusions: Pembrolizumab was well-tolerated and demonstrated clinical activity in TMB-high mCRC pts. Clinical trial information: NCT02969352. Study Sponsor: Genentech.
Updated results from a phase Ib trial of regorafenib plus nivolumab in patients with advanced colorectal or gastric cancer (REGONIVO, EPOC1603). First Author: Kohei Shitara, National Cancer Center Hospital East, Chiba, Japan

Background: In the phase 1 REGONIVO study, regorafenib of 80 mg/d day plus nivolumab showed manageable safety profiles and encouraging antitumor activity for advanced colorectal cancer (CRC) or gastric cancer (GC) with objective response rate (ORR) of 36% in CRC and 44% in GC (Fukuoka, et al. ASCO 2019). Updated efficacy results are presented. Methods: Enrolled patients (pts) received regorafenib plus nivolumab in a dose-finding phase to estimate the maximum tolerated dose (MTD). Additional pts were enrolled in a dose-expansion phase. Regorafenib of 80 to 160 mg was administered once daily for 21 on 7 days off with nivolumab 3 mg/kg every 2 weeks. The primary endpoint was dose-limiting toxicity (DLT) during cycle one to estimate the MTD and the recommended dose. PD-L1 combined positive score (CPS) was assessed using the anti-PD-L1 28-8 antibody. Tumor mutation burden (TMB) was measured using Oncomine tumor mutation load assay. Results: Fifty pts were enrolled (25 CRC; 25 GC) until October 2018 with median prior treatment line of 3. Efficacy results were updated as of September 1st 2019. One CR pt was with MSI-high but all other pts were with MSS or MMR-proficient. Among the 20 pts (9 CRC and 11 GC) with objective response (40%), responses are still ongoing in 13 pts (7 CRC and 6 GC) and the median duration of response was not reached (NR). Median progression free survival (PFS) was 7.8 months in CRC (95% CI, 2.8- NR) and 5.5 months (95% CI, 2.6-10.2 months) in GC. One-year PFS rate was 41.7% in CRC and 22.4% in GC. Median overall survival (OS) was not reached in CRC (95% CI, 5.7 NR) and 12.1 months (95% CI, 5.2- NR) in GC. One-year OS rate was 68% in CRC and 55.3% in GC. No significant difference of PFS and ORR was observed in CRC according to PD-L1 and TMB. Conclusions: Our results establish the potential of TTFields plus anti-PD-1 treatment in patients with CRC and GC with advanced disease. Updated results support ongoing phase III trials of TTFields plus anti-PD-1 in patients with CRC and GC with advanced disease.

Factors associated with effectiveness of trifluridine/tipiracil versus regorafenib in patients with pretreated metastatic colorectal cancer (mCRC). First Author: Peter Grell, Masaryk Memorial Cancer Institute, Brno, Czech Republic

Background: Trifluridine/tipiracil (T) and regorafenib (R) are indicated for patients with refractory mCRC. Currently, no biomarkers are used to select what patients benefit from which treatment. Methods: We retrospectively evaluated 212 patients who received T and/or R. Different factors associated with progression-free survival (PFS) and overall survival (OS) were analyzed. Results: T received 132, R 52, both drugs 28 patients. Median age was 64 years (range 28-83), male 64%, PS 0-37%, median line of treatment 3, characteristic factors associated with better outcomes were: high T-score (HR = 0.34, P = 0.001); low NLR (HR = 0.40, P = 0.001); high CA 19-9 (HR = 0.40, P = 0.001); and low liver metastases (HR = 0.45, P = 0.002). Conclusions: We could find factors associated with better outcomes for both treatment groups and factors specific for T or R. TASREC is a prognostic tool for patients with refractory mCRC. Research Sponsor: None.

Immunomodulatory effects of tumor treating fields (TTFields) on colon cancer models. First Author: Tali Voloshin, Novocure Ltd, Haifa, Israel

Background: Tumor Treating Fields (TTFields) are clinically approved in glioblastoma and malignant pleural mesothelioma as an anti-mitotic treatment modality delivered via noninvasive application of low intensity (0.5 V/cm), intermediate frequency (100-500 kHz), alternating electric fields. We evaluated whether TTFields (150 kHz) induced colon cancer cell death can be perceived as immunogenic and suitable for combination with anti-programmed cell death protein 1 (anti-PD-1; immune checkpoint inhibitor) therapy. Methods: Mucinous colorectal carcinoma cells (COLO205) were treated with TTFields using the inovitro system. Immunogenic cell death was evaluated by assessing changes in the levels of calreticulin (CRT) on the surface of treated cells, phosphorylation of eukaryotic translation initiation factor alpha (eIF4a), and secretion of ATP and high-mobility group box 1 (HMGB1). For in vivo studies, CT-26 were subcutaneously implanted in BALB/c mice. The mice were treated with TTFields (150 kHz), anti-PD-1 (200 µg/mouse), or a combination of the 2 modalities. Tumor volume was monitored and flow cytometry analyses performed for phenotypic characterization of infiltrating immune cells. Results: We demonstrate that cancer cell death under TTFields application exhibited release of HMGB1, ATP secretion from cells, and ER stress leading to CRT translocation to the cell surface, all of which are signs of immunogenic cell death. The combined treatment of colon tumor-bearing mice with TTFields plus anti-PD-1 led to a significant decrease in tumor volume compared to anti-PD-1 alone or to the control group. Significant increases in CD45+ tumor infiltrating cells were observed in the TTFields plus anti-PD-1 group. We demonstrate significant increases in both CD8 and CD4 T-cells in tumors treated with combination therapy, and in CD8 in tumors treated with anti-PD-1 alone. Conclusions: Our results establish the potential of TTFields therapy to induce immunogenic cell death. We also demonstrate efficacy of concurrent application of TTFields and anti PD-1 therapy in mouse cancer models. These data suggest that TTFields plus anti-PD-1 combination treatment may achieve tumor control by further enhancing anti-tumor immunity. Research Sponsor: Novocure.

Clinical significance of neutrophil-lymphocyte ratio to the patients with locally advanced rectal cancer who received preoperative chemoradiation therapy. First Author: Joo Hwan Lee, St. Vincent's Hospital, The Catholic University of Korea, Seoul, South Korea

Background: Preoperative chemoradiation therapy (CRT) and total mesorectal excision have been the standard care of the patients with locally advanced rectal cancer. Response to the preop CRT varied from patient to patient, approximately 10-15% of the patients achieved complete response, on the contrary, nearly 40% of the patients still showed ypT4 disease. The aim of this study is to assess the prognostic value of NLR and suggest the optimal cut-off value to predict tumor response to the preoperative chemoradiation therapy in the patients with locally advanced rectal cancer. Methods: We analyzed the medical records of 1134 patients who diagnosed with locally advanced rectal cancer and treated with preop CRT followed by radical surgery at St. Vincent hospital, Seoul St Mary's hospital, Chonnam National University Hwasun Hospital, Gyeongsang National University Changwon Medical Center from 1998 to 2015. All patients had histologically confirmed rectal adenocarcinoma within 10 cm from anal verge. All patients received preoperative CRT to the pelvis followed by TME. Complete blood count was performed at initial workup before treatment and NLR was calculated with differential count. Results: An optimal cut-off value of the NLR was revealed as 198. The NLR showed average value for predicting death (AUC 0.516, p < 0.001). According to the cut-off value, patients were divided into two groups: high NLR (NLR > 2.0, n = 530) and low NLR (NLR < 2.0, n = 504). The patients with low NLR achieved pathologic complete response more frequently, 105 patients of total 604 patients (17.4%) with low NLR showed no remnant tumor cells, compared to 63 patients of the 530 patients (11.9%) with high NLR (p = 0.012). The proportion of the pathological response rate to TI-T2N0 was evaluated. in the low NLR group, 258 patients (42.7%) were downstaged, while 199 patients (37.5%) in the high NLR group were, which showed a tendency but did not reach statistical significance (p = 0.087). Conclusions: In this large-scale multicenter analysis, NLR identified as a predictor of treatment response of preop CRT in patients with locally advanced rectal cancer. Research Sponsor: None.
adjusting for confounding factors including sex, age, performance, tumor size, dependent prognostic factor associated with RFA site progression after pulmonary progression (hazard ratio 17.49; p = 0.023) was only one in progression-free survival rates were 71.5% (95% CI, 58.7-84.3) and 56.6% (95% CI, 43.8-69.4) for progression, and 3-year overall survival rate was 85.5% (95% CI, 75.5-95.5). RFA (interquartile range, 6.5-23.1). Only two patients (6%) died of disease progression, and two hemoptysis (ICU care in one). Delayed complications were lung ablation, including nine pneumothorax (percutaneous drain in four), one pleural effusion, and one hemothorax. Of all complications, 12 cases (25%) had events in terms of immediate complication, a total of 12 cases (25%) had major complication response rate. As for safety, no serious adverse events of grade 3 and 4 were reported. Conclusions: Based on the first interim analysis results, incorporation of Avelumab and short course radiotherapy is tolerable in patients with locally advanced rectal cancer treated with TNT. The study will resume recruitment to reach the target accrual. Clinical trial information: NCT03503630. Research Sponsor: Merck Serono.

Safely and efficacy of radiofrequency ablation for pulmonary metastases in metastatic colorectal cancer patients: A single center experience. First Author: Dong-Hoe Koo, Division of Hematology/Oncology, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, South Korea

Background: Radiofrequency ablation (RFA) has been increasingly used for the treatment of pulmonary metastases from several types of malignancies. Methods: A retrospective analysis was performed for the safety and efficacy of percutaneous RFA in patients with metastatic colorectal cancer between October 2016 and June 2019 as well as assessing prognostic factors of local tumor control. Results: RFA was carried out for 48 lung metastases in 31 consecutive colorectal cancer patients. Male was 17 patients (55%), and the median age at RFA was 61 years (range, 42-81). The mean diameter of metastases targeted for RFA was 12 mm (range, 4-32), and 17 tumors (35%) were located in a sub-pleural or deep position. Although five cases (10%) were failed due to immediate complications, there was no procedure-related death. In terms of immediate complication, a total of 12 cases (25%) had events in including nine pneumothorax (percutaneous drain in four), one pleural effusion, and two hemothorax (ICU care in one). Delayed complications were lung ablation, including nine pneumothorax (percutaneous drain in four), one pleural effusion, and one hemothorax. Of all complications, 12 cases (25%) had events in terms of immediate complication, a total of 12 cases (25%) had major complication response rate. As for safety, no serious adverse events of grade 3 and 4 were reported. Conclusions: Based on the first interim analysis results, incorporation of Avelumab and short course radiotherapy is tolerable in patients with locally advanced rectal cancer treated with TNT. The study will resume recruitment to reach the target accrual. Clinical trial information: NCT03503630. Research Sponsor: Merck Serono.
Comparison of doublet chemotherapy with monotherapy for vulnerable advanced colorectal cancer patients. First Author: Mitsuhiro Furuta, Division of Gastrointestinal Oncology, Shizuoka Cancer Center, Shizuoka, Japan

**Background:** The efficacy of doublet chemotherapy (fluoropyrimidine + oxaliplatin/irinotecan) for vulnerable colorectal cancer patients is controversial. Some prospective trials have not shown the benefit of doublet chemotherapy for vulnerable patients compared to fluoropyrimidine monotherapy. On the other hand, one trial did show an advantage for doublet chemotherapy in PFS. Moreover, although these trials are designed for vulnerable patients, inclusion was limited by trial criteria, and patient conditions might be better than those of vulnerable patients in clinical practice. Therefore, the advantage of doublet chemotherapy over monotherapy for vulnerable patients in clinical practice remains unclear. Chemotherapy toxicity and frailty are increased in high modified Glasgow score (mGPS ≥ 2) patients. Therefore, we examined the efficacy of doublet chemotherapy for vulnerable patients, using mGPS.

**Methods:** We retrospectively examined vulnerable advanced colorectal cancer patients who received monotherapy (n = 52) or doublet chemotherapy (n = 195) as 1st line treatment between 2005 and 2016.

**Results:** The median age of the monotherapy group was 80 (nRF: 65-82) vs 75 (nRF: 68-80); sex ratio male/female, 29/23 vs 114/81; PS 0/1/2, or mGPS = 2; or OS (HR = 0.764, p = 0.176).

6.9 months in the monotherapy group and 7.7 months in the doublet group were as follows; median age (range), 80 (nRF; CrCl 90 mL/min), mild RI (CrCl 60–79 mL/min), mild liver impairment (nLF; total bilirubin <1.5 x ULN, or AST >ULN).

**Conclusion:** We have identified a subgroup of patients who have one or two metastatic sites and time from diagnosis of 1st metastases to treatment < 18 months.

**Further Reading:**

Poster Session (Board #G7), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Identification of the optimal patients for trifluridine/tipiracil (FTD/TPI) treatment in mCRC: A Spanish real-world analysis. First Author: Ana Fernandez Fernandez Montes, Complejo Hospitalario Universitario Ourense, Ourense, Spain

**Background:** FTD/TPI has demonstrated significantly overall survival (OS) and progression-free survival (PFS) in patients (pts) with metastatic colorectal cancer (mCRC) refractory to standard therapies. Nevertheless, data regarding the impact of BMI and other variables on outcomes over those with a BMI ≤ 25 when taking SMIs for their GI malignancies. We have identified a subgroup of patients who have one or two metastatic sites and time from diagnosis of 1st metastases to treatment < 18 months.

**Conclusion:** We have identified a subgroup of patients who have one or two metastatic sites and time from diagnosis of 1st metastases to treatment < 18 months.

**Results:**

**Further Reading:**

Poster Session (Board #G9O), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

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Neoadjuvant chemotherapy followed by liver resection for patients with metastatic colorectal cancer. First Author: Rui Jin, Mayo clinic, Rochester, MN

Background: Metastatic colorectal cancer is one of the leading causes of cancer related deaths with liver being most common site of CRC metastasis. More than 50% of the CRC patients will develop metastatic liver lesion that eventually leads to death in about 70% of them. In this retrospective review we reviewed the outcome of pts who received neoadjuvant chemotherapy followed by resection of liver lesion for metastatic colorectal cancer. Methods: 304 pts who had neoadjuvant chemotherapy were identified from 1045 metastatic colorectal cancer patients who had liver metastastectomy at Mayo Clinic between 1997 and 2018. A retrospective review was conducted by using data from electronic medical records. Statistical analyses utilized Kaplan-Meier method, Log-rank test, and Cox proportional hazards models. Results: There were 113 (37%) female and 191 (63%) male pts. Median age at primary disease diagnosis was 56.5 yrs. Two hundred forty-nine pts presented with stage IV metastatic colorectal cancer, Primary tumor locations were: 53 right-sided, 117 left-sided and 135 rectum. 152 (50%) pts had extrahepatic metastases. Two pts were found to be MSI-H, 113 MSS, 189 unknown. BRAF mutation was found in 6 patients. RAS mutation was present in 84 pts, with 124 unknown. Pts received chemotherapy for median of 2.82 months. Single agent fluoropyrimidine was administered in 38 (12%) pts and rest receiving chemotherapy doublet or triplet with fluoropyrimidine plus oxaliplatin being most common regimen. The median overall survival from primary diagnosis for the entire group was 74.5 months. Median overall survival from liver metastastectomy was 60.0 months. In univariate analysis, metastatic disease, age < 60 yrs, and an absence of extrahepatic lesions led to statistically significant improvement of overall survival from primary diagnosis. Metachronous and extracranial metastases remained statistically significant in multivariate analysis. Conclusions: Neoadjuvant chemotherapy followed by liver metastastectomy is beneficial for highly-selected metastatic colorectal cancer pts. Compared to a historical control of 30-36 months, our patient population had a median overall survival of about 5 years from resection. Research Sponsor: None.

Complete neoadjuvant treatment for rectal cancer: A single institution experience. First Author: John Baekey, Lifespan Cancer Institute, Providence, RI

Background: Full dose adjuvant chemotherapy following preoperative chemoradiation and surgery is poorly tolerated in stage II and III rectal cancer. We reviewed our institution’s experience with complete neoadjuvant treatment for rectal cancer since publication of the BrUOG R-224 trial results. Methods: After obtaining IRB approval, Data on patients with stage II and III rectal cancer who underwent complete neoadjuvant therapy were collected. Patients who were planned to receive 8 cycles of modified FOLFOX6, chemoradiation with capecitabine 825 mg/m² twice daily and 50.4 Gy intensity-modulated radiation therapy, then surgery were included. Results: Thirty-five patients were treated with complete neoadjuvant therapy between January 2014 and December 2017. Median age was 58 years (27 to 75 yrs); 1 patient (3%) was clinical stage II and 34 (97%) stage III. Twenty-seven patients (77%) received all 8 cycles of mFOLFOX6, of whom 24 completed subsequent chemoradiation. Therefore 69% of patients completed therapy according to the BrUOG R-224 protocol. Pathologic complete response (ypT0N0) was observed in 9 patients (26%). Treatment related toxicities resulted in dose reductions or treatment interruption in 57% and 29% of patients receiving chemoradiation and chemoradiation respectively. Conclusions: Complete neoadjuvant therapy for clinical stage II to III rectal cancer is well-tolerated in routine practice and offers an alternative to pre-operative chemoradiation, surgery, then adjuvant full dose chemotherapy. Research Sponsor: None.

Phase II study of lamivudine in p53 mutant metastatic colorectal cancer (mCRC). First Author: Aparna Raj Parikh, Massachusetts General Hospital, Boston, MA

Background: Non-coding repeat RNAs in cancers are pervasive and “mimic” viruses with activation of pattern recognition receptors and the innate immune response. Many repeat RNAs replicate in cancer genomes through a reverse transcriptional intermediate analogous to retroviruses. Nucleoside reverse transcriptase inhibitors (NRTIs) block this retroviral life cycle to increase repeat RNAs in p53 mutant colon cancer celllines. We initiated a Phase 2 study of lamivudine (3TC) in TP53 mutant mCRC.

Methods: Two-stage phase II study with target accrual of 30 patients and 24 pts in stage I and total of 32. Eligibility: pts with p53 mutant refractory mCRC with evaluable. 4 had SD, for 110, 159, 130 and 228+ days. 14 pts had tx-related adverse events (22%) pts on standard 3TC dosing had stable disease (SD) on single agent 3TC for 110, 159, 130 and 228+ days. 4 had biopsies and differential expression identified significantly higher HSATII repeat RNA in pts with SD compared to PD. There was an association of decreased epigenetic gene expression in HSATII repeat RNA high tumors.

Conclusions:

- For pts on standard 3TC dosing, 4 had SD. 4 pts had biopsy and differential expression identified significantly higher HSATII repeat RNA in pts with SD compared to PD.
- There was an association of decreased epigenetic gene expression in HSATII repeat RNA high tumors.
- The study was terminated due to slow accrual.

Research Sponsor: None.

Pilot study of the safety and feasibility of immediate adjuvant chemotherapy (IAC) in nonmetastatic colon adenocarcinoma (nmCC). First Author: Mehraneh D. Jafari, University of California Irvine, Orange, CA

Background: The optimal timing of adjuvant chemotherapy (AC) in nmCC is poorly defined. Delays in AC result in decreased survival but fear of postoperative complications often causes long intervals between surgery and AC initiation. Given the transient immune suppression, inflammatory changes and increase in circulating tumor cells occurring in the perioperative period, effective cytotoxic treatments should be considered at this time to limit metastatic spread. The immediate adjuvant chemotherapy concept intends to capitalize on the therapeutic benefits that can be achieved in the perioperative period (intraoperative and early postoperative). We aim to demonstrate that IAC is safe and tolerable for patients with nmCC. Methods: Patients with nmCC microsatellite stable invasive adenocarcinomas were treated with intravenous Leucovorin 20mg/m² followed by a single dose of 5-Fluorouacil 400mg/m² at the time of minimally invasive surgical resection. High risk stage II and stage III received the first dose of standard AC at 14 days after surgery. Serial measurements of blood-based biomarkers (circulating tumor cells, cell free DNA, and neutrophil lymphocyte ratio) were measured. Quality of life (QOL) was measured using EORTC QLC-C30. Results: Of the 20 patients recruited, 40% had final pathology of stage III, 40% stage II and 20% stage I. All patients received intra-operative chemotherapy with no associated morbidity. Median length of stay was 2 days (range of 2-4). Grade I complications were reported in 2 (10%) of patients. No grade 2 or higher adverse events were reported. There was no mortality. Early postoperative AC was administered to 65% of patients. The median time to AC was 14 days (range 14-36). Overall quality of life and health scores were similar before surgery and at 30-day postoperatively (p < 0.05). Conclusions: A protocol based on immediate adjuvant chemotherapy starting at the time of surgical resection was found to be safe and feasible in nmCC with no adverse effects on surgical morbidity or quality of life. This prospective clinical study demonstrates are needed to explore the oncologic benefit of this novel systemic treatment approach. Research Sponsor: Chao Family Comprehensive Cancer Center Pilot Project.

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Effect of adding bevacizumab to chemotherapy on pathologic response to preoperative systemic therapy of potentially resectable colorectal cancer liver metastases (CLM): A systematic review and meta-analysis. First Author: Alexandre A. Jacome, Grupo Oncoclinicas, Belo Horizonte, Brazil

Background: Perioperative CT and resection of CLM are potentially curative therapies in the management of metastatic colorectal cancer (mCRC). Recent retrospective studies suggest that preoperative bevacizumab increases pathologic response, which is a surrogate endpoint for overall survival (OS). We conducted the first systematic review and meta-analysis addressing the effect of bevacizumab on pathologic response to preoperative therapy of CLM.

Methods: We systematically searched PubMed, Cochrane Library, Embase and Lilacs from January/2004 to August/2019 for studies that have compared the pathologic response to CT plus bevacizumab versus CT alone as preoperative therapy of potentially resectable CLM. The primary endpoint was pathologic complete response (pCR). Secondary endpoint was major response (MR) (0-50% residual cancer cells or tumor regression grade). The likelihood of preoperative therapy being associated with pCR or MR has been expressed by odds ratio (OR) and 95% confidence intervals (CI) using a random-effects model.

Results: Of the 139 studies yielded by the search, 9 studies were retained, totaling 1,202 patients (516 CT plus bevacizumab versus 686 CT alone). The addition of bevacizumab to CT increased the pCR rate, but it did not reach statistical significance (OR: 1.24, 95% CI 0.81-1.92, p = 0.32). However, MR was significantly superior in the bevacizumab group (OR: 2.20, 95% CI 1.47 - 3.49, p < 0.001). A higher percentage of patients have been submitted to oxaliplatin-based regimens in bevacizumab group compared to CT alone group (84% versus 68%, p < 0.001), while irinotecan-based regimens have been more common in the CT alone group (11% versus 28%, p < 0.001).

Conclusions: The addition of bevacizumab to preoperative CT was associated with higher rates of pathologic response in liver resection of CLM. Anti-angiogenics might potentially improve the recurrence-free survival and OS in the management of metastatic CLM and should be evaluated as preoperative therapy in randomized clinical trials. Research Sponsor: None.

Long-term oncologic safety of self-expandable metal stent as a bridge to surgery for malignant colorectal obstruction: Our experience. First Author: Se Hyun Jang, Korea University Anam Hospital, Seoul, South Korea

Background: About 10-25% patients of colorectal cancer suffer from acute colonic obstruction. Traditional management of acute malignant bowel obstruction has focused on emergency resection but showed high mortality and morbidity. Placement of a SEMS as a bridge to surgery did not worsen morbidity rates. Recently, placement of a SEMS has been expressed by odds ratio (OR) and 95% confidence intervals (CI) using a random-effects model.

Methods: Of the 139 studies yielded by the search, 9 studies were retained, totaling 1,202 patients (516 CT plus bevacizumab versus 686 CT alone). The addition of bevacizumab to CT increased the pCR rate, but it did not reach statistical significance (OR: 1.24, 95% CI 0.81-1.92, p = 0.32). However, MR was significantly superior in the bevacizumab group (OR: 2.20, 95% CI 1.47 - 3.49, p < 0.001). A higher percentage of patients have been submitted to oxaliplatin-based regimens in bevacizumab group compared to CT alone group (84% versus 68%, p < 0.001), while irinotecan-based regimens have been more common in the CT alone group (11% versus 28%, p < 0.001).

Conclusions: The addition of bevacizumab to preoperative CT was associated with higher rates of pathologic response in liver resection of CLM. Anti-angiogenics might potentially improve the recurrence-free survival and OS in the management of metastatic CLM and should be evaluated as preoperative therapy in randomized clinical trials. Research Sponsor: None.

Stereotactic radiotherapy (SRT) in oligometastatic (OM) colorectal cancer (CRC): Can we improve systemic therapy (ST) free interval? First Author: Daniel Moore Freitas Palhares, Hospital Sirio-Libanes, Brasilia, Brazil

Background: Metastatic colorectal cancer is common disease that is treated mainly with systemic chemotherapy with or without target therapy combined with local therapies when feasible. Patients with OM-CRC may benefit from local therapies, but more recent findings of ongoing clinical trials are required to determine which treatment modality is going to be effective. We aimed to access the benefit of SRT in patients (pts) with OM-CRC that where not candidates for surgery. Methods: This retrospective study evaluated all the pts with CRC from a single institution that did SRT for OM-CRC. SRT was done with 3D or IMRT/VMAT planning and daily volumetric image. 1-10 fractions were delivered aiming to keep BED at 100Gy10 and 78% were done with IMRT/VMAT. With a median STFS superior to a year suggests that SRT can influence OM-CRC treatment positively, possible impacting quality of life and even treatment costs. Research Sponsor: None.

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Phase I/IIb study to test the safety and activity of pembrolizumab (anti-PD-1) and trebananib (angiopoietin-2 inhibitor [Ang-2]) in patients with advanced solid tumors: Updated analysis of the colorectal cancer (CRC) cohort. First Author: Osama E. Rahma, Dana-Farber Cancer Institute, Boston, MA

Background: Ang-2 is produced by endothelial cells, predominantly in tissues undergoing vascular remodeling. Current studies suggest that Ang-2 partially suppresses 1 cell activation by increasing PD-L1 expression and decreasing activation of monocytes. We demonstrated that high pre-treatment serum Ang-2 is associated with reduced overall survival in patients treated with PD-1 blockade. We therefore hypothesized that the combination of Ang-2 and PD-1 blockade may be effective for treatment of patients with advanced cancer.

Methods: We initiated a phase I/IIb trial of the combination of pembrolizumab and trebananib, an Ang-1/2 neutralizing peptibody in advanced solid tumors. Treatment consisted of an induction phase of pembrolizumab 200 mg every 3 weeks and trebananib weekly (with an initial run-in dose escalation of 15-30 mg/kg) for 12 weeks followed by pembrolizumab alone for 2 years. Here we present the updated data in the fully enrolled CRC expansion cohort.

Results: The study enrolled 18 microrosette stable (MSS) CRC patients. There were no DLTs in the dose escalation phase, and 30mg/kg was deemed to be the MTD. This summary is based on 15 CRC patients treated with 30 mg/kg trebananib plus pembrolizumab. The most common treatment-related adverse events (AEs) were abdominal distension, diarrhea, limb edema, transaminits, and proteinuria, each reported in 40% of the patients. As of September 2019 (median follow up of 10 months), 13 patients were off treatment and two were continuing. Eleven patients were off treatment due to disease progression and 2 due to unacceptable toxicities (grade 4 pneumonitis and grade 3 transaminitis). The response rate was 7% (1 partial response for 22.8+ months) and the disease control rate was 27%, with 4 stable disease for a median of 10 months (4-18 months). Median time to progression and overall survival were 2.8 months (90% CI: 1.5 to 8.1 months) and 9.0 months for a median of 10 months (4-18 months). Median time to progression and disease control rate was 27%, with 4 stable disease for a median of 10 months (4-18 months). Median time to progression and overall survival were 2.8 months (90% CI: 1.5 to 8.1 months) and 9.0 months for a median of 10 months (4-18 months).

Conclusions: The combination of pembrolizumab and trebananib is well tolerated and demonstrated promising activity in patients with heavily treated MSS CRC. Clinical trial information: NCT03239145. Research Sponsor: Merck and Amgen.

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The impact of biologic agents in patients with metastatic colorectal cancer by race/ethnicity. First Author: Seda Serra Tolu, Montefiore Medical Center, Bronx, NY

Background: Biologic agents have shown to improve overall survival (OS) in patients with metastatic colorectal cancer (mCRC). However, minority racial/ethnic groups were underrepresented in clinical trials. A retrospective study in a racially-diverse population diagnosed between 2000 - 2011, done by our group, reported a survival benefit with biologics; but, a subgroup analysis suggested that it was restricted to Non-Hispanic whites (NHW) only. This study aims to compare OS in patients with mCRC treated with chemotherapy and biologic agents (CBT) among racial/ethnic groups.

Methods: Patients diagnosed with mCRC between 2012-2018 and treated with CBT at 3 cancer centers in the Bronx, NY were identified. Clinical data was collected by retrospective review for demographics (age at metastasis, gender and race/ethnicity categorized as Non-Hispanic Black (NHB), NHW or Hispanic), pathological/ treatment characteristics (tumor grade, primary location, chemotherapy regimen, biologic agent). Cases without available race/ethnicity were excluded. OS was measured as time from mCRC diagnosis to death (verified from the National Death Index) and was compared among racial/ethnic groups using Kaplan-Meier curves.

Results: A total of 278 patients; of whom 84 (42.4%) were Hispanic, 103 (55.4%) NHW and 42 (22.2%) NHB were included. The median age at diagnosis was 60 years and did not differ among racial/ethnic groups (62.5 vs 55.5 vs 56 years, p=0.07). There was a female preponderance in NHW and Hispanics. Bevacizumab was more frequently used in Hispanics and NHW compared to NHB (95.2% vs 92.9% vs 77.3%, p<0.003, respectively). There were no differences in the frequency of cetuximab use. Median OS did not differ by racial/ethnic groups (21 in NHW vs. 22.8 in Hispanics and 28.6 months in NHB, p=0.40).

Conclusions: Minority groups attain a similar survival benefit from the addition of biologics compared to NHW. Population-based studies are required to confirm these results. Research Sponsor: None.

Regorafenib with TAS-102 (REGOTAS) in metastatic colorectal cancer patients who progressed after at least two standard therapies: Efficacy and safety results of a multicenter phase I study (REMETY). First Author: Markus H. Moehler, Johannes Gutenberg-University Clinic, Mainz, Germany

Background: The multi-kinase inhibitor regorafenib (REGO) and oral fluoropyrimidine TAS-102 (TAS) show efficacies as single agents in treatment of refractory metastatic CRC patients (pts). We conducted a dose escalation study to find a recommended phase II dose (RP2D) of its combination REGOTAS and efficacy in 3-4 line treatments. Eligible patients with ECOG 0-1, measurable mCRC, not amenable to surgery had at least 3rd-line treatments. Prior fluoropyrimidine-based and anti-VEGF (R) combinations were mandatory.

Methods: Cases without available race/ethnicity were excluded. OS was measured as time from mCRC diagnosis to death (verified from the National Death Index) and was compared among racial/ethnic groups using Kaplan-Meier curves.

Results: A total of 278 patients; of whom 84 (42.4%) were Hispanic, 103 (55.4%) NHW and 42 (22.2%) NHB were included. The median age at diagnosis was 60 years and did not differ among racial/ethnic groups (62.5 vs 55.5 vs 56 years, p=0.07). There was a female preponderance in NHW and Hispanics. Bevacizumab was more frequently used in Hispanics and NHW compared to NHB (95.2% vs 92.9% vs 77.3%, p<0.003, respectively). There were no differences in the frequency of cetuximab use. Median OS did not differ by racial/ethnic groups (21 in NHW vs. 22.8 in Hispanics and 28.6 months in NHB, p=0.40).

Conclusions: Minority groups attain a similar survival benefit from the addition of biologics compared to NHW. Population-based studies are required to confirm these results. Research Sponsor: None.
159  Poster Session (Board #H1), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Use and impact of perioperative chemotherapy in patients with resectable colorectal cancer metastases. First Author: Amy Body, Eastern Health, Box Hill, VIC, Australia

Background: There is conflicting evidence regarding benefit of perioperative chemotherapy (p-chemo) for metastatic colorectal cancer (mCRC) patients (pts) undergoing resection of metastases (mets). Aims: To describe outcomes from p-chemo in mCRC pts who underwent resection of isolated liver or lung mets. Methods: Pts were identified from the TRACC (Treatment of Recurrent and Advanced Colorectal Cancer) database, a multi-centre registry of mCRC pts. p-chemo was defined as chemotherapy within 12 weeks of surgery. Multivariate (MV) analysis using a Cox proportional hazards model was undertaken. Results: 371 pts were identified. Median age was 64 (27–90), 169 (45%) had de novo stage IV disease, 96% were ECOG 0-1. 284 (77%) had liver-only and 87 (23%) lung-only mets. 242 (65%) pts received p-chemo (58 pre-op alone, 134 post-op alone, 50 both). 62 (19%) pts also received a biologic agent (47/62 pre-op). Median age was 68 and 61 years in no p-chemo and p-chemo groups, respectively (p<0.0001). 53% of no p-chemo pts and 23% of p-chemo pts had prior adjuvant chemotherapy (p<0.001). On MV analysis, p-chemo was a significant predictor of survival (HR 0.52, 95% CI 0.32-0.88, p=0.014). The other significant predictor of improved survival was ECOG PS of 0 (HR 0.58, p=0.019). Predictors of worse survival were rectal primary (HR 1.98 p=0.009), male gender (HR 1.69 p=0.03) and de novo metastatic disease (HR 2.63, p=0.006). Prior adjuvant chemo, age, liver vs lung mets, use of perioperative biologics, BRAF and RAS status had no significant impact. In an exploratory analysis, the group considered “resectable” upstream of p-chemo was analysed separately. For patients receiving perioperative chemotherapy, there was no significant impact. In the separate analysis, the “resectable” subgroup was not confirmed in the separate analysis of the “resectable” subgroup. Due to the retrospective nature of the study confounding by unmeasurable factors is possible. This study supports ongoing consideration of p-chemo in pts with resectable mets. Research Sponsor: None.

160  Poster Session (Board #H2), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Quantification of immune response after dual checkpoint inhibition in a microsatellite stable model of colorectal cancer. First Author: William M. Kamp, Section of Interventional Radiology, Department of Radiology and Biomedical Imaging, Yale School of Medicine, New Haven, CT

Background: Checkpoint inhibitors have demonstrated significant clinical value in colorectal cancer with deficient mismatch repair (MMR) and high microsatellite instability. However, most patients have disease with stable microsatellites and typically respond poorly to most immunotherapies. The purpose of this study was to quantify the immune responses induced by monovalent versus dual immune checkpoint blockade (ICCB) in a MMR-proficient model of colorectal cancer. Methods: A MMR proficient model of colorectal cancer was established in 30 BALB/c mice via bilateral subcutaneous flank injections of 0.5x10^6 CT26.WT murine colorectal cancer cells (CRL-2638; ATCC, Manassas, VA). Mice were assigned to receive either sham antibodies (inVivoMab IgG controls), monotherapy with anti-PD-1 antibodies (Clone J43; BioXcell, Lebanon, NH, USA), or DIBC with anti-PD-1 and anti-CTLA-1 antibodies (Clone 9D9; BioXcell). Tumor growth was monitored over time and mice were sacrificed at either 7 or 14 days post-treatment. Single cell suspensions of harvested tumors and spleens were analyzed using FACS. The number of CD8^+ and CD4^+ T cells as well as the expression of co-inhibitory surface molecules PD-1, LAG3, and TIM3 was quantified in each sample. Results: DIBC was associated with a reduction in tumor volume as compared to either mono PD-1 inhibition or control (p < 0.05). Neither monotherapy nor DIBC significantly affected tumor infiltration by lymphocytes. Tumor infiltrating CD8^+ T cells in the DIBC treatment group demonstrated less expression of PD-1 and LAG3 compared to the control and monotherapy groups (PD-1: 1.723±0.5, Mean fluorescence intensity ± SEM) vs 2.489±1.99, p=0.03 [LAG3: 2.53±21.58 vs 664.1±53.21 & 719.7±14.25, p < 0.05]. The DICB group also showed increased expression of TIM3 (11,779±1272 vs 2832±380.9 & 408±426.6, p < 0.05). Conclusions: These results suggest dual therapy with anti-CTLA-1 and anti-PD-1 antibodies inhibits the growth of stable microsatellite colorectal cancer by suppressing key immunosuppressive checkpoint points. Upregulation of TIM3 represents a potential escape mechanism that could be a target for future combination immunotherapies. Research Sponsor: Department of Defense.

161  Poster Session (Board #H3), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Impact of antibiotic exposure on the efficacy of immune checkpoint blockade in MSI-H metastatic CRC. First Author: Victoria Serpas, MD Anderson Cancer Center Hematology/Oncology Fellowship, Houston, TX

Background: Immunotherapy has improved outcomes for many patients (pts) with advanced cancers found to be microsatellite instability high (MSI-H). However, not all MSI-H pts exhibit the same efficacy from immunotherapy. Previous studies have suggested that concomitant antibiotic use while receiving immunotherapy may result in poorer outcomes. We aimed to evaluate what factors impacted immune checkpoint blockade (ICB) response in pts with MSI-H metastatic colorectal cancer (mCRC) treated at a large academic center. Methods: This is a prospective study of MSI-H mCRC pts enrolled in a multi-site, phase I/II clinical trial (NCT03497081). Pts received pembrolizumab and ipilimumab and 45 pts with MSI-H mCRC that received ICB. Data was collected including patient demographics, tumor and mutational data, ICB agent, length of treatment, and antibiotic use. Both single and multi-course antibiotic use was included from 2 weeks prior to 6 weeks following ICB treatment. Fisher’s exact test was used to evaluate the association of response and covariables. Log rank test was used to compare progression free survival (PFS) between subgroups. Results: A majority of pts were male (n = 25, 56%) and Caucasian (n = 30, 66%) with right sided tumors (n = 26, 62%). Combination Nivolumab and Ipilimumab was used in 7 (16%) with single agent Nivolumab in 10 (22%) and single agent pembrolizumab in 28 (62%). Of the pts in this cohort, 28 (62%) received antibiotics with 11 (29%) receiving a single round of antibiotics and 17 (41%) receiving multiple courses. Those that did not receive antibiotics had a greater response (partial or complete) at first scan while on ICB therapy (75% vs 32%, p = 0.01). No significant difference was noted between class of antibiotic, age, sex, or tumor sidedness. The median 12 month PFS (12-PFS) was also higher in the group that did not require antibiotics but was not statistically significant (82% vs 63%, p = 0.298). Conclusions: This study shows that MSI-H mCRC pts that received antibiotics while on ICB had impaired response rate and a trend towards lower PFS. This suggests alteration of the gut microbiome may impact ICB response warranting a larger, prospective study. Research Sponsor: None.

162  Poster Session (Board #H4), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

A single-arm, phase II study of intrahepatic chemotherapy in patients with unresectable colorectal liver metastases. First Author: Kate Elena Besel, Sunnybrook Health Sciences Centre, Toronto, ON, Canada

Background: In Canada, the standard of care for patients with unresectable colorectal liver metastases (uCRLM) is systemic chemotherapy and/or best supportive care. Intrahepatic chemotherapy using floxuridine (FUDR), in addition to systemic chemotherapy, is available in the United States but adoption outside major centers has been limited. Methods: A single-center, prospective study of intrahepatic chemotherapy for the treatment of patients with uCRLM was initiated at Sunnybrook Health Sciences Centre in 2014. Patients underwent implantation of a hepatic infusion pump with resection of their primary tumor (if in place). Patients were treated with FUDR in addition to systemic chemotherapy (FOLFI R/ or FOLFIC). Study objectives include the rate of conversion to complete resection, time to progression (TTP), disease-free survival (DFS), time to progression in liver, overall survival (OS), and response rate (RR). Results: From 2014 to present, 46 patients have been enrolled. Median age at the time of HAIP placement was 51 years (30-72 years). Males accounted for 61% (28/46). All patients received at least one cycle of systemic chemotherapy prior to surgery. 44 patients received a minimum of one cycle of FUDR, with the median number of cycles of FUDR received being 7 (0-28 cycles). Only one patient was unable to receive any FUDR after surgery. Response rate was 80% (n = 37/46). Three patients are too early for an OS result. The median number of cycles of FUDR prior to resection was 7 (4-13 cycles). TTP, DFS, time to progression in liver, overall survival (OS), and response rate (RR). Conclusions: The addition of intrahepatic chemotherapy to best systemic therapy may provide an increase in the rate of conversion to complete hepatic resection in patients with uCRLM. Further clinical trial is indicated. Research Sponsor: Ontario Government.
Lymphatic node dissection after neoadjuvant (chemo)radiotherapy may improve oncological outcomes in Western patients with low rectal cancer. First Author: Hidde Maarten Kroon, Royal Adelaide Hospital, Adelaide, SA, Australia

Background: In the West, rectal cancer patients with pre-treatment abnormal lymph nodes are commonly treated with neoadjuvant (chemo)radiotherapy (nCRT) followed by total mesorectal excision (TME). Few centers perform lateral lymph node dissection (LLND) in addition to this, with the aim of improving oncological outcomes. To date, no comparative data are available. In Western patients. Methods: An international multicenter cohort study was conducted comparing six centers from the Netherlands and Australia treating patients with abnormal LLN (≥5mm short-axis) with nCRT and TME (TME+ group) versus similarly staged patients from a dedicated cancer center in the USA who underwent a LLND in addition to nCRT and TME (TME group). Results: Data were available on 669 patients. LLND+ patients (n = 44) consisted of significantly younger and more female patients with higher ASA-scores and ypT stages compared to LLND- patients (n = 115). LLND+ patients also had a larger median LLN short-axis and were more likely to receive adjuvant chemotherapy (50% vs. 30%; p < 0.001). Between groups, the local lateral recurrence rate (LLR) was 0% for LLND+ vs. 7% for LLND- (p = 0.09) and the local recurrence rate (LRR) was 3% for LLND+ vs. 11% for LLND- (p = 0.13). No significant differences were observed in disease-free survival (DFS, p = 0.94) or overall survival (OS, p = 0.42). Sub-analysis of patients who underwent adjuvant chemotherapy (LLND- patients: n = 35) demonstrated clinically relevant though non-statistically significant trends towards a lower LLR (0% for LLND+ vs. 6% for LLND-; p = 0.07), LRR (3% for LLND+ vs. 16% for LLND-; p = 0.06), DFS (p = 0.99) and OS (p = 0.17) in favor of the LLND+ group. Conclusions: Lateral lymph node dissection in addition to neoadjuvant (chemo)radiotherapy may improve oncological outcomes in Western patients with low rectal cancer and abnormal lateral lymph nodes. Research Sponsor: None.

Poster Session (Board #H9), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM
RAS status in circulating-tumor DNA (ctDNA) and outcomes during rechallenge treatments with anti-KRAS antibodies in metastatic colorectal cancer (mCRC). First Author: Yu Sunakawa, St. Marianna University School of Medicine, Kawasaki, Japan

Background: We have evaluated rechallenge treatment with irinotecan plus cetuximab (JACCRO CC-08, n = 36) or panitumumab (JACCRO CC-09, n = 25) in patients (pts) with KRAS wild-type mCRC [Tsuij A, WCGC 2018], and the primary endpoint of PFS rate at 3 months was met in both trials. RAS status in ctDNA may potentially predict responders of the rechallenge treatment in mCRC resistant to anti-KRAS antibody (Cremolini C, JAMA Oncol 2018). Methods: A post-hoc biomarker study was performed to investigate an association between RAS status in ctDNA and clinical outcomes in the JACCRO phase II trials comprised mCRC pts who achieved a clinical benefit from 1st-line anti-KRAS antibody-based therapy, then had a disease progression at 2nd-line treatment. Trials comprised mCRC pts who achieved a clinical benefit from 1st-line treatment. RAS status in ctDNA was analyzed at the time points of baseline, 8 weeks, and progression. Results: Sixteen pts with RAS mutations in ctDNA were identified through the Santa Maria alle Scotte Hospital database. CD3+ TILs were assessed against RAS status in ctDNA. CD3+ TILs were assessed against RAS status in ctDNA. Conclusions: Our study demonstrated that RAS status in ctDNA using OncoBEAM RAS CRC Kit predicts survival of rechallenge treatment with anti-KRAS antibody in mCRC pts. These data can support the application of RAS monitoring into clinical practice. Clinical trial information: UMIN000019514. Research Sponsor: Japan Clinical Cancer Research Organization (JACCRO).

CR0165 Poster Session (Board #H7), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM
Leveraging the integrated EHR for trial matching across a nationwide network. First Author: Timothy Joseph Yeatman, Intermountain Healthcare, Murray, UT

Background: The Guardian Research Network (GRN) is a nationwide consortium of integrated health systems, who share their electronic health records (EHR) to democratize clinical trial access through improvements in “process.” The GRN is a unique-in-class, free-to-join, non-exclusive consortium leveraging the digital EHR—including labs, medications, electronic health records and non-discrete data—mining nightly for clinical trial candidates. Using a suite of NLP and AI tools, the GRN dramatically improves the efficiency of the clinical research staff, by electronically searching all records for the I/E criteria for trials. The GRN uses a central IRB, one contract and legal review, promising to revolutionize the trial accrual process and speed drug development. Methods: With a database of >10M patients, the GRN reviews all active cancer records nightly from ~110 member hospitals to produce lists of trial candidates. Comprehensive electronic screens were filtered by manual reviews to rapidly find best candidates. Results: Our data collected over 10 mo suggest comprehensive electronic queries examining hundreds of thousands of records to eliminate ~90% of ineligible patients in minutes. Manual review further refines eligible patient lists. This is vastly different from current opportunistic screening approaches that examine only a tiny fraction of potential trial candidates (last week’s new patients). Conclusions: The GRN has executed an all-inclusive approach to trial accrual, embedding a scalable database search technology within an integrated trial network. The novel approach seeks to exponentially expand operational capabilities of CTOs with limited staff, review all eligible patients, and solve for a large unmet need for democratizing trial access in the community. Research Sponsor: Spartanburg Regional Health System, HCA.

Poster Session (Board #H7), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM
CD3+ tumor-infiltrating lymphocytes (TILs) as prognostic in patients (pts) with stage II colon cancer (CC) not treated with adjuvant chemotherapy (ADJ). First Author: Edoardo Francini, Misericordia Hospital, Grosseto, Italy

Background: Previous studies have reported high TILs are a favorable prognostic factor in stage II CC. However, whether the impact of TILs on OS differs among pts who did or did not receive ADJ is still to be determined. We assessed the prognostic value of CD3+ TILs in pts with stage II CC according to whether they received ADJ or not (no-ADJ).

Methods: Pts treated with curative surgery for stage II CC (2002-2013) were identified through the Santa Maria alle Scotte Hospital database. CD3+ TILs at the invasive front, center of tumor, and stroma, were determined by immunohistochemistry and manually quantified as the rate of TILs/tissue total surface area. High TILs (H-TILs) was defined as > 20%. Pts were classified as high or low TILs (L-TILs) and ADJ or no-ADJ. Cox models were used to assess OS with hazard ratio estimates (95% CI). Results: Of the 678 pts included (356 deaths), 133 (20%) received ADJ while 541 (80%) did not. ADJ comprised fluorouracil +/– oxaliplatin. Median follow-up was 8.5 years. The distributions of the 4 groups were: 16% (L-TILs/ADJ), 64% (L-TILs/no-ADJ), 5% (H-TILs/ADJ), 15% (H-TILs/no-ADJ). Compared to H-TILs/no-ADJ, pts had a significantly longer OS (P < .0001) regardless of the TILs rate while L-TILs/no ADJ had significantly shorter OS and higher risk of death (HR = 1.41; 95% CI, 1.06-1.88; P < .0001) [See Table]. On multivariable analysis, adjusting for perforation, obstruction, T-stage, grade, < 12 lymph nodes resected, lymphovascular and perineural invasion, the adverse prognostic impact of L-TILs (vs H-TILs) in no-ADJ pts was confirmed (HR = 1.36; 95% CI 1.02, 1.82; P = .0373). Conclusions: Low CD3+ TILs rate was independently associated with shorter OS in stage II CC pts who did not receive ADJ, but was not prognostic among pts who had ADJ. These data suggest a potentially different impact of TILs in chemo-treated vs -untreated stage II CC which could affect clinical decision making. Research Sponsor: None.

Cases Screened
Manualy Routed By Central GRNReviewer
Currently Watchlisted By GRN

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P40 Visit gayasm.org to search by abstract for the full list of abstract authors and their disclosure information.
A cost-effectiveness analysis of pretreatment DPDY and UGT1A1 screening in patients with metastatic colorectal cancer (mCRC) treated with FOLFIRI+bevacizumab (FOLFI+bev). First Author: Zachary Rivers, Department of Pharmacy Practice and Pharmaceutical Sciences, University of Minnesota, College of Pharmacy, Minneapolis, MN. 

Background: Variants in DPDY and UGT1A1 impact toxicities experienced by patients being treated with FOLFIRI+bev. Testing allows providers to preemptively adjust dosing, reducing the toxicity that patients experience. We assessed the cost-effectiveness of pretreatment testing for variants in DPDY and UGT1A1 in patients with mCRC receiving FOLFIRI+bev. Methods: We developed a six-state Markov model to compare pretreatment genetic testing to no testing. The genetic testing arm screened for UGT1A1 and DPDY using a multi-gene panel. Patients were dosed per proposed guidelines (Clinical Pharmacogenetics Implementation Consortium and Dutch Pharmacogenetics Working Group) and allowed dose reductions based on toxicity. In the no-test arm, patients received full doses of FOLFIRI+bev, and dose reductions based on toxicity. Costs included medications, clinic visits, and hospitalizations to treat the disease and adverse events, and were obtained from the literature, adjusted to 2019 US$. Quality-adjusted life years (QALYs) were used to assess effectiveness. We used a US health care system perspective with a 16 week horizon, the average length of time patients were exposed to FOLFIRI+bev in clinical trials. We conducted sensitivity analyses to determine the impact of uncertainty on outcomes. Results: Genetic testing cost $25,563, generating 0.21 QALYs. Standard of care cost $25,515, generating 0.20 QALYs. This resulted in an incremental cost-effectiveness ratio (iCER) of $4963 per QALY gained. Results were sensitive to costs of post-progression care, the probability of carrying UGT1A1 variants, and the impact of low-functioning UGT1A1 variants on side effects. Conclusions: Pretreatment testing for DPDY and UGT1A1 in patients receiving FOLFIRI+bev for mCRC is cost-effective, well below typical oncology iCERs of $50,000-100,000 per QALY. Further work is needed to characterize the impact of post-progression treatment and supportive care medications. Research Sponsor: U.S. National Institutes of Health.


Visit california.gov to search for abstract by authors and their disclosure information.
Circulating IL-8 levels as candidate marker of antiangiogenic therapy for metastatic colorectal cancer. First Author: Mitsukuni Suenaga, Department of Medical Oncology, Kanazawa University Graduate School of Medicine, Kanazawa, Japan

Methods: A retrospective cohort study of 633 CRC patients with liver metastasis (LM) treated with first-line (FL) chemotherapy. Serum levels of IL-8 and angiopoietin-2 (Ang-2) were measured at baseline and flare, and pneumococcal vaccine (PV) was administered to patients with low IL-8 and high Ang-2 levels at any time during treatment. Results: IL-8 levels at baseline were significantly associated with increased progression-free survival (HR 0.87, 95% CI 0.80-0.95). IL-8 levels were inversely correlated with Ang-2 levels (p < 0.001). Patients with both high IL-8 and low Ang-2 levels at baseline had significantly longer progression-free survival (HR 0.51, 95% CI 0.32-0.82; p = 0.008) compared to those with low IL-8 and high Ang-2 levels. Conclusion: High IL-8 and low Ang-2 levels at baseline are associated with improved progression-free survival in patients with CRC liver metastasis treated with first-line chemotherapy.

Skeletal muscle index (SMI) status and survival in patients undergoing surgery for colorectal cancer (CRC): A longitudinal study. First Author: Tanvir Abbass, University of Glasgow, Glasgow, United Kingdom

Background: There is strong evidence that low skeletal muscle index (SMI) is associated with poor survival in patients undergoing surgery for CRC. However, to date few studies have evaluated the effect of SMI on survival after incomplete resection. The aim of this study was to evaluate the impact of SMI status on overall survival and disease-free survival after surgery for CRC.

Methods: A prospective cohort study of 125 patients undergoing colorectal cancer surgery. SMI was calculated as the area of cross-section of the thigh at the level of the femoral neck divided by the length of the thigh. The primary endpoint was overall survival, and the secondary endpoint was disease-free survival. Patients were divided into two groups: low SMI (≤ 50 cm²/m²) and high SMI (> 50 cm²/m²). Kaplan-Meier survival analysis was used to compare survival between the two groups. Multivariate analysis was performed using Cox proportional hazards regression to identify independent predictors of survival.

Results: The median follow-up time was 24 months (range 6-60 months). The median age of the study population was 65 years (range 29-87 years). The median SMI was 62 cm²/m² (range 36-88 cm²/m²). The 5-year overall survival rate was 50% (95% CI 39-61%) in the low SMI group and 65% (95% CI 54-76%) in the high SMI group (p = 0.04). In multivariate analysis, SMI status was an independent predictor of overall survival (HR 0.50, 95% CI 0.30-0.84; p = 0.01). Other significant predictors of overall survival included age, presence of lymph node metastasis, and preoperative Eastern Cooperative Oncology Group performance status.

Conclusion: Low skeletal muscle index is associated with poor survival after surgery for colorectal cancer. This finding highlights the importance of assessing and maintaining muscle mass in patients with CRC to improve outcomes after surgery.
Correlation of mesothelin (MSLN) expression with future peritoneal metastases (PM) in colorectal cancer (CRC). First Author: Midhun Malia, Oklahoma University of Health Sciences Center, Oklahoma City, OK

Background: CRC patients with PM have a significantly worse median overall survival (OS) when compared to those with liver and lung metastases. We studied MSLN expression using immunohistochemistry (IHC) on primary resected CRC (PRC), its correlation with future development of PM and its effect on OS. Our hypothesis is that PRC tumors from patients who later developed PM will have an increased proportion of positive MSLN scores based on IHC. Methods: We performed a retrospective case control study of all localized CRC (Stage I, II, III) patients who underwent curative resection from 2000-2017 at the University of Oklahoma. The target population consisted of PRC patients who had distant recurrence during surveillance. Control group comprised of patients who never recurred after a minimum of 5 years of surveillance. MSLN score was calculated by the sum of staining percentage and intensity scores on each MSLN stained slide. Kaplan-Meier method was used to estimate OS and differences in survival were estimated using log-rank test. Results: Among 100 patients with recurrent CRC, 19 patients had PM, 51 had solid organ only metastases (SOM) and 66 are in the control group. A significant association between MSLN score and future development of PM was observed (p<0.001) based on Fisher’s exact test. Sensitivity of MSLN as a marker for future PM was 93% and specificity was 58%. Patients with a positive MSLN score had a poor OS when compared to those with a negative MSLN score on univariate analysis (95% CI: 4.1-NR (not reached), p<0.001), which lost significance on multi-variable cox proportional analyses. Conclusions: A higher proportion of patients in the PM group had a positive MSLN score on PRC compared to when the SOM and control groups. MSLN was found to be a highly sensitive marker for future PM development. We expand this work by examining an additional cohort to validate these findings. Research Sponsor: Pilot award from Stephenson Cancer Center support grant from NCI P30CA225520.

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OS and MSLN score in three groups.

Plasma VEGF-D and PIGF levels according to prior use of biologics among metastatic colorectal cancer: Preliminary results from GI-SCREEN CRC-Ukut study. First Author: Hiyori Taniguchi, National Cancer Center Hospital East, Kashiwa, Japan

Background: Plasma vascular endothelial growth factor-D (VEGF-D) level is a potential predictor for ramucirumab efficacy in patients (pts) with metastatic colorectal cancer (mCRC) while a high VEGF-D/PIGF (Placental Growth Factor; PIGF) level in bevacizumab naive pts receiving 2nd-line FOLFIRI plus afibbercept may suggest relatively higher activity. However, there are a few data associating t-statistic antiangiogenic treatments as well as anti-EGFR with angiogenic factors. Methods: This prospective longitudinal study aims to investigate the association between plasma angiogenesis-related mediators and clinical outcomes in mCRC. Serial plasma collections were done at time points of pre- and post-treatments of either 1st- or 2nd-line. Comprehensive measurements of 17 mediators were analyzed by the multiplex assay with Luminex technology. Here we report an association between levels of VEGF-D, PIGF and MSLN score in three groups. Kaplan-Meier method was used to estimate OS and differences in survival were estimated using log-rank test. Results: Among 100 patients with recurrent CRC, 19 patients had PM, 51 had solid organ only metastases (SOM) and 66 are in the control group. A significant association between MSLN score and future development of PM was observed (p<0.001) based on Fisher’s exact test. Sensitivity of MSLN as a marker for future PM was 93% and specificity was 58%. Patients with a positive MSLN score had a poor OS when compared to those with a negative MSLN score on univariate analysis (95% CI: 4.1-NR (not reached), p<0.001), which lost significance on multi-variable cox proportional analyses. Conclusions: A higher proportion of patients in the PM group had a positive MSLN score on PRC compared to when the SOM and control groups. MSLN was found to be a highly sensitive marker for future PM development. We expand this work by examining an additional cohort to validate these findings. Research Sponsor: Pilot award from Stephenson Cancer Center support grant from NCI P30CA225520.

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Preclinical drug testing for clinical trial planning of novel combinatorial therapy with P3I3K and MAPK inhibitors in colorectal cancer(CRC). First Author: Cha Len Lee, Department of Molecular Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland

Background: Combinatorial inhibitors with multiple actions to target downstream effectors are good strategy to reduce resistance occurrence. This is a preclinical study to evaluate efficacy of the combination of PI3K (PIK3CA(E545G) + mTOR dual inhibitors) and RAS (BRAFV600E + MEK2 inhibitor) in CRC cell models. Methods: CRC cell lines with hot-spots mutations in PI3K and MAPK pathways genes were used. Cell growth assay was used to evaluate antiproliferative response to P, G and P-G alone and in combination. RPPA is used to clarify the role actions of combinatorial drugs on intracellular metabolism and nuclear factor activations. Shared-transfer microarrays were used. Results: CRC cell lines except LS1034 (IC50 = 7.2 μM) were sensitive to G. LS401N and SNUC4 were sensitive to PI3K inhibitor (P=0.06) with IC50 of 6.9 μM and 15 μM, respectively. All cell lines were sensitive to PD. When tested in combination, P+G had synergistic response in all cell lines, except for LS401N (CI=0.06; p=0.02). P+G is highly synergistic in LS1034 with KRAS mutation (CI=0.01; p=0.1). P+G is also synergistic in LS401N with co-occurring PIK3CA and KRAS mutations (CI=0.6; p=0.04). P+PD is synergistic in all cell lines except for LS401N. In SNUC4 with PIK3CA mutation, both drug combinations have equal synergism (CI=0.5; p=0.05). RPPA analysis is in progress and will be included in final abstract. Conclusions: This offers good rationale for further clinical development of P+G as beneficial therapy in treatment-resistant CRC patients. P+G offers better alternative to P+PD since MEX inhibitor resistance had been associated with tumours harbouring KRAS with(out) PIK3CA mutations. BRAFV600E and ERBB2 mutations are useful negative predictors in this cohort. Research Sponsor: None.
NeORAS: Incidence of RAS reversion from RAS mutated to RAS wild type.

Background: RAS mutations are found in ~50% of patients (pts) with metastatic colorectal cancer (mCRC) and associated with resistance to anti-EGFR. Circulating tumor DNA (ctDNA) enables detection of resistant RAS(+) tumors arising from RAS(−). Recently there has been interest in defining the converse: RAS(−) tumors that revert to RAS(+) with early results suggesting rates of ~7%. Clinical trials in this population are in development, though the incidence has not been calculated with robust methodologies. Methods: We identified 74 mCRC pts with baseline RAS(−) and longitudinal ctDNA or tissue data enrolled in ATTACC (NCT0199630), a prospective genomics matching protocol utilizing paired tissue/ctDNA samples at baseline. We evaluated serial samples for RAS loss. 2 L Using an external cohort of pts with mCRC and serial ctDNA with a targeted NGS assay sequencing all KRAS/NRAS exons (Guardant360, Guardant Health), we screened pts for baseline RAS(−) with no evidence of prior anti-EGFR exposure and evaluated for RAS loss. Results: 74 pts met criteria of RAS(−) CRC with serial samples in ATTACC. Of these, 51 retained RAS(−). 22 pts had very low or absent levels of other clonal alterations such as APC or TP53 and are therefore unable to reliably detect RAS loss. One patient had true RAS loss with NRAS G13R, APC and TP53 mutations at baseline and persistent high-level APC and TP53 mutations without a detectable NRAS mutation, for an overall rate of RAS loss of 2% (1/52). In the second cohort we identified 162 pts, 34 of which had insufficient ctDNA to assess RAS loss on the serial sample as defined by loss of clonal alterations like APC and TP53. Of the remaining 128 patients, 11 had RAS loss (8.5%, with 1 NRAS, 10 KRAS). We next compared the relative mutant allele frequency (rMAF) between RAS retainers and RAS loss. The median baseline rMAF for pts who lost RAS was 0.74, compared to 0.86 in pts retaining RAS (p = 0.045). Conclusions: RAS reversion in mCRC from RAS(−) to RAS(+) is uncommon and occurs at a rate between 2-8% in our two cohorts. RAS reversion is associated with a lower rMAF at baseline, suggesting subclonality. Liquid biopsies must be interpreted carefully, such that a determination of RAS mutation status is most informative in the presence of truncal APC and/or TP53 mutations. Research Sponsor: None.

Exosomal markers (CD63 and CD9) expression and their prognostic significance using immunohistochemistry in right-sided and left-sided colon cancer.

Background: Exosomes play pivotal roles in cancer progression, metastasis and chemoresistance. CD63 and CD9 are widely accepted exosomal markers. The prognostic and prognostic impact of expression in patients with RSCC and LSCC is unknown. This study explored CD63 and CD9 expression and prognostic significance in patients with RSCC and LSCC using immunohistochemistry (IHC). Methods: Between 2015 and 2016, 63 patients underwent surgical resection of colon cancer for whom we had available tissues for CD63 and CD9 IHC staining. Two pathologists independently scored the CD63 and CD9 expression in the tumor and adjacent normal mucosa (ANM). Staining intensity was graded 1-3 and staining percentage was estimated in 10% increments. Mean Quick-score (Q-score) (intensity X percentage of staining) was calculated. Results: RSCC and LSCC represented 52% and 48% of the patients respectively. The ANM and Tumor CD63 Q-scores were 225 vs 191 (p = 0.009) in RSCC and 224 vs 154 (p = 0.0001) in LSCC, respectively. The ANM and Tumor CD9 Q-scores were 134 vs 152 (p = 0.042) in RSCC and 135 vs 154 (p = 0.137) in LSCC, respectively. In patients with RSCC and LSCC, the mean Tumor CD63 Q-score was 191 vs 154 (p = 0.024), while the mean ANM CD63 Q-score was 225 vs 224 (p = 0.920). The mean Tumor CD9 Q-score was 152 and 154 (p = 0.883), and the mean ANM CD9 Q-score was 134 vs 135 (p = 0.926). In our cohort, there was no difference in progression free survival (PFS) between patients with RSCC and LSCC (p = 0.2349). In all patients, there was no difference in PFS in patients with CD63 expression < 100 and ≥100 (p = 0.8284). Among patients with RSCC, there was a significantly lower PFS in patients with CD63 expression < 100 vs. ≥100 (p = 0.0349). Conclusions: To our knowledge, this is the first study to show a difference in exosomal marker (CD63) expression pattern and its prognostic significance in patients with RSCC and LSCC. Research Sponsor: None.

Circulating miR-203 secreted from metastatic tissues could exacerbate myopericardial dysfunction in colorectal cancer patients.

Background: Sarcopenia is commonly observed in advanced cancer patients with distant metastases. In addition, biological functions of microRNAs (miRNAs) in cell-to-cell communication by qRT-PCR and in situ hybridization in 58 pairs of primary CRC (pCRC) and corresponding matched liver metastasis (LM) tissues. We further evaluated miR-203 levels using pCRC tissues and matched preoperative serum to clarify its clinical significance in independent 183 CRC patients. Second, we assessed miR-203 expression using immunohistochemistry in human skeletal muscle cells (SMC), and cells were analyzed for proliferation and apoptosis. Expression of several, putative, miR-203-target genes was also validated in SMC cells. Results: MiR-203 expression was significantly upregulated in LM compared with matched pCRC tissues. Serum miR-203 levels were significantly downregulated in patients with CRC in both patient cohorts. In contrast to IMAC, decreased PFS significantly correlated with well-established disease development factors, and decreased PFS was an independent prognostic factor for overall survival, and disease-free survival in CRC patients. Conclusions: Assessment of serum miR-203 could be used for risk assessment of metastasis-related myopericardial dysfunction in CRC. Research Sponsor: None.
The intersection of age and tumor biology with postoperative outcomes in patients after cytoreductive surgery and HIPEC. First Author: Michael K. Turgeon, Winship Cancer Institute, Division of Surgical Oncology, Department of Surgery, Emory University, Atlanta, GA

Background: Patient age is an often significant factor in preoperative selection for major abdominal surgery. Its association with postoperative outcomes in patients undergoing cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) remains ill-defined. Methods: The US HIPEC Collaborative database (2000-2017) was reviewed for patients who underwent a CRS/HIPEC. Age was categorized into < 65 or ≥ 65yrs. Primary outcomes were postoperative major complications, readmission, 30-day mortality, and non-home discharge (NHD). Analysis was stratified by disease histology: non-invasive (appendiceal LAM/HAMN), and invasive (appendiceal/colorectal adenocarcinoma). Results: Of 1090 pts identified, 22% ≥ 65yrs (n = 240, 59% were female, n = 64), 25% had non-invasive (n = 276) and 51% had invasive (n = 555) histology. Median PCI was 13 (IQR 7-20). Patients ≥ 65yrs had a higher rate of major complications (37%vs26%, p = 0.02), readmission (28%vs22%, p = 0.05), 30-day mortality (3%vs1%, p = 0.02), and NHD (21%vs5%, p < 0.01) compared to those < 65yrs. On multivariable analysis, accounting for extent of disease as measured by PCI, for non-invasive histology, age ≥ 65yrs was an independent predictor for NHD (OR 2.54, 95% CI 1.08-5.99, p = 0.03), but not major complications. For invasive histology, even when accounting for PCI, age ≥ 65yrs was an independent predictor for both NHD (OR 2.54, 95% CI 1.08-5.99, p = 0.03) and major complications (OR 2.04, 95% CI 1.16-3.59, p = 0.02). Age was not associated with hospital readmission or 30-day mortality for any histology. Conclusions: Regardless of histology, patients ≥ 65yrs are at an increased risk for both non-home discharge after CRS/HIPEC. For invasive histology, age ≥ 65yrs is also associated with increased major complication rates, but the procedure seems to be better tolerated when performed for indolent biology. These data inform preoperative counseling and risk stratification. Early planning for discharge after CRS/HIPEC is ill-defined. For invasive histology, age ≥ 65yrs was an independent predictor for NHD (OR: 2.54, 95% CI: 1.08-5.99, p = 0.03). Age was not associated with hospital readmission or 30-day mortality for any histology. 

Plasma deoxyuridine levels in metastatic colorectal cancer (mCRC) patients and clinical response after SFU based therapy in combination with arfolitixorin. First Author: Helena Anna Talfin, Surgical Oncology Laboratory; Department of Surgery, Sahlgrenska Academy at the University of Gothenburg, Gothenburg, Sweden

Background: 5-Fluorouracil (SFU) is one of the most commonly used cancer drugs. FU is a metabolite from SFU which inhibits thymidylate synthase (TS). TS inhibition causes a rise in the intracellular pool of the natural TS substrate dUMP leading to increased global levels of deoxyuridine (dUr). In order to increase TS inhibition, SFU is combined with folates, usually leucovorin (LV). However, LV needs enzymatic conversion to become active. The LV conversion capacity differs between patients, with the consequence that many patients will have a reduced effect of SFU-based treatment. Arfolitixorin is a biologically active folate, 5,10-methylenetetrahydrofolate, which doesn’t need enzymatic conversion; hence it could potentially be more efficacious. Methods: ISO-C-C005 is a phase I/II safety and tolerability study in mCRC patients receiving SFU/arfolitixorin alone or in combination with irinotecan or oxaliplatin bevacizumab. Efficacy was evaluated as Overall Response Rate (ORR) after 4 cycles of indoleamine and clinical finding. A LC-MS/MS method was developed for quantification of plasma dUr and SFU. Blood samples were collected before and 24 h after SFU administration at the first (C1) and fourth (C4) treatment cycle (n = 33). The C4/C1 ratio for dUr and SFU, respectively, were calculated. The clinical response, which is an ordered categorical data, was modelled using nominal logistic regression using the ratio C4/C1 and the absolute values C1 and C4 as explanatory variables. Results: A positive correlation between dUr and SFU levels was seen (r = 0.89, p = 0.001) at C4. The C4/C1 ratio for dUr and SFU positively (r = 0.9, p = 0.001) correlated at C1. The C4/C1 ratio was also found to be related to arfolitixorin and plasma levels of dUr (r = 0.44, p = 0.016) at C1, but not at C4. In the model test, the C4/C1 dUr ratio, as well as the individual dUr levels at C1 and C4, had a highly significant effect on ORR (p = 0.0075). Conclusion: The results from this study suggest that arfolitixorin dose has an impact on plasma levels of dUr and also on clinical response. dUr could potentially be an early surrogate marker for TS inhibition in mCRC patients treated with SFU/arfolitixorin. Clinical trial information: NCT02244632. Research Sponsor: Isofil Medical, Swedish Medical Association.

Immune modulation after Toca 511 and Toca FC treatment of colorectal cancer patients. First Author: Gerald Steven Falchook, Sarah Cannon Research Institute, Denver, CO

Background: Toca 511 (vocimagene amiretrorepvec) is a cancer-selective, retroviral replicating vector encoding yeast cytosine deaminase that converts 5-fluorocytosine (5FC) into 5-fluorouracil in the tumor microenvironment (TME). Toca FC is a combination of Toca 511 and 5-fluorouracil (5FU) to augment immunosuppressive cells, leading to antitumor immune activity. A Phase 3 study of Toca 511 & Toca FC (extended-release 5FC) in patients with recurrent high grade glioma revealed results consistent with this proposed mechanism. A Phase 3a clinical trial is ongoing. Methods: Toca 6 (NCT02576665) is a Phase 1b, single-arm, multicenter study designed to investigate immunological changes after Toca 511 & Toca FC treatment in patients with advanced solid tumors, including colorectal cancer (CRC). Patients received intravenous (IV) Toca 511 for 3 days, and underwent biopsy of metastatic tumor before and ~ 4 weeks after starting oral Toca FC. Toca FC was repeated every 4-6 weeks. Peripheral blood mononuclear cells and tumor biopsies were evaluated for treatment related immune responses. Results: 17 CRC patients with a median 5 lines of prior chemotherapy were enrolled. At last data cut-off, 9 patients were alive and the median overall survival was 9.4 months. A patient receiving concomitant panitumumab had a partial response. IV Toca 511 led to viral expression in tumor, which decreased post-Toca FC while maintaining a reservoir of virus in the remaining tumor. T cells shifted from naïve to effector phenotypes, CD4 memory T cells expanded, and/or B cells increased after Toca FC treatment in 36% of patients. Marked changes in tumor infiltrating cells (CD8+ myeloid cells, Tregs, exhausted T cells and CDB T cells) occurred after Toca FC treatment. Treatment has been generally well tolerated. We also plan to report insights gained from RNA analysis of TME and update on clinical finding. Conclusions: Clinical data suggest a signal of activity in these heavily pre-treated CRC patients warranting further exploration. IV Toca 511 administration led to viral expression in tumor. Toca 511 treatment may be associated with T cell mediated immune activity in peripheral blood and metastatic tumor, consistent with pre-clinical data in multiple tumor types. Clinical trial information: NCT02576665. Research Sponsor: Tocagen.
Prognostic and predictive impact of primary tumor sidedness in first-line trials for advanced colorectal cancer: An analysis of 7,828 patients in the ARCAD database. First Author: Jun Yin, Department of Health Science Research, Mayo Clinic, Rochester, MN

Background: Unplanned subgroup analyses from several studies have suggested primary tumor sidedness (PTS) as a potential prognostic and predictive parameter in metastatic colorectal cancer (mCRC). We aimed to investigate the prognostic and predictive impact of PTS on outcomes.

Methods: PTS data of 7,828 mCRC patients (pts) from 10 first-line randomized trials in the ARCAD database were pooled. Pts were defined as right-sided (RS) or left-sided (LS) if tumor arose from the cecum to the hepatic flexure or from the splenic flexure to the rectum, respectively. Transverse colon cancers were not included. Overall survival (OS) and progression-free survival (PFS) were assessed using Kaplan-Meier and Cox models adjusting for age, sex, performance status (PS), prior radiation/chemo, and stratified by treatment arm. Predictive value was tested by interaction term between PTS and treatment (anti-EGFR plus chemotherapy vs. chemotherapy alone).

Results: Compared to RS pts (5421, 69%), LS pts (5421, 69%) had better OS (median: 21.6 vs 19.2 mos; HRadj: 0.73, 95% CI 0.69-0.79, P < .001) and PFS (median 8.4 vs 6.7 mos; HR: 0.81, 95% CI 0.76-0.86, P < .005). Results were consistent among subgroups defined by age, sex, PS, metastatic site, and IBD status. Survival benefit from anti-EGFR was observed for LS, but not for RS (table).

Conclusions: The prognostic value of PTS is restricted to the KRAS wt population. PTS is predictive of anti-EGFR efficacy, with a significant improvement of survival for LS vs RS pts. These results suggest that treatment stratification in mCRC trials should be based on PTS and KRAS status.

Poster Session (Board #30), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Genetic variants in R-Spondin/RNF43 complex and gene expression levels to predict efficacy of cetuximab (cet) in patients (pts) with metastatic colorectal cancer (mCRC): Data from the FIRE-3 phase III trial. First Author: Francesca Battaglin, Division of Medical Oncology, USC Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, CA

Background: Wnt signaling deregulation is a primary driver of colorectal carcinogenesis. RNF43 is a key suppressor of Wnt activation while R-Spodin inhibits RNF43 activity. RNF43 mutations are associated with the serrated neoplasia pathway, BRAF mutation and MSI. We hypothesized that genetic variants in the R-Spodin/RNF43 complex and corresponding genes expression levels may predict cetuximab efficacy in mCRC pts. Methods: Genomic DNA from blood samples of pts enrolled in the randomized FIRE-3 trial was genotyped through the OncoArray, a custom array manufactured by Illumina. The impact on colorectal cancer (CRC) risk associated with known genetic variants in RNF43 and TSPO1/2/3 was analyzed in 129 pts treated with first-line FOLFIRI/cet and 107 pts treated with FOLFIRI alone. Genomic DNA (DNA) was extracted from blood samples of pts enrolled in the randomized FIRE-3 trial and genotyped through the OncoArray, a custom array manufactured by Illumina. Results: Compared to RS pts (5421, 69%), LS pts (5421, 69%) had better OS (median: 21.6 vs 19.2 mos; HRadj: 0.73, 95% CI 0.69-0.79, P < .001) and PFS (median 8.4 vs 6.7 mos; HR: 0.81, 95% CI 0.76-0.86, P < .005). Results were consistent among subgroups defined by age, sex, PS, metastatic site, and IBD status. Survival benefit from anti-EGFR was observed for LS, but not for RS (table).

Conclusions: The prognostic value of PTS is restricted to the KRAS wt population. PTS is predictive of anti-EGFR efficacy, with a significant improvement of survival for LS vs RS pts. These results suggest that treatment stratification in mCRC trials should be based on PTS and KRAS status.

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192 Poster Session (Board #J12), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM and Poster Walks, Sat, 12:30 PM-1:15 PM

Genomic characterization of rectal cancer and molecular determinants of response to neoadjuvant chemoradiotherapy. First Author: Walid K. Chatila, Memorial Sloan Kettering Cancer Center, New York, NY

Background: Rectal cancers are clinically different from colon cancers and have not yet been molecularly characterized due to the scarcity of pre-treatment specimens. Discovery of molecular determinants of response to chemotheraphy and radiation in patients with locally advanced rectal cancer (LARC, stage II and III) are needed to select those who can avoid surgery and benefit from watch-and-wait strategies. Methods: We profiled 371 pre-treatment specimens using targeted-exome sequencing of 468 cancer genes (n = 325), whole-exome sequencing (n = 100), and RNA-sequencing (n = 113). The targeted-sequencing cohort included patients with stage I (n = 44), II (n = 41), III (n = 176), and IV (n = 64) disease. Primary tumors were divided into lower (LR: 0-4 cm to anal verge, n = 62), middle (MR: 4-8 cm, n = 115), and upper rectum (UR: 8-12 cm, n = 107). We examined molecular determinants of complete response (CR) and relapse free survival (RFS) in LARC patients treated with chemoradiotherapy only (CRT: n = 39), induction chemotherapy + CRT (INCT: n = 87) and consolidation chemotherapy after CRT (CCNT: n = 63).

Results: Among MSS cases, oncogenic gene and signaling pathway alterations did not vary by clinical stage. WNT pathway alterations, driven by APC checkpoint, EMT transition, and DNA repair were overexpressed in the UR, but not in the MR or LR. WNT alterations are more frequent in the UR while RTK/RAS alterations were more frequent in the LR (54% UR v 69% MR v 72% LR, p < 0.001) while RTK/RAS alterations were more frequent in the LR (54% UR v 69% MR v 72% LR, p < 0.003). A set of genes enriched in mTOR signaling, G2M checkpoint, EMT transition, and DNA repair were overexpressed in the UR (FDR < 0.1). The 5-yr RFS rate for LARC was 75% (CI: 68%-82%) and 24% of the cases had a CR (n = 45). MSS cases had a higher rate of CR compared to MSS cases (50% v 23%, p = 0.07) and non-relapse (n = 8). KRAS-altered MSS tumors exhibited RFS in cases treated with CNT (5-yr: 74% v 97%, p = 0.03), but not in cases treated with INCT (5-yr: 67% v 72%, p = 0.7).

Conclusions: WNT alterations are more frequent in the UR while RTK/RAS alterations are more frequent in the LR, suggesting differences in tumor biology between proximal and distal rectal cancer. Further, we report correlations between distinct molecular profiles and response to treatment paradigms that could guide the design of future clinical trials. Research Sponsor: None.

194 Poster Session (Board #J14), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Effect of previous chemotherapy treatments on circulating tumor-associated cells in colorectal cancer. First Author: Sewanti Limaye, Kokilaben Dhirubai Ambani Hospital, Mumbai, India

Background: Resistance to combination regimens of fluorouracil, oxaliplatin and irinotecan are commonly observed in Colorectal cancers (CRC). There are presently no viable approaches for ‘real-time’ monitoring of innate and acquired chemoresistance. We used a novel method for chemoresistance by harvesting from peripheral blood sufficient numbers of Circulating-Tumor Associated Cells (CTACs) which are defined as apoptosis-resistant cells of tumorigenic origin which are positive for Epithelial Cell Adhesion Molecule (EpCAM) and pan-cytokeratins (pan-CK) irrespective of CD45 status. Associated Cells (CTACs) which are defined as apoptosis-resistant cells of tumorigenic origin which are positive for Epithelial Cell Adhesion Molecule (EpCAM) and pan-cytokeratins (pan-CK) irrespective of CD45 status. Methods: Peripheral blood was collected from 110 patients with confirmed diagnosis of CRC, among whom 56 were recently diagnosed and therapy naive while 54 were pre-treated. Peripheral blood mononuclear cells (PBMCs) were harvested by centrifugation and treated with commercially available stabilizing agents by a proprietary protocol to stabilize apoptosis resistant C-TACs. Surviving C-TACs were confirmed by immunostaining for EpCAM and pan-CK. Harvested C-TACs were cultured in vitro with 5-fluorouracil, irinotecan and oxaliplatin and the fraction of surviving cells estimated to determine resistance profiles. Results: Among the 56 cases of recently diagnosed therapy naive CRC, innate chemoresistance was observed in 37.5%, 47.3% and 41.8% of samples (unique patient-drug combinations) towards 5-fluorouracil, irinotecan and oxaliplatin respectively. Among the 54 cases of previously treated CRC, acquired chemoresistance was observed in 92.6%, 92.6% and 95.5% of samples towards 5-fluorouracil, irinotecan and oxaliplatin respectively. Conclusions: We show for the first time that sufficient C-TACs can be harvested for meaningful CI in newly diagnosed treatment naive CRC as well as refractory CRCs. Post-treatment chemoresistance being an order of magnitude higher than the untreated cohort indicates that C-TACs in CRC are resistance-educated by previous treatments and can guide treatment strategy. Research Sponsor: Datar Cancer Genetics Limited.

195 Poster Session (Board #J15), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

5-hydroxymethylcytosine signatures in plasma circulating cell-free DNA as markers for appendiceal and colorectal peritoneal metastasis. First Author: Yaniv Berger, University of Chicago, Chicago, IL

Background: Noninvasive tests for peritoneal metastasis (PM) detection lack sensitivity. Genome-wide mapping of 5-hydroxymethylcytosine (5hmC) on nanogram quantities of peripheral plasma circulating cell-free DNA (PcfDNA) was previously shown to differentiate non-metastatic colorectal cancer from healthy subjects. We aimed to examine if patients with colorectal cancer (CRC), high grade appendiceal cancer (HGA) or low grade appendiceal cancer (LGA) with PM have distinct signatures of 5hmC in PcfDNA compared to each other and to healthy subjects. Methods: We analyzed plasma samples from a prospectively collected tissue bank. To correlate 5hmC signatures with intraoperative findings, only patients who underwent abdominal surgery in proximity to plasma collection were selected. Key steps of PcfDNA processing included extraction from plasma, nano-hmC-Seal chemical labeling and enrichment of 5hmC-modified fragments, next-generation sequencing, and mapping to the reference human genome. Conclusions: The DESeq2 R package was finally used to compare relative 5hmC enrichment and detect distinct 5hmC signatures according to disease histology and PM presence. Results: Plasma samples were collected between 11/2016 - 3/2019 from 46 patients with CRC (n = 21), HGA (n = 17) and LGA (n = 8). Of those, 32 (70%) had PM based on intraoperative findings (median peritoneal cancer index score = 15, range 2-39) and 14 did not have PM. Most samples (91%) were collected on the same day as surgery. An average of 24 million paired-end reads were sequenced for each sample. Four samples (8.7%) were excluded from the analysis due to low sequencing coverage or high duplication level. Unique 5hmC enrichment patterns were found to discriminate with p < 0.05 between CRC PM and LGA PM (n = 106, differentially 5hmC-modified genes (DHMGs)), CRC/HGA PM and LGA PM (n = 1074 DHMGs), and CRC/HGA PM and CRC/HGA patients without PM (n = 1576 DHMGs). Conclusions: Distinct signatures of 5hmC in PcfDNA could differentiate patients with CRC/HGA/LGA PM from each other and from patients with similar tumor histologies without PM. Thus 5hmC signatures in PcfDNA might potentially serve as a sensitive marker of occult PM. Research Sponsor: None.
Association of KRAS and BRAF mutations with progression-free survival (PFS) with second-line FOLFIRI +/- regorafenib in metastatic colorectal cancer (mCRC). First Author: Federico Innocenti, The University of North Carolina at Chapel Hill, Chapel Hill, NC

Background: LCCCO1029 was a 2:1 randomized phase II trial of 2nd-line FOLFIRI +/- regorafenib in mCRC. The addition of regorafenib improved PFS (median PFS 6.1 vs 5.3 mo, HR 0.73, 95% CI 0.53-1.01). However, the effect of somatic mutations on regorafenib activity has not been tested. Methods: We performed whole exome sequencing on archival primary tumors, and all patients of LCCCO1029 were compared PFS and OS using Kaplan-Meier method and log-rank tests, and hazard ratios (HR) were estimated using Cox proportional hazards method. Results: Among the 85 subjects, 54 (64%) had tumors wild-type (WT) for KRAS and BRAF, 26 (31%) had tumors with KRAS mutations in exons 2-4, and 5 (6%) had tumors with BRAF V600E. The addition of regorafenib improved PFS in the KRAS/BRAF WT subgroup (median PFS 8.0 vs 4.9 mo, HR 0.68, 95% CI 0.48-0.97, log-rank p=0.028), but not in the KRAS mutant subgroup (median PFS 6.8 vs 5.5 mo, HR 0.90, 95% CI 0.61-1.35, log-rank p=0.617) or the BRAF mutant subgroup (log-rank p=0.04). Conclusions: The addition of regorafenib to FOLFIRI improves PFS among the subgroup of patients with KRAS and BRAF dual WT CRC, but not among the KRAS mutant subgroup. These results indicate that the addition of anti-angiogenic therapy to second-line chemotherapy backbones may be more effective in KRAS/BRAF WT tumors in particular. More confirmatory studies are needed to corroborate this finding. Research Sponsor: Bayer.

Poster Session (Board #J6), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

198 Systemic impact on tumor growth after combined immuno-thermal ablation in a murine model of colorectal cancer. First Author: Ryan J. Slovak, Section of Interventional Radiology, Department of Radiology and Biomedical Imaging, Yale School of Medicine, New Haven, CT

Background: Cryoablation exposes tumoral antigens capable of provoking an anti-cancer immune response. The addition of immunotherapy alongside cryoablation may synergistically promote a more robust systemic response. The purpose of this investigation was to study the growth of targeted and off-target tumors after combined cryoablation and dual immune checkpoint blockade (DICB). Methods: Thirty BALB/c mice were implanted with bilateral flank injections of 0.5 x 106 CT26.WT colorectal cancer cells (CRL-2638; ATCC, Manassas, VA). Tumor volume was measured every other day via caliper (LxW2). Mice were randomly assigned to receive either sham injections (InVivoMAB IgG controls), dual anti-PD-1 and anti-CTLA-4 (Dicarb) (Clone J43 & Clione 9DF; BioXcell, West Lebanon, NH, USA), or Dicarb plus either partial or full cryoablation on the single targeted tumor. Treatment day 0 began once tumors reached a volume of >300mm3. Injections of antibodies were given on treatment day 0, 3, and 5. Cryoablation was performed on treatment day 2. Full ablation was achieved via two 3 minute cycles at 100% power and partial ablation was defined as a single 3 minute cycle at 70% power ablation (Visual-ICE System, Galil Medical, St. Paul MN). Animals were sacrificed at 7 and 14 days after treatment. Results: There was an average of 77.15± 75.22 (SD) increase in tumor volume among control animals and 14.47± 9.69 decrease in animals treated solely with DICB. Mice that received full ablation demonstrated an average 72.39%± 29.21 decrease in volume in the target tumors and 48.94%± 25.97 decrease in the off-target tumors. Partially ablated mice averaged 81.22%± 16.43 decreased volume in the target tumors and 35.87%± 16.95 decreased volume in the off-target tumors. The mean change in volume of every group was significantly less than that of the control (p < 0.05) and there was a significantly larger reduction in volume between both the full and the partial target tumors versus the DICB group (p < 0.05). Conclusions: The addition of cryoablation to DICB resulted in a significant reduction in volume of the targeted tumors. Additionally, this combination led to larger volume reductions in off-target tumors as compared to immunotherapy alone. Research Sponsor: Department of Defense, Society of Interventional Radiology & Radiological Society of North America.
Establishing novel mutation subtypes in peritoneal carcinomatosis of appendiceal origin.

First Author: Mary Garland-Kledzik, John Wayne Cancer Institute at Providence St. John’s Health Center, Santa Monica, CA

Background: Appendiceal cancer (AC) is a rare disease process with complex treatment strategies. The objective of this study was to identify mutation-based genetic subtypes that may differ from the current histological classification, compare genetic make-up of primaries and metastases, and to find novel targetable alterations. Methods: The analysis involved the curation and normalization of mutation panels from adenocarcinoma and mucinous adenocarcinoma (n = 196) stored in the AACR GENIE Database v6.0. Genes mutated in less than two patients and tumors profiled with incomplete mutation panels were excluded from the study. The optimal number of AC subtypes was established using the Non-negative Matrix Factorization algorithm. Statistical comparisons of mutation frequencies were performed by using the Pearson’s x² test. Results: AC patients were stratified into five mutation subtypes. ACO had no mutations in the 41 genes in the study. The most frequently mutated genes varied between the subtypes. AC KRAS (91.9%) and GNAS (77.4%); AC2 KRAS (52.5%), APC (32.5%), and GNAS (30%); AC3: KMT2D (38.7%), TP53 (38.7%), KRAS (35.5%), EP300 (22.6%); and AC4: TP53 (97.2%), KRAS (77.8%), and SMAD4 (36.1%). Additionally, AC3 was less likely to be mucinous (22.6% v 50.0-74.2%, p < 0.001) and had a higher mutation frequency (3.6 v 0-3.1, p = 0.035). Conclusions: Characterization of these subtypes suggest a need for molecular rather than anatomic staging for AC. Histone regulation by KMT2D and EP300 may be considered for targeted therapy for AC patients with AC3. A prospective comparison of subtype prognosis and response to surgery and adjuvant treatment is needed. Research Sponsor: None.

Prediction of hepatic metastasis and relapse: Concordance analysis among noninvasive liver fibrosis scores from colorectal cancers.

First Author: Sanjun Cai, Fudan University Shanghai Cancer Center, Shanghai, China

Background: Liver fibrosis, resulted from several liver diseases, are in- Important, in validation cohort, the discriminatory capacity of the fibrosis score incorporated was superior to that of the CRS score in predicting RFS, as documented by the C-index and AUC. The concordance study showed well agreement among NFS, FIB4 and APRI in predicting DFS and RFS. Among these three noninvasive liver fibrosis scores, NFS score performed the best in predicting hepatic specific DFS and RFS. Conclusions: The liver fibrosis was a powerful predictor of hepatic specific DFS and RFS in CRC. Fibrosis niche may be a favorable microenvironment for metastatic formation in the liver. Research Sponsor: None.
Multimodality management of brain metastasis from colorectal cancer.

**First Author:** Zhachou Jin, Mayo Clinic, Rochester, MN

**Background:** More than 50% of colorectal cancer (CRC) patients will develop metastatic disease. Brain metastasis (BM) from colorectal cancer is uncommon (0.6-1.36%). This study aims to investigate the prognostic characteristics, treatment modalities and prognostic factors in this rare population. **Methods:** 104 patients with brain metastasis from CRC were identified from over 30,000 colorectal cancer patients at the Mayo Clinic Rochester between 1999/4 and 6/2020. A retrospective review was conducted using data from electronic medical records (EMR). Statistical analysis utilized the Kaplan-Meier method, Log-rank test, and Cox proportional hazards models. **Results:** Among the 104 patients, 62 were male (59.6%) and 42 were female (40.4%). Median age at CRC diagnosis was 58.4 and at BM diagnosis was 62.0 years. Three patients had right-sided colon cancers, 27 patients had left-sided colon cancers and 39 patients had rectal cancer. Median time from CRC diagnosis to BM was 9.0 months. The majority of patients (58.7%) presented with a solitary brain lesion. Eighty-six patients (82.7%) had extracranial metastatic disease at BM diagnosis. Median survival was 7.0 months (95% CI 1.26-16.9) from BM diagnosis. Age <70, solitary BM, surgery, radiation, and chemotherapy were associated with statistically significant improved survival on univariate and multivariate analysis. Multimodality treatment including surgical brain lesion resection, postoperative stereotactic radiation (SRS) with/without whole brain radiation (WBRT), and chemotherapy significantly improved median overall survival (Table). **Conclusions:** Although BM from CRC carries poor prognosis, multimodality treatment (surgery, radiation and systemic chemotherapy) for patients with limited BM improves clinical outcome. Research Sponsor: None.

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**Poster Session (Board #K5), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM PM**

Prognostic phenotypic subtypes to predict recurrence and response to adjuvant chemotherapy for colorectal cancer. **First Author:** Antonia K. Rosewar, University of Glasgow, School of Medicine, Glasgow, United Kingdom

**Background:** Histological phenotypic subtypes have been proposed that stratify survival in a discovery cohort of patients with stage I-III colorectal cancer (CRC). However, clinical utility has not been validated nor associations with recurrence and chemotherapy assessed. Therefore, this study assessed prognostic value in patients with stage I-III CRC as well as predictive value for recurrence and chemotherapy response. **Methods:** Two independent stage I-III CRC patient cohorts were utilized to assess associations between phenotypic subtypes, survival, and recurrence. Stage I-II patients, from the SCOT adjuvant chemotherapy trial, were utilized to assess associations between phenotypic subtypes and adjuvant chemotherapy response. Log rank analysis compared immune and stromal subtypes. **Results:** In an 867-patient internal cohort, phenotypic subtype stratified patients by disease-free survival (DFS) (HR 2.18 95% CI 1.22-4.47, p < 0.01); independent of stage and location. The stromal subtype also predicted increased local and distant recurrence (p < 0.001). In a 146-patient external validation cohort, phenotypic subtype significantly stratified patients by DFS (HR 3.43 95% CI 1.60-7.35, p = 0.001). In 1343 SCOT trial patients, phenotypic subtype significantly stratified patients by DFS (HR 1.59 95% CI 1.13-2.25, p = 0.010). Furthermore, there was evidence that the effect of regimen depended on phenotypic subtype (p = 0.048), only significantly stratifying DFS in patients receiving FOLFOX (HR 3.73 95% CI 1.58-8.81, p = 0.003) but not CAPOX (HR 0.84 95% CI 0.56-1.26, p = 0.396) adjuvant chemotherapy. Interestingly, the immune subtype associated with improved DFS in patients that received FOLFOX chemotherapy (HR 0.56 95% CI 0.36-0.91, p = 0.022). Where patients with a stromal subtype trended towards improved DFS in patients receiving CAPOX compared to FOLFOX adjuvant chemotherapy (HR 0.72 95% CI 0.50-1.05 p = 0.088). **Conclusions:** Histological phenotypic subtype segmentation can be dependent prognostic classification for patients with stage I-II CRC that can predict response to FOLFOX adjuvant chemotherapy as well as the presence of local and distant recurrence. Research Sponsor: University of Glasgow.

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**Poster Session (Board #K6), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM PM**

Validation of the Glasgow Microenvironment Score in patients with colon cancer: A pathology-based prognostic tool. **First Author:** Peter G. Alexander, University of Glasgow, Glasgow, United Kingdom

**Background:** The Glasgow Microenvironment Score (GMS), comprised of assessment of the tumour inflammatory cell infiltrate (using Klintrup-M¨ akinen (KM) grade) and tumour-associated stroma (TSP), has been reported as a stage-independent prognostic score in patients with colorectal cancer. **Methods:** 104 patients with colorectal cancer were included. The Glasgow Microenvironment Score (GMS), comprised of (KM) grade) and tumour-associated stroma (TSP), has been reported as a stage-independent prognostic score in patients with colorectal cancer. The present study aims to validate the GMS and examines its prognostic utility in stage I-III colorectal cancer. It should be further validated in prospective randomised trials. Research Sponsor: Gilead & Freenome.

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**Poster Session (Board #K7), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM PM**

Exploratory longitudinal analysis of cfDNA to reveal potential biomarkers of CRC progression and treatment response. **First Author:** Francesco Vallania, Freenome, South San Francisco, CA

**Background:** Blood-based tests can predict drug response and disease progression. Many tests rely on detecting tumor DNA, which represents only a fraction of all cell-free DNA (cfDNA). Here, we used a novel methodology to interrogate cfDNA to provide insights into biological processes that may inform patient care. **Methods:** This unique platform offers the ability to identify potential non-tumor derived biomarkers that may be associated with clinical outcomes in colorectal cancer (CRC). **Results:** Longitudinal plasma samples from metastatic CRC patients enrolled in NCT01630322 guided the development of cfDNA biomarkers. 92 patients with untreated CRC were evaluated. Patients were classified as responders (SD+PD) or responders (CR+PR) based on objective response. Gene activation was inferred from cfDNA fragment length and counts around transcription start sites using whole-genome sequencing. Transcription factor activity was estimated by measuring binding site accessibility across the genome. **Conclusions:** Longitudinal plasma cfDNA samples from CRC patients were evaluated for potential markers of clinical progression or treatment response. Gene activation profiles inferred from cfDNA across the entire genome identified several genes differentially expressed in responders or non-responders. Specifically, all patients with elevated KIR2DL1, an inhibitory NK cell receptor, progressed (p = 0.05). Additionally, BMPRIA activation decreased in responders (p = 0.002) while the DNA- binding activity of SMADI, which functions directly downstream of BMPRIA in the BMP2 pathway, increased in responders post-therapy (p = 0.03). These 3 genes (i.e., KIR2DL1, BMPRIA and SMADI) are related to NK cell maturation, suggesting an immunological mechanism. Notably, pre-therapy TF did not predict response. **Conclusions:** In this pilot study, we demonstrated the ability of a unique cfDNA platform to interrogate multiple features to reveal genes associated with drug response and their underlying mechanism. We identified that KIR2DL1 is associated with progression, and BMPRIA and SMADI are associated with response. This work highlights the potential of cfDNA to probe beyond TF and to provide early identification of non-tumor-derived signals that may benefit biomarker discovery and drug target identification. Research Sponsor: Gilead & Freenome.
Emergence of RAS mutations in patients with metastatic colorectal cancer receiving cetuximab-based treatment. First Author: Jaw-Yuan Wang, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

Background: In management of patients with RAS wild-type mCRC, anti-EGFR therapy can demonstrate clinical benefit. However, the correlation between emergence of RAS mutations in circulating tumor DNA (ctDNA) and secondary resistance to anti-EGFR therapies requires further elucidation. In this study, we aim to examine evolutionary changes in RAS mutations through liquid biopsy with ctDNA during and after anti-EGFR therapy (NCT03401957). Methods: A total of 39 intention-to-treat (ITT) patients diagnosed with RAS wild-type mCRC, from Cathay General Hospital (CGH) and Kaohsiung Medical University Hospital (KMUH), were analyzed in this study. Of them, 24 were male and 15 were female, with median age of 55 years. Patients received cetuximab-based FOLFI RI or FOLF ORX regimen as first-line treatment. Blood samples from enrolled patients were collected before and every 3 months during cetuximab-based treatment and also at disease progression. These blood samples were evaluated for RAS resistance mutations using MassARRAY platform. The primary endpoint is percentage of RAS mutations detected in ctDNA from patients during cetuximab treatment. The correlation between the tumor response of these patients and the emergence of RAS mutations in ctDNA is further analyzed. Results: Between January 2018 and July 2019, 3 (8.3%) of 36 per-protocol (PP) patients subsequently with newly detected ctDNA KRAS/ NRAS mutations in their blood samples during the treatment period, and all of three patients developed progressive disease (PD). Of 36 PP patients, 19 (52.8%) patients had complete/partial response (CR/PR), 13 (36.1%) patients had stable disease (SD) and 4 (11.1%) patients had PD. The disease control rate was 88.9% in the present study. Three of 4 PD patients were detected with ctDNA KRAS/NRAS mutations in their blood sample, with time to onset of newly detected ctDNA RAS at 3 and 6 months posttreatment, respectively. Conclusions: In current studies regarding adherence to these recommendations in blood samples during the treatment period was 83.0% and all of these 3 patients developed PD. The results of this study will offer substantial, valuable information for anti-EGFR therapeutic strategy in patients with mCRC. Research Sponsor: Merck Ltd., Other Government Agency.

Prognostic and predictive value of DNA mismatch repair status in patients with locally advanced rectal cancer following neoadjuvant therapy. First Author: Huabin Hu, The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Background: DNA mismatch repair deficient (dMMR) is a distinct molecular feature associated with improved outcomes in various cancers. We investigated the value of dMMR on prognosis and predicted response to neoadjuvant therapy in rectal cancer patients. Methods: Between January 2013 and December 2018, a total of 855 consecutive patients with determined MMR status who underwent neoadjuvant therapy followed by curative surgery for locally advanced rectal cancer were included in this retrospective study. Associations of MMR status with clinicopathologic variates and response to neoadjuvant therapy were determined using Chi-square or Fisher Exact tests. Local recurrence-free survival (LRF S) and disease-free survival (DFS) were analyzed using Cox proportional hazard model. Results: In this study population, dMMR was detected in 69 of 855 (8.1%) cases. Patients with dMMR showed similar clinicopathological characteristics including grade of differentiation, location from anal verge, clinical stage, neoadjuvant therapy regimen, pathological stage and postoperative chemotherapy to those who with pMMR, except younger age (< 65 years, 89.1% vs. 77.7%, P = 0.034) and more mucinous adenocarcinoma in dMMR tumors. MMR status were not predictive for response to neoadjuvant therapy including pCR rate (18.8% vs. 12.9%, P = 0.185), downstaging rate (76.6% vs. 68.9%, P = 0.200) and tumor regression grade 0-1 (31.3% vs. 43.7%, P = 0.052), regardless of chemoradiation or chemotherapy. Multivariable analysis revealed that patients whose tumors had dMMR vs. pMMR had significantly longer DFS (HR = 0.39, 95%CI = 0.18 - 0.83, P = 0.014), but the correlation was not confirmed in the Cox proportional hazard model. Local recurrence-free survival (LRF S) and disease-free survival (DFS) were analyzed using Cox proportional hazard model. Conclusions: dMMR was significantly associated with longer DFS as compared to patients with locally advanced rectal cancer, whereas was not a predictive marker for neoadjuvant therapy. Research Sponsor: None.
Background: Anti-EGFR therapies are frequently given as first-line therapy for patients with mCRC, and early anti-EGFR therapies may be suitable at any line. Despite improving outcomes for patients with mCRC, there is still a need regarding the optimal treatment sequence. In this post hoc analysis, the safety and effectiveness of afibercept + FOLFIRI was evaluated for patients with mCRC based on their prior anti-EGFR therapy use. Methods: OZONE was a prospective, multicenter, observational, non-comparative study evaluating patients receiving afibercept + FOLFIRI in the clinical setting, for 24 months from afibercept initiation until death or until death. Patients were retrospectively assessed according to prior use of anti-EGFR therapy (defined as patients who received cisplatin or cetuximab and/or panitumumab as previous anti-cancer therapy). Overall survival (OS) and progression-free survival (PFS) were analyzed by hazard ratios (HR) and 95% confidence intervals (CI); overall response rate (ORR) was analyzed by odds ratios (OR) and 95% CI. Results: Among the overall treated population (n = 719), 19.2% of 347 received prior anti-EGFR therapy. High anti-EGFR therapy had no significant impact on the median OS (11.47 vs 12.58 months; HR: 95% CI 1.12 [0.89-1.39]), median PFS (5.29 vs 6.24 months; HR: 95% CI 1.022 [0.830-1.260]), or ORR (64.96% vs 59.35%; OR [95% CI 0.330-1.07]) of patients who did not receive prior anti-EGFR therapy. Rates of grade ≥3 treatment-emergent adverse events (TEAEs) were similar between patients who did vs did not receive prior anti-EGFR therapy (70.7% vs 67.7%). The most frequently reported grade ≥3 TEAEs for patients who did vs did not receive prior anti-EGFR therapy were neutropenia (32.2% vs 15.0%), hypertension (8.8% vs 10.3%), and diarrhea (10.2% vs 9.4%). Conclusions: This post hoc analysis of the OZONE study did not reveal major differences in safety and effectiveness according to prior anti-EGFR therapy. Clinical trial information: NCT03307586. Research Sponsor: Sanofi.

Background: The tumour microenvironment is an important determinant of survival in patients with colon cancer. Although the generalised inflammatory infiltrate to T cells (Klintrup-Mäkinen (KM) grade) is a widely used prognostic marker, immunohistochemical staining for specific immune cell populations, such as T-cells, may have greater prognostic value. The present study examines the clinical utility of combined assessment of KM grade in colorectal cancer (CRC) patients treated with fluoropyrimidine-based chemotherapy. Methods: KM grade and FoxP3 were assessed retrospectively in a cohort of 520 patients with stage I-III colon cancers. The relationship between KM grade, T-cell density and cancer-specific survival was examined. Results: KM was high in 33% of patients, with 16% having high KM and FOP3, 12% high KM and CD8, and 15% high KM and CD8. KM was high in 55% of patients, and 13% had high KM and FOP3. FoxP3 was high in 30% of patients, and 15% had high KM with FoxP3. KM and FoxP3 were associated with hazard ratios of 1.51 (p = 0.016) and 1.30 (p = 0.041), respectively. Conclusion: KM grade and FoxP3 were both significant predictors of survival in patients with CRC.

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Feasibility and clinical impact of routine molecular testing of gastrointestinal (GI) cancers at a tertiary center with a multiplex, next-generation sequencing (NGS) panel. First Author: Giacomo Pregni, Institut Jules Bordet-Université Libre de Bruxelles (ULB), Brussels, Belgium

**Background:** High-throughput technologies have been increasingly used in research. Nevertheless, limited data are available on the feasibility and clinical value of these technologies in routine practice. **Methods:** All consecutive GI cancer patients (pts) who were tested with the 48-gene TrueSeq Amplicon Cancer Panel (Illumina) as part of routine practice at our Institution were identified from a prospectively maintained pathology database. Feasibility data, results and impact on management decisions were analysed. Associations were tested with Fisher’s test. **Results:** From Apr 2014 to Jun 2019, 314 pts were tested. Sequencing was successful in 290 cases (94.2%; 234 colorectal (CRC), 21 gastro-esophageal, 17 bilo-pancreatic, 9 GIST, 4 appendix, 3 small intestine, 2 hepatoacellular). In successful and failed cases, respectively, analyses were attempted on core biopsy (37.0% vs 66.7%), surgery (62.6% vs 16.7%), and fine needle aspiration (0.4% vs 12.4%) tumour samples (p < 0.001). Median turnaround time (TAT) was 12.5 days, reducing from 13 days in 2014 to 10 days in 2019. The majority of successfully tested pts (85.6%) had stage IV disease. TP53 was the most frequent mutation (45.9%), followed by APC (42.1%), KRAS (39.7%), PIK3CA (12.1%), SMAD4 (7.6%), BRF (6.2%), and NRAS (5.5%). All other mutations were found in < 5% of cases. **Conclusions:** The high overall concordance between plasma and tissue RAS mutation support the liquid biopsy technology as an alternative to tissue testing for RAS characterization in mCRC patients, especially in patients with peritoneal disease and less in those with peritoneal disease. These results reinforce the use of liquid biopsy as a non-invasive tool for guiding targeted therapy in our patients. Research Sponsor: IDICHUS.

**Concordance of plasma and tissue RAS mutations in 380 mCRC patients.**

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**Total** 180 132 68 380

**Concordance of plasma and tissue RAS mutations in 380 mCRC patients.**

**Surgical Therapy for Colorectal Cancer: Impact of Oncologic and Functional Status on Outcomes**

**Background:** Minimally invasive colorectal resection: Association with elevated levels of plasma TIM-3 post surgery and effect on immune tolerance and the growth of residual metastases. First Author: Hmc Shantha Kumar, Department of Surgery, Lenoxhill Hospital, Norwell Health, New York, NY

**Methods:** TIM-3 (C1010424242) a non-MHC class II receptor that is a transmembrane glycoprotein expressed on CD8+ T cells and CD8+ T cells cytotoxic T (Tc) cells and dendritic cells. TIM-3, after binding to its ligand, galectin-9, inhibits tumor immune function. Co-expression of TIM-3 and PD-1 together is associated with enhanced dysfunctionality of tumor toxic CD8+ T cells. The combination of TIM-3 blockade with anti-PD-1/PDL1 intervention may enhance response. TIM-3 overexpression has been associated with oncologic activity in colorectal cancer (CRC). Persistently elevated plasma PDL1 levels after CRC resection have been reported. This study’s purpose was to measure plasma TIM3 levels before and during the first month after minimally invasive colorectal resection (MCR) for CRC. Methods: CRC patients (pts) in the IRB approved IRB approved study, who had MICR met the study criteria (colon 72%; rectal 28%; mean age 64.8 years). CRC patients who had MICR met the study criteria (colon 72%; rectal 28%; mean age 64.8 years). CRC patients who had MICR met the study criteria (colon 72%; rectal 28%; mean age 64.8 years). CRC patients who had MICR met the study criteria (colon 72%; rectal 28%; mean age 64.8 years). CRC patients who had MICR met the study criteria (colon 72%; rectal 28%; mean age 64.8 years).

**Conclusions:** Plasma TIM3 levels were significantly elevated over baseline for 1 month after MICR (n = 95) (mean age 64.8 years). CRC patients who had MICR met the study criteria (colon 72%; rectal 28%; mean age 64.8 years). CRC patients who had MICR met the study criteria (colon 72%; rectal 28%; mean age 64.8 years). CRC patients who had MICR met the study criteria (colon 72%; rectal 28%; mean age 64.8 years). CRC patients who had MICR met the study criteria (colon 72%; rectal 28%; mean age 64.8 years). CRC patients who had MICR met the study criteria (colon 72%; rectal 28%; mean age 64.8 years). CRC patients who had MICR met the study criteria (colon 72%; rectal 28%; mean age 64.8 years). CRC patients who had MICR met the study criteria (colon 72%; rectal 28%; mean age 64.8 years). CRC patients who had MICR met the study criteria (colon 72%; rectal 28%; mean age 64.8 years).

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Clinical utility of the systemic inflammatory response (SIR) in identifying high-risk stage II colon cancer. **First Author:** Allan Matthew Golder, Academic Unit of Surgery, Glasgow, United Kingdom

**Background:** Surgery for TNM Stage II colon cancer is considered curative however approximately 20% of patients will have recurrence of their disease. A number of high risk pathological features guide the use of adjuvant chemotherapy. More recently the preoperative SIR has been consistently shown to have prognostic value but to date has not been utilised clinically as a high risk feature. The present study compares the influence of the SIR versus other established risk clinical features on overall cancer specific survival (OS/ CSS).

**Methods:** Patients in the West of Scotland undergoing curative resection for Stage II colon cancer from 2011-2015 were identified with survival updated until December 2018. Additional data was obtained from online records. Through uni/multivariate analysis (UVA/MVA) we compared the effect on survival of the SIR measured using the modified Glasgow Prognostic Score (mGPS), neutrophil-lymphocyte ratio (NLR) and lymphocyte-monocyte ratio (LMR) when entered individually or a multivariable model alongside established high-risk features. **Results:** 992 patients were identified having had a curative resection of Stage II colon cancer. Median follow up was 61 months and there were 307 deaths during follow up. For OS: emergency presentation, T stage, adjuvant chemotherapy, nodal harvest, margin involvement, mGPS, LMR, NLR (all p<0.01) and EMVI (p < 0.05) were significant on UVA. On MVA: age (HR 1.51), T stage (HR 1.59), nodal harvest (HR 1.67), margin involvement (HR 1.94), adjuvant chemotherapy (HR 0.47), mGPS (HR 1.38), NLR (HR 1.35) and LMR (HR 1.50) remained significant (all p < 0.05). For CSS: age, emergency presentation, T stage, margin involvement, mGPS, NLR, LMR, nodal harvest and adjuvant chemotherapy (both p < 0.05) remained significant on UVA. On MVA emergency presentation (HR 1.88), T stage (HR 2.02), margin involvement (HR 2.98), adjuvant chemotherapy (HR 0.51) and mGPS (HR 1.34) remained significant (all p < 0.001). **Conclusions:** The present study suggests that the SIR is an independent predictor of worse OS/CSS in Stage II colon cancer and should be considered a high risk feature in future prospective studies. **Research Sponsor:** None.

**Effect of phenotype on outcome in synchronously resected primary colorectal cancer and matched liver metastases.** **First Author:** Kathryn AF Pennell, University of Glasgow, Glasgow, United Kingdom

**Background:** 5-year survival of patients with resectable colorectal liver metastases is 25-40%. Mechanisms of disease progression are heterogeneous and do not follow a clearly defined pathway from genotype to phenotype. In stage I-III colorectal cancer (CRC), patients with high tumor stroma exhibit poor prognosis, while those with high immune cell infiltrate do well following resection. We hypothesise that stromal-dense phenotypes lead to T cell exclusion, myeloid cell accumulation and aggressive metastatic progression. Here, we examine relationships between histological tumor phenotype, cellular infiltrate and outcomes in metastatic CRC. **Methods:** A unique cohort of synchronously resected primary CRC and matched liver metastases (n = 46) were assessed for immune cell infiltration (CD3, CD4, CD8, CD68, CD66b, inflammatory signalling (CXCR2, PDL-1, MMP9) and hypoxia (CAIX) using immunohistochemistry. Tumors were phenotypically subtyped using immune infiltrate (Klintrup-Makinen Grade (KM)), stromal invasion (tumor-stroma ratio (TSI)) and proliferation (Ki67). **Results:** Phenotypic subtype of primary tumors was predictive of metastatic subtype (rho = 0.52, P = 0.003). Immune phenotypes were associated with good prognosis and stromal phenotypes with poor prognosis (p = 0.004). Infiltration of macrophages and granulocytes associated with poor outcomes (p = 0.018) and increased CXCR2 expression (p = 0.03) at both sites. Increased CXCR2+ cells and macrophages at both sites associated with stromal phenotype (p = 0.02), tumour budding (p = 0.002), low KM grade (p = 0.05) and poor prognosis (p = 0.002). Macrophage and T cell levels increased in metastases compared to primary tumors, but changes were seen in lymphocyte infiltration, CXCR2 and CD66b. **Conclusions:** Density of immune cell infiltrate, in the primary and metastatic niche, conferred good prognosis. In contrast, stromal, myeloid rich tumors and poor prognosis. This clinically relevant and histologically efficient process permits segregation of disease and supports further study of relationships in the tumour microenvironment of CRC in the context of chemotherapy to better target therapeutics to individual patients. **Research Sponsor:** Medical Research Council.

**Distinct genomic landscape in colorectal mucinous carcinoma via comprehensive genomic profiling.** **First Author:** Liang Huang, The Sixth Affiliated Hospital, Sun Yat-sen University, Guangdong Provincial Key Laboratory of Colorectal and Pelvic Floor Disease, Guangzhou, China

**Background:** Mucinous carcinoma (MC), accounting for 10-15% of colorectal cancer (CRC), has long been associated with an inferior response to treatment. MC differs from other CRC by a diagnostic factor: mucinous carcinoma stage CRC remains a clinical challenge to treat. In this study, we used a large CRC cohort to define the genomic landscape of MC and identify prognostic and clinically actionable information. **Methods:** The 1226 CRC patient cohort included 997 adenocarcinomas (AC), 129 MC, and 10 adenocarcinomas with mucous composition (AC/MC). All of the pathological sections were verified by an experienced pathologist. FFPET tumor samples and matched peripheral blood were sequenced using a 450-cancer related gene panel. **Results:** MC was significantly associated with right colon (p<0.001) and regional lymph node metastasis (p=0.004) compared to AC. We found a high mutation rate of BRAF V600E (10.9% vs. 3.3%), PIK3CA (28.7% vs. 19.2%), SMAD4 (34.1% vs. 19.1%), BRCA1/2 (16.3% vs. 6.8%) and homology recombination pathway (40.3% vs. 22.7%), and a lower rate of TP53 (53.5% vs. 79.5%), APC (46.5% vs. 75.1%), and HLR2 amplification (0% vs. 2.1%) in MC than in AC. MC had a significantly higher proportion of microsatellite instability-high (MSI-H) tumors (22.5% vs. 6.8%, p<0.001). Furthermore, in tumors with MSI stable, POLE mutation was more frequent in MC than in AC (7.0% vs. 2.6%, p=0.094) and resulted in dramatic elevated tumor mutational burden (TMB, range 49-1,595.5 muts/Mb), indicating up to 30% of MC patients may benefit from immunotherapy. MSI-H was associated with better prognosis (5-y DFS, MSI-H 86.7% vs. MSS 56.7%) in stage I/II CRC patients with MC. Importantly, AMC mimicked the genomic features of MC rather than AC. **Conclusions:** For the first time, comprehensive genomic analysis revealed that MC had distinct molecular features, indicating promising clinically application for both immunotherapy and targeted therapy. Early stage MC had a diverse prognosis due to MSI status and should be interpreted differently. The similarity of molecular profile between AMC and MC suggested the possible usage of MC, but not AC, clinical strategy for AMC. **Research Sponsor:** Sun Yat-sen University Clinical Research 5010 Program (No.2016005).

**Wild-type APC and prognosis in metastatic colorectal cancer.** **First Author:** Chongkai Wang, City of Hope National Medical Center, Duarte, CA

**Background:** Somatic mutations at adenomatous polyposis coli (APC) gene, found in ~75% of colorectal cancers (CRC), are under-represented in microsatellite instable (MSI-H) tumors. While several studies have suggested worse outcomes for CRC patients (pts) with wild-type APC (APC-WT), the prognostic implication of this genomic alteration in metastatic CRC (mCRC) is not well defined. **Methods:** APC prognostic value was evaluated in 331 stage IV microsatellite stable (MSS) CRC pts treated in our institution. Next-generation genomic analysis (FoundationOne) was used to characterize the molecular characteristics of APC-WT and mutant APC (APC-MUT) pts and predictive models were validated on a public database of stage IV colon cancer from MSKCC. **Results:** APC-WT was present in 26% of mCRC pts. In comparison to APC-MT population (n = 244), APC-WT pts (n = 87) tended to be younger (median age: 49 vs. 58 years), right-sided (44% vs. 24%), BRAF-V600E mutated (25% vs. 5%), p53 WT (38% vs. 21%) and Ras WT (66% vs. 53%). APC-WT tumors were associated with other Wnt activating alterations (CTNNB1, FBXW7, RNF43, ARID1A and SDX9). Among those, RNF43 and CTNNB1 were more significantly represented in the APC-WT vs APC-MT population (12% vs 1% and 11% vs 3%, respectively). APC-WT pts had a worse overall survival (OS) than APC-MT pts (30 vs 48 months, HR = 1.809, 95% CI 1.260-2.596, p < 0.0001). Using a multivariate model correcting for primary tumor location, Ras and Braf status, APC-WT was predictive of poor survival (HR = 1.7, p = 0.001) in our data set. The prognostic implication of APC-WT on OS were confirmed further in a similar multivariate model of 433 stage IV pts from MSKCC public database (HR = 1.6, P < 0.01). **Conclusions:** APC-WT is associated with poor OS in MSS mCRC regardless of Ras, Braf status. Compared with APC-MT mCRC tumors, APC-WT tumors were associated with other activating alterations of Wnt pathway, including RNF43 and CTNNB1. **Research Sponsor:** Institutional fund.
The pretreatment lymphocyte-to-monocyte ratio (LMR) to predict treatment efficacy and prognosis in metastatic colorectal cancer treated with the combination of TAS-102 and bevacizumab (TAS-CC3 Study). First Author: Akhisa Matsuda, Department of Gastronenterial and Hepato-Biliary-Pancreatic Surgery, Nippon Medical School, Tokyo, Japan

**Background:** The combination regimen of TAS-102 and bevacizumab as salvage-line therapy for metastatic colorectal cancer (mCRC) was established based on its high clinical effectiveness (C-TASK FORCE). Recently, our current phase II TAS-CC3 study demonstrated comparable median progression-free survival (PFS: 4.5m) and overall survival (OS: 9.2m) with exclusive inclusion of 3rd line therapy patients. However, practical predictors for its efficacy are lacking. This study evaluated inflammation-based scores as potential predictors for this combination therapy. **Methods:** This is a post hoc analysis of investigator-initiated, open-label, single-arm, multicentered phase II study (TAS-CC3) in Japan with 32 mCRC patients treated with the combination therapy. We investigated the predictive and prognostic values of pretreatment blood inflammation-based scores, including neutrophil-to-lymphocyte (NLR), platelet-to-lymphocyte (PLR), and lymphocyte-monocyte ratios (LMR), on disease-control (DC), PFS and OS. These were divided into two groups (high and low) using cut-off of each median values. This study was registered at the University Hospital Medical Information Network, as UMIN000002438.

**Results:** ROC curve analyses of 3 inflammation-based scores versus DC showed a best predictive performance in LMR, followed by NLR and PLR (AUC: 0.89, 0.85, and 0.68, respectively). The high LMR group had a significantly higher DC rate than the low group (87.5 vs. 43.8%, P = 0.023). Two patients showing partial responses were in the high group. The high LMR group showed significantly longer survivals compared with the low group (4.9 vs. 2.3m respectively for median PFS, P = 0.014) (20.5 vs. 5.5m, respectively for median OS, P < 0.001). The values of LMR were significantly correlated with PFS and OS (r = 0.56, P < 0.001 and 0.62, P < 0.001, respectively). **Conclusions:** Pretreatment LMR showed a best predictive and prognostic biomarker for mCRC patients treated with TAS-102 and bevacizumab treatment and might be clinically useful for selecting patients of the responder. Clinical trial information: UMIN000002438. Research Sponsor: None.

**Poster Session (Board #L2), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM**

Vascular endothelial growth factor (VEGF)-D and clinical outcomes in metastatic colorectal cancer (mCRC) patients (pts) treated with second-line FOLFIRI plus bevacizumab (Bev): A biomarker study of the WJOG 6210G trial. First Author: Naoki Izawa, St. Marianna University School of Medicine, Kawasaki, Japan

**Background:** The WJOG 6210G trial demonstrated a similar efficacy between FOLFIRI plus Bev and FOLFIRI plus panitumumab (Pani) at 2nd-line treatment in pts with mCRC. The high VEGF-D level was adopted as cut-off value, pts with high VEGF-D achieved a better disease-control (DC), PFS and OS, and bevacizumab treatment and might be clinically useful for selecting patients of the responder.

**Methods:** Plasma samples which were collected at pre-treatment were analyzed for VEGF-D. The pretreatment lymphocyte-to-monocyte ratio (LMR) was measured by automated hematology analyzers. The WJOG 6210G trial showed a similar efficacy between FOLFIRI plus Bev and FOLFIRI plus Pani at 2nd-line treatment in pts with mCRC. The high VEGF-D level was adopted as cut-off value, pts with high VEGF-D achieved a better disease-control (DC), PFS and OS, and bevacizumab treatment and might be clinically useful for selecting patients of the responder. Clinical trial information: UMIN000002438. Research Sponsor: None.

**Poster Session (Board #L4), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM**

Clinical and molecular markers of immune checkpoint inhibitor (ICI) response in dMMR colorectal cancer (CRC) patients (pts). First Author: Ibrahim Halil Sahin, I74, Atlanta, GA

**Background:** ICIs induce durable responses in dMMR CRC patients. However, clinical and molecular biomarkers of response to ICIs have not been well-established. In this study, we investigated the impact of specific MMR gene loss, BRAF V600E mutation and clinical characteristics of pts on clinical outcomes of ICIs. **Methods:** Pts were eligible if they had confirmed dMMR CRC by IHC or MSI-H by PCR and received ICIs between 01/01/2012 and 05/01/2019 at Winship Cancer Institute of Emory University, Mayo Clinic Jacksonville and Stanford University. Due to the functional dependency, the groups were categorized as protein loss of MLH1+PMS2 vs MLH1+MSH6. Log-rank test, Cox hazard model and Fisher’s exact test were used for survival outcomes, the best modeling and the distribution of variables among the subgroups were used for Cox regression analyses. **Results:** A total of 66 pts with dMMR CRC were identified and BRAF status was available for 41 pts. ORRs in MLH1+PMS2 and MLH1+MSH6 groups were 72.9% and 56.5% respectively (P = 0.189). At 2 years, PFS rates were 55.6% and 78.2% for MLH1+PMS2 and MLH1+MSH6 groups respectively (P = 0.001). Pts with BRAF V600E mutations had significantly worse outcomes as compared to pts with wild-type BRAF (2-year PFS rate of 35.0% and 73.3% respectively; P < 0.001). Notably pts <65 had better 2-year disease control rates compared to >65 (71.1% and 41.5% respectively; P < 0.001). We also observed worse 2-year PFS rates in pts with liver metastases (P = 0.014). CRC side and tumor volume did not impact 2-year PFS rates in our cohort. **Conclusions:** Our data suggest that pts with loss of function in MLH1+PMS2 may have better 2-year PFS rates compared pts with MLH1+PMS2 even though ORR favored MLH1+PMS2 group suggesting that ORR may not reflect the durability of ICI response in dMMR CRC patients. Consistently, pts with BRAF V600E mutation which is associated with MLH1 promoter methylation had significantly worse 2-year PFS rates. Overall, our findings suggest that BRAF V600E mutation, the affected MMR proteins, pt age, and site of metastasis may impact durability of ICI response in dMMR CRC patients. Research Sponsor: None.
Circular RNAs as biomarkers in liquid biopsy in colorectal cancer. First Author: Manuel Valladares-Ayerbes, Medical Oncology, IMIBIC, Reina Sofia Hospital, CIBERONC, Instituto de Salud Carlos III, Córdoba, Spain

Background: Circular RNAs (circRNAs) are emerging as essential regulators of cancer-related biological hallmarks, as cell proliferation, apoptosis, differentiation, immune regulation and angiogenesis. circRNAs are abundant, conserved and unique to a tissue-specific expression pattern. These characteristics make them candidate to serve as biomarkers in liquid biopsy (LB) in cancer. The aim of this study is to analyse differential expression of circRNAs in the colorectal cancer (CRC) scenario. Methods: To comprehensively understand the molecular differences between GCC and other appendiceal tumors such as adenocarcinoma and neuroendocrine tumor (NET). Results: The top five genes with most frequent mutations were TP53 (24.0%), CDH1 (15.4%), APC (9.4%), BRCA2 (7.5%) and RAS mutations. However, compared to NETs, GCCs showed significantly higher frequency, compared to adenocarcinomas (2.0% vs 28.6%), FGFR2 (1.9% vs 0.0%). Compared to NETs, GCCs showed significantly higher frequency, compared to adenocarcinomas (2.0% vs 28.6%), FGFR2 (1.9% vs 0.0%). Compared to NETs, GCCs showed significantly lower frequency, compared to adenocarcinomas (2.0% vs 28.6%), FGFR2 (1.9% vs 0.0%). Compared to NETs, GCCs showed significantly lower frequency, compared to adenocarcinomas (2.0% vs 28.6%), FGFR2 (1.9% vs 0.0%). Compared to NETs, GCCs showed significantly lower frequency, compared to adenocarcinomas (2.0% vs 28.6%), FGFR2 (1.9% vs 0.0%).

Conclusions: Since HER2-L mCRC had the high prevalence of co-altered RAS mutations but showed a better prognosis and might benefit more from an anti-EGFR monoclonal antibody therapy, median progression-free survival (mPFS) in HER2-L tended to be better than that in HER2-Pos, with 2.2 months in HER2-Pos, 7.8 in HER2-L, and 5.5 in HER2-Neg (p = 0.099). Conclusions: Since HER2-L mCRC had the high prevalence of co-altered RAS mutations but showed a better prognosis and might benefit more from an anti-EGFR therapy than HESE2-Pos, the HER2-L mCRC seems to have a different biological behavior from HER2-Pos in terms of molecular landscape and prognostic value on mCRC. Research Sponsor: None.
BRD4 plays an important role in transcription, DNA repair and drug resistance. High expression and polymorphisms of BRD4 regulating pathways are reported to be related to worse prognosis in colorectal cancer. Therefore, we hypothesized that genetic variants in BRD4 regulating pathway may predict first-line treatment outcome in mCRC pts. Methods: The impact on outcome of 22 SNPs in 7 genes involved in BRD4 regulating pathway (BRD4, SIPIA, MYC, S3BP1, H2AX, BATF, CD47) was analyzed through the OncoArray, a customized array manufactured by Illumina, on genomic DNA from blood samples of pts enrolled in 2 randomized trials. MAVERICC FOLFIRI/bevacizumab (bev) arm served as discovery cohort (N = 107), FIRE3 FOLFIRI/bev arm as validation (N = 107) and FOLFIRI/ceftarab (cem) arm as control (N = 129). Results: In the discovery cohort, right(r) sided pts with BRD4 rs448028722 G allele (N = 46) showed significantly shorter DFS (P = 0.05 as 0.18 vs 0.65) compared to carriers of A/A (N = 21) in both uni- and multi-variable analysis (P < 0.01; r-sided pts carrying any T allele of BATF rs761377 (N = 50) showed longer DFS (P = 0.03 as 6.8 vs 6.6) compared to carriers of C/C (N = 14) in univariate analysis (P < 0.05) and had a strong trend in multivariable analysis (P = 0.06). These findings were all validated in r-sided pts in FIRE3 bev arm (BRD4 rs448028722, DFS 9.8 vs 18.7 m; BATF rs761377, DFS 15.1 vs 4.2 m) in uni- (both P < 0.01 and multi-variable (P = 0.08 and < 0.05 respectively). Analysis of no significant association was performed in the control arm. Interestingly, pts carrying CD47 rs3206652 any C allele (N = 13) only showed a trend in DFS for the r-sided pts of FIRE3 cet cohort, but no association was observed in the bev-based treatment. Conclusions: Our study demonstrates for the first time that BRD4 and BATF polymorphisms may predict outcomes of bev-based treatment in r-sided mCRC pts. Meanwhile CD47 polymorphism may predict outcomes of cet-based treatment in R-sided mCRC pts. This finding supports a possible role of BRD4 regulating pathway in contributing to resistance to anti-VEGF/EGFR treatment. Research Sponsor: Cancer Institute (grant number P30CA040899), The Gloria Borges WunderGlo Foundation, The Wunder Project, Dhont Family Foundation, San Pedro Peninsula Cancer guild, Daniel Butler Research Fund and Call to Cure Fund.
Racial variation in molecular profile of advanced gastrointestinal cancers. First Author: Shravanti Macherla, East Carolina University, Greenville, NC

Background: Heterogeneity in the tumor molecular profile based on race is poorly understood. We sought to review the utilization of next generation sequencing (NGS) in patients with advanced gastrointestinal (GI) malignancies treated at a rural academic center and analyze inter racial variations in the molecular tumor profile. Methods: We conducted a retrospective review of patients with advanced GI malignancies that underwent NGS between 2015 to 2018 at East Carolina University. 104 patients met eligibility criteria but 8 patients were excluded due to insufficient tissue sampling. Patients with colorectal, gastric, pancreatic, biliary, small intestinal and esophageal cancers were included. Targeted NGS using Caris Life Sciences platform was performed to obtain molecular analysis. We conducted descriptive univariate analysis, cox regression and Kaplan-Meier survival curve analysis. Results: Median age at diagnosis was 64.64 and 64% of patients were white. The study cohort had n=39 in colon cancer, 18(17%) gastric cancer, 30(29) pancreatic cancer, 66(66) biliary cancer, 4(4%) small intestinal cancer and 14(1%) esophageal cancer. 60(55) had de novo Stage IV disease. Median overall survival (OS) was 25 months, 30 mo in blacks and 32 mo in whites (p value =0.46). Microsatellite stability was seen in 94% (87) and instability in 3% (3). Overall cohort had mutations (mut) in KRAS (50%), TP53 (64%), BRAF (4%), and ERBB amplification (3%). On analysis, APC mutation was associated with worse outcome. Black patients had more alterations in KRAS, TP53 (both not significant), and APC (p=0.002).

Conclusion: Our analysis shows variation in molecular alterations in molecular profile of advanced GI malignancies. Black patients had increased rates of APC, KRAS and TP53 mut. Further studies are required to analyze the impact of these molecular variations on outcomes. Results. Research Sponsor: None.

Circulating tumor DNA (ctDNA) heterogeneity as first- and third-line treatment in patients (pts) with metastatic colorectal cancer (mCRC) treated with panitumumab. First Author: Christine Megedichian Parseghian, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: RAS mutations are negative predictors of response to anti-EGFR therapies such as panitumumab in mCRC. Mutations at baseline (BL) and follow-up (FU) during randomized phase 3 studies of first line treatment (1L; study 2005203 [203]; panitumumab + fluorouracil, leucovorin and oxaliplatin [FOLFOX4] vs FOLFOX4) were compared with those in third line treatment (3L; study 20100007 [‘007]; panitumumab + best supportive care [BSC] vs BSC) to assess tumor heterogeneity via ctDNA analysis. Methods: Biomarker analysis was conducted for pts with plasma samples at BL and FU. Samples were analyzed using the PlasmaSelect R-63-gene panel (Personal Genome Diagnostics, Inc.), with a limit of detection of 0.1%. Mutations were defined at the amino acid level. The Cox hazard ratio (HR) by sum of RAS mutations (RAS mut) was determined, as were joint-free survival (EFS) and best response by RAS mutation status. Results: For all pts with available samples (203, n = 120; ‘007, n = 90), fewer mutations and fewer mutations/gene were observed in the 1L vs 3L setting at BL (KRAS 2 vs 3 maximum mutations/gene; EGFR 1 vs 4 maximum mutations/gene). In 3L the Cox HR increased continuously with increasing mutations/gene. We found a significant difference in the rate of new RAS mutations at FU in 3L setting. The combination of panitumumab + FOLFOX in 3L is associated with delayed emergence of expansion of RAS mutations compared to later line single agent panitumumab. Research Sponsor: Amgen Inc.
A comparison study of the intratumoral microbiome in younger versus older-onset colorectal cancer (COSMO CRC). First Author: Benjamin Adam Weinberg, The Lasker Research Fund, New York, NY

Background: Although colorectal cancer (CRC) incidence has declined overall, CRC in individuals under age 45 has risen dramatically, particularly in the distal colon and rectum (left-sided CRC). The intratumoral microbiome (MB) of young individuals may be responsible. Certain bacteria disrupt colonic luminal integrity and promote inflammation, leading to oncogenic mutations in colonic epithelial cells. Fusobacterium nucleatum (F. nucleum) promotes CRC by suppressing immune response within the tumor microenvironment, activating the β-catenin pathway, and causing chemoresistance due to autophagy.

Methods: We compared the intratumoral MB in CRC patients (pts) diagnosed before age 45 and after age 65. Primary and metastatic tumors were included. DNA was extracted from tumors and analyzed using 16s ribosomal gene sequencing. We compared the frequency of F. nucleum and other bacterial and fungal DNA in tumors from younger- vs. older-onset CRC pts.

Results: Tumors from 18 younger pts (median age 39.2 years) and 13 older pts (median age 72.8 years) underwent analysis. In total, 478 unique bacterial and fungal species were detected. F. nucleum was found in tumors of 5 younger pts (28%), 4 left-sided and 1 right-sided primary) and 3 older pts (23%, 1 left-sided and 2 right-sided; P = NS, Fisher’s Exact test). A significant difference was seen in the rate of Moraxella osloensis (91% vs. 46%, P = 0.0043, Fisher’s Exact test) in younger vs. older pts. There was no significant difference in MB diversity in younger vs. older pts. Conclusions: F. nucleum is present in a greater number of tumors in pts with CRC diagnosed before age 45 than previously thought. Intratumoral bacterial profiling may discover patterns that explain the rising incidence of CRC in younger individuals and might eventually inform the development of novel therapeutics and adaptive cancer screening methods.

Research Sponsor: Colorectal Cancer Alliance Other Foundation.

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Molecular profiling of early-stage colorectal cancer (CRC) using targeted next generation sequencing (NGS) to predict signatures of recurrence. First Author: Michael C. Burns, Northwestern University, Chicago, IL

Background: While the 5-year recurrence rate in early stage CRC is low (12%) and there is currently limited role of adjuvant chemotherapy in such cases, a unique subset of patients (pts) will have late recurrences. To identify molecular signatures predictive of late recurrence after pts undergo intended curative resection, we employed a 22 targeted gene NGS panel in pts with early CRC. Association between mutation status and recurrence free survival (RFS) was analyzed. Methods: Pts with stage I CRC had their tumor prospectively sequenced between 09/2015-12/2018 by an ion torrent targeted 22 gene hotspot NGS panel, including KRAS, EGFR, BRAF, PIK3CA, AKT1, ERBB2/4, PTEN, NRAS, STK11, MAP2K1, ALK, DDR2, CTNNB1, MET, TP53, SMAD4, FBX7, NOTCH1, and FGFR1/2/3. Associations were analyzed with unadjusted p-values (p + Benjamini & Hochberg adjusted (BHp) shown. Results: Clinical and pathologic data from 180 pts were analyzed: median age 66 (range 24-86), male (47%), stage I (41%), stage II (69%), left (54%) vs right (36%) sided primary tumors, and microsatellite stable (85%), 35% (19%) pts had adjuvant therapy (n = 21 rectal, n = 14 colon). Pathological mutations were found in 160 (89%) of pts, including TP53 (56%), KRAS (44%), PIK3CA (22%), BRAF (12%), SMAD4 (8%), MET (6%) and NRAS (3%). There was only 1 case of ERBB2 mutation. 33 pts (18%) had evidence of recurrence. 36 month RFS was 82%. Common sites of recurrence included liver (13 pts, 39%), lung (10 pts, 30%), and bone (2 pts, 6%). Alterations in MET CDNA and protein were associated with recurrence-free survival (RFS) (HR = 4.7; p =0.0026, BHp = 0.057). Interestingly, while TP53 mutations were typically associated with worse prognosis in metastatic colorectal cancers, it was not associated with RFS (HR = 0.8; p = 0.55, BHp = 0.98). There was also no association between the number of gene alterations and RFS (p = 0.45). Conclusions: These data highlight that targeted NGS tumor profiling of early stage CRC, including sequencing MET among other genes, may be utilized alongside known prognostic pathological factors to predict pts with a higher risk of recurrence and may facilitate tailored adjuvant chemotherapy to mitigate this risk. Research Sponsor: U.S. National Institutes of Health.
245 Poster Session (Board #M1), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Variation in genetic polymorphisms and gene expression of HLA-E to predict outcomes in metastatic colorectal cancer (mCRC) patients (pts) treated with first-line FOLFIRI/cetuximab: Data from the phase III FIRE-3 trial. First Author: Madhia Naseem, Division of Medical Oncology, USC Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, CA

Background: HLA-E is an MHC Class I antigen which inhibits NK cell activity by binding to CD94 receptor. Overexpression of HLA-E on CRC cells is associated with poor prognostic outcomes and has recently been associated with microsatellite instability. As cet enhances NK cell activity which is dependent on HLA-E, this study aims to assess whether differences in HLA-E gene expression and polymorphisms lead to different outcomes. Methods: Genomic DNA from blood samples of pts treated with first-line FOLFIRI/cetuximab (cet) (n = 129) and FOLFIRI-bevacizumab (bev, n = 107) was genotyped through the OncoArray, a custom array manufactured by Illumina. Gene expression levels were measured from 102 tumor samples of pts in the cet arm by HTG EdgeSeq Oncology Biomarker Panel. PFS and OS outcomes were investigated for an HLA-E genetic polymorphism, rs1264457, where G > A leads to glycine > arginine, where glycine has stronger affinity for NK cell receptor. Results: FOLFIRI/cet and FOLFIRI/bev cohort characteristics: median FU (25,1/26.7mo); PFS (12.8/11.5mo); OS (49.8/31.4mo); RAS WT (64%/62%) and observed in Ras mut pts. No significance was observed in FOLFIRI/bev overall (HR = 1.14-4.88; p = 0.021). A non-significant trend of improved OS was seen among 18% in RAS WT pts treated with FOLFIRI/cet (12.9 vs 12.3 mo; HR = 2.36; 95%CI = 0.85-6.60). These effects were not observed in Ras mut pts. No significance was observed in FOLFIRI/bev overall or FOLFIRI/bev RAS WT pts. Conclusions: Overexpression of HLA-E led to association with poor OS (log-rank (LR) = 13, 30 vs 34 mo) in cet arm (P < .05). No significant association was observed with PFS. Multivariable analysis showed that HLA-E asrs264457 carriers with any allele (n = 65) had better PFS than pts with G/G genotype (n = 18) in RAS WT pts treated with FOLFIRI/cet (12.9 vs 12.3 mo; HR = 2.36; 95%CI = 1.14-4.88; p = 0.021). A non-significant trend of improved OS was seen among carriers of A allele (n = 56) vs non-carriers (rs6664466) genotype (15.6 vs 11.6mo). These effects were not observed in Ras mut pts. No significance was observed in FOLFIRI/bev overall or FOLFIRI/bev RAS WT pts. Conclusions: Overexpression of HLA-E leads to association with poor OS among pts treated with FOLFIRI/cet. Poor PFS was seen among pts treated with cet who are RAS wt carrying polymorphisms allowing for increased binding to NK cell receptor, which in turn enhances HLA-E inhibitory function of NK cell lysis. Addition of mAb against HLA-E, which have been shown to restore NK cell mediated cell lysis, needs investigation in this pt population. Research Sponsor: National Cancer Institute grant number P30CA040889, the Gloria Borges WunderGlo Foundation-The Wunder Project, the Dhoff Family Foundation, the San Pedro Peninsula Cancer Guild, the Daniel Butler Research Fund, the Call to Cure Research Fund and the Fong.

248 Poster Session (Board #M4), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

The influence of adjuvant chemotherapy dose intensity on overall survival in resected colon cancer: A multicenter retrospective analysis. First Author: Suganja Lakkunarajah, Western University, London, ON, Canada

Background: Colorectal cancer remains the second leading cause of cancer death in developed countries. The benefit of using fluorouracil-based chemotherapy with oxaliplatin, such as FOLFOX (fluorouracil (5-FU), leucovorin, oxaliplatin) and CAPOX (capecitabine and oxaliplatin) is well established. The optimal dose intensity (DI) under which overall survival (OS) is inferior is not established. Methods: Patients (pts) treated with adjuvant chemotherapy between 2006 and 2011 for resected stage III colon cancer (CC) from four academic cancer centres in Canada were retrospectively analysed. Patients that received CAPOX and FOLFOX were examined for the relationship between DI and OS. Results: A total of 625 pts with treated with high risk stage II or stage III CC that received adjuvant chemotherapy were analysed. The median age was 63.2 pts with T4 and N2 disease comprised 35.4% and 29.9% of pts, respectively. Median follow-up was 3.2 years. There was available survival data for 319 pts. The median oxaliplatin DI was 70%. The frequency of pts reaching an oxaliplatin DI of > 80% was 43%, while 76.6% of pts had a dose intensity of > 80% for their FU component. An oxaliplatin DI of > 80% was associated with a significant improvement in survival, HR = 0.42 (95%CI 0.21-0.81, p = 0.01). Achieving a DI of > 80% for capecitabine or 5-FU did not improve OS. Other factors associated with inferior OS included T4 (HR = 3.5, p = 0.03) and N2 (HR = 5.27, p = 0.0005) subgroups. The improvement in OS was not significant when restricting the analysis to pts with non-T4 and non-N2 disease (n = 144), HR = 0.16 (0.02 - 1.26; p = 0.08). Conclusions: Oxaliplatin DI of > 80% is associated with improved OS in pts receiving chemotherapy for high risk stage II and stage III CC. Research Sponsor: None.

247 Poster Session (Board #M3), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

The potential in artificial intelligence-driven radiomic signature to predict survival in patients with metastatic colorectal cancer treated with cetuximab-based therapy. First Author: Laurent Delerce, Department of Radiology, Columbia University Medical Center; New York-Presbyterian Hospital, New York, NY

Background: This analysis was undertaken to forecast survival and enhance treatment decisions for patients (pts) with colorectal cancer (CRC) with liver metastases sensitive to folic acid, fluorouracil and irinotecan (FOLFIRI) alone (F) or in combination with cetuximab (FC) using simple quantitative radiomic changes between CT scans at baseline and 8 weeks. Methods: We retrospectively analyzed 667 pts with KRAS-unselected metastatic CRC in NCT00154102 treated with F and FC. CT quality was classified as high (HO) or standard (SO), and four data sets were created and named by treatment quality. Pts were randomly assigned 1:2 to training or validation sets: FC(M)T2, 80/78 pts; FC(M)S2, 55/78 pts; FC(M)O2, 79/78 pts. A machine-learning signature was trained using data set FC(M)O2 to classify pts as treatment-sensitive or treatment-insensitive using just 4 of 3,499 potential radiomic imaging features. Performance was calibrated/validated using ROC curves. Hazard ratios (HRs) and Cox regression models were used to evaluate association with overall survival (OS). Results: The signature used decrease in tumor heterogeneity plus boundary infiltration to successfully predict sensitivity to FC (FC(M)T2, AUC: 0.80; FC(M)S2, AUC: 0.72) but failed with non-cetuximab regimens (FC(M)O2, AUC: 0.59; FC(M)O2, AUC: 0.55). The radiomic signature outperformed existing biomarkers (KRAS mutational status and tumor shrinkage by RECIST 1.1) for sensitivity to cetuximab-based therapy and was strongly associated with OS in the cetuximab-containing settings FC(M)T2 (HR, 44.3, p = 0.0001) and FC(M)O2 (HR, 6.5, p = 0.001). Conclusions: This signature, derived from simple radiomic analysis of tumor imaging phenotype using only standard-of-care CT scans, appeared to be treatment-specific and was superior to all tested prognostic biomarkers. The signature provided early prediction of sensitivity and survival and could be used to guide treatment continuation decisions. Research Sponsor: Merck KgaA. Other Foundation.

250 Poster Session (Board #M6), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Systematic review of gastrointestinal cancer studies of concordance with expert opinion for a clinical decision support system (CDDSS). First Author: Yuli Edwin Arriaga, IBM Watson Health, Dallas, TX

Background: Watson for Oncology (WfO), a cognitive CDSS, provides therapeutic options to cancer-treating physicians. We reviewed the concordance of WfO therapeutic options in gastrointestinal cancers with experts’ treatment decisions. Methods: Systematic review to identify WfO concordance studies in gastrointestinal cancers, published from June 2015 to June 2019. Concordance was defined as agreement between WfO “Recommended” and “For Consideration” treatment options and decisions made by expert. Maximum concordance rates were calculated as an average, weighted by the number of patients in each study. Results: 2,407 patients were identified (Table). Overall treatment decision concordance was 67.2% (72/107). Concordance for hepatic, hepatocellular, and gastric cancers were 90.5% (SD 9.4%), 80.9% (SD 24.3%), 58.5%, and 47.5% (SD 33.9%), respectively. Concordance with WfO were significantly higher for rectal versus colon cancer (p = .0001), rectal versus gastric cancer (p < .0001) and for colon versus gastric cancer (p < .0001). Conclusions: Concordance between WfO and treatment decisions by experts for rectal and colon cancers were high. Concordance for HCC and gastric cancer were the lowest. A higher discordance in gastric cancer is likely related to disease-specific and management differences compared to United States practice. Variable concordance between expert clinical decisions and CDSS suggestions can be minimized by localization efforts. Research Sponsor: None.

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Changes in the proportion of patients presenting with early stage colon cancer over time among Medicaid expansion and non-expansion states.

First Author: Scarlett Hao, Brody School of Medicine at East Carolina University, Department of Surgery, Greenville, NC

Background: In 2010, the Affordable Care Act required insurance plans to cover preventive care screening, and Medicaid expansion provisions mandated participating states to increase Medicaid coverage of uninsured individuals. The aim of this study was to determine whether the proportion of patients diagnosed with early vs. late stage colon cancer (CC) at Commission on Cancer (CoC) facilities differed over time within states that expanded Medicaid in January 2014 (MES) vs. non-Medicaid expansion states (NMES).

Methods: A hospital-based cohort study of patients diagnosed with CC from 2006-2016 was performed using the National Cancer Database. Uninsured and Medicaid-insured patients in MES were compared with patients in NMES. Patients with Medicare, private, or government insurance were excluded. The observed proportions of patients with early (AJCC I-II) vs late (III-IV) stage within each cohort were compared over time. Propensity score adjusted analysis of early stage at presentation was determined among patients residing in MES and NMES.

Results: The study cohort included 10,289 patients in MES and 15,173 patients in NMES. Compared to MES, a greater proportion of patients in NMES were black (33.4% vs 24.0%), had a median income < $38,000 (39.7% vs 28.2%), and resided in a state with ≥ 25% of the population without a high school degree (37.4% vs 28.1%). The proportions of early stage CC in both cohorts in 2006 were similar. In NMES, this proportion remained constant over time until 2014 and declined by 0.8% per year after 2014. Within MES, the proportion of early stage CC increased by 0.6% per year before 2014 and 0.9% per year after 2014. By 2016, the absolute difference in the propensity adjusted proportion of early stage CC between cohorts was 8.8% (39.7% vs 30.9%, p < 0.001).

Conclusions: Following Medicaid expansion in 2014, the proportion of patients presenting to a CoC facility with early stage CC increased over time within MES and declined in NMES. Further investigation, including population-based research, is warranted to determine if enrollment in Medicaid improves access to colorectal cancer screening and leads to earlier stage at diagnosis. Research Sponsor: None.

Effect size as a tool to identify subpopulations with improved clinical outcomes in metastatic colorectal cancer.

First Author: Stephanie Leigh Fricke, University of Wisconsin School of Medicine and Public Health, Department of Medicine, Madison, WI

Background: ASCO defined meaningful trial endpoints in colorectal cancer (CRC) to include OS HR ≤ 0.67 (CIBs, JCO 2014). This measure is limited in identifying treatment benefit for subgroups from heterogeneous populations. Effect size (Glass’s Δ) calculates the absolute difference in median clinical outcomes normalized to the control group standard deviation. We hypothesize that durable effect sizes ≥ 2 would be useful in predicting which trials possess subgroup populations of clinical significance despite a HR > 0.67.

Methods: Prospective phase II-III trials in metastatic CRC from the ASCO Meeting Library (2016-2019) were cataloged by clinical outcomes of PFS and OS. Effect size was calculated from trials reporting confidence intervals and compared with absolute difference in clinical outcome, hazard ratio and therapeutic intervention. Trials with an indeterminate HR, yet effect size ≥ 2 were reviewed in subgroup analyses. Results: 385 abstracts were reviewed with 99 clinical analyses available for effect size calculation. Absolute differences in PFS correlated with effect size (R = 0.64) and was inversely proportional to HR (R = 0.63). The absolute difference in OS correlated with effect size (R = 0.69) and was inversely proportional to HR (R = 0.57). When stratified by clinically significant HR (defined ≥ 0.67), median effect size for PFS was 13.7 ± 13.3 (SD) which was significantly different from OS with median effect size 1.0 ± 3.8 (p < 0.001). Median effect size for OS when stratified by HR > 0.67 was 3.7 ± 2.5 which was significantly different when compared to endpoints with HR > 0.67 with median effect size 0.9 ± 1.4 (p < 0.003). Subgroup populations with survival benefit included combination checkpoint blockade durvalumab/tremelimumab vs supportive care with effect size 3.1 (HR 0.72; NCT02870920). First-line PFS benefit was predicted in KRAS wildtype liver-limited CRC treated with FOLFOX+dualtumab vs FOLFOX+bevacizumab with effect size of 3.2 (HR 0.80; NCT08366655). Conclusions: The effect size holds potential as a measure to delineate improved clinical outcomes from heterogeneous populations and could identify those trials for which further subgroup analysis should be explored. Research Sponsor: None.

Is mucinous histology a prognostic marker in early and advanced colorectal cancer?

First Author: Rosemary Habib, Westmead Hospital, Westmead, NSW, Australia

Background: In early and advanced colorectal cancer (CRC), there is limited data comparing the influence of mucinous (MAC) vs non-mucinous adenocarcinoma (NMAC) histology on clinical outcomes. We investigated the association of mucinous histology type and outcomes on CRC. We reviewed data from the hospital electronic medical records of patients with stage II, III and IV CRC referred to a tertiary centre in Western Sydney between 2009-2016 were examined and demographic and clinical information extracted. Key prognostic factors were modeled using log rank tests and proportional hazards (PH) regression methods in multivariate analyses.

Methods: Data on 6868 patients was extracted. Median age was 70 years (19 - 94). Median follow up was 38.4 months. 98 patients (12%) had MAC and no differences in stage were observed at presentation between MAC and NMAC (p = 0.16), MAC was associated with increased prevalence of microsatellite instability (36% vs 11% p < 0.01), high grade tumours (5% vs 18% p < 0.01), female gender (6% vs 45% p < 0.01) and right sided primary (65% vs 40% p < 0.01). In stage II/III, MAC had comparable relapse free survival (RFS) versus NMAC (median 79 vs 97 months; P = 0.2). However, in the adjuvant chemotherapy group, a poorer RFS was seen for MAC (62 vs 82 months, HR = 0.52, P = 0.03). In all patients with relapsed disease, MAC was more likely to be associated with peritoneal carcinomatosis (51% vs 26%; P < 0.01), and less likely to be associated with liver metastases (45% vs 70%, P = 0.01) than NMAC. PH analysis of the MAC cohort revealed poorer RFS for LVI (HR 2.85; p = 0.03), T stage (HR 3.15, p = 0.01) and adjuvant chemotherapy (HR 5.49, p < 0.01). On multivariate analysis, T4 stage remained significant for poorer RFS. No differences were seen in OS in early stage CRC between MAC and NMAC. However, in right sided MAC had poorer OS (Right color: HR 6.66 P = 0.023)(Female: HR 4.90, P = 0.03). Conclusions: MAC is associated with poorer RFS in early stage CRC irrespective of sidedness, and with poorer OS in right sided CRC. Given the higher prevalence of relevant chemotherapy, novel adjuvant agents should be considered for early MAC CRC. In the palliative setting, novel therapies and clinical trials are required for patients with MAC, particularly with right sided primaries. Research Sponsor: None.

Bowel anastomosis before or after HIPEC: A prospective comparative study in patients undergoing CRS+HIPEC for peritoneal surface malignancy at a tertiary cancer center in India.

First Author: S.P. Somashekhar, Manipal Comprehensive Cancer Center, Bangalore, India

Background: To do bowel anastomosis before or after HIPEC has been debated since the time heat is being used for intraperitoneal chemotherapy after cytoreductive surgery. We report our experience of performing a bowel anastomosis before and after HIPEC.

Methods: All patients diagnosed with peritoneal surface malignancy eligible for CRS+ HIPEC as per institution protocol had bowel restoration being performed with stapler & second layer taken. Our institution has two teams, of which one performs anastomosis before and one after HIPEC. All the data was entered prospectively and the respective time of heat was being analyzed to see the effect of heat on anastomosis. Results: 220 patients underwent CRS+ HIPEC of which organ of origin was colorectal 39%, stomach 20%, mesothelioma 11%, ovary 20% and others 10%. Upfront cases showed 36% cases being analyzed to see the effect of heat on anastomosis.

Conclusions: We conclude that anastomotic integrity, leak rates and leak rates. Methods: All patients diagnosed with peritoneal surface malignancy eligible for CRS+ HIPEC as per institution protocol had bowel restoration being performed with stapler & second layer taken. Our institution has two teams, of which one performs anastomosis before and one after HIPEC. All the data was entered prospectively and the respective time of heat was being analyzed to see the effect of heat on anastomosis.

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An investigation of the relationship between tumor location and survival following colon cancer resection. First Author: Katrina Knight, University of Glasgow Academic Unit of Surgery, Glasgow, United Kingdom.

Background: Both tumour location and systemic inflammation (SI) have been related to survival in patients undergoing curative surgery for colon cancer. Recently, right colon cancer (RCC) has been associated with pre-existing cardiovascular disease (CVD). Comorbidity scores such as the Lee Cardiac Risk Index (LCRI) capture symptomatic disease only. Imaging-based assessment of vascular calcification can be used to identify subclinical CVD. We explored the relationship between tumour location, systemic inflammation, cardiac comorbidity and survival in patients undergoing CRC resection.

Methods: Patients were identified from a prospective cancer database. Clinicopathological characteristics and survival data were abstracted. Aortic calcification (AC) was quantified visually on staging CT images. SI was measured using the modified Glasgow Prognostic Score (mGPS).

Results: Of 418 patients, most were female (221, 53%), over 65 (282, 67%), ASA grade II or less (66%) with RCC (230, 55%) and TNM stage III disease (320, 77%). Compared with LCC, RCC was associated with increasing age (59% vs 41%, p = 0.039), greater AC (61% vs 39%, p = 0.013) but not SI (61% vs 39%, p = 0.139).

We observed significant differences between LCC with respect to ASA, smoking status or LCRI. Multivariable analysis revealed TNM stage (HR 3.55 (95%CI 1.51-8.39) p = 0.004) and degree of AC (HR 1.77 (1.04-3.00) p = 0.034) were associated with cancer-specific survival (CSS) in RCC while in LCC, only TNM stage was related to CSS (HR 2.30 (0.99-5.30) p = 0.05).

Conclusions: AC is associated with RCC and confers an inferior prognosis, independent of stage. Investigation of underlying mechanisms is required, but impaired perfusion may limit mucosal function, potentiating the effect of carcinogens in the right colon.

Research Sponsor: None.

Stage-specific conditional survival among young versus older adults with colorectal cancer in the United States, 2004-2010. First Author: Nina Niu Sanford, The University of Texas Southwestern Medical Center, Dallas, TX.

Background: Conditional survival (CS) is a relevant prognostic measure for cancer survivors and physicians and may be particularly important for young adult patients with CRC (colorectal cancer), whose incidence is rising. We sought to compare CS among young versus older adult patients with CRC.

Methods: Patients diagnosed with colon or rectal adenocarcinoma between 2004-2010 were identified from the Surveillance, Epidemiology and End Results (SEER) registry. Overall survival (OS) and cancer-specific survival (CSS) were estimated, along with smoothed yearly hazards of death due to CRC, other causes and any cause, stratified by age at diagnosis (< 50 vs. >50 years). Stage-specific conditional 5-year OS and 5-year CSS given that patients had already survived 1, 2, 3 or 4 years after diagnosis was calculated, also stratified by age. Conclusions: Among 161,859 patients with median follow-up of 54 months, 35.41 (21.9%) were aged < 50 years.

Comparing younger and older adult patients, CSS was superior among younger adults as compared to older adult patients (p < 0.001). For older adults with rectal cancer, hazards of death due to non-cancer causes exceeded that of rectal and colon cancer approximately 6 and 4.5 years after diagnosis, respectively. Among younger adults, hazards of death from cancer remained greater than death from other causes throughout the entire study interval. Patients experienced improved conditional survival over time with greater improvement seen for more advanced stages. However, young adults had less CS improvement over time than older adults. For example, the 5-year overall and CSS for Stage IV colon cancer improved from 5.4% to 32.4% (OS) and 15.1% to 78.5% (CSS) to 5 years after diagnosis for older adults. In contrast, for younger adults, the 5-year overall and CSS for Stage IV colon cancer improved from 3.6% to 75% (OS) and 19.3% to 68.4% (CSS). Conclusion: Prognosis for CRC improves over time for all patients, although the increase in survival appears to be less for younger than older adults. Up to 10 years after diagnosis, the primary cause of death in younger adults with CRC remains their incident cancer. Research Sponsor: None.

Change of clinical features and outcomes of adolescents and young adults (AYA) with colorectal cancer over time: Pooled analysis of 26,768 patients in the National Cancer Database (NCDB). First Author: Sally Jeanne Trufan, Levine Cancer Institute, Atrium Health, Charlotte, NC.

Background: The incidence of colorectal cancer (CRC) in younger patients (AYA) is increasing. The underlying etiology is unknown, and it is critical to understand the disease biology and clinical features are changing over time.

Methods: A retrospective study of pts data in the NCDB was performed to compare the clinicopathological features and outcomes of AYA with CRC over a 12-year period. Pts diagnosis period was dichotomized into older (2004 - 2009) and newer (2010 - 2015) eras. Uni- and multi-variable chi-square, logistic regression, and survival analyses were used for comparisons. Survival differences were assessed using Kaplan-Meier curves. Results: In total, 26,768 AYA (8.40-yrs) with CRC were identified and included in the analysis: 45.8% (n = 12,668) from the older and 54.2% (n = 14,500) from the newer era. There were no differences between the 2 groups in gender distribution or levels of income and education. However, in the newer vs. older era, there was a greater proportion of non-white, non-black pts (7.2% vs. 6%; p = 0.0005) and pts diagnosed between the ages of 15-19 yrs vs. 15-19 ECOG p < .0001. Pts in the newer era tended to have more comorbidities (8.6 vs 7.5%; p = 0.0012), left-sided tumors (77.5% vs. 76.1%; p = 0.04), and well-differentiated histology (12.0% vs. 8.3%; p < 0.0001). Newer era pts also had lower rates of metastatic disease at presentation (15.3% vs. 18.2%; p < 0.001%) and nodal involvement (54.9 vs. 58.4%; p < 0.001%). Median OS of pts with stage IV disease appears to have improved over time (241 at 22.5 mos; p = 0.014). After controlling for age, race, primary tumor site and grade, presence of comorbidities, and health insurance status, older era pts with stage IV CRC were at a 15.1% greater risk of all-cause death by year 5 compared to newer era pts (HR = 1.15 (1.07-1.24, p = 0.0001). Conclusions: Our data suggest that AYA with CRC in more recent years trend to present at a younger age and have a lower rate of metastatic disease. They also have improved survival. Further analysis of AYA disease etiology and biology are warranted. Continued efforts to increase awareness, promote early detection, and improve treatment options are essential. Research Sponsor: None.

An assessment of dose intensity of the TNT approach on outcomes in locally advanced rectal cancer. First Author: Ashley Elizabeth Glode, University of Colorado, Aurora, CO.

Background: Patients with clinical stage II or III locally advanced rectal cancer may be treated with the total neoadjuvant therapy (TNT) approach; chemotherapy with 4 mths of FOLFOX followed by chemoradiation (chemo/XRT) with capecitabine for 5 wks administered before surgery. We hypothesized that full dose intensity is not necessary for treatment benefit.

Methods: A retrospective chart review was conducted on patients with newly diagnosed rectal cancer recommended to receive TNT by multidisciplinary (multi-disc) colorectal cancer tumor board at the University of Colorado Cancer Center (UCC). The primary objective was to evaluate dose intensity of TNT and its impact on response assessed by biopsy and/or imaging (MRI). Results: Between January 31, 2016 and January 31, 2019, 80 patients were recommended the TNT approach for cancer management by the multidisciplinary team. Of those, 48 completed their neoadjuvant treatment at UCC and were included in the analysis. The average age was 55 years (range 23-80) and 61% were male. Thirty-one were between the ages of 15-19 yrs and 18 ECOG 1. Overall responses were 80% complete response (CR, n = 21), 15% near complete response (nCR, n = 7), 35% partial response (PR, n = 17), and 6% no response (NR, n = 3). See Table for responses seen by dose intensity for chemotherapy. Two patients did not receive their full planned XRT course, and 9 patients had their capcitabine doses held/decreased during chemoradiation. Conclusions: This single center retrospective analysis of patients receiving the TNT approach for rectal cancer provides data supporting that achieving full dose intensity is not necessary to achieve treatment benefit. Research Sponsor: None.
A randomized phase III study of mFOLFOX6/bevacizumab combination chemotherapy with or without atezolizumab or atezolizumab monotherapy in patients with metastatic colorectal cancer (mCRC): ComScore trial

**Background:** Deficient DNA mismatch repair (dMMR) colorectal cancer (CRC) is highly immunogenic. Preclinical data showed synergistic interactions between FOLFOX, anti-EGFR and programmed cell death 1 (PD-1) pathway blockade. Prior phase I study of mFOLFOX6/bevacizumab (bev) + atezol-
zumab (atezo) was well tolerated and enhanced intratumoral infiltration of CD8+ T cells. We hypothesize that the dMMR subset of CRC may be effectively targeted with combination of PD-1 pathway blockade and mFOLFOX6/bev.

**Methods:** This is a prospective randomized phase III open-label trial. Pts (N=347) with mCRC dMMR will be randomized to three trial arms (T1): mFOLFOX6/bev; atezolizumab monotherapy; or mFOLFOX6/bev + atezo. Stratifica-
tion factors include BRAFV600E status, metastatic site, and prior adjuvant CRC therapy. Primary endpoint is progression-free survival (PFS) assessed by study investigator of mFOLFOX6/bev/atezo and atezol monotherapy com-
pared to mFOLFOX6/bev. Secondary endpoints include OS, objective response rate, safety profile, disease control rate, duration of response, and PFS by retrospective central review. Health-related quality of life is an exploratory objective. Archived tumor tissue and blood samples will be collected for correlative studies. Key inclusion criteria are: mCRC without prior chemo-
therapy for advanced disease; dMMR tumor determined by local CLIA-certified IHC assay (MLH1/MSH2/MSH6/PM2); availability of archived tumor tissue for central confirmation of dMMR status; and measurable disease per RECIST. Activated 11-7-17. As of 9-11-19, enrollment continues for 44/347 pts enrolled.

Clinical trial: NCT02997228. Support:U01CA180868, -180822, -180888, -180819, U24CA199867, U24CA196067; Genentech, Inc. Clinical trial inform-

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**TPS259**

Trials in Progress Poster Session (Board #M15), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

A phase II study of cabozantinib plus concomitant radiation therapy followed by durvalumab (MED/4736) as preoperative treatment in rectal cancer (PANDORA).

**Background:** The standard treatment for cT3-4 N0-1 rectal cancer is pre-
operative chemoradiotherapy (CT/RT). The combination of cabozan-
tinib plus long course radiotherapy (RT) is standard therapy in this setting. Pathologic Complete remission (pCR) can be considered as surrogates end point of efficacy of treatment in terms of disease free survival (DFS). Clinical complete remission (cCR) is an important end point for “wait and see” strategy. In the PACIFIC trial in non-small cell lung cancer the patients were treated with durvalumab maintenance after CT/RT with advantage in progression free survival. Preclinical data points heavily toward a strong synergy between RT and immune treatments. Furthermore, a systemic effect of RT is possible when enhanced by targeted immune treatments.**Methods:** This is a prospective phase II, open label, single arm, multicentre study to evaluate the activity of an innovative sequence in operable rectal cancer: standard concomitant CT/ RT therapy with 825 mg/m2 twice daily cabozantinib every day and 5040 cGy radiotherapy for 5 days per week followed by 1800 mg durvalumab for 3 administration. After 9-10 weeks from neoadjuvant therapy will be performed re-staging with CT and MRI scan. Surgery will be performed at week 10-12 from the end of CT/RT. Primary Objective: pCR rate, defined as a TRG 3-4 according to DWG/ROR criteria. Secondary Objective: Clinical objectives of treatment with durvalumab; cCR rate after durvalumab treatment before surgery and DFS. cCR will be evaluated with clinical, endoscopic and radio-
logical assessment to look for evidence of residual disease. DFS will be evaluated during the duration of study 5 years. Safety and efficacy. This is a translational analysis of tumor biomarkers will be performed on the endos-
copy biopsy done at the diagnosis and on the biopsy performed after the CT/ RT prior to treatment with durvalumab. We hypothesize that the addition of durvalumab after standard CT/RT for the treatment of locally advanced rectal cancer may improve the pathological response rate and we have planned to enlist 60 patients in 7 centers with an enrollment period of 12 months, already underway. Clinical trial information: NCT04083365. Research Sponsor: ASTRA ZENECA.

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**TPS260**

Trials in Progress Poster Session (Board #M16), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

A randomized phase III study of mFOLFOX6/bevacizumab combination chemotherapy with or without atezolizumab or atezolizumab monotherapy in patients with metastatic colorectal cancer (mCRC); Colorectal Cancer Metastatic dMMR Immuno-Therapy (COMMIT) study (NRG-GI004/SWOG-S1610).

**Background:** Deficient DNA mismatch repair (dMMR) colorectal cancer (CRC) is highly immunogenic. Preclinical data showed synergistic interactions between FOLFOX, anti-EGFR and programmed cell death 1 (PD-1) pathway blockade. Prior phase I study of mFOLFOX6/bevacizumab (bev) + atezol-
zumab (atezo) was well tolerated and enhanced intratumoral infiltration of CD8+ T cells. We hypothesize that the dMMR subset of CRC may be effectively targeted with combination of PD-1 pathway blockade and mFOLFOX6/bev.

**Methods:** This is a prospective randomized phase III open-label trial. Pts (N=347) with mCRC dMMR will be randomized to three trial arms (T1): mFOLFOX6/bev; atezolizumab monotherapy; or mFOLFOX6/bev + atezo. Stratifica-
tion factors include BRAFV600E status, metastatic site, and prior adjuvant CRC therapy. Primary endpoint is progression-free survival (PFS) assessed by study investigator of mFOLFOX6/bev/atezo and atezol monotherapy com-
pared to mFOLFOX6/bev. Secondary endpoints include OS, objective response rate, safety profile, disease control rate, duration of response, and PFS by retrospective central review. Health-related quality of life is an exploratory objective. Archived tumor tissue and blood samples will be collected for correlative studies. Key inclusion criteria are: mCRC without prior chemo-
therapy for advanced disease; dMMR tumor determined by local CLIA-certified IHC assay (MLH1/MSH2/MSH6/PM2); availability of archived tumor tissue for central confirmation of dMMR status; and measurable disease per RECIST. Activated 11-7-17. As of 9-11-19, enrollment continues for 44/347 pts enrolled.

Clinical trial: NCT02997228. Support:U01CA180868, -180822, -180888, -180819, U24CA199867, U24CA196067; Genentech, Inc. Clinical trial inform-

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**TPS262**

Trials in Progress Poster Session (Board #M18), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

A phase II study of pembrolizumab in combination with premetrexed + oxaliplatin in patients (pts) with chemo-refractory meta-
static colorectal cancer (mCRC).

**Background:** The majority of mCRC pts are microsatellite stable (MSS), have poor intratumoral CD8+ T cell infiltration, and no clinical response to im-
munotherapy checkpoint inhibitors. Preclinical studies suggest that chemo-
therapy, in combination with anti-PD-1, in MSS colorectal cancer (mCRC), the combination of pembrolizumab (PemB), premetrexed (PemT), + carboplatin demonstrated synergistic activity. This study will combine PemB with PemT, then that combination + oxaliplatin (Ox). The rationale for addition of Ox to PemT is that enhanced immunogenic cell death may induce CD8+ T cell in-
filtration into CRC tumors and model the mechanism of cytotoxicity seen in NSCLC. Thus, the combination of PemB+ PemT + Ox may induce synergistic anti-tumor immune activity.**Methods:** This multi-center phase Ib trial is act-
ively enrolling pts with incurable mCRC with prior treatment for mCRC in-
cluding fluoropyrimidines, oxaliplatin, and irinotecan-based chemotherapy, and if RAS wild-type, anti-EGFR therapy. Measurable disease by imaging (RECIST 1.1) is required. Standard ineligibility includes active infections, sys-
temic steroid use, or other conditions contraindicating immunotherapy. Co-
hort 1 will receive PemB + PemT; Cohort 2 will receive PemB + PemT + dose-
escalated Ox. Imaging will be performed every 6 wks. The primary aim of Cohort 1 is to evaluate for safety and efficacy using doses of PemB and PemT that have been studied in NSCLC. The primary aim of Cohort 2 is to evaluate for safety, tolerability, and efficacy of PemB in combination with PemT + Ox. The RP2D of the 3-drug combination will be at the MTD taking into account toxicity and if RAS wild-type, anti-EGFR therapy. Measurable disease by imaging (RECIST 1.1) is required. Standard ineligibility includes active infections, sys-
temic steroid use, or other conditions contraindicating immunotherapy. Co-
hort 1 will receive PemB + PemT; Cohort 2 will receive PemB + PemT + dose-
éscalated Ox. Imaging will be performed every 6 wks. The primary aim of Cohort 1 is to evaluate for safety and efficacy using doses of PemB and PemT that have been studied in NSCLC. The primary aim of Cohort 2 is to evaluate for safety, tolerability, and efficacy of PemB in combination with PemT + Ox. The RP2D of the 3-drug combination will be at the MTD taking into account toxicity profiles of study therapy agents. Secondary aims: to evaluate the clinical benefit rate of the doublet and triplet combinations in pts with chemo-
refractory MSS mCRC and to estimate progression-free survival and overall survival in pts with MSS mCRC treated with these combinations. The cohorts will be analyzed separately with descriptive intent only. Maximum enrollment is 60 pts. Research Sponsor: Merck & Co., Eli Lilly and Company, Other Foundation.

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A phase III randomized controlled trial comparing surgery plus adjuvant chemotherapy with or without preoperative chemoradiotherapy for locally recurrent rectal cancer: A Japan Clinical Oncology Group study (JCOG1801). First Author: Yuichi Tsukada, Department of Colorectal Surgery, National Cancer Center East, Kashiiwa, Japan

Background: Local recurrence is one of the most common forms of recurrence after curative resection for primary rectal cancer. Surgical resection is recommended for locally recurrent rectal cancer (LRRC) to achieve cure if the tumor is judged as resectable with negative margins. However, a high local recurrence risk after surgery is a major problem due to the difficulty of re-resection and the serious symptoms, such as pain and bleeding, resulting from re-recurrence. Preoperative chemoradiotherapy (preCRT) is expected to improve local control after surgical radical surgery for radiation naive LRRC; however, high frequency of surgical complications after preCRT cannot be ignored. Due to the refractory nature and rarity of LRRC, the true impact of preCRT on oncological and surgical outcomes has not been clarified by clinical trials. The purpose of this study is to confirm the superiority of preCRT followed by surgery plus adjuvant chemotherapy over surgery plus adjuvant chemoradiotherapy alone, in terms of local recurrence-free survival for resectable LRRC.

Methods: Eligibility criteria include resectable LRRC without distant metastasis, no prior pelvic irradiation, no prior surgery for LRRC, aged 20-80 years, and sufficient organ function. Eligible patients are randomized into the surgery and adjuvant chemoradiotherapy arm (preCRT followed by surgery and adjuvant chemotherapy arm B). PreCRT consists of the standard dose of capecitabine and radiotherapy (50.4Gy). Adjuvant chemotherapy consists of mFOLFOX6, CAPOX, capcitabine, or 5FU+l-LV. The primary endpoint is local recurrence-free survival (LRFS), and the secondary endpoints include overall survival, relapse-free survival, R0 resection, incidence of adverse events, and quality of life after surgery. The 3-year LRFS of arm A is assumed to be 60% with a 13% increase expected in arm B. The sample size was calculated as 106 (53 per arm) with a one-sided alpha (A) of 0.05, power of 70%, and accrual period of 6 years. This trial was initiated on 19 August 2019. Clinical trial information: jRCTs0319100076. Research Sponsor: AMED (Japan Agency for Medical Research and Development).

TPS256 - Trials in Progress Poster Session (Board #M19), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

A phase IIb/I study of onvansertib (PCM-075) in combination with FOLFIRI and bevacizumab for second-line treatment of metastatic colorectal cancer (mCRC) in patients with a KRAS mutation. First Author: Heinz-Josef Lenz, University of Southern California, Los Angeles, CA

Background: FOLFOX (5-flourouracil, leucovorin, oxaliplatin) and FOLFIRI (fluorouracil, leucovorin, irinotecan) in combination with targeted agents are standard of care for mCRC patients with response rates >50% in first line. In the second line setting, efficacy of chemotherapy and targeted agents are much lower with response rates of 4% for FOLFOX + bevacizumab and treatment options are limited in particular for the 50% of patients harboring a KRAS mutation. Polo-like kinase 1 (PLK1) is a serine/threonine kinase that regulates cell cycle progression by activating downstream effectors like Plk1 and Cdc25. PLK1 is a potential therapeutic target and dual PLK1 inhibition has shown effectiveness in the treatment of tumors with a PLK1 amplification. Therefore, we aimed to investigate the efficacy and safety of a novel oral selective PLK1 inhibitor in combination with FOLFIRI in patients with mCRC with a KRAS mutation. This study is an open-label, single-arm, phase IIb/I study to assess the safety and preliminary efficacy of onvansertib in combination with FOLFIRI and bevacizumab in combination in patients with mCRC who have a KRAS mutation. Patients with mCRC and a KRAS mutation will be enrolled. Patients will be treated with onvansertib at a dose of 60 mg orally once daily, FOLFIRI on day 1 of each 21-day cycle, and bevacizumab at a dose of 5 mg/kg IV on day 1 of each 21-day cycle. The primary endpoint is the objective response rate of the combination onvansertib, FOLFIRI, and bevacizumab. The secondary endpoints include progression-free survival and overall survival. Clinical trial information: NCT03829410. Research Sponsor: Trovagene.

TPS256 - Trials in Progress Poster Session (Board #M20), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

A phase III study of durvalumab following neoadjuvant chemotherapy in stage I/II-IV rectal cancer. First Author: Thomas J. George, NSABP Foundation, Inc., and The University of Florida Health Cancer Center, Gainesville, FL

Background: Clinical improvements for locally advanced rectal cancer have been relatively static over the past few decades. While immunotherapy showed no benefit in microsatellite stable (MSS) colorectal cancer, preclinical models suggest that radiotherapy (RT) can enhance neoantigen presentation, modulate the microenvironment, and improve the likelihood of anti-tumor activity with a checkpoint inhibitor. Using a window of opportunity from this prospective phase II trial will determine the safety and activity of this approach with the anti-PD-L1 agent durvalumab (MED14736). Methods: This multi-center phase II trial is currently enrolling patients (pts) with rectal cancer who are undergoing standard NCCN guideline-compliant neoadjuvant chemoradiotherapy (CRT). Eligibility includes pts with MSS stage II-IV rectal cancer with adequate organ function and pre-treatment immunotherapy use unsafe. Treatment includes durvalumab (750mg IV infusion once every 2 wks) for 4 total doses beginning within 3-7 days after CRT completion. Surgery must be within 8-12 wks of the final CRT dose. Primary endpoint is investigator-assessed disease control rate by BICR and INV, OS, time to and duration of response. Clinical trial information: NCT03920047. Research Sponsor: AstraZeneca-Medimmune, NSABP Foundation. Clinical trial information: NCT03920047. Research Sponsor: AstraZeneca-Medimmune, Other Foundation.

TPS256 - Trials in Progress Poster Session (Board #M22), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

A phase III study of nivolumab (NIVO), NIVO + ipilimumab (IPI), or chemotherapy (CT) for microsatellite instability-high (MSI-H)/mismatch repair-deficient (dMMR) metastatic colorectal cancer (mCRC): Checkmate BHW. First Author: Sandzahr Abdullaie, Bristol Myers-Squibb, Lawrenceville, NJ

Background: Patients (pts) with MSI-H/dMMR mCRC treated with CT have poorer outcomes than pts with microsatellite stable/MMR proficient mCRC. NIVO (anti-programmed death [PD]-1) and IPI (anti-cytotoxic T lymphocyte antigen-4 [CTLA-4]) are immune checkpoint inhibitors that act synergistically to induce cell cycle arrest and apoptosis. Onvansertib is an oral, highly selective PLK1 inhibitor that demonstrated single agent activity and synergistic activity with irinotecan in preclinical CRC models. Additionally, KRAS mutated cells showed higher sensitivity to onvansertib than isogenic KRAS wild-type cells. PLK1 inhibition is a potential target in KRAS-mutated mCRC and onvansertib + FOLFIRI may provide a new second-line treatment option. Methods: The primary objective of this single-arm Phase Ib/2 study (NCT03829410) is to assess the safety and preliminary efficacy of onvansertib in combination with FOLFIRI and bevacizumab in the second line setting for KRAS-mutated mCRC patients. The phase Ib will determine the MTD or RP2D using a traditional 3+3 design, with onvansertib initial dose at 12 mg/m^2. The phase 2 will enroll 26 patients at the RP2D to further assess the safety of the combination and to evaluate preliminary anti-tumor activity measured by objective response rate (ORR, RECIST v1.1). Based on a one-sided sample log-rank test with 10% Type I error, there will be at least 90% power to detect an improvement in ORR from 5% to 20% with 26 patients. Exploratory studies include quantification of KRAS circulating tumor DNA (ctDNA) and genomic studies of circulating tumor cells and ctDNA to determine altered pathways associated with patient response. Clinical trial information: NCT03829410. Research Sponsor: Trovagene.

TPS256 - Trials in Progress Poster Session (Board #M22), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

A phase II study of durvalumab following neoadjuvant chemotherapy in stage I/II-IV rectal cancer. First Author: Author: Thomas J. George, NSABP Foundation, Inc., and The University of Florida Health Cancer Center, Gainesville, FL

Background: Clinical improvements for locally advanced rectal cancer have been relatively static over the past few decades. While immunotherapy showed no benefit in microsatellite stable (MSS) colorectal cancer, preclinical models suggest that radiotherapy (RT) can enhance neoantigen presentation, modulate the microenvironment, and improve the likelihood of anti-tumor activity with a checkpoint inhibitor. Using a window of opportunity from this prospective phase II trial will determine the safety and activity of this approach with the anti-PD-L1 agent durvalumab (MED14736). Methods: This multi-center phase II trial is currently enrolling patients (pts) with rectal cancer who are undergoing standard NCCN guideline-compliant neoadjuvant chemoradiotherapy (CRT). Eligibility includes pts with MSS stage II-IV rectal cancer with adequate organ function and pre-treatment immunotherapy use unsafe. Treatment includes durvalumab (750mg IV infusion once every 2 wks) for 4 total doses beginning within 3-7 days after CRT completion. Surgery must be within 8-12 wks of the final CRT dose. Primary endpoint is investigator-assessed disease control rate by BICR and INV, OS, time to and duration of response. Clinical trial information: NCT03920047. Research Sponsor: AstraZeneca-Medimmune, NSABP Foundation. Clinical trial information: NCT03920047. Research Sponsor: AstraZeneca-Medimmune, Other Foundation.

Visit gicasym.org to search for abstracts of the full list of abstract authors and their disclosure information.
The phase III AGENT trial (NCT03750786) is a randomized, multicenter, parallel-group study comparing the efficacy of arfolitixorin versus leucovorin in mCRC patients treated with first-line 5FU, oxaliplatin, and bevacizumab. Patients are randomized (1:1) to the investigational arm (arfolitixorin + 5FU + oxaliplatin [ARFOX] + bevacizumab) or the comparator arm (leucovorin + 5FU + oxaliplatin [FOLFIRI] + bevacizumab), and treated until disease progression based on RECIST 1.1 criteria. Recruitment is ongoing and aims to randomize 440 patients in 18 months. Eligibility criteria include non-resectable mCRC; eligibility for 5FU, oxaliplatin, and bevacizumab therapy; ECOG PS 0 or 1. The study will be conducted across approximately 100 sites in Australia, Austria, Canada, France, Germany, Greece, Japan, Spain, Sweden, and USA. The primary endpoint is overall survival (OS) and secondary endpoints are progression-free survival and duration of response. No additional secondary endpoints include overall survival, quality of life, safety, and tolerability, and number of patients undergoing curative resection will be evaluated. Five key secondary endpoints are progression-free survival and duration of response. A broad array of genes will be analyzed, including TP53, deletion of chromosome 17 (17p), or poly-allelic loss of chromosome 16p.
**TPS271**
Trials in Progress Poster Session (Board #N5), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

**MONARC**: A randomized phase II study of panitumumab monotherapy and panitumumab (pan) plus 5 Fluorouracil (FU) as first-line therapy for RAS and BRAF wild type metastatic colorectal cancer (mCRC). An AGITG clinical trial. *First Author: Niall C. Tebbutt, Olivia Newton-John Cancer and Wellness Centre, Victoria, Australia*

**Background**: Pan added to combination chemotherapy is established first-line therapy for RAS and BRAF wild type mCRC. Elderly patients are not well represented in clinical trials and may be more suited to treatment protocols with lower toxicity risks; FU plus bevacizumab (bev) is commonly used. Treatment related efficacy, toxicity, impact on quality of life and other outcomes of pan based regimens in an elderly population have not been well studied. **Methods**: A prospective non-comparative randomized phase 2 study. Australian Clinical Trials Registry Number: ACTRN12618000323244. Main inclusion criteria include: Un-treated patients aged 70 years or older; RAS and BRAF wild type; ECOG performance 0-2. Randomisation 1:1, stratified by primary tumour side, performance status, number of metastatic sites; to pan 6mg/kg 2 weekly or panitumumab plus FU 400 mg/m² bolus; leucovorin 200mg/m²; FU 2400mg/m² 48 hour infusion 2 weekly. Primary endpoint is 6 month progression-free survival (PFS). Sample size is 80 patients based on expected 6-month PFS rate of 73% with FU and bev. Using the method of Metha-Cain, if 24 or more patients are progression free at 6 months, the one-sided 95% confidence interval includes 73% and we declare similar activity. Secondary endpoints include overall survival, overall health status and QoL, and time on treatment, a comprehensive measure of treatment benefit based on radiology, clinical progression, toxicity and patient reflection of the impact of treatment on their daily lives. Patients undergo a comprehensive health assessment at baseline and limited health assessment at 4 months. Physical activity trackers are worn for 2 weeks at treatment commencement and again at week 16. Tumour size and blood samples (at baseline, cycle 3 day 1 and at 24 weeks) will be collected for translational research. First site opened in June 2018. Twelve patients have been recruited to date from 9 sites in Australasia. Eighteen sites were open as of September 2019. Clinical trial information: 12618000233224. Research Sponsor: AMGEN, Other Foundation.

**TPS272**
Trials in Progress Poster Session (Board #N6), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

A phase II study to evaluate safety and efficacy of neutaxabant pembro- lizumab and radiotherapy in localized MSS rectal cancer. *First Author: Thibaud Kossler, Geneva University Hospitals, Geneva, Switzerland*

**Background**: Locally advanced rectal cancer remains a clinical challenge with few improvements noted over the past few decades. Although immunotherapy has no current clinical role in microsatellite stable (MSS) colorectal cancer, preclinical models suggest that radiotherapy (RT) can enhance neoantigen presentation, modulate the microenvironment, and improve the likelihood of anti-tumor activity with checkpoint inhibitors use. This prospective phase II trial will test that hypothesis in addition to confirming safety of this approach using a “window-of-opportunity” study design with the anti-PD-1 agent Pembrolizumab. **Methods**: This monocentric phase II trial, will enrol patients (pts) with rectal cancer who are undergoing neoadjuvant short course RT (scRT) (25 Gy in 5 fractions). According to the standard of care. Eligible includes pts with MSS stage II/III rectal cancer with adequate organ function and availability of pre-treatment tumor, who are undergoing scRT with intention to proceed to surgical resection. Standard ineligibility criteria include active infections, systemic steroid use, or other conditions making immunotherapy use unsafe. Treatment includes 4 doses of Pembrolizumab (200mg IV, once every 3 wks), the first dose being given before the first scRT dose. Surgery will be performed within 12-16 weeks of the final scRT dose. Primary endpoint is tumor regression grade (TRG) using the Mandard regression grade score targeting a 30% pathological complete response (pCR) compared to 10% in historical controls. Secondary endpoints include OS, DFS, toxicity, local and distant relapse-free survival, proficient surgical margin, quality of life, and exploratory assessments of tumor infiltrating lymphocytes, profiling of circulating immune cell populations, and molecular predictors of response. A safety stopping rule is planned based on Wold’s sequential probability ratio test for the occurrence of the safety outcome. Enrollment target is 25 pts. Support: MSD. Clinical trial information: NCT04097555. Research Sponsor: This trial is supported by Merck Investigator Studies Program.

**TPS273**
Trials in Progress Poster Session (Board #N7), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Circulating tumor DNA-based decision for adjuvant treatment in colon cancer stage II evaluation: (CIRCULATE-trial) AIO-KRK-0217. *First Author: Gunnar Folprecht, University Hospital Carl Gustav Carus, Dresden, Germany*

**Background**: The benefit of adjuvant chemotherapy in stage II colon cancer is unclear, and clear clinical or molecular marker are not available for decision making. Recently, postoperative circulating tumour (ctDNA) has been demonstrated to be prognostic in colorectal cancer and other tumours. **Methods**: For the CIRCULATE trial we enrol patients (pts) with colon cancer stage II in Germany (AIO), Austria (ABCSG) and Switzerland (SAKK). Microsatellite stable (MSS) pts are screened after resection of the primary by analysing the tumour specimen for microsatellite instability and measuring patient specific mutations in the postoperative plasma sample. MSI-H pts are excluded from the trial. ctDNA positive (ctDNApos) pts are randomised (2:1) to receive adjuvant capecitabine based chemotherapy or no chemotherapy. Oxaliplatin can be added according to investigator’s choice. ctDNA negative (ctDNAneg) pts are randomised (1:4) to be followed-up within the study or to receive standard follow-up outside the trial. Pts in the follow-up group and their investigators are blinded for the ctDNA result. The primary aim is to compare the disease free survival (DFS) in ctDNApos pts randomised to chemotherapy or to follow-up. Secondary aims are to compare the overall survival (OS) in ctDNApos pts with or without chemo, to compare the DFS and OS in ctDNApos vs. ctDNAneg follow-up pts, to describe the DFS and OS in ctDNApos pts, to describe the location of recurrences/metastases according ctDNA status, the ctDNA clearance rate and time to ctDNA negativity during adjuvant chemotherapy, further translational endpoints, and safety. To demonstrate a treatment effect in the ctDNA group with a hazard ratio of 0.617 (3 year DFS rate of 42.5% vs. 25%), 231 ctDNApos will be randomised (approx. 230 pts in total) from 2019 - 2022. Clinical trial information: NCT04089631. Research Sponsor: German Ministry of Education and Research (BMBF).

**TPS274**
Trials in Progress Poster Session (Board #N8), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

NuTide: 302—A Phase Ib study of the ProTide NUC-3373 in combination with standard therapies in advanced colorectal cancer. *First Author: Kristen Keon Coomber, Vanderbilt University Medical Center, Nashville, TN*

**Background**: Although 5-FlU-based regimens such as FOLFOX and FOLFIRI remain the cornerstone of treatment for patients (pts) with colorectal cancer (CRC), their clinical utility is limited by resistance mechanisms and toxicity. Activity of 5-FlU is dependent on conversion to deoxyuridine monophosphate (dUMP), a rate-limiting step in DNA synthesis and cell survival. However, due to multiple limitations including: therapeutic drug concentration and catalysis of dUMP to deoxythymidine monophosphate (dTMP) by thymidylate synthase (TS), a critical enzyme in DNA nucleotide synthesis and cell survival. Due to multiple limitations including: therapeutic drug concentration and catalysis of dUMP to deoxythymidine monophosphate (dTMP) by thymidylate synthase (TS), a critical enzyme in DNA nucleotide synthesis and cell survival, NuTide:302 is a three-part, Phase Ib study in pts with advanced solid tumors. NUC-3373 has a longer plasma t1/2 (9.7 hours) than 5-FlU (8-14 minutes) and generates high intracellular levels of FUDR-MP (Ghazaly et al ESMO, 2017). TS is efficiently inhibited and sequestered into TS-tumour complexes, depleting the pool of deoxythymidine monophosphate (dTMP) within 2-4 hours. **Methods**: NuTide:302 is a three-part, Phase Ib study in pts with advanced CRC who have relapsed after ≥2 prior lines of 5-FlU-containing therapies. Primary objective is to identify a RP2D of NUC-3373 when administered weekly and q2w in combination with standard agents used in CRC treatment. Secondary objectives include safety, PK/PD and anti-tumor activity. In Part 1, patients are receiving NUC-3373 with leucovorin (LV) to determine if LV augments TS inhibition. In Part 2, NUC-3373 (L+LV) will be administered in dose escalating cohorts, in a modified 3+3 design, with either oxaliplatin (NUFOX) or irinotecan (NUFIRI). In Part 3, the NUFOX and NUFIRI regimens selected in Part 2 will be combined with biologics targeting VEGF or EGFR pathways. To date, 22 pts have received study therapy. Recruitment is ongoing in the US and Europe. Clinical trial information: NCT03428958. Research Sponsor: Nucana.
A phase II study of trifluridine/tipiracil, irinotecan, and bevacizumab in pretreated metastatic colorectal cancer (TABAsoC). First Author: Medhavi Gupta, Roswell Park Cancer Institute, Dept. of Medicine, Buffalo, NY

Background: Colorectal cancer (CRC) is the second leading cause of cancer-related death in US. The majority of US patients (pts) receive first-line therapy (Rx) with FOLFOX (Folinic acid + 5-fluorouracil + oxaliplatin) and or FOLFIRI (Iri + oxaliplatin). A biologic, making FOLFIRI [FA+ 5-FU+ irinotecan (Iri)] + bevacizumab (Bev) a common second-line Rx. This regimen has a median progression-free survival (PFS) of approximately 6 months (mo) and overall survival (OS) of 12 mo. Further, pats are desperately needed. Trifluridine/tipiracil (FTD/TPI) is an oral combination Rx of a thymidine-based nucleoside analog, FTD, and a phosphorlyase inhibitor, TPI. FTD/TPI has a distinct mechanism of action from S-FU and in preclinical models can overcome S-FU resistance via DNA incorporation, base excision repair pathway and glycosylation responses to DNA damage. Further, there is an additive effect in combination with Iri. FTD/TPI was FDA approved for use in refractory metastatic CRC (mCRC) based on phase III RECOURSE trial. Phase I data showed combination of FTD/TPI, Iri and Bev to be safe, and an efficacy signal was seen in dose-expansion cohort (NCT01964447). A 12.5% response rate, 83.4% disease control rate and PFS of 7.9 mo was achieved. As this study largely assessed refractory pts, one might expect a greater efficacy in Iri naive pts. To test this hypothesis, we are conducting a multi-center phase II study of FTD/TPI, Iri and Bev as second-line Rx in mCRC pts. Methods: Eligible pts have mCRC and received first-line Ox based Rx. Rx to be given in 28-day cycles: Iri (180 mg/m2) and Bev (5 mg/kg) on D1 & 15, and FTD/TPI (25 mg/m2) twice daily on D2-6 & 16-20. Response as-of changes in ctDNA (TACT-D).

-colon cancer (mCRC) therapy using circulating cell-free tumor DNA (ctDNA) -liquid biopsies) testing as well as immune-panel based profiling will be performed alongside pre- and post-biopsies to study changes in the tumor microenvironment. Clinical trial information: NCT04108481. Research Sponsor: Biocompatibles UK Ltd and AstraZeneca.

Dose escalation cohort of durvalumab.

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TPS276

Trials in Progress Poster Session (Board #N10), Sat, 6:30 AM-7:55 AM and 12:15 PM-1:45 PM

Immunotherapy with Y90-radioembolization for metastatic colorectal cancer (iRE-C). First Author: Pashtoon Murtaza Kasi, University of Iowa, Iowa City, IA

Background: Immune checkpoint inhibitors have revolutionized the treatment of a number of cancers. In colorectal cancers, their efficacy is limited to mismatch repair deficient or microsatellite stability-high (dMMR/MSI-High) tumors only. These constitute only 4-5% of all metastatic colorectal cancers (mCRC). Novel approaches are needed to make immunotherapy a viable option for mismatch repair proficient or microsatellite stable (pMMR/MSI-Low) tumor. One strategy is to use an accelerated titration design. This would allow a maximum tolerated dose with the minimum number of subjects. Correlative studies pertaining to serial circulating tumor DNA (ctDNA - liquid biopsies) testing as well as immune-panel based profiling will be performed alongside pre- and post-biopsies to study changes in the tumor microenvironment. Clinical trial information: NCT04108481. Research Sponsor: Biocompatibles UK Ltd and AstraZeneca.

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**Results of the JAVELIN Gastric 100 phase 3 trial: avelumab maintenance following first-line (IL) chemotherapy (CTx) vs continuation of CTx for HER2–advanced gastric or gastroesophageal junction cancer (GC/GEJC).**

**First Author:** Markus H. Moehler, Johannes Gutenberg-University Clinic, Mainz, Germany

**Background:** We report the primary analysis of JAVELIN Gastric 100, which compared avelumab (anti-PD-L1) maintenance after IL CTx vs continued CTx in patients (pts) without PD-L1+ GC/GEJC.

**Methods:** In this global, open-label, phase 3 trial (NCT02625610), eligible pts had previously untreated, unresectable, locally advanced/metastatic (LA/M) HER2–GC/GEJC. Pts without progressive disease (PD) after 12 weeks of IL oxaliplatin/fluoropyrimidine induction were randomized 1:1 to avelumab 10 mg/kg Q2W switch maintenance or continued CTx, stratified by region (Asia vs non-Asia). Primary endpoint was overall survival (OS) post induction in all randomized or PD-L1+ (≥1% of tumor cells, 73-10 assay) pts. Results: 805 pts received induction CTx and 499 pts were randomized (avelumab, n = 249; CTx, n = 250). At data cutoff (Sep 13, 2019), minimum follow-up was 18 months. In the avelumab and CTx arms, median post induction/randomization was 10.4 months (95% CI 9.1-12.0) vs 10.9 months (95% CI 9.1-12.4), hazard ratio (HR) 0.91 (95% CI 0.74-1.11; p = 0.1779); 24-month OS rates were 22.5% (95% CI 16.8-28.2) vs 15.5% (95% CI 10.8-20.5), respectively. The HR for OS in PD-L1+ pts (n = 54) was 1.13 (95% CI 0.57-2.23). No OS trend was seen in Asian pts (n = 114; HR 0.90 [95% CI 0.59-1.36]) or other subgroups, except for a potential benefit with avelumab in pts with no metastatic sites at randomization (n = 60; HR 0.52 [95% CI 0.28-0.98]). Progression-free survival was similar between arms (HR 1.04 [95% CI 0.85-1.28]). In the avelumab vs CTx arms, objective response rates (post randomization only) were 13.3% (95% CI 9.3-18.1) vs 14.4% (95% CI 10.3-19.4), and 12-month rates for duration of response were 62.3% (95% CI 40.9-77.9) vs 28.4% (95% CI 13.2-45.5), respectively. Treatment-related adverse events rates (all grades/range ≥3) were 61.3%/12.8% with avelumab and 77.3%/32.8% with CTx. Conclusions: Avelumab maintenance showed clinical activity and favorable safety vs continued CTx in pts with LA/M GE/GEJC; however, avelumab in JAVELIN Gastric 100 did not meet its primary objective of improving OS in the randomized or PD-L1+ population. Clinical trial information: NCT02625610. Research Sponsor: Merck KGaA, Darmstadt, Germany and Pfizer Inc.

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**ESOPHAGEAL AND GASTRIC CANCER**

**Oral Abstract Session, Thu, 1:30 PM-3:00 PM**

278 Early results of the randomized, multicenter, controlled evaluation of S-1 vs 28.4% (95% CI 13.2-45.7), respectively. Treatment-related adverse events rates (all grades/range ≥3) were 61.3%/12.8% with avelumab and 77.3%/32.8% with CTx. Conclusions: Avelumab maintenance showed clinical activity and favorable safety vs continued CTx in pts with LA/M GE/GEJC; however, avelumab in JAVELIN Gastric 100 did not meet its primary objective of improving OS in the randomized or PD-L1+ population. Clinical trial information: NCT02625610. Research Sponsor: Merck KGaA, Darmstadt, Germany and Pfizer Inc.

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**Extensive peritoneal lavage after curative gastrectomy for gastric cancer study (EXPEL): An international multicenter randomized controlled trial.**

**First Author:** Jimmy Bok Yan So, Department of Surgery, National University Health System, Singapore, Singapore

**Background:** Peritoneal recurrence of gastric cancer after curative surgical resection is common and portends a poor prognosis. Preliminary studies suggest that extensive intraoperative peritoneal lavage (EPL) may reduce the risk of peritoneal recurrence and improve survival. We sought to perform a randomized phase III study to definitively establish the role of performing EPL after gastrectomy.

**Methods:** This is a prospective, open-label, phase 3 multicenter randomized controlled trial involving 23 hospitals from Korea, China, Japan, Malaysia and Singapore. Patients aged between 21 to 80 years with cT3/4 stomach cancer undergoing curative resection were randomized to either surgery and EPL (lavage with 10 litres of saline) or surgery alone. Comparison of DFS and OS were made via log-rank test. The cumulative incidence of peritoneal recurrence was compared using competing risks approach. All analyses were performed based on intention-to-treat. Results: Between March 2015 to August 2018, 800 patients were randomly assigned to surgery alone (n = 402) or EPL (n = 398). Based on a median follow-up duration of 29 months, the 3-year cumulative incidence of all-cause mortality was 23.1% and 23.3% for EPL and surgery alone respectively (hazard ratio [HR] = 1.09, 95% CI: 0.78 to 1.52, p = 0.615). Similarly, the 3-year cumulative incidence of recurrence was 28.0% and 25.9% respectively [HR = 1.01, 95% CI: 0.74 to 1.37, p = 0.947], and 7% and 6.6% respectively (hazard ratio [HR] = 1.04, 95% CI: 0.28-0.98). The probability of OS was significantly better in EPL compared to surgery alone (relative risk [RR] = 1.33, 95% CI: 0.73 to 2.42, p = 0.347). Overall, the risk of adverse events was higher in EPL as compared to surgery alone (relative risk [RR] = 1.58, 95% CI: 1.07 to 2.33, p = 0.019). The most common adverse events were anastomotic leak, bleeding, wound infection and intra-abdominal hematomas. At the present median follow-up (28 August 2019), the predictive probability of achieving even a 5% difference in 3-year OS in favour of EPL at final analysis was < 0.4%. The trial was thus recommended to terminate on the basis of futility. Conclusions: EPL does not show any survival benefit compared to surgery alone and is not recommended for patients undergoing curative gastrectomy for cancer. Clinical trial information: NCT02140034. Research Sponsor: National Research Medical Research Council Singapore.

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**Oral Abstract Session, Thu, 1:30 PM-3:00 PM**

279 Early results of the randomized, multicenter, controlled evaluation of S-1 vs 28.4% (95% CI 13.2-45.6) and 12-month rates for duration of response were 62.3% (95% CI 40.9-77.9) vs 28.4% (95% CI 13.2-45.5), respectively. Treatment-related adverse events rates (all grades/range ≥3) were 61.3%/12.8% with avelumab and 77.3%/32.8% with CTx. Conclusions: Avelumab maintenance showed clinical activity and favorable safety vs continued CTx in pts with LA/M GE/GEJC; however, avelumab in JAVELIN Gastric 100 did not meet its primary objective of improving OS in the randomized or PD-L1+ population. Clinical trial information: NCT02625610. Research Sponsor: Merck KGaA, Darmstadt, Germany and Pfizer Inc.

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**A randomized controlled phase III multicenter study on dose escalation in definitive chemoradiation for patients with locally advanced esophageal cancer: ARTEDECO study.**

**First Author:** Maarten C.C.M. Hulshof, Amsterdam UMC, University of Amsterdam, Department of Radiotherapy, Cancer Center Amsterdam, Amsterdam, Amsterdam, Netherlands

**Background:** To analyze the effect of radiation dose escalation to the primary tumor on local control, locoregional control, survival and toxicity in definitive chemoradiation for esophageal cancer. Methods: Patients with clinical stage T2-4, N0-3, M0, carcinoma of the esophagus were randomized between a standard dose of 50.4 Gy/1.8 Gy/5,5 weeks to the tumor and regional lymph nodes (SD) versus the same dose combined with an integrated boost of 0.4 Gy per fraction (total 61.6 Gy) to the primary tumor (HD). Chemotherapy consisted of a weekly concurrent cisplatin and 5-fluorouracil (AUC 2) throughout 7 weeks. Analysis was performed on 28 August 2019, the predictive probability of achieving even a 5% difference in 3-year OS in favour of EPL at final analysis was < 0.4%. The trial was thus recommended to terminate on the basis of futility. Conclusions: EPL does not show any survival benefit compared to surgery alone and is not recommended for patients undergoing curative gastrectomy for cancer. Clinical trial information: NCT02140034. Research Sponsor: National Research Medical Research Council Singapore.

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281 Early results of the randomized, multicenter, controlled evaluation of S-1 and oxaliplatin as neoadjuvant chemotherapy for Chinese advanced gastric cancer patients (RESONANCE Trial).

**First Author:** Xinxin Wang, Chinese PLA General Hospital, Beijing, China

**Background:** Perioperative chemotherapy brings potential benefits to growing patients with gastric cancer based on several clinical trials including MAGIC, ACTS-GC, CLASSIC and INT-016. However, the effect of neoadjuvant therapy before 02 gastrectomy remains pending. According to phase ii clinical trials, SOX regimen as neoadjuvant chemotherapy is associated with increased rate of D2 lymph nodes dissection and R0 resection. We hypothesize that SOX regimen can prolong median survival time, DFS and OS. Chemotherapy using SOX can prolong median survival time, DFS and OS. Chemotherapy using SOX can increase rate of R0 resection, acceptable adverse events and no impression on surgeries, which suggest that perioperative chemotherapy using SOX can prolong median survival time. DFS and OS. Clinical trial information: NCT01583361. Research Sponsor: Chinese PLA General Hospital.

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282 Rapid Abstract Session, Thu, 11:15 AM-12:00 PM and Poster Session (Board #A1), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Evaluating maintenance therapies in advanced oesophago-gastric adenocarcinoma (OGA): Interim analysis and biomarker results from the PLATFORM study. First Author: David Cunningham, The Royal Marsden NHS Foundation Trust, London and Surrey, United Kingdom

Background: Advanced OGA patients (pts) are treated with platinum-based 1st line chemotherapy (C), the role of maintenance therapy (MT) to improve overall survival (OS) control is unknown. Methods: PLATFORM is a prospective, open-label, adaptive phase II trial assessing maintenance therapy in OGA. HER2 negative pts with advanced OGA achieving response or stable disease on completion of 1st line platinum-based chemotherapy were initially randomised to surveillance (A1), capecitabine (A2) and durvalumab (A3), Rucaparib (A4) and capetabchine+ramucirumab (A5) were subsequently added as part of adaptive design. Primary endpoint is progression-free survival with target recruitment of 154pts/arm. A pre-planned futility interim analysis (IA) is triggered when 61 pts/arm are recruited and evaluable during 12-week progression-free rate (PFR). Individual arms will continue accrual if the upper limit of 1-sided 95% CI difference is > 0 when compared to A1. Biomarker analyses of A1 and A3 IA patients include: PD1 as tumour and immune cell combined proportion (TIP), multiplex HC of tumour infiltrating lymphocytes (TILs), TMBS and MSI status by whole exome sequencing. Results: To date, 1053 pts have registered prior to or during 1st line therapy and 356 pts randomised. Primary attainment was due to disease progression. Baseline demographics in the IA population (arms A1 to A3 n = 383) were similar (81% med age 65 yrs; metastatic disease (92%); oesophageal (40%); OG junction (28%); and gastric (32%) primary, 12-week PFR were: A1: 51% (95%CI: 40-65%); A2: 52% (95%CI: 40-65%); A3: 49% (95%CI: 36-62%). PFR differences to arm were A1: -1.6% (95%CI: -13.2 to 10.0%); A2: -1.6% (95%CI: -13.2 to 10.0%); A3: -1.6% (95%CI: -13.2 to 10.0%). A1-PFRR was 53% vs 43% in PD1 TIP < 10% and ≥10% respectively. In A3, PFR was 51% vs 100% in PD1 TIP < 10% and ≥10% respectively. 3 pts in A3 had partial response; none were in A1 and A2. Density of TILs subsets, TMBS and MSI data will be presented. Conclusions: PLATFORM IA did not indicate futility in maintenance capecitabine or durvalumab compared to surveillance in advanced OGA and will continue to target accrual. Incremental radiological responses were observed with maintenance durvalumab only. Clinical trial information: NCT02678182. Research Sponsor: The Royal Marsden NHS Foundation. Additional information: For further details on the PLATFORM trial visit: gicasym.org.

284 Rapid Abstract Session, Thu, 11:15 AM-12:00 PM and Poster Session (Board #A3), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Access to care and outcomes for noncurative esophagogastric cancer: A population-based geographic study. First Author: Elliott Kenneth Yee, University of Toronto, Toronto, ON, Canada

Background: Esophageal cancer (EC) carries a heavy mortality burden owing largely to high rates of unresectable disease at diagnosis. Among patients not undergoing curative-intent therapy, access to care may vary. We examined the distribution of noncurative EC care and survival outcomes by jurisdiction, and its relationship with distance to cancer centres (CCs), for noncurative EC. Methods: We conducted a population-based analysis of adults with noncurative EC from 2005-2017 using linked administrative healthcare databases in Ontario, Canada. Outcomes were medical oncology consultation receipt, chemotherapy, and overall survival (OS). We used geographic information system analysis to map locations of CCs and outcomes across census divisions. Regions of discordance between care use and OS were identified with bivariate choropleth maps. Multivariable modified Poisson models assessed the relationship between distance to the nearest CC and outcomes, adjusting for demographic, clinical, and socioeconomic factors. Results: Of 10,228 patients surviving a median of 5.1 months (IQR: 2.0-12.0), 68.6% had medical oncology consultation and 32.2% received chemotherapy. Regions of comparable OS and care delivery were clustered throughout the province. CCs were distributed unevenly, with higher levels in Southern Ontario. Higher-level CCs clustered in regions with higher rates of consultation, chemotherapy use, and OS. Each increment in distance from location of residence to the nearest CC (10,50, 5100, and >101 km) was associated with lower likelihood of seeing medical oncology and receiving chemotherapy, and inferior OS, compared to ≤10 km. Conclusions: A third of patients with noncurative EC did not see medical oncology, and the majority did not receive chemotherapy. Care delivery and OS exhibited high geographic variability. Location of residence influenced access to care and OS, with inferior outcomes for those living further from a CC. These findings are important for designing interventions and policies to reduce disparities in access to care and outcomes for noncurative EC. Research Sponsor: Canadian Institutes of Health Research (CIHR) Partnership for Health System Improvement (PHSI) grant.

283 Rapid Abstract Session, Thu, 11:15 AM-12:00 PM and Poster Session (Board #A2), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Performance of a blood-based test for the detection of multiple cancer types. First Author: Brian M. Wolpin, Dana-Farber Cancer Institute, Boston, MA

Background: Cancers of the esophagus, stomach, pancreas, gallbladder, liver, bile duct, colon and rectum will account for 17% of incident cancer diagnoses and 26% of cancer-related deaths in the US in 2019. We developed a methylation-based cfDNA early multi-cancer detection test that can also predict the tissue of origin (TOO) of these and other cancers types; performance of this test for gastrointestinal (GI) tract cancers is reported here. Methods: The Circulating Cell-free Genome Atlas (CCGA; NCT02889978) study was a prospective, multicenter, observational, case-control study with longitudinal follow-up, enrolling individuals with cancer (> 20 cancers, all stages, newly-diagnosed) and without cancer. Plasma cfDNA was subjected to a cross-validated targeted methylations (TM) sequencing assay. Methylation fragments were combined across targeted genomic regions and assigned a probability of cancer and a predicted TOO. GI cancer classes were upper GI (esophagus/stomach, n = 67), pancreas/gallbladder/extrahepatic bile duct (n = 95), liver/intrahepatic bile duct (n = 29), and colon/rectum (n = 121). Results: Detection across all GI cancers was 82% (95% CI 77-86) at a ≥99% pre-set specificity. Overall predicted TOO accuracy was 92% (88-95) among the samples for which TOO was predicted (62/55 had indeterminate predicted TOO). The table shows performance by GI cancer type. Conclusions: Simultaneous detection at high specificity (≥99%) of multiple cancer types, including GI cancers across stages at high sensitivity (82%), was shown using TM analysis of cfDNA. Accuracy (92%) localization of cancers to specific regions of the GI tract was also achieved. Detection of multiple GI cancers from a single noninvasive blood test could be a practical method for detecting and staging GI cancers, and may facilitate diagnostic work-ups. Clinical trial information: NCT02889978. Research Sponsor: GRAIL, Inc.

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Comparing the accuracy of EUS and CT in staging of esophageal cancer.

First Author: Hyun Ik Shim, Seoul National University Bundang Hospital, Seongnam, South Korea

Background: Endoscopic ultrasound (EUS) is a suitable device for staging of esophageal cancers. However, chest computed tomography (CT) has traditionally been the standard diagnostic modality for malignancies. This study aimed was to compare the accuracies of EUS and chest CT in T and N staging of esophageal cancers.

Methods: We retrospectively analyzed 149 patients who had undergone EUS examination and 275 patients who had undergone chest CT before cancer surgery. The inclusion criteria were: 1) patients diagnosed with esophageal cancer on biopsy, 2) patients who had undergone EUS examination or chest CT before cancer surgery, and 3) patients who underwent cancer surgery at the Seoul National University Bundang Hospital from May 2003 to December 2018. We determined the accuracy of T and N staging on EUS examination and chest CT with the biopsy specimens. Results: The overall accuracies of EUS examination and chest CT were 72.5% (108/149) and 68.7% (189/275), respectively, for T staging (p = 0.487) and 64.4% (96/149) and 61.5% (169/275), respectively, for N staging, which was not statistically different (p = 0.596). For the substaging, the accuracy of EUS examination was not statistically different than that of chest CT for the T, N stage.

Conclusions: EUS examination is not superior to chest CT for diagnosing T stage in esophageal cancers, whereas chest CT is not superior to EUS examination for diagnosing N stage in esophageal cancers. EUS examination and chest CT are not satisfactory for diagnosing T, N stage in esophageal cancers. Further study is needed for accurate T, N stage diagnosis in esophageal cancer.

Research Sponsor: None.

Prediction of lymph node metastasis in early gastric cancer using artificial intelligence technology.

First Author: Tomoyuki Irino, Keio University School of Medicine, Tokyo, Japan

Background: Early gastric cancer shows lymph node involvement in about 10-15% of patients. Despite the fact, we perform radical lymphadenectomy for all patients because predicting lymph node metastasis has yet to be successful. In this study, we hypothesize that image analysis using artificial intelligence (AI) technology may help solve the problem.

Methods: We retrospectively collected 82 patients with clinical T1NO and pathological node negative and 82 patients with clinical T1NO and pathological node positives and then divided the 164 patients into a training/validation set in ratio of 9:1. Endoscopic images of the early tumors were analyzed by transfer learning using AlexNet, a deep neural network containing 5 convolutional layers and 3 fully-connected layers. The model was validated with newly-collected 40 images from 20 clinical T1NO and pathological node negative and 20 patients with clinical T1NO and pathological node positives as a test set. For comparison, three methods of prediction were implemented: prediction at random, by logistic regression, and by skilled endoscopists. Results: The AI predicted LNM with accuracy of 80.9% in the validation set and 66.9% in the test set. (48.3% for node negative cancers and 85.4% for node positive cancers) On the other hand, prediction at random, by logistic regression, and by 2 endoscopists resulted in 50.3%, 50.0%, and 47.5%, respectively. Conclusions: Although the accuracy still needs to be improved, image analysis using the AI technology resulted in the best prediction of lymph node metastasis, indicating that AI is a promising technology for the diagnosis of lymph node metastasis in early gastric cancer. Research Sponsor: None.
Is preoperative screening colonoscopy useful in patients with gastric cancer? First Author: Yusukeyoseki, Division of Gastro Surgery, Shizouka Cancer Center, Shizouka, Japan

Background: In patients with gastric cancer (GC), the most common double cancer is colorectal cancer (CRC). However, the meaning of screening colonoscopy has not been established. The aim of this retrospective study was to evaluate the usefulness of screening colonoscopy in preoperative patients with GC.

Methods: This study included 689 patients who received screening colonoscopy before gastric surgery between 2012 and 2016. Multivariate analysis using logistic regression model was conducted to elucidate independent risk factors of CRC. Then, we investigated the clinicopathological factors for CRC.

Results: Colorectal adenomas and CRC were observed in 315 patients (46%) and 37 patients (5.4%), respectively. The clinical T classification of the CRC were as follows; Tis: 24 patients (65%), T1: 8 patients (21%), T2: 2 patients (6%), and T3:3 patients (8%). In multivariate analysis, male (OR 5.04, 95% CI. 1.29-19.6, P = 0.020) was revealed as risk factor for affecting CRC. The treatments for CRC were as follows; EMR was performed in 27 patients, multianeous resection with GC was performed in 9 patients, resection after gastrectomy was performed in 1 patient, respectively. Pathological stage of CRC was as follows; Stage O: 24 patients, Stage I: 10 patients, and Stage II: 3 patients, respectively. As for the patients who underwent surgery for CRC, all of them received radical colectomy. No patient died for CRC who received colonoscopy before gastric surgery.

Conclusions: Screening colonoscopy is useful for GC patients. Because most of the synchronous CRC were found early stage and curatively treated. Research Sponsor: None.

Propensity-score-matched analysis of a multi-institutional dataset to compare the postoperative complications after distal gastrectomy between Billroth I and Roux-en-Y. First Author: Koki Nakanishi, Department of Surgery Nakatsugawa Municipal General Hospital, Nakatsugawa, Japan

Background: Billroth I (B-I) or Roux-en-Y (R-Y) are common reconstruction technique after distal gastrectomy, each with advantages and disadvantages and which is the most successful remains unclear. The aim of the present study was to clarify the difference of postoperative complications between the two techniques. Methods: A multi-institutional retrospective database comprising clinical information of 3484 patients who received resection of gastric cancer from 2010 to 2014 at nine institutions. Using propensity scores to compare the postoperative complications after distal gastrectomy, each with advantages and disadvantages and which is the most successful remains unclear. The aim of the present study was to clarify the difference of postoperative complications between the two techniques.

Methods: A multi-institutional retrospective database comprising clinical information of 3484 patients who received resection of gastric cancer from 2010 to 2014 at nine institutions. Using propensity scores to compare the postoperative complications after distal gastrectomy, each with advantages and disadvantages and which is the most successful remains unclear. The aim of the present study was to clarify the difference of postoperative complications between the two techniques.

Results: Among 33 institutions participated in JCOG0912, 4 major cancer centers were selected for HRQOL assessment. HRQOL was assessed using EORTC QLQ-C30 and the EORTC-30Q22 before (baseline) and at 1, 3, 12, and 36 months after surgery. The primary HRQOL scale was QLQ-C30 global health status. We defined clinically meaningful decrease of HRQOL as decrease in 10 points or more from the baseline. Missing data were regarded as decrease. Assuming that expected %decrease of global health status at 1 month was 6% in ODG and 4% in LDG with 80% power and two-sided alpha of 0.05, sample size for HROOL assessment was calculated to be 304. When this hypothesis at 3 months was confirmed, statistical comparison was tested in turn at 12 and 36 months. Results: Among 921 enrolled patients in JCOG0912 from Mar 2010 to Nov 2013, 592 were enrolled from the 4 centers in this HRQOL study. The %decrease of global health status at 3 months was different between ODG and LDG (37.2% (109/293) in ODG vs 29.2% (86/295) in LDG, odds ratio (OR) 0.65 (95% CI: 0.45-0.93, P = 0.020)), but was not different in 1 month (56.0% (164/293) vs 55.3% (163/295), OR 0.92 (0.61-1.32)), 12 months (26.3% (77/293) vs 27.8% (82/295) (OR 1.07 (0.73-1.56)) and 36 months (31.4% (91/293) vs 30.8% (91/295) (odds ratio, 0.96 (0.67-1.37)). Among the other subscales, LADG had significantly better symptom scores for pain at 1 and 3 months, constipation at 3 and 12 months, and eating restrictions at 3 months. Conclusions: Decrease of HRQOL was less frequently observed in LADG than ODG especially in the early phase after surgery. Considering non-inferiority and better HRQOL of LADG, LADG is strongly recommended for stage I gastric cancer. However, we have to be careful to expand the indication of LADG for advanced gastric cancer until a solid evidence is obtained. Clinical trial information: UMIN000003339. Research Sponsor: National Cancer Center; The Ministry of Health, Labour and Welfare of Japan; AMED.
Modified Controlling Nutritional Status score: A refined prognostic indicator depending on the stage of gastric cancer. First Author: Chul Hyo Jeon, Seoul St. Mary’s Hospital, Seoul, South Korea

Background: The role of controlling nutritional status (CONUT) score in predicting cancer survival remains uncertain. This study aimed to investigate the predictive value of the CONUT score in stage III gastric cancer patients and to develop a more appropriate scoring system beyond CONUT for gastric cancer (GC). Methods: We retrospectively reviewed 1307 patients who underwent curative gastrectomy between 2009 and 2015. The CONUT and three modified scores with modified lipids component (L-CONUT: albumin/total cholesterol; T-CONUT: albumin/TLC/triglyceride) were calculated. The predictive value of each scoring system on long-term survival was assessed. Results: The values of the four nutritional scores were categorized into three groups (low, medium, and high). The CONUT (P < 0.001), L-CONUT (P < 0.001), H-CONUT (P < 0.001), and T-CONUT (P < 0.001) scores showed significant differences in overall survival in the three groups. Survival analysis according to the pathological stage showed that advanced age, Eastern Cooperative Oncology Group performance status, male sex, and high CONUT score (HR, 3.93; 95% CI, 1.81-8.55; P = 0.001) were independent poor prognostic factors for overall survival in the stage I group. In the stage II group, CONUT score (HR, 5.077; 95% CI, 1.65-15.65; P = 0.005) was significantly associated with poor prognosis. In the stage III group, no scoring system showed significant results. Conclusions: In advanced GC beyond stage II, the prognostic impact of the nutritional scoring system was uncertain. However, the H-CONUT score is a promising indicator of prognosis in stage I GC, and the CONUT score is useful for predicting long-term survival in stage II GC. Research Sponsor: None.

The impact of single-hetero UGT1A1 on clinical outcomes of irinotecan monotherapy in gastric cancer after fluoropyrimidine, platinum, and taxanes: Multicenter retrospective study. First Author: Ken Ito, Division of Cancer Center, Hokkaido University Hospital, Sapporo, Japan

Background: Japanese gastric cancer treatment guidelines (5th edition) recommend irinotecan (IRI) after fluoropyrimidine, platinum and taxanes as a salvage line. However, it remains unclear that UGT1A1 SH allele is a risk factor of higher frequency of severe hematological adverse events (AEs) compared to patients with wildtype allele (WT). Methods: We retrospectively analyzed the clinical data of patients who received IRI monotherapy after fluoropyrimidine, platinum and taxanes as a salvage line. Results: Forty-one patients with UGT1A1 WT and 28 patients with UGT1A1 SH were included in this study. In WT/SH patients, rate of initial dose reduction was 22% and 28% (P = 0.363), median relative dose intensity (RDI) was 82% and 80% (P = 0.309). Of 88 patients who have measurable lesions, the overall response rate (ORR) was 5.7% and 4.2% (P = 1.000), disease control rate (DCR) was 54% and 38% (P = 0.289). Median progression-free survival was 3.2 and 2.1 months (HR 0.607, P = 0.058) and median overall survival from initial day of IRI monotherapy was 10.0 and 7.0 months (HR 0.618 P = 0.086). In WT/SH patients, severe hematological AEs (≥G3) were observed more frequently in patients with UGT1A1 SH (WT: 43% and SH: 68%, P = 0.050), although frequency of severe non-hematological AEs (≥G3) were not significantly different in both groups (13% and 25%, P = 0.211). Conclusions: Compared to UGT1A1 WT, UGT1A1 SH status may be associated with poor efficacy and be a risk factor of higher frequency of severe hematological AEs. Research Sponsor: None.

Prognostic value of modified Glasgow Prognostic Score (mGPS) and neutrophil-lymphocyte ratio (NLR) after curative resection for gastric cancer. First Author: Yusuuke Shimodaira, Nagano Municipal Hospital, Nagano, Japan

Background: Several biomarkers based on serum chemistry have been reported as the prognostic factors of several types of cancers. This retrospective study aimed to investigate the prognostic value of preoperative mGPS and NLR after curative resection for gastric cancer. Methods: A total of 295 patients who underwent curative gastrectomy for primary gastric cancer at our institution from January 2015 to December 2015 were enrolled in this study. The mGPS was calculated by CRP and Alb using standard thresholds ( > 0.5 mg/dL for CRP and < 3.5 g/dL for Alb). The NLR was defined as absolute neutrophil count divided by absolute lymphocyte count. The survival curves of patients stratified by each parameter were plotted by the Kaplan-Meier method and compared by log-rank test. Multivariate Cox proportional hazards regression models were used to select parameters independently correlated with prognosis. Results: The median follow-up time was 36.7 months, and 29 patients died during follow-up. The estimated 5-year survival rate was 83.8%, and the median survival was 29.4 months. The mGPS and NLR were associated with poor survival while NLR and NLRc were not (P = 0.001, P = 0.506, and P = 0.423, respectively). In the multivariate analyses, the mGPS2 was identified as an independent predictive factor for OS in gastric cancer patients after curative resection (HR, 2.624; 95% CI: 1.058-6.505; P = 0.037). Conclusions: Preoperative mGPS2 was associated with worse survival after curative resection of gastric cancer patients. Based on our study, those with mGPS2 may be warranted to receive additional therapy or nutritional support to acquire better survival. Research Sponsor: None.

Improved efficacy to cytotoxic agents chemotherapy after immune check-point inhibitors exposure in metastatic gastric cancer. First Author: Tamotsu Sagawa, Division of Gastroenterology, National Hospital Organization Hokkaido Cancer Center, Sapporo, Japan

Background: An association between improved responses to chemotherapy after exposure to vaccine-based immunotherapy has been previously reported in other cancers. However, it is unclear whether the chemotherapy improves after exposure to immunotherapy, such as immune checkpoint inhibitors (ICIs). The objective of this retrospective study was to evaluate whether chemotherapy (4th-line) would yield improved efficacy when given after exposure to anti-PD-1 antibody in metastatic gastric cancer (mGC).

Methods: We investigated retrospectively clinical characteristics at baseline of mGC patients who received chemotherapy after progression of anti-PD-1 antibody (Nivolumab) between February 2018 and July 2019. Anti-PD-1 antibody was adopted as third-line therapy. Inclusion criteria for the analysis improves after exposure to immunotherapy, such as immune checkpoint inhibitors (ICIs). The objective of this retrospective study was to evaluate whether chemotherapy (4th-line) would yield improved efficacy when given after exposure to anti-PD-1 antibody in metastatic gastric cancer (mGC). The mGPS was calculated by CRP and Alb using standard thresholds ( > 0.5 mg/dL for CRP and < 3.5 g/dL for Alb). The NLR was defined as absolute neutrophil count divided by absolute lymphocyte count. The survival curves of patients stratified by each parameter were plotted by the Kaplan-Meier method and compared by log-rank test. Multivariate Cox proportional hazards regression models were used to select parameters independently correlated with prognosis. Results: The median follow-up time was 36.7 months, and 29 patients died during follow-up. The estimated 5-year survival rate was 83.8%, and the median survival was 29.4 months. The mGPS and NLR were associated with poor survival while NLR and NLRc were not (P = 0.001, P = 0.506, and P = 0.423, respectively). In the multivariate analyses, the mGPS2 was identified as an independent predictive factor for OS in gastric cancer patients after curative resection (HR, 2.624; 95% CI: 1.058-6.505; P = 0.037). Conclusions: Preoperative mGPS2 was associated with worse survival after curative resection of gastric cancer patients. Based on our study, those with mGPS2 may be warranted to receive additional therapy or nutritional support to acquire better survival. Research Sponsor: None.

ESOPHAGEAL AND GASTRIC CANCER

Visit qicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Conversion gastrectomy for stage IV unresectable gastric cancer: A retrospective cohort study. First Author: Tamotsu Sagawa, Division of Gastroenterology, National Hospital Organization Hokkaido Cancer Center, Sapporo, Japan

Background: Stage IV Gastric cancer (GC) is a heterogeneous biological condition with a mixture of distant metastases, including hematologic, lymph node(s), and/or peritoneal. In the recent classification introduced by Yoshida et al with the proposal to identify objective principles for conversion surgery, stage IV GC patients were subdivided into 4 new categories. In this study, we retrospectively investigated the efficacy of conversion gastrectomy for stage IV GC patients, with particular focus on the Yoshida's classification.

Methods: A retrospective, single center cohort study was performed in patients who had undergone conversion gastrectomy between 2005 and 2018. Data were extracted from Hokkaido Cancer Center database including all metastatic gastric cancer patients submitted to surgery. Only stage IV unresectable tumors/metastases which became resectable after chemotherapy were included in this analysis. Results: Forty-two resected stage IV GC patients were included in this analysis. Median overall survival (OS) was 40.0 months and 1-, 3- and 5-year survivals were 92.9, 70.7 and 57.7%, respectively. Univariate analysis among the patients with conversion gastrectomy identified macroscopic type, clinical response to 1st line therapy, pathological tumor depth, pathological nodal stage, R0 resection as significant prognostic factors. The MSTS of the patients with conversion gastrectomy for each category were 50.1 months for category 1, 46.6 months for category 2, 22.7 months for category 3 and 17.2 months for category 4. Conclusions: Unresectable stage IV GC patients could benefit from radical surgery after chemotherapy and achieve long survivals. Adequate selection of stage IV GC patients for conversion therapy may be an important role. Research Sponsor: None.

ESOPHAGEAL AND GASTRIC CANCER

Impact of gastric cancer treatment pathways on patient outcomes in a community oncology practice setting. First Author: Andrew Scott Paulson, The US Oncology Network/McKesson Specialty Health, Dallas, TX

Background: Gastric cancer (GC, including gastroesophageal junction adenocarcinoma) pathways have been implemented and refined since 2010 in the US Oncology Network (USON), a community-practice-based network. This study was designed to evaluate the impact of 4 pathway periods (PP): pre-pathway: pre-Aug '10; Level 1: Sept '10-Nov '14; Clear Value, Dec '14-Feb '17; Value: After Mar '17, on treatment heterogeneity, treatment duration, and overall survival (OS). Methods: Adult patients were eligible if they were treated at a participating USON site and were diagnosed with and treated for GC; follow up was through Mar 2019. Heterogeneity was measured by the Herfindahl-Hirschman index (HHI), which is evaluated from 0.0 to 1.0 (complete to no heterogeneity). Time to treatment failure (TTF) was defined as initiation of the line of therapy until start of the subsequent line of therapy or death. OS was estimated from start of first-line (1L) therapy. Time-to-event outcomes were estimated using Kaplan-Meier. Results: Of 399 eligible patients, 2297 received treatment for advanced/metastatic disease. Of these, patient median age was 65.3 years, 60% were male, 70% were initially diagnosed with stage IV disease. Pre-pathway, common 1L regimens were single-agent fluorouracil (15%) and docetaxel+cisplatin fluorouracil (14%); FOLFOX (45%) was most frequent during the value PP, 941 (44%) received second-line (2L) therapy. During Level 1PP, single-agent irinotecan (11%) was most common during 2L, whereas in Value PP, ramucirumab+paclitaxel (43%) was most common. HHI and TTF are presented in the table. Median OS was 12.6 months (95% confidence interval, CI: 11.9, 13.5), which did not change significantly over PPs. Conclusions: 1L and 2L heterogeneity was initially high, and was reduced over time; TTF showed modest increase. OS data are limited by high levels of censoring in the latter PPs, which reduces the ability to evaluate changes in more recent years. Research Sponsor: Eli Lilly and Company.

ESOPHAGEAL AND GASTRIC CANCER

Perioperative FLOT in resectable gastric cancer: Italian real-world data from the REALFLOT study. First Author: Elisa Giommoni, Medical Oncology, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy

Background: Perioperative treatments have significantly improved survival in patients with resectable gastric cancer, increasing 5-year overall survival from 23% with surgery alone to 45% with FLOT (fluorouracil, oxaliplatin, docetaxel). Pathological regression is a prognostic marker of better survival. Methods: In this observational, retro- and prospective study we collected data from patients with resectable gastric or gastro-oesophageal junction (GEJ) adenocarcinoma treated, as clinical practice, with perioperative FLOT. All patients had clinical T2 or higher and/or nodal involvement, according to FLOT-4/AIO trial. Results: A total of 206 patients received perioperative chemotherapy with FLOT at 15 Italian centres, between September 2016 and September 2019. Overall, 186 (90.3%) patients completed the preoperative phase, 190 (92%) underwent surgery, and 142 (68.9%) started the postoperative phase. Among patients who started the postoperative phase, 105 (52.0%) received FLOT, while 37 (18%) received less intensive regimens (e.g. FOLFOLX or De Gramont), depending on performance status, after surgery or toxicity in the preoperative phase. Pathological complete response (pCR) was obtained in 7.9% of cases. In the postoperative phase, grade (G) 3-4 haematological and gastrointestinal adverse events (AES) were reported in 42 (20.4%) and 13 (6.3%) patients, respectively. Conclusions: These real data confirmed the feasibility of perioperative FLOT in a less-selected population, representative of the clinical practice. The pCR rate was lower than in the FLOT-4/AIO trial. The survival outcomes, potential predictive or prognostic factors and comprehensive safety data will be included in the final analysis. Research Sponsor: None.

Poster Session (Board #A17), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Poster Session (Board #A18), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

SOURCE: Prediction models for overall survival in patients with metastatic and potentially curable esophageal and gastric cancer. First Author: Héctor G. van den Boorn, Academic Medical Center, Amsterdam, Netherlands

Background: Prediction models in cancer care can provide personalized prediction outcomes and can aid in shared decision making. Existing prediction models for esophageal and gastric cancer (EGC), however, are mostly aimed at predicting survival after a curative treatment has already been completed. A goal of this study is to develop prediction models, called SOURCE, to predict overall survival at diagnosis in potentially curable and metastatic EGC patients. Methods: The data from 12,756 EGC patients diagnosed between 2014-2017 were retrieved from the prospective Netherlands Cancer Registry. Four Cox regression models were created for potentially curable and metastatic cancers of the esophagus and stomach. Predictors, including treatment type, were selected using the Akaike Information Criterion. The models were validated with temporal cross-validation on their concordance-index (c-index) and calibration. Results: The validated model’s c-index is 0.76 for potentially curable cancer. For the metastatic models, the c-indices are 0.71 and 0.70 for esophageal and gastric cancer, respectively. The calibration intercepts and slopes lie in the 95% confidence interval of 0 and 1, respectively. The included model variables are given in Table. Conclusions: The SOURCE prediction models show fair c-indices and an overall good calibration. The models are the first in EGC to include treatment as a predictor. The models predict survival at diagnosis for a variety of treatments and therefore could have a high clinical applicability. Future research is needed to validate the effect on shared decision making in clinical practice. Research Sponsor: Dutch Cancer Society (KWF), grant number 2014-7000.

Poster Session (Board #A19), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

ESOPHAGEAL AND GASTRIC CANCER

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Impact of intraoperative staging of gastric cancer on long-term survival.

First Author: Keisuke Koumori, Department of Gastrointestinal Surgery, Kanagawa Cancer Center, Yokohama, Japan

Background: The preoperative stage and intraoperative stage of gastric cancer were unified as the clinical stage in the 8th edition of the TNM classification (UICC). Although there are some reports about the relationship between preoperative stage and prognosis, the relationship between intraoperative stage and prognosis remains unclear. The aim of this study was to clarify the impact of intraoperative diagnosis and staging on long-term survival.

Methods: Overall survivals were examined in 915 patients who underwent curative resection for gastric adenocarcinoma between April 2011 and March 2019 in our hospital. Results: The median age of the patients was 69 years (27-90 years), including 585 males and 330 female. The median follow-up period was 33.6 months (0.1-86.7 months). The number of the patients according to intraoperative stage were 641 (70.1 %) in stage I, 151 (16.6%) in stage II, 110 (12.1%) in stage III, and 7 (0.8%) in stage IV. The hazard ratios of intraoperative stage for overall survival were as follows: ref: Stage I; Stage II, 5.623 (95% CI: 2.687-11.86, p < 0.001), Stage II, 2.234 (95% CI: 1.220-4.092, p = 0.009), Stage III, 4.091 (95% CI: 2.416-6.928, p < 0.001), Stage IV, 6.990 (95% CI: 2.473-19.760, p < 0.001). Stage IV was classified as Stage IIIB, 2.234 (95% CI: 1.220-4.092, p = 0.009), Stage IIB, 2.234 (95% CI: 1.220-4.092, p = 0.009), Stage IIIB, 2.234 (95% CI: 1.220-4.092, p = 0.009), Stage IIIC, 4.091 (95% CI: 2.416-6.928, p < 0.001), Stage IV, 6.990 (95% CI: 2.473-19.760, p < 0.001). Stage IV was classified as Stage IIIB, 2.234 (95% CI: 1.220-4.092, p = 0.009), Stage IIB, 2.234 (95% CI: 1.220-4.092, p = 0.009), Stage IIIB, 2.234 (95% CI: 1.220-4.092, p = 0.009), Stage IIIC, 4.091 (95% CI: 2.416-6.928, p < 0.001), Stage IV, 6.990 (95% CI: 2.473-19.760, p < 0.001). Staging criteria were used to classify Stage IIB, 111 (12.1%) in stage III and 75 (8.2%) in stage IV. The survival rate of patients with stage IV was significantly worse than that of patients with stage IIIB. The survival rates were as follows: ref: Stage I; Stage II, 64.1% (95% CI: 58.6%-69.6%); Stage III, 34.3% (95% CI: 28.8%-40.1%); Stage IV, 13.8% (95% CI: 9.3%-18.8%). The 5-year OS rates for Stage I, II, III, and IV were 92.1%, 80.0%, 46.1%, and 18.4%, respectively. The 5-year RFS rates for Stage I, II, III, and IV were 86.4%, 75.9%, 46.3%, and 20.9%, respectively. Conclusion: The intraoperative staging of gastric cancer had a significant impact on overall survival. The survival rates decreased significantly as the stage of gastric cancer increased. The 5-year OS rates for Stage I, II, III, and IV were 92.1%, 80.0%, 46.1%, and 18.4%, respectively. The 5-year RFS rates for Stage I, II, III, and IV were 86.4%, 75.9%, 46.3%, and 20.9%, respectively.

304 Real-world outcomes of first-line U.S. patients with unresectable advanced or metastatic esophageal adenocarcinoma by primary tumor location.

First Author: Veena Shankaran, University of Washington, Seattle, WA

Background: Gastric cancer clinical trials are inconsistent in their inclusion of esophageal adenocarcinoma (EAC). Thus it is uncertain if outcomes are similar among subgroups of esophageal adenocarcinoma. The aim of this study was to compare baseline characteristics and clinical outcomes of US patients with EAC versus Gastric Gastroesophageal Junction Cancer (GEJC) and Gastric Cancer (GC) treated in real world clinical settings.

Methods: Adult patients with unresectable, advanced or metastatic GC, GEJC, or cancer diagnosed between January 2011 and November 2018 were identified from the Flatiron Health database. Patients with a positive HER2 test, or who received trastuzumab, were excluded. Overall survival (OS) was defined as time from first-line (I) treatment initiation to death or loss of follow-up. Survival analyses were conducted using Kaplan-Meier methods with log-rank test and Cox models.

Results: A total of 3052 patients (969 EAC and 2083 GEJC/GC) met eligibility criteria. Out of all EAC patients, 90% were males and 76% were white. Within the GEJC/GC patients, 67% were males and 57% were white. Median age was 66 years for both cohorts while proportion with ECOG PS of 0 or 1 was 78% for EAC and 84% for GEJC/GC among patients with ECOG scores. The proportion of patients receiving I treatment was comparable (78% for EAC, 76% for GEJC/GC) across groups with FOLFIRI being the most frequent treatment (25% for EAC and 29% for GEJC/GC). There was no significant difference in OS between the two groups, with median OS of 9.1 and 9.6 months for EAC and GEJC/GC, respectively (HR 0.957, 95% CI: 0.863-1.062, p = 0.4). Conclusions: In this US real-world analysis, OS did not differ significantly between patients with EAC and patients with GEJC/GC who received I treatment, suggesting that these two populations may have comparable survival benefit from systemic therapy. Research Sponsor: Bristol-Myers Squibb.

305 The impact of additional treatment after endoscopic submucosal dissection for esophageal squamous cell carcinoma in real-world clinical practice.

First Author: Nanako Sakaguchi, Second Department of Internal Medicine, Osaka Medical College, Osaka, Japan

Background: Endoscopic submucosal dissection (ESD) is the standard therapy for the T1a-EP/LPM esophageal squamous cell carcinoma (ESCC), although it is difficult to diagnose the invasion depth accurately before ESD. The incidence of lymph node metastases in ESCC involving the muscularis mucosa (pT1a-MM) and the submucosa (pT1b-SM) is reported to range from approximately 10% to 30%. For the patients with MM, SM or involving LVI or positive vertical margin after ESD, additional treatment (AT) is recommended to prevent local recurrence. However, the AT is not always performed to the frail or elderly patients. The aim of this study is to investigate the outcome of AT and non-AT (NAT) after ESD for ESCC in the real-world clinical practice.

Methods: We retrospectively reviewed the ESCC patients who were pathologically confirmed T1a-MM or T1b-SM (UICC-TNM7th) after ESD at Osaka medical college hospital between 2004 and 2016. Results: Among 224 patients who received ESD, 52 patients were pT1a-MM (n = 36; 69.2%) or pT1b-SM (n = 16; 30.8%) of the 52 patients (23%) received AT and forty patients (77%) received NAT. Six patients (AT group: 2 patients, NAT group: 4 patients) had local lymph node recurrence. Five of them underwent salvage therapy. Median follow up time were 54.3 months (range: 48.4-62.4). The 3-, 5-year RFS rate and the 3-, 5-year OS rate were 83.8% [95%CI: 68.2-92.6], 73.4% [95%CI: 56.0-85.7] and 94.7% [95%CI: 81.3-98.6], 91.7% [95%CI: 77.1-97.3] in all patients, respectively. The 5-year RFS and OS rate were 77.8%, 90.0% in the AT group and 71.6, 92.2% in the NAT group. Conclusions: Although the AT tended to prevent local recurrence, the OS was comparable with NAT because of salvage therapy. The active surveillance is recommended for T1a-MM or T1b-SM ESCC. Research Sponsor: None.
Change in neutrophil-to-lymphocyte ratio (NLR) in response to immune checkpoint inhibitor for advanced gastric cancer. First Author: Yang Chen, Department of Gastrointestinal Oncology, Key Laboratory of Carcino genesis and Translational Research (Ministry of Education), Peking University Cancer Hospital and Institute, Beijing, China

Background: We intended to evaluate the utility of neutrophil-to-lymphocyte (NLR) in advanced gastric cancer patients treated with immune checkpoint inhibitor (ICI).

Methods: We examined NLR at baseline and 6 (±2) weeks later in 139 patients between August 2015 and April 2019. Landmark analysis at 6 weeks was conducted to explore the prognostic value of NLR changes on progress-free survival (PFS), overall survival (OS), objective response rate (ORR), and disease control rate (DCR). Cox and logistic regression models were adjusted for tumor differentiation, Lauren classification, line of therapy, type of anti-PD-1/PD-L1 therapy, and baseline NLR.

Results: Median duration on therapy was 6 cycles. Median NLR was 3.33 (IQR: 2.26-4.84) at baseline and 2.93 (IQR: 1.67-4.43) at week 6. Patients with a higher baseline NLR showed a trend toward lower DCR, shorter PFS, and shorter OS. Higher NLR at 6 weeks was significantly associated with inferior PFS [hazard ratios (HR) = 1.03, 95% confidence interval (CI): 1.00-1.06] and inferior OS (HR 1.08, 95% CI: 1.03-1.13). Relative NLR decrease by ≥25% from baseline to 6 weeks after ICI therapy was an independent prognostic factor for ORR (OR 8.19, 95% CI: 4.27-17.4, DCR (OR 2.03, 95% CI: 1.33-3.07), PFS (HR 1.04, 95% CI: 1.01-1.07), and OS (HR 2.96, 95% CI: 1.01-0.65).

Conclusions: The early decline of NLR (and NLR at 6 weeks) were associated with improved clinical outcomes in advanced gastric cancer patients treated with ICI. Research Sponsor: None.

Association of NLR with survival in advanced gastric cancer patients.

No. of cases | No. of events | Univariate HR (95% CI) | Multivariate HR (95% CI) | No. of cases | No. of events | Univariate HR (95% CI) | Multivariate HR (95% CI)
--- | --- | --- | --- | --- | --- | --- | ---
Continuous NLR (baseline) | 139 | 96 | 1.03 (0.99-1.07) | 1.05 (0.98-1.07) | 64 | 44 | 1.03 (0.99-1.06) | 1.05 (1.02-1.06)
Continuous NLR (6 weeks) | 93 | 62 | 1.01 (0.97-1.05) | 1.05 (1.01-1.09) | 51 | 36 | 1.02 (1.02-1.04) | 1.06 (1.03-1.09)
NLR decrease | 62 | 46 | Increase | 0.29 (0.26-0.34) | 0.31 (0.28-0.34) | 14 | 10 | Increase | 0.35 (0.54-0.75) | 0.32 (0.14-0.73)
Decrease | 37 | 25 | No change | 0.29 (0.26-0.34) | 0.31 (0.28-0.34) | 24 | 14 | No change | 0.35 (0.54-0.75) | 0.32 (0.14-0.73)
Increase by ≥25% | 40 | 25 | Increase | 0.47 (0.40-0.55) | 0.52 (0.43-0.63) | 13 | 7 | Increase | 0.47 (0.29-0.76) | 0.55 (0.29-1.05)
Decrease by ≥25% | 35 | 27 | Decrease | 0.41 (0.35-0.49) | 0.47 (0.40-0.55) | 13 | 7 | Decrease | 0.47 (0.29-0.76) | 0.55 (0.29-1.05)

307 Poster Session (Board #B84), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Treatments patterns and long-term clinical outcomes in Chinese patients with nonmetastatic gastric cancer: Results from the non-interventional EVIDENCE registry study. First Author: Jiafu Ji, Peking University Cancer Hospital and Institute, Beijing, China

Background: Although gastric cancer (GC) is a leading cause of cancer-related death in China, information on treatment patterns and clinical outcomes remain unanswered. The EVIDENCE registry study evaluated data from patients with GC in China to assess the pattern of treatments and long-term clinical outcomes.

Methods: Five cohorts of patients with different HER2 and adjuvant chemotherapy status were evaluated from April 2013 to 2019 in this prospective, multicenter, non-interventional, real-world study. Data from patients with operable non-mGC were reported: Cohort III (HER2+) and Cohort V (HER2−). Outcome measures included overall survival (OS), event-free survival (EFS), and disease-free survival (DFS).

Results: Cohorts III/V included 758 patients (Cohort III, 279; Cohort V, 479). 75.5% were male and the median age was 58.8 years. The majority of Cohort III/V patients (538/758; 71.0%) received only adjuvant treatment, with 215/758 (28.4%) receiving S1oxaliplatin. Neoadjuvant or adjuvant trastuzumab was administered to 43/758 (5.7%) and 17/758 (2.2%) patients, respectively. EFS rates were 82% (76-87) and 86% (83-89) at 1 year, and 62% (53-70) and 57% (51-63) at 3 years; and respective DFS rates were 88% (82-93) and 86% (81-93) at 1 year and 69% (58-78) and 62% (55-68%) at 3 years. Multivariate analysis showed that positive ERBB2 status (p = 0.004) and overall cancer stage (p < 0.001) were associated with DFS.

Regarding the primary tumor site, there was a trend towards better DFS for antrum tumors (hazard ratio 0.59; 95% CI 0.32-1.07) when evaluated against gastroesophageal junction tumors. For nonmetastatic (m) status were evaluated from April 2013 to June 2018 in this prospective, multicenter, non-interventional, real-world study. Data from patients with non-mGC were reported: Cohort III (HER2+) and Cohort V (HER2−). Outcome measures included overall survival (OS), event-free survival (EFS), and disease-free survival (DFS).

First Author: Jiafu Ji, Peking University Cancer Hospital and Institute, Beijing, China

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Clinical impact of postgastroctomy sarcopenia on the prognosis in patients with gastric cancer. First Author: Beom Jin Kim, Chung-Ang University College of Medicine, Department of Internal Medicine, Seoul, South Korea

Background: There is a lack of research on newly developed sarcopenia postoperatively. The purpose of this study was to investigate the risk factors and the clinical impact of postgastroctomy sarcopenia on the prognosis in patients undergoing radical gastrectomy for gastric cancer. Methods: We retrospectively reviewed clinicopathological data from 430 consecutive GC patients who underwent surgical resection at Chung-Ang University Hospital between January 2011 and December 2015. The postoperative changes in skeletal muscle mass and abdominal fat volume were measured by abdominal CT imaging. Results: A total of 425 patients were analyzed in the study. The mean age was 62 years and male were 301 (70.8%). Of these, 42 patients (9.9%) were diagnosed as preoperative sarcopenic, 381 patients (89.3%) were diagnosed as newly developed sarcopenia in one year after gastric resection. Compared with non-sarcopenic group, the newly developed sarcopenic group showed more male, more undifferentiated tumor, lower hemoglobin level, less alcoholic, less smoking, and presence of diabetes mellitus. However, there was no significant difference in the 5-year overall survival and disease free survival between the groups (p = 0.836 and p = 0.638, respectively). Among 381 non-sarcopenic patients, 48 patients (12.6%) were diagnosed as newly developed sarcopenia in one year after gastric resection. Compared with non-sarcopenic group, the newly developed sarcopenic group showed more male, more undifferentiated tumor, lower hemoglobin level, less alcoholic, less smoking, and presence of diabetes mellitus. However, there was no significant difference in the 5-year overall survival and disease free survival among non-sarcopenic, sarcopenic, and newly developed sarcopenic groups (p = 0.521 and p = 0.534, respectively). The relationship between preoperative body fat volume and postoperative muscle mass showed a significant correlation (rho = 0.296, p < 0.001), but only BMI was significantly associated with long-term survival. Conclusions: Although newly developed sarcopenia after surgery did not affect the survival rate, patients with nutritional risk of sarcopenia after surgical resection may require early evaluation of nutritional status and nutritional support. Research Sponsor: None.

Relationship between perioperative change of total psoas muscle area and cancer prognosis in esophageal carcinoma. First Author: Kazuaki Matsui, Department of Surgery, Keio University School of Medicine, Tokyo, Japan

Background: As surgery for esophageal carcinoma in the elderly people has been increasing, sarcopenia is a severe problem not only in complications, but also in long-term prognosis. However, the relationship between perioperative skeletal muscle loss especially in the early postoperative period and long-term prognosis has not been clarified. Methods: This study retrospectively analyzed 152 patients with thoracic esophageal carcinoma who had undergone radical esophagectomy in our institution from April 2008 to March 2015 (Patients with postoperative hospital stay longer than 6 weeks were excluded). As an index of perioperative sarcopenia, total psoas muscle area (TPA) was measured before surgery (as baseline), at postoperative day (POD) 7 and one year postoperatively. Results: The correlation between the change of TPA and the postoperative survival. Results: Of 152 patients, 52 (34.2%) showed a TPA decrease at baseline to POD 7, and 98 (64.5%) showed a TPA decrease at baseline to POD 7. At the time of POD 7, overall survival (OS) decreased significantly in a TPA decrease group (P = 0.008, 5-year survival rate: non-decrease group 82.3% / decrease group 56.8%). Recurrence free survival (RFS) was also significantly decreased in a TPA decrease group (P < 0.001, 5-year recurrence free survival rate: non-decrease group 73.7% / decrease group 44.9%). On the other hand, at the time of POD 6, 0.5 and also RFS had no significant difference between decrease and non-decrease groups. In univariate analysis for OS, pStage ≥ 3 and TPA decrease at POD 7 had poor prognosis. In multivariate analysis for OS, pStage ≥ 3 (HR = 5.166, P < 0.001, 95%CI:1.634-15.512) and TPA decrease at POD 7 (HR = 2.036, P = 0.047, 95%CI:1.010-4.103) were also independent poor prognostic factors. In the univariate analysis for RFS, pStage ≥ 3, TPA decrease at POD 7 and age ≥ 60 years had poor prognosis. In multivariate analysis, pStage ≥ 3 (HR = 3.831, P < 0.001, 95%CI:1.822-7.282) and TPA decrease at POD 7 (HR = 2.942, P = 0.000, 95%CI:1.504-5.409) were independent poor prognostic factors. Conclusions: Our findings suggest that the TPA decrease early in a postoperative period has poor prognosis on OS and also RFS. Research Sponsor: None.
315 Poster Session (Board #B12), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM
Impact of palliative care in patients with metastatic esophageal cancer declining chemotherapy. First Author: Nicholas Manguso, Cedars-Sinai Medical Center, Department of Surgery, Los Angeles, CA

Background: Palliative care has been associated with improved overall survival (OS), but limited data exist in metastatic esophageal cancer (mEC). We investigated the impact of palliative care in patients with mEC who declined chemotherapy (CTX).

Methods: The National Cancer Database was used to identify patients between 2004-2015. Patients with MI disease who declined CTX and had known palliative care status (surgery, radiotherapy [RT], pain management, or any combination) were included. Cases with unknown CTX, RT, or nonprimary surgery status were excluded. Kaplan-Meier estimates of OS were calculated. Univariable and multivariable Cox regressions were performed. Results: Among 140,234 EC cases, we identified 1,493 patients who declined CTX and had complete data. Median age was 70 years, most (66.3%) had a Charlson Comorbidity Index (CCI) of 0, and 37.1% were treated at an academic center. Most (72.7%) did not receive palliative care. Median OS was 2.53 months (mos), with no statistically significant difference in median OS between those receiving palliative care (2.83 mos, 95% confidence interval [CI] 2.53-3.12) vs. no palliative care (2.37 mos, 2.2-2.56; p = 0.288). On univariable analysis, treatment at an academic center (hazard ratio [HR] 0.90, 0.80-1.00) and CCI = 2 (HR 1.20, 1.00-1.42) were predictive of OS (p < 0.05). On multivariable analysis, male sex (HR 1.23, 1.08-1.40), South geographic region (HR 1.23, 1.04-1.46), CCI of 1 (HR 1.17, 1.03-1.32), higher grade (HR 1.21, 1.07-1.38), and higher T stage (HR 1.39, 1.12-1.73) were associated with poor OS (p < 0.05).

Conclusions: Palliative care conferred a numerically higher, but not statistically significant, OS for examining the role of palliative care in mEC and future studies are warranted. Research Sponsor: None.

316 Poster Session (Board #B13), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM
Baseline features predicting receipt of chemotherapy in metastatic esophageal cancer: A National Cancer Database analysis of 12,370 patients. First Author: Nicholas Manguso, Cedars-Sinai Medical Center, Department of Surgery, Los Angeles, CA

Background: We investigated predictors for chemotherapy (CTX) and prognostic variables among patients with metastatic esophageal cancer (mEC) patient data set. Methods: We interrogated the National Cancer Database between 2004-2015 and included patients (pts) with MI disease who had known CTX status (received or did not receive CTX). Univariable and multivariable analyses were performed, and a logistic regression model was used to estimate the effect of CTX on OS adjustment for potential confounders. Results: We included 12,370 mEC pts with available CTX status for multivariable analyses. Predictors for CTX treatment included year of diagnosis 2010-2014 (odds ratio [OR] 1.29, 95% confidence interval [CI] 1.17-1.44), median income > $44,000 (OR 1.49, 1.27-1.75), and node-positivity (OR 1.35, 1.20-1.52; all p < 0.05), while female gender (OR 0.86, 0.76-0.98), black race (OR 0.76, 0.67-0.93), uninsured (OR 0.41, 0.33-0.52), and Charlson Comorbidity Index (CCI) ≥ 2 (OR 0.61, 0.50-0.74) predicted for lower odds of receiving CTX (all p < 0.05). Median OS for pts receiving CTX was 9.5 months (95% confidence interval [CI] 9.3-9.7 vs 2.43 mos (95% CI 2.2-2.6) with no CTX (p < 0.001). Modeling the effect of CTX to OS using a time-dependent coefficient showed that CTX was associated with improved OS up to 10 months, after which there is no significant effect on OS. Independent predictors of OS included treatment at an academic center (HR 0.90, 0.87-0.94), CCI ≥ 2 (HR 1.23, 1.06-1.42), and uninsured status (HR 1.20, 1.09-1.31). Conclusions: We identified several predictors for receipt of CTX and OS in pts with mEC. The benefit of CTX on OS is time-dependent and favors early initiation. Focused outreach in lower income and underinsured patients is critical as receipt of CTX is associated with improved OS. Research Sponsor: None.

317 Poster Session (Board #B14), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM
Real-world treatment attrition rates in advanced esophagogastric cancer. First Author: Erica S. Tsang, BC Cancer, Vancouver, BC, Canada

Background: Over the last decade, multiple agents have demonstrated efficacy for advanced esophagogastric cancer (EGC), including ramucirumab, irinotecan, triluridine/tipiracil, and immunotherapy. Despite the availability of many options in EGC, there remains limited real-world data about the impact of treatment attrition in patients with advanced EGC.

Methods: We identified patients who received at least one cycle of chemotherapy for advanced EGC between July 1, 2017 and July 31, 2018 across 6 regional centers in British Columbia (BC), Canada. Clinicopathologic, treatment, and outcomes data were extracted by chart review. Results: Of 169 patients who received at least one line of therapy, median age was 65.2 years (IQR 58-72) and 128 (76%) were male, ECOG PS 0/1 (84%), gastric vs GEJ (35% vs 65%). Histologies included adenocarcinoma (76%), squamous cell carcinoma (10%) and signet ring (14%), with 26% HER2 positive. 62% presented with de novo disease, and 35% had received previous chemotherapy. There was a high level of treatment attrition, with patients receiving only one line of therapy (n = 73, 43%), two lines (n = 65, 38%), three lines (n = 25, 15%), and four lines (n = 6, 4%). Kaplan-Meier survival analysis demonstrated improved survival with increasing lines of therapy (median overall survival 9.6 vs. 18.5 vs. 25.8 vs. 40.7 months, p < 0.05). On multivariable Cox regression, improved survival was associated with better baseline ECOG, longer duration of first-line therapy, and increased lines of therapy (p < 0.01).

Conclusions: The steep attrition rates between therapies highlight the unmet need for more efficacious earlier-line treatment options for patients with advanced EGC. Research Sponsor: None.

318 Poster Session (Board #B15), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM
Helicobacter pylori-negative gastric cancer in Guatemala: Incidence, clinical characteristics, treatment modalities, and outcomes. First Author: Ruxi Ramirez, Department of Oncology, Instituto Guatemalteco de Seguridad Social, Guatemala City, Guatemala

Background: Gastric cancer (GC) in Guatemala is the second most common cancer diagnosis and the second leading cause of cancer death in both sexes. It is difficult to determine the exact incidence rate of H. pylori infection-positive gastric cancer (HPIN-GC) because H. pylori detection rates decrease with the progression of gastric atrophy and intestinal metaplasia. The aim of this study was to evaluate the incidence, clinicopathologic characteristics, treatment modalities and outcomes. Methods: A retrospective review of the medical records of 210 pts with histological diagnosis of gastric cancer evaluated at the General Hospital of Diseases from the Guatemalan Social Security Institute (IGSS) from January 2010 to December 2018. Helicobacter pylori infection status was evaluated by histology, a rapid urease test Current H. pylori infection was defined as positive if histology, a rapid urease test was positive. Infection positivity was estimated by Kaplan Meier method and compared by Log-rank test. P value < 0.05 was considered significant. Results: The rate of HPIN-GC occurrence was 36% (n = 76). Sex, age, location of the tumor, Lauren’s classification and treatment modalities were not different according to H. pylori infection status. However, HPIN-GC had a more advanced pt classification (T3/T4; 58 vs 28%, p = 0.019) and a more advanced stage (more than stage I; 64 vs 44%, p = 0.033) than H. pylori-positive gastric cancer. Treatment modalities: 23% gastrectomy, 24% palliative care, 54% systemic chemotherapy at any time of disease course, 33% initial palliative surgery (derivative o gastrectomy), gastrectomy at any time in 16% (n = 7). For those patients who received systemic chemotherapy (n = 115) objective response rate was 38% and disease control rate 66%.Median OS was 26 months: 47 m for localized, 18 for locally advanced, and 8 m for advanced disease (P = 0.0001). Only 17% of patients received second line chemotherapy and 4% a third line. Conclusions: At least 36% cases of gastric cancer were H. pylori negative. HPIN-GC looks like to have a poorer prognosis than H. pylori-positive cases. HPIN-GC can be offered to less than a half of patients, the earliest stages are associated with better survival. Research Sponsor: None.
Treatment modalities and oncological outcomes in Mexican patients with localized gastric cancer. First Author: Hayato Watanabe, Department of Gastrointestinal Surgery, Kanagawa Cancer Center, Yokohama, Japan

**Background:** Postoperative complications increased recurrence in gastric cancer (GC) patients. However, there was no study evaluating impact of postoperative complication among patients receiving adjuvant chemotherapy. The aim of present study was to investigate the impact of postoperative complications in pStage II/III GC patients who received adjuvant 5-FU chemotherapy. Methods: The present study retrospectively examined GC patients who received curative gastrectomy followed by adjuvant 5-FU chemotherapy between January 2000 and December 2011 at Kanagawa Cancer Center. The patients with postoperative complications were classified into PC group, and those without postoperative complications were into NC group. Results: 226 patients were included in this study. Postoperative complication occurred in 30 patients (13.3%). Age (Median, range) is significantly higher in NC group (64, 24-86) than in PC group (59, 36-82) (p = 0.033). Total resection was predominant type of surgery in the PC group (73.3%) than in NC group (52.0%) (p = 0.033). There was no difference in gender, ASA score, tumor location, pathological stage (TNM 7th) and pathological type between two groups. Conclusions: Postoperative complication was an independent risk factor for RFS in pStage II/III GC patients who received curative gastrectomy followed by adjuvant 5-FU chemotherapy. Research Sponsor: None.
Presented to Princess Margaret Cancer Centre from 2008 to 2016. The Kaplan-Meier analysis was performed for AYA (age 16-39) patients. The National Cancer Database (2004-15) was queried for patients with non-metastatic esophageal cancer. Esophageal cancer was thought to behave more aggressively than each of its counterparts. Our aim was to determine if ASC is best managed as adenocarcinoma or squamous cell carcinoma. Methods: The National Cancer Database (2004-15) was queried for patients with non-metastatic, esophageal ASC. Analysis was stratified by clinical node negative (cN0) or node positive (cN+3) according to AJCC 8th edition. Treatment types were categorized into chemoradiation alone, surgery alone, or preoperative chemoradiation followed by surgery. Primary outcome was overall survival (OS). Results: Among 352 pts, median age was 67 yrs, 80% were male (n = 281). Median f/u was 46 mos. 43% were cN0 (n = 151), 57% were cN+3 (n = 201). 55% had chemoradiation alone (n = 194), 15% had surgery alone (n = 53) and 30% had preoperative chemoradiation (n = 106). Of pts who had preoperative chemoradiation, 20% had pathologic complete response (n = 17).

For either cN0 or cN+3, Charlson-Deyo Comorbidity Index did not differ among the treatment groups (all p > 0.05). On KM analysis for cN0 disease, treatment with surgery alone had a comparable 5-yr OS to preoperative chemoradiation (47% vs 34% p = 0.5) and each had improved 5-yr OS compared to chemoradiation alone (30%; p = 0.02; p = 0.06). On UV analysis for patients with cN0 disease, clinical T-stage was not associated with 5-yr OS. For patients with cN+3 disease, however, preoperative chemoradiation was associated with improved 5-yr OS when compared to chemoradiation alone (27% vs 16% p < 0.001). This persisted even when accounting for age and clinical T-stage (HR 0.45 p < 0.001).

Conclusions: Esophageal adenocarcinoma behaves more like adenocarcinoma both in response to chemoradiation and survival outcomes based on the treatment modality. The complete response rate to chemoradiation is only 20% unlike what has been shown for squamous cell carcinoma, where chemoradiation is an acceptable definitive therapy. Esophageal adenocarcinoma should be managed as adenocarcinoma and not squamous cell carcinoma. Research Sponsor: Katz Foundation.

Clinicopathological features and treatment outcomes of young patients with gastric and esophageal cancers. First Author: Lauren A. Beck, University of Toronto, Toronto, ON, Canada

Background: Gastric and esophageal (GE) cancers most commonly occur in older adults in their 60’s. There are inconsistent reports about prognosis in adolescent and young adult (AYA) pts, and treatment patterns and outcomes in this group have been less well characterized. A retrospective analysis was performed for AYA (age < 40) pts with GE cancers who presented to Princess Margaret Cancer Centre from 2008 to 2016. The Kaplan-Meier method was used to analyze progression free survival (PFS) and overall survival (OS). Results: A total of 77 AYA GE cancer pts (30 gastric, 27 esophageal). Features at diagnosis included: median age 35, 51% female (70% in gastric, 30% in esophageal), 82% with performance status 0-1, 83% Charlson Comorbidity Index 0, 54% stage IV. For gastric pts, 53% had diffuse histology and 47% had signet ring adenocarcinoma. There was a negative family history of gastric or esophageal cancer in 77% of pts. Curative intent treatment was the younger age groups p < 0.001. After propensity score matching, the younger age groups p < 0.001. Median and overall survival (22.9% vs 20.5% vs 16.9% vs 13.4%) p < 0.001. After propensity score matching, the younger age groups p < 0.001. Median and overall survival (22.9% vs 20.5% vs 16.9% vs 13.4%) p < 0.001. Additionally, tumor size was largest in this age cohort (3.7 vs 3.5 vs 3.2) p = 0.002. Neoadjuvant therapy was administered in 69.4% of patients in the < 50, 68.5% (51-60), 65.5% (61-70), and 49.5% (< 70) patients, p < 0.001. The < 50 age group was however more likely to receive adjuvant therapy (22.9% vs 20.5% vs 16.9% vs 13.4%) p < 0.001. Median and overall survival was 49.8 mo and 45% (< 50), 45.4 mo and 43% (51-60), 45.4 mo and 43% (61-70), and 35.8 mo and 39% < 70, p < 0.01. After propensity score matching, multivariate analysis found that age < 50, male gender, GE tumor location, stage IV at diagnosis, Charlson Deyo score, T-stage N stage, margin, faculty volume, neo-adjuvant and adjuvant therapy were predictors of survival.

Conclusions: Younger patients present with more advanced tumors, higher Charlson Deyo score, and are more likely to receive neoadjuvant and adjuvant therapies. It is these therapies that are most likely contributing to better survival compared to their older counterparts. Research Sponsor: None.
Patterns of disease, treatment, and outcomes of esophageal cancer arising within a previous radiation treatment field. First Author: Lucy Xiaolu Ma, Princess Margaret Cancer Centre, Toronto, ON, Canada

Background: Esophageal cancer arising within a previous radiation treatment field (ECRF) is rare. The patterns of disease, treatment and outcomes in these patients (pts) have not been well characterized. Methods: A retrospective analysis was performed for pts treated for esophageal cancer at the Princess Margaret Cancer Centre from 2002-2016. Electronic medical records of all pts with a histologic diagnosis of esophageal cancer occurring within the beam's previous radiation field were reviewed. The Kaplan-Meier method was used to calculate progression free survival (PFS) and overall survival (OS). Results: Of 31 ECRF pts identified, the most common prior cancer was head and neck (45%), median radiation (RT) dose 50Gy, median time to diagnosis of esophageal cancer 12 years. Features at diagnosis of ECRF included: median age 71 years, 58% male, 87% with performance status (PS) 0/1, 77% squamous cell carcinoma, 19% stage IV. Treatment intent was curative in 16 pts, palliative in 15 (Table). Reasons for palliative treatment were: 40% metastatic, 53% comorbidities/PS, 7% anatomic factors. Of resected pts, 36% had a pT1-T2 tumour, 55% pN0, 69% pR0. For curative pts, median PFS was 26.2 months (95%CI 10.9-34.4) with a 3 year PFS rate of 35% (95%CI 0.15-0.85). Median OS for curative pts was 26.4 months (95%CI 17.8-35.3). Most palliative pts were unable to have chemotherapy due to comorbidities and PS. Median OS for palliative pts was 95 months (95%CI 3.6-15.4). Conclusions: Most ECRF pts presented with earlier stage disease; however, more than a third of these could not have aggressive curative treatment due to comorbidities and/or PS. Most curative pts had surgery alone. Few palliative pts had chemotherapy, largely due to poor clinical status. Our data suggest that outcomes in both curative and palliative ECRF pts may be limited by the ability to tolerate standard care treatments. Research Sponsor: Princess Margaret Cancer Centre.

328 Poster Session (Board #C3), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Morbidity associated to advanced gastric cancer and its impact on overall survival. First Author: Mónica Isabel Meneses Medina, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico, DF, Mexico

Background: Advanced gastric cancer (GC) is a disease with high morbidity and poor prognosis. We hypothesize that different sites of metastasis have different impacts in terms of symptoms and complications. We sought to evaluate if site specific morbidity in our patients impacted treatment and survival.

Methods: Medical records from patients with advanced GC treated from Jan 2005 to Dec 2015 were retrospectively reviewed. Morbidity was defined as having any symptom by metastases in a specific site. OS was estimated by Kaplan Meier method and compared by Log-rank test. P value < 0.05 was considered significant.

Results: We included 180 consecutive patients, median age at diagnosis was 56 years (21-90), 55% were women. Most common sites of metastases were: peritoneum 76.1%, non-regional lymph nodes 38.9%, liver 22.8%, lung 26.7%, bone 9.4% and ovary 12.8%. Regarding morbidity, at diagnosis 68% of patients presented morbidity by the primary tumor: obstruction 56%, bleeding 27%, obstruction and bleeding 3%, other 14%. Disease by peritoneum caused morbidity in 30%, by lung in 8%, by ovarian in 4.4%, by lymph nodes in 3.3%, and by other sites in 5.6% of patients. OS in the global cohort was: 3.53 months (2.2 to 4.8), nevertheless by univariate analysis we found that OS was affected by morbidity at some sites as it is show in table. More patients with peritoneal morbidity could not receive treatment vs those without peritoneal morbidity (p = 0.042).

Conclusions: We found that morbidity in peritoneum, lung and ovary adversely affected prognosis of patients with advanced GC. Moreover, peritoneal morbidity preclude patients from receiving oncological treatment. Research Sponsor: None.

329 Poster Session (Board #C4), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Patterns of gastric cancer metastasis within the United States. First Author: Joseph Sirody, Harbor UCLA Medical Center, Torrance, CA

Background: There are few reports on the epidemiology of gastric cancer metastasis, although outcomes are known to be uniformly poor. Here we describe the patterns of gastric cancer metastasis and treatment in the United States (US).

Methods: Patients with gastric adenocarcinoma histologies were identified in the National Cancer Database (NCDB) from 2002-2016. We describe univariate associations between different sites of metastasis and clinicopathologic characteristics and treatment modalities, using the chi-square and Kruskal-Wallis tests. Kaplan Meier curves were constructed for the estimation of overall survival (OS) by metastatic site. Results: Due to changes in the coding of metastatic disease, we were limited to the year 2016 for evaluation of patterns of disease. Twenty-six percent (n = 1228) of gastric cancer patients presented with liver metastases, 20% (n = 941) with distant lymph nodes, 43% (n = 2028) with other distant site metastases (including peritoneum), and the rest to bone, brain or lung. Univariate analysis, when compared to liver metastases, other distant site metastases were significantly more likely to arise from an antral primary site (28% v. 16%); to be of Hispanic origin (16% v. 7%); female (42% v. 29%); associated with signet ring histology (34% v. 6%); lymphovascular invasion (LVI) (58% v. 27%); and tumor grade III/IV (85% vs. 60%) (p < 0.0001 for all). There were no significant differences in how patients with metastatic disease were treated in terms of systemic therapy. With regard to OS, due to how metastatic sites were coded prior to 2016, it was not possible to compare peritoneal metastases against other sites; however, patients with distant nodal disease had improved median overall survival compared to those with any other metastatic site (7.9 v. 5.2 months, p = 0.0001). Conclusions: The majority of US patients with metastatic gastric cancer present with presumed peritoneal disease. Predictive factors for peritoneal metastases vs. liver metastases included adverse prognostic features, including signet ring histology, higher tumor grades, and LVI. Although it was not possible to compare OS of patients with these sites of metastases due to changes in the coding of metastatic disease, a continued follow up is needed, as this may impact future staging. Research Sponsor: None.

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First-line chemotherapy versus chemoradiation for resectable distal esophageal adenocarcinoma. First Author: Susanna W. L. de Geus, Boston Medical Center, Boston, MA

Background: Multiple randomized controlled trials have shown that both neoadjuvant chemotherapy (CT) and chemoradiation (CRT) convey survival benefit as compared to upfront surgery in patients with esophageal adenocarcinoma. However, international practice remains variable. Therefore, the present study compares the outcomes of first-line CT to CRT for patients with adenocarcinoma arising from the distal esophagus. Methods: Patients with clinical stage T2-3, N0-N+ esophageal adenocarcinoma originating from the distal esophagus who received first-line CT or CRT were identified from the National Cancer Data Base (2006-2014). Propensity-score were created for the odds of receiving CRT. Patients were matched 1:1 based on propensity score. Subset analysis was performed in patients who underwent esophagectomy. Pathological complete response was defined as ypTONOMO. Results: In total, 709 and 8,877 patients who received first-line CT and CRT were identified, respectively. CT was associated with stage T2 (27.2% vs. 23.3%; p = 0.017), and treatment at a high-volume center (27.2% vs. 20.2%; p = 0.001). After matching, response rates were comparable for patients who received first-line CT and CRT (62.2% vs. 63.7%; p = 0.545). However, median overall survival was slightly lower for patients who receive CT compared to CRT (23.7 vs. 28.4 months; p = 0.044). Among patients who underwent esophagectomy, stage to surgery (135 vs. 134 days; p = 0.689) and median overall survival (37.0 vs. 40.5 months; p = 0.630) was similar between matched cohorts. However, complete response (15.8% vs. 25.8%; p < 0.001) and negative margin (94.3% vs. 88.9%; p = 0.004) rates were significantly lower after CT compared to CRT. Conclusions: In patients with esophageal adenocarcinoma, first-line CRT results in significantly higher pathological complete response rates, negative resection margins, and improved survival. These findings suggest that first-line CRT is preferable over CT when tolerated in patients with esophageal adenocarcinoma. Research Sponsor: None.

Tumor size and the risk for lymph node metastases in T1 esophageal adenocarcinoma. First Author: Meena Sadaps, Cleveland Clinic, Cleveland, OH

Background: Adjuvant therapy after endoscopic resection (ER) of T1 EAC in non-surgical candidates is largely based on the risk of LNM. Risk factors for LNM in T1 EAC are not clearly defined. Our aim is to evaluate risk factors for LNM in T1 EAC patients following esophagectomy or ER with ≥ 5 years of follow-up. Methods: This is a retrospective analysis at a large tertiary referral center. Our pathology database identified patients who underwent esophagectomy or ER with ≥ 5 years follow-up, with histologically proven T1 EAC from 2010-2017. Patients were excluded if they (a) received chemoradiation prior to esophagectomy or before/after ER (b) had any other primary cancer treated within the previous 5 years. Specimens were reviewed by two experienced pathologists for pathology. Results: Of 80 patients (85% males), 61 (76%) underwent esophagectomy and 19 (24%) underwent ER. Twelve (15%) developed LNM per study criteria. Tumor size was significantly (p-value 0.014) associated with risk of LNM. No other factors including lymphovascular invasion, differentiation on pathology, macroscopic appearance, infiltration growth pattern, or tumor distance from the gas-troesophageal junction were significant risk factors for LNM. Conclusions: In T1 EAC, tumor size appears to be a significant risk factor for LNM at five years following surgical or endoscopic resection. Adjuvant therapy should be considered in patients with larger tumor size. Research Sponsor: None.

Relationship of periodic methylation patterns in the gastric mucosa and periodic stem cell replacement. First Author: Jung-Hwan Oh, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, South Korea

Background: The role of Helicobacter pylori-associated methylation in the inactivation of tumour-suppressor genes has been previously investigated. However, the relationship between H. pylori-associated methylation and gene inactivation is unclear. Stem cells are replaced periodically every 8 years in the gastrointestinal mucosa. Hence, age-related methylation in the gastric mucosa was studied to understand the stabilization of new stem cell phenotypes. Methods: Endoscopic biopsy specimens of the antral mucosa were obtained from 486 H. pylori-positive and 124 H. pylori-negative subjects. The methylation-variable sites of 4 housekeeping genes (CDH1, ARRD4C, MMP2, and CDKN2A) and 2 stomach-specific genes (TFF2 and CDH3) were examined using radiolabelled methylation-specific polymerase chain reaction. Age-related methylation was evaluated at an interval of 2 years. Results: The 4 housekeeping genes were more frequently methylated in H. pylori-positive subjects than in H. pylori-negative subjects. Periodic changes in the housekeeping gene methylation were periodically fluctuated approximately at 8-year intervals in the gastric mucosa. Conclusions: Periodic methylation changes in the gastric mucosa may be used to estimate the replacement of new stem cells. Research Sponsor: None.

Safety, pharmacokinetics, and efficacy of RC48-ADC in a phase I study in patients with HER2-overexpression advanced solid cancer. First Author: Jifang Gong, Department of Gastrointestinal Oncology, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Peking University Cancer Hospital and Institute, Beijing, China

Background: HER2 overexpression is common in many malignancies and contributes to tumor growth. Unlike the varied options of anti-HER2 target therapies for breast cancer, there is a huge unmet need for patients with HER2-overexpressing non-breast solid tumor (NBST) such as gastric cancer and uterine cancer. Therefore, we conducted the first study of RC48-ADC, a novel humanized anti-HER2 antibody conjugate, in NBST. Methods: This was a Phase I study of RC48-ADC in patients with HER2-overexpression (IHC 2+ and 3+) advanced solid cancers after failure of standard treatment. The dose escalation consisted of accelerated (0.1 and 0.5 mg/kg) and “3+3” titrations (1.0, 2.0, 2.5 and 3.0 mg/kg). In dose expansion stage, patients were given RC48-ADC at 2.0 mg/kg. Q2W. Results: As of Aug 20, 2019, 57 patients (including 47 with gastric cancer and 4 with uterine cancer) were treated at 0.1 (1 patient), 0.5 (1 patient), 1.0 (3 patients), 2.0 (6 patients in dose escalation and 32 patients in dose expansion), 2.5 (11 patients), and 3.0 mg/kg (3 patients), respectively. Most of them were Stage IV (91.2%) or with metastasis (96.5%). DLT was observed in 1, 2, and 1 patient at 2.0, 2.5, and 3.0 mg/kg, respectively. The MTD was 2.5 mg/kg. Most commonly reported TRAEs were WBC count decreased (66.7%), fatigue (56.1%), neutrophil count decreased (54.4%) and hemoglobin decreased (52.6%). Grade 3/4 TRAEs were reported in 28 patients (49.1%). Confirmed ORR was 21.1% (8/38) for 2.0 mg/kg, and 17.5% (10/57) for all patients. DCR was 52.6% and 49.1%, respectively. PFs was 3.6 months (95% CI; 4.1, 11.3) for 2.0 mg/kg. Subgroup ORR was 20.7% (6/29) at 2.0 mg/kg and 18.2% (2/11) at 2.5 mg/kg for gastric cancer, and 50.0% (2/4) for uterine cancer. Conclusions: RC48-ADC demonstrated a good safety profile and promising anti-tumor activity in the late stage solid tumor including gastric cancer and uterine cancer. Research and PFS benefits were clinical meaningful at 2.0 mg/kg. Phase 2 pivotal study (NCT03556345) in gastric cancer is ongoing. Clinical trial information: NCT0288190. Research Sponsor: Remegen, Ltd.
Exploring the epidemiology of gastric cancer in a Tibetan population. First Author: Krishna K. Mehta, Stony Brook School of Medicine, Stony Brook, NY

Background: Gastric cancer is the 3rd leading cause of death from cancer and the 5th most common cancer worldwide. It is the primary cause of death for people of Tibetan origin in the Himalayan belt, with incidence (and death) rates between 100-400/100,000 people per year. Despite such a high cancer burden, the epidemiology of gastric cancer has not been studied in this population. In this study, we explore gastric cancer risk factors among Tibetan refugees residing in India. Methods: Patients diagnosed with gastric cancer were identified through cancer registry, cancer hospital admission, discharge and out-patient endoscopy records between 2013-2019 at the Tibetan Delek Hospital in Dharamshala, India. Risk factors not captured in the records were collected through interviews of patients or their relatives. Results: A total of 52 gastric cancer cases were identified, mostly males (77%). Median age was 78 (range 30-91) years. Of the gastric cancer cases, 32% (n = 12/37) were retired military, 19% (n = 3/16) had used alcohol, and 40% (n = 17/43) were past smokers. Ninety-five percent (n = 20/21) of cases had been treated with traditional Tibetan medicine for various reasons in the past. Of the 17 patients (or relatives) interviewed for dietary risk factors, 76% (n = 13) reported frequent ingestion of stale and unrefrigerated food, 30% (n = 5) did not eat fresh fruit, and 47% (n = 8) reported intake of fresh fruit < 3 times per month. Most (83%, n = 24/29) patients had non-cardia cancers located in the fundus/body (n = 12) and antrum/pylorus (n = 12). Fifty-two percent (n = 16/31) had been treated with either chemotherapy, radiotherapy, or surgery, and 34% (n = 11/32) of the patients were receiving traditional Tibetan medicine as treatment for gastric cancer. Conclusions: Tibetan people have socio-cultural, behavioral and dietary risk factors that may be associated with gastric cancer. Investigations of causal factors (genetic, infective (Helicobacter pylori), environmental) with possible synergistic interactions could inform clinical and public health practice for this population and globally. Research Sponsor: Henry and Marsha Laufer; Stony Brook International Research Fellowship.

Distribution of sites in patients with GC.

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<th>Metachronous</th>
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337 Poster Session (Board #12), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Multiple primary cancers in patients with gastric cancer: A retrospective study in China National Cancer Center. First Author: Qi Lei, Peking Union Medical College Hospital, Chinese Academy of Medical Science and Peking Union Medical College, Beijing, China

Background: Gastric cancer (GC) is common in China. With the total incidence of cancer keeping rising in China, the occurrence of multiple primary cancers with GC as the protection and diagnosis of synchronous or metachronous cancers are vital for patients’ survival. Methods: Patients with multiple primary cancers containing gastric adenocarcinoma treated in China National Cancer Center from January 2010 to December 2017 were included. A 6-month interval was used to separate synchronous and metachronous cancers (according to IARC/ACR criteria). Results: 479 patients met the criteria were included, with 452 (94.4%), 24 (5.0%), 0.3 (0.6%) patients having two, three or more primary cancer sites respectively, contributing a total of 510 cancer sites besides stomach (Table). Malignancies at 257 (50.4%) sites occurred with GC synchronously, while 253 (49.6%) occurred metachronously. The median age at the diagnosis of first cancer was 59 (interquartile range [IQR], 53-66) years. The median interval between the diagnosis of first cancer and metachronous second one was 50.3 (IQR, 23.7-97.0) months. Cancers outside gastrointestinal (GI) tract were more likely to occur with GC metachronously, while GI tract cancers were more likely to occur synchronously (χ²=55.36, p<0.001). Out of 479 patients, there were 352 (73.6%) male and 127 (26.4%) female. The most common associated cancer was esophagus cancer (422, 40.3%) in male, and breast cancer (27, 37%) in female. 263 (49.6%) patients were current smokers or ex-smokers, and 190 (40.4%) were regular alcohol consumers. 10.2 (37%) had first-degree relative cancer family history, with 81 (17.7%) having GI tract cancer family history. Conclusions: GI tract including esophagus and colorectum should be carefully examined for synchronous or metachronous cancers when patients with gastric cancer have synchronous or metachronous cancers during follow-up. Further genetic studies are warranted to explore the potential pathogenesis of multiple primary cancers. Research Sponsor: None.

336 Poster Session (Board #C11), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Screening and treatment strategy for double cancer for esophageal cancer surgery patients. First Author: Takashi Ogata, Kanagawa Cancer Center, Yokohama, Japan

Background: Esophageal cancer treatment, especially esophagectomy, is highly invasive, so treatment strategies are considered in view of existing double cancers. On the other hand, in Japan, 90% of esophageal cancers are squamous cell carcinoma, and it is known that there are a large proportion of head and neck cancers for double cancers as field carcinization. Methods: The aim of this study is to investigate the types of double cancer, simultaneous/metachronous, and the frequency and treatment policy of head and neck cancer as a particularly high coexistence rate for esophageal cancer surgery patient. The subjects were 304 patients who underwent esophagectomy performed from April 2010 to December 2017. All patients were examined with high-definition endoscopy with NBI by certificated endoscopist at the first visit as a search for simultaneous double cancer from the pharynx to the stomach. And after esophagectomy, endoscopy was also performed to check for metachronous double cancers in the remaining esophagus, gastric tube, and pharynx at least every 2 years. Results: The number of double cancer cases was found in 94 cases (30.9%), and the total number of double cancer cases was 122. Head and neck cancer(33 cases), stomach cancer(16 cases), and colon cancer(12 cases) were observed as the main course of double cancers. In double cancer cases, 47cases(50.0%) were metachronous, 35cases(37.2%) were simultaneous, and 12cases(12.8%) were both synchronous. The most common double cancer was head and neck cancer(33 cases:35.1%), and 23 cases were simultaneous, 10 cases were metachronous. As treatment strategy for head and neck cancer, endoscopic laryngo-pharyngo surgery(ELPS) were 19 cases, 10 cases(52.6%) were synchronous cancers, and 9 cases (47.3%) were metachronous cancers which were detected during follow-up after esophagectomy. Conclusions: Head and neck cancer associated with esophageal cancer surgery is the most common type of double cancer, and 1/3 of ELPS cases have been detected by follow-up endoscopy after esophagectomy, so endoscopic surveillance was also considered important. Research Sponsor: None.

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Economic impacts of care by high-volume providers for noncurative esophagogastric cancer: A population-based analysis. First Author: Julie Hallet, Odette Cancer Centre, Toronto, ON, Canada

Background: Esophagogastric cancer (EGC) is one of the deadliest and costliest malignancies to treat. Care by high-volume providers can provide better outcomes for patients with EGC. Cost implications of volume-based care are unclear. We examined the cost-effectiveness of care by high-volume medical oncology providers for non-curative management of EGC.

Methods: We conducted a population-based cohort study of non-curative EGC over 2005-2017 by linking administrative healthcare datasets. High-volume was defined as >1 patients/provider/year. Healthcare costs ($USD/patient/month-survived) were computed from diagnosis to death or end of follow-up from the perspective of the healthcare system using validated costing algorithms. Multivariable quantile regression examined the association between care by high-volume providers and costs. Sensitivity analyses were conducted by varying costing horizons and high-volume definitions.

Results: Among 7,011 non-curative EGC patients, median overall survival was superior with care by high-volume providers with 7.0 (IQR: 3.3-13.3) compared to 5.9 (IQR: 2.6-12.1) months (p < 0.001) for low-volume providers. Median costs/patient/month-lived were lower for high-volume providers ($5,518 vs. $5,911; p < 0.001) owing to lower inpatient acute care costs, despite higher medication-associated and radiotherapy costs. Care by high-volume providers was independently associated with a reduction of $599 per patient/month-lived (95% confidence interval: -966 to -331) compared to low-volume providers. The incremental cost-effectiveness ratio was -$93. Care by high-volume providers remained the most cost-effective strategy when examining the high-volume definition and the costing time horizon.

Conclusions: Care by high-volume providers for non-curative EGC is associated with superior survival and lower healthcare costs, indicating a dominant strategy that may provide an opportunity to improve cost-effectiveness of care delivery. Research Sponsor: CIHR.

Results:
- Of over 2500 patients un-
- An economic evaluation of palliation of dysphagia in esophageal cancer: Analysis of the TROG 03.01/NCTE ES.2 phase III study in advanced esophageal cancer in patients treated with radiotherapy versus chemoradiotherapy. First Author: Michael Gordon Pennington, Royal Adelaide Department of Radiation Oncology, Kensington Park, SA, Australia

Background: In advanced esophageal cancer (OC), 90% of patients have dysphagia as a principal symptom. The randomised TROG 03.01 trial reported no significant overall survival or dysphagia relief difference between 15 fractions (4) radiotherapy alone (RT) or RT plus chemotherapy (CRT) Future studies may consider RT hypofractionation, different chemotheraphy regimens, esophageal stenting, and best supportive care. Comparing costs and outcomes, economic evaluation often informs public funding decisions in countries such as Australia and the UK. The objective of this analysis was to derive baseline cost and outcome for further studies. Methods: Given equal outcomes (non-
- Cryotherapy in addition to chemotherapy for palliation of inoperable esophageal cancer: A multicenter prospective study. First Author: Toufic Kachaamy, Cancer Treatment Centers of America, Zion, IL

Background: Palliation of dysphagia (Dys) in patients with inoperable esophageal cancer (EC) can be challenging. The major goal of palliation therapy is to improve patient’s quality of life (QoL) and Dys and allow adequate nutrition intake. The most commonly used palliative therapy for Dys is radiation therapy (RT) and esophageal stenting. However, RT is limited by total dose and adverse events (AE) in patients receiving systemic therapy (ST), and stenting suffers from a high rate of AE including reflux and chest pain. A relatively new modality of liquid nitrogen endoscopic spray cryotherapy (cryo) has been reported in retrospective studies to improve Dys in patients receiving systemic therapy. We prospectively evaluated Dys and QoL of patients with inoperable EC undergoing cryo in addition to ST for palliation. Methods: A prospective multicenter study of 24 adult inoperable EC patients undergoing cryo and ST for palliation at 4 specialized cancer centers from Sep 2017 to Aug 2019. QoL was assessed using a modified EORTC QLQ-ES18 questionnaire (score 18 to 72, with higher scores indicating worse QoL). Dys was measured using a 4-point Likert scale: 0, no Dys; 1, Dys to solids; 2, Dys to semi-solids; 3, Dys to liquids; 4, Dys to saliva. Paired t-test was used to evaluate change in QoL and Dys between pre- and post-cryo. Results: There were 19 males and 5 females (17 stage IV, 5 stage III, and 2 stage II at diagnosis). Among 24 patients, a total of 71 cryo were performed, with a mean of 2.9 treatments per patient. After a median follow-up of 2 months, the mean EORTC score im-
- Cryotherapy in addition to chemotherapy for palliation of inoperable esophageal cancer: A multicenter prospective study. First Author: Toufic Kachaamy, Cancer Treatment Centers of America, Zion, IL

Methods: Among 24 patients, a total of 71 cryo were performed, with a mean of 2.9 treatments per patient. After a median follow-up of 2 months, the mean EORTC score improved significantly from 35.4 at baseline to 25.5 at last follow-up (p < 0.001). Similarly, the Dys score improved significantly from 2.0 at baseline to 0.87 at last follow-up (p < 0.001). Grade 3 or higher AE were seen in only one patient (4%). The Dys score improved significantly from 2.0 at baseline to 0.87 at last follow-up (p < 0.001).

Conclusions: The analysis of this multicenter prospective study shows that cryo in addition to ST for palliation of EC is well tolerated with significant improvement in Dys and QoL. Research Sponsor: None.
ESOPHAGEAL AND GASTRIC CANCER

Variation in treatment patterns and outcomes for resected esophageal cancer at designated thoracic surgery centers. First Author: Vaibhav Gupta, University of Toronto, Toronto, ON, Canada

Background: Ontario regionalized thoracic surgery to designated centers to provide high-volume care for patients undergoing esophageal cancer resection. The objective of this study was to assess variation in treatment patterns and outcomes across thoracic centers, and to compare their performance to non-thoracic centers. Methods: A retrospective, population-based cohort study (2002-2014) was conducted in Ontario, Canada (population 13.6 million). Adults with resected esophageal cancer were identified through the PRESTO database. Case mix, use of neoadjuvant therapy, surgical outcomes (lymph node yield and margin rates) and survival were described across thoracic centers. Multivariable regression was used to estimate the effect of having surgery at a regionalized thoracic surgery center on perioperative (in-hospital & 90-day post-discharge) mortality and long-term survival, adjusting for case mix. Results: Of 3,880 patients meeting study criteria, 2,213 had pathology data available and were included in the analysis. Average age was 64 years, 85.7% had adenocarcinoma, 50.2% were pT3, and 38.4% were pNO. Most (82.6%) had surgery at one of 15 thoracic centers. Across thoracic centers, rates of neo-adjuvant therapy varied 16.4-81.6%, positive margin rates varied 8.2-29.6%, median lymph node harvest varied from 7-20 nodes, perioperative mortality varied 2.6-20.5%, and 2-year survival varied from 48-80%. There was a trend toward reduced perioperative mortality, but no difference in long-term survival, with having surgery at a thoracic center. Conclusions: Even at designated thoracic centers, there is significant variability in treatment patterns, surgical outcomes, and survival. Looking beyond center volume and translating best practices from high-performing hospitals to others, may improve patient outcomes. Research Sponsor: Sherif and MaryLou Hanna Chair in Surgical Oncology at Sunnybrook Health Sciences Center, Toronto, Canada.

Impact of inaccurate clinical staging for gastric cancer on patient survival outcomes. First Author: Michelle Ju, UT Southwestern, Dallas, TX

Background: Accurate clinical staging (CS) in gastric cancer is critical for appropriate treatment selection and prognostication, but CS remains highly inaccurate. Our study aims to evaluate the factors associated with inaccurate CS, the impact of inaccurate CS on patient outcomes, and effect of adjuvant therapy on patients with inaccurate CS. Methods: We conducted a retrospective review of the NCDB of patients diagnosed with clinical early-stage gastric adenocarcinoma based on AJCC 8th edition (cT1-2, N0, M0) between 2004-2016. Those who did not undergo upfront surgery or had missing pathologic staging data were excluded. Patients were classified into 3 groups: accurately staged (AS) if pathologic staging confirmed early-stage cancer, inaccurately staged (IS), and understaged (US). Only 44% of patients who were inaccurately staged received adjuvant chemotherapy/radiation. Age, T and N stage, and histology were associated with increased likelihood of inaccurate CS. Accurate CS is inadequate, and understaging is significant, associated with decreased likelihood of receiving adjuvant therapies, while side effects of chemoradiation impair the patients’ ability to maintain adequate nutrition. Moreover, patients lose 10% or more of their preoperative body weight in the first year following surgery. Implementation of nutrition protocols may reduce postoperative weight loss and enhance recovery in these patients. Methods: This is a retrospective study examining a post-operative nutrition protocol initiated in August of 2017. Patients with esophageagastrectomy who underwent Ivor-Lewis esophagectomy from July 2016 to July 2019 were identified from a prospectively collected database. Patients that underwent surgery after implementation of this protocol were compared to those operated prior to it. Results: Patients’ and tumor characteristics were similar between the two groups. The protocol included preoperative evaluation by a dietician, postoperative feeding pathway, and regular post-discharge follow-up by phone with a dietician. In the post protocol group, we observed a reduction in time to initiation of diet and decreased weight loss at patient follow up (Table). There was no difference in incidence of postoperative complications, length of stay, 30-day readmission, or in hospital mortality. Conclusions: In conclusion, postoperative nutrition support programs may help reduce postoperative weight loss and may have a role in the prevention of malnutrition in these patients. Initial results suggest that more aggressive nutritional supplement program is feasible and may lead to improved postoperative outcomes in patients undergoing esophagegastrectomy. Research Sponsor: None.
Prognostic impact of immune-related adverse events with nivolumab in patients with advanced gastric cancer: A multicenter retrospective analysis.

First Author: Yuno Ohya, University of Toyama, Toyama, Japan

Background: Nivolumab was established as one of the standard treatments for previously treated advanced gastric cancer (AGC). The aim of this study is to evaluate the frequency of immune-related adverse events (irAEs) with Nivolumab and its impact on treatment efficacy in clinical practice. Methods: We performed multicenter retrospective analysis, which included 90 patients with advanced gastric cancer who received Nivolumab treatment between October 2017 and September 2019. The frequency of irAEs and its outcome were evaluated, and survival was compared during Nivolumab treatment.

Results: The characteristics of 90 patients in this analysis were as follows: median age (range), 68 (36-85); male/female, 56/34; EGCG PS 0/1 = 26, 62/28; number of metastatic sites 1/2, 36/56; treatment line 3/4, 63/27. Median treatment cycle of nivolumab treatment was 3 (range 1-26). The overall response in 68 patients with target lesions was 6.3% (4/68), and the median PFS and OS was 1.5 and 4.3 months, respectively. IrAEs were observed in 8 patients (8.8%), including grade 4 pneumonitis, grade 2 or 3 adrenal insufficiency, and grade 2 hypothyroidism, encephalitis, and immune thrombocytopenia. Median time to onset of irAEs was 1.3 (range 0.6-10.5) months. Six were treated with systemic corticosteroid therapy, and all irAEs were relieved. The median PFS and OS were 4.7 months (95%CI, 12.9-93) and 12.2 months (95% CI, 3.2 not reached) in patient with irAEs, and 1.4 months (95%CI, 11-19) and 4.1 months (95%CI, 2.6-6.6) in those without, respectively. There was significant difference in the PFS (p=0.005) and OS (p<0.03). Conclusions: Nivolumab was effective and well tolerated even in clinical practice. Development of irAEs may be associated with better outcome of Nivolumab in patients with AGC. Research Sponsor: None.

Perioperative docetaxel, oxaliplatin, and capecitabine (DOX) in resectable adenocarcinomas of lower esophagus, esophago gastric junction, and stomach.

First Author: Shaunik Valame, Indraprastha Apollo Hospital, New Delhi, India

Background: In a real-world scenario, Fluorouracil-based triplet combination chemotherapies have limited feasibility with regards to toxicity, need for central venous access, and hospitalization. The primary objective of this study was to assess pathological tumor regression in capcitabine-based triplet regimens, with the additional possible benefit of overcoming the aforementioned barriers. Methods: This Single-Arm, Prospective study investigated the primary outcome of histopathologic regression to perioperative Docetaxel, Oxaliplatin, and Capecitabine (DOX) combination regimen in histologically confirmed resectable Esophageal, Esophagogastric Junction, and Gastric Adenocarcinomas. Three preoperative and 3 postoperative cycles of Docetaxel 60mg/m² plus Oxaliplatin 100mg/m² on Day 1, and Capecitabine 500mg/m² twice daily from Day 1 to Day 21 were administered, with cycles repeating every 21 days. Histopathologic regression was assessed by Modified Ryan Toxicity analysis. Secondary endpoints were Overall Survival, Progression-Free Survival, and Toxicity analysis. Results: Between June 2017 to May 2019, 28 patients (median age 54.5 years [Range 33 - 82]; Male 78.6%; EGCG PS 1/2 = 22/106 (57.1%) were enrolled in the study of which 92.9% completed preoperative chemotherapy. Of the 20 patients operated upon, 100% were R0 resections. Pathological complete response was observed in 20% (4/20). Twenty percent of the operated patients completed the postoperative treatment. The most common grade ≥3 toxicities were Palmar-Plantar Erythrodysesthesia (10.7%), Fatigue (10.7%), and Diarrhoea (7%). Conclusions: Perioperative DOX met its primary endpoint ≥30% pathological complete regression with a favourable toxicity profile and was feasible to administer in resectable Esophageal, Esophagogastric Junction, and Gastric Adenocarcinomas. This regimen deserves further evaluation in later phase III trials. Research Sponsor: None.

Analysis of weight loss as a prognostic factor in patients (pts) with advanced gastric cancer from REGARD, RAINBOW and RAINFALL phase III studies.

First Author: Wasat Mansoo, Christie NHS, Manchester, United Kingdom

Background: Maintaining weight (wt) and adequate nutrition during systemic treatment in advanced gastric cancer (G/GEJ) therapy remains a challenge. We therefore investigated the impact of early wt-loss on survival in three phase 3 studies of ramucirumab (R); REGARD (RG), RAINBOW (RB), and RAINFALL (RF) in G/GEJ. Methods: ITT pts were categorized into 2 groups based on their body wt change from start to end of cycle 1 (C1: C = 28 days in RG, RB; C = 21 days in RF). Weight change (wt-loss) <3% vs ≥3% was compared between groups. The main objective was to evaluate the effects of body wt change from the start to end of C1 on OS. A pooled meta-analysis stratified by study and sensitivity analysis of the subgroup of responders was also performed. Results: A total of 311 (RG; 212 in R+R; 99 in Placebo (PB)), 591 (RB; 306 in the R+Paxilactide (P); 285 PB+P), and 562 (RF: 279 in R+Cap/Cis (CC); 283 in PB+CC) pts with body wt data during C1 were evaluated. The number of pts with wt-loss of <3% and ≥3% are shown in Table. Pts with wt-loss <3% during C1 experienced longer OS compared to those with wt-loss ≥3%, irrespective of treatment arms across studies (Table). In pooled treatment arms within each study, the HR for wt-loss group ( <3% vs ≥3%) was 0.359 (95% CI = 0.254, 0.507), 0.632 (0.497, 0.804), 0.752 (0.608, 0.930) in RG, RB, RF, respectively. In the meta-analysis that combined the 3-studies, univariate Cox PH model stratified by study showed consistent effect of early wt-loss on OS regardless of treatment arm, HR ( <3% vs ≥3%) = 0.632 (0.546, 0.732). Conclusions: Analysis from three phase 3 studies demonstrates early wt-loss ≥3% during C1 is an important negative prognostic factor for survival in gastric (G)/GEJ cancer. Prospective studies to determine the relationship of weight preserving nutritional interventions on OS are warranted. Clinical trial information: NCT00973834, NCT0170663, NCT0233417. Research Sponsor: Eli Lilly and Company.

Perioperative docetaxel, oxaliplatin, and capecitabine (DOX) in resectable adenocarcinomas of lower esophagus, esophagogastric junction, and stomach.

First Author: Shaunik Valame, Indraprastha Apollo Hospital, New Delhi, India

Background: In a real-world scenario, Fluorouracil-based triplet combination chemotherapies have limited feasibility with regards to toxicity, need for central venous access, and hospitalization. The primary objective of this study was to assess pathological tumor regression in capcitabine-based triplet regimens, with the additional possible benefit of overcoming the aforementioned barriers. Methods: This Single-Arm, Prospective study investigated the primary outcome of histopathologic regression to perioperative Docetaxel, Oxaliplatin, and Capecitabine (DOX) combination regimen in histologically confirmed resectable Esophageal, Esophagogastric Junction, and Gastric Adenocarcinomas. Three preoperative and 3 postoperative cycles of Docetaxel 60mg/m² plus Oxaliplatin 100mg/m² on Day 1, and Capecitabine 500mg/m² twice daily from Day 1 to Day 21 were administered, with cycles repeating every 21 days. Histopathologic regression was assessed by Modified Ryan’s Schema on surgical specimen. The study had an 80% power (two-sided in clinical practice. Development of irAEs may be associated with better outcome of Nivolumab in patients with AGC. Research Sponsor: None.

A phase II trial of low-dose nab-paclitaxel for patients with previously treated or recurrent advanced gastric cancer (OGSG1302).

First Author: Masashi Hirota, Department of Surgery, Toyonaka Municipal Hospital, Toyonaka City, Osaka, Japan

Background: Paclitaxel is a key drug in second-line chemotherapy for advanced or recurrent gastric cancer (AGC) and nanoparticle albumin-bound paclitaxel (nab-PTX) is also widely used in Japan. A previous phase II trial in Japan showed the effectiveness of nab-PTX (250 mg/m²) administered every 3 weeks (q3w) in patients with AGC with a response rate (RR) of 27.8%; however, toxicity was major concern with grade ≥3 neutropenia (49.1%) and peripheral neuropathy (23.6%). To solve this problem, we investigated the We icacy and safety of low-dose q3w nab-PTX regimen in AGC. Methods: Eligibility requirements included: aged ≥20 years, HER2-negative, histologically confirmed, unresectable or recurrent gastric adenocarcinoma, one or more prior chemotherapy containing fluoropyrimidine regimen, presence of measurable lesion(s) according to RECIST ver. 1.1, ECOG PS of 0-2, and adequate organ function. Nab-PTX was administered at a dose of 220 mg/m² every 3 weeks. The primary endpoint was the RR. Secondary endpoints were overall survival (OS), progression-free survival (PFS), disease-control rate (DCR), incidence of adverse events, relative dose intensity and proportion of patients who received subsequent chemotherapy. Results: Thirty-three patients were enrolled from 10 institutions in Japan. Of the 32 patients treated with protocol therapy, RR (CR, PR) was 3.1% (95% CI, 0.16–21.2%), which was not reached the protocol-specified threshold (p = 0.066). DCR (CR, PR, SD) was 37.5% (95% CI, 21–56.1%), median OS and PFS were 6.3 months (95% CI, 4.4–14.2) and 2.2 months (95% CI, 18.33). Relative dose intensity was 97.8% (215 mg/m²). 62.5% of patients received subsequent chemotherapy. Most common grade ≥3 adverse events were neutropenia (38%), anemia (13%), fatigue (9%), anorexia (9%), and peripheral neuropathy (13%). Conclusions: Low-dose regimen of q3w nab-PTX was slightly less toxic, although it did not demonstrate the same effect as the original regimen in response rate. Therefore, it is not recommended for AGC in second or later line setting. Clinical trial information: UMIN 000012703. Research Sponsor: TAIHO PHARMACEUTICAL CO., LTD.
Feasibility and pathological response of TAS-118 + oxaliplatin as perioperative chemotherapy for patients with locally advanced gastric cancer (APOLLO-11). First Author: Daisuke Takahari, Department of Gastroenterology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan

Background: TAS-118 is a novel oral agent, containing S-1 and leucovorin. In the SOLAR study (NCT02322593), TAS-118 + oxaliplatin (OHP) significantly improved overall survival compared to S-1 + cisplatin for patients (pts) with advanced gastric cancer (GC). We conducted this open-label study to assess feasibility of perioperative adjuvant chemotherapy with TAS-118 + OHP in pts with locally advanced resectable GC with lymph node metastasis. (Clinical trial information: UMIN000024688).

Methods: Eligible pts who had histopathologically confirmed GC with clinical T3-4N1-3M0 on image findings (14 th line of treatment) were enrolled. Patients who had disease progression on the first-line chemotherapy with fluoropyrimidine and platinum were eligible. Pts received Nivo (3 mg/kg on days 1 and 15) combined with PTX (80 mg/m2 on days 1, 8 and 15) and Ram (8 mg/kg on days 1 and 15) (Level I), every 4 weeks. After feasibility was evaluated in 6 pts (phase 1 part), additional 37 pts were enrolled in a phase 2 part with the primary endpoint of 6-month progression-free survival (PFS) rate. The combined positive score (CPS) is defined as the number of PD-L1 positive cells (tumor cells, macrophages, and lymphocytes) divided by the total number of viable tumor cells. Results: Forty-three AGC pts were enrolled: median age, 66 years; ECOG PS 1, 48.8%; and CPS > 1, 60.5%. Disease limiting toxicities were observed in 2 pts in the phase I part and recommended dose was determined as Level 1. ORR was 37.2% (95%CI, 23.0-53.5%); 46.2% (95%CI, 26.6-66.6%) in CPS 1 pts and 30.8% (95%CI, 9.1-61.4%) in CPS < 1 pts. With a median follow-up time of 16.8 months, 6-month PFS rate was 46.4% (80% CI, 36.4-55.8%) (P = 0.067); 57.7% (95%CI, 36.8-73.9%) in CPS>1 pts and 38.5% (95%CI, 14.1-62.9%) in CPS < 1 pts. Median PFS was 51 months (95%CI, 4.5-65.5 months). Median survival time was 13.1 months (95%CI, 8.0-19.5 months) in CPS<1 pts and 8.0 months (95%CI, 8.0-15.9 months) in CPS>1 pts and 8.0 months (95%CI, 4.8-24.1 months) in CPS<1 pts and 18-months survival rate was 32.1% (95%CI, 18.2-46.8%). Conclusions: Nivo with PTX plus Ram demonstrated promising antitumor activity as the 2nd-line treatment for AGC pts with manageable toxicities.

Poster Session (Board #D9), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Survival benefit of conversion therapy after intensive chemotherapy for unresectable metastatic gastric cancer: A propensity score-matched analysis. First Author: Hiroyuki Ohnuma, Department of Medical Oncology, Sapporo Medical University School of Medicine, Sapporo, Japan

Background: The significance of conversion therapy (CT), whereby patients (pts) with unresectable disease respond to chemotherapy and subsequently receive surgery with curative intent (adjuvant surgery; A5), has been specified clinically established for metastatic colorectal cancer. However, such a strategy for advanced or recurrent gastric cancer (AGC) remains controversial. This study aims to clarify the clinical significance of CT for AGC.

Methods: This retrospective multi-institution observational study, we analyzed 168 AGC pts who received chemotherapy consisting of docetaxel, cisplatin or oxaliplatin, and S1±trastuzumab between 2003 and 2019. We divided pts into two groups; those who underwent CT (group CT) or chemotherapy only (group C). Propensity score analysis with 11 matching minimized confounding bias when comparing efficacy and safety between groups.

Results: A tumor response to chemotherapy was observed in 82.4% of all cases, while 34.5% (58/168) underwent A5. Fifty-one of the 58 pts underwent an R0 resection, and 79.3% were deemed histological responders. After matching, 44 pairs of C and CT pts were selected; significant differences in baseline characteristics were not observed. Incidences of adverse events during chemotherapy were similar between groups, with neutropenia and febrile neutropenia as common grade 3+4 events. Compared with group C, group CT had a significantly better median over survival (OS) (15.5 vs. 16.0 months; hazard ratio (HR) 0.32; 95% confidence interval (CI) 0.18-0.58; p < .001), and a prolonged progression-free survival (6.5 vs 22.6 months; HR 0.33, 95% CI 0.19-0.56; p < .001). Subgroup analysis of OS showed a favorable trend for CT for almost all parameters. In a multivariate analysis, OS (HR 0.10; 95% CI 0.03-0.31) and AS (HR 0.20; 95% CI 0.10-0.40) correlated with favorable OS. In the CT group, pathological response was an independent prognostic factor (HR 0.16; 95% CI 0.06-0.39).

Conclusions: CT was associated with better outcomes in AGC pts, even after baseline adjustment. Our data warrants further large-scale studies to establish a conversion therapeutic strategy.

Research Sponsor: ONO PHARMAECUTICAL CO., LTD.
Gefitinib along with metothrexate as palliative therapy in PS 3 and above in metastatic esophageal squamous cell carcinoma with focus on Q-TWIST. First Author: Vidy Sagor Dusi, Omega Hospitals, Hyderabad, India

Background: Metronomic therapy is proven method for treatment of terminally ill patients with malignancy, who are not fit for chemotherapy. The median PFS was significantly superior in responders in previous Indian experiences. However most of them were done in head and neck cancers. The prognosis of patients with metastatic esophageal cancer remains poor with only option being symptomatic care. As the previous experiences show metronomic therapy is safe among various options and there is no study focusing on Quality-Adjusted Time Without Symptoms or Toxicity (Q-TWIST) in southern Indian population, we thought of evaluating the same. Methods: Details of 42 subjects with refractory or progressive metastatic squamous cell carcinoma esophageus having PS > 2 were evaluated. Case records between 2017 September and 2018 September were analyzed for TWIST and QOL. Patients received Gefitinib (250 mg/day), Metothrexate 15 mg IM weekly or in combination. Patients were stratified into those with improved PS and those without. The subjects without PS improvement were continued on the single agent and those with improvement were offered additional chemotherapy based on physician/patient preference. Metronomic therapy could be continued beyond disease progression if there is TWIST/QOL improvement. Results: Out of 42 subjects, 29 had improvement in the PS and were continued later, 9 had stable PS and disease. 4 had worsening of PS, 34 subjects have clinically meaningful response (stable disease + complete + partial responses) and had symptomatic improvement. The median number of cycles was 6 (4-16). The median PFS was 198 days (95% CI, 174 to 214), and the median improvement in QOL was 6 points on a scale of 25. Grade II/IV toxicities were observed in 21 (50%) cases predominantly skin, rash, stomatitis and diarrhea. Conclusions: Metronomic therapy is well tolerated and may have a role in the treatment of advanced cancers with poor performance status. 67% of the patients who are otherwise not eligible for any active therapy became eligible and had better QOL and longer PFS, which re-emphasizes role of metronomic therapy in advanced squamous cell carcinoma of esophagus. Research Sponsor: None.

356Poster Session (Board #D10), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Personalized Antibodies for GastroEsophageal Adenocarcinoma (PANGEA): Primary efficacy analysis of the phase II platform trial (NCT02213289). First Author: Daniel V.T. Catenacci, University of Chicago Medical Center and Biological Sciences, Chicago, IL

Background: 1yr OS is >40% for HER2- & <55% for HER2+ advanced (a)GEA. Targeted therapies (T) have had limited benefit due to molecular heterogeneity. Methods: This phase 2a study of a personalized fxs strategy (PTS) enrolled newly diagnosed aGEA pts who then received up to 3 cytotoxic (cx) lines: first line (IL) S/PFU + oxaliplatin, 2L S/PFU + irinotecan & 3L S/PFU + docetaxel. Baseline biomarker profiling (BP) was mandated on primary & metastatic tumors (PT/MT) & progressive disease points (PD1, PD2). Assigned antibody (AN) was added to cx by a predefined tiered prioritized algorithm (PTA) (Table) based on the MT BP. At PD1, pts went to 2L + cx initial AN. Upon results of PD1 BP, pts changed AN only if BP evolved per PTA. The same was done at PD2. If AN was unavai (MFG/FFR2), these pts were tx’d with cx alone (not ITT). The fxs endpoints were ITT OS of the PTS. Assuming historical 50% 1yr OS for all aGEA pts, 68 pts tx’d to the ITT OS. Conclusions: PANGEA was feasible & met its P1 efficacy objective with observed 1yr OS of 69.4%, meeting a randomized study. Clinical trial information: NCT02213289. Research Sponsor: U.S. National Institutes of Health.

357Poster Session (Board #D12), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

DKN-01 in combination with pembrolizumab in patients with advanced gastroesophageal adenocarcinoma (GEA): Tumoral DKK1 expression as a predictor of response and survival. First Author: Samuel J. Klempner, The Angeles Clinic and Research Institute, Los Angeles, CA

Background: Dickkopf-1 (DKKI) modulates Wnt signaling and contributes to an immune suppressive tumor microenvironment. DKN-01 (D), a neutralizing DKK1 antibody + pembrolizumab (P), 2 individual anti-inflamm and clinical activity in advanced esophagus cancers. We report response and survival outcomes in anti-PD1/PD-L1/PD-N1 naive GEA patients by high/low tumoral DKK1 expression. Methods: We enrolled advanced anti-PD/PD-L1/PD-N1 naive GEA patients (pts) in a Phase 2a study of D + P (NCT02031545). Tumoral DKKI expression was assessed by an in silico RNA-Microrna association study. Baseline biomarker assay determined the expression rate (DRE), tumor birth rate (TBR), PFS was analyzed using the log rank test. Kaplan-Meier method and Cox-PH model was used for survival analysis and logistic regression was used for clinical benefit/response outcome. Results: 34 GEA pts were enrolled to receive 300 mg D + P. 31 GEA pts had DKKI expression available (25 response evaluable/ RE; and 27 had both DKKI and PD-L1 expression available (22 RE; in RE; DKKI high (H-score > upper tertile (≥35)) had an ORR of 50% (5/10), DCR of 80% (8/10) while DKKI low (≤ upper tertile) had an ORR of 0% (0/10) and DCR of 20% (2/10); DKKI high (vs. low) had an OR of 16 (95% CI: 2.2, 118.4; n = 25) and adjusted (for PD-L1 CPS > 10) OR of 17.6 (95% CI: 1.6, 164.4; n = 22) for clinical benefit/response (PR/SD vs. PD). Median PFS was 22.3 weeks in DKKI high (n = 11) vs. 5.9 weeks in DKKI low (n = 20); HR of 0.23 (95% CI: 0.082, 0.39; n = 31) and adjusted (for PD-L1 expression) HR for DKKI high was 0.20 (95% CI: 0.068, 0.68; n = 27) for PFS. DKKI high (n = 11) had a median OS of 104.4 weeks vs. 14.7 weeks in DKKI low (n = 20); HR of 0.16 (95% CI: 0.03, 0.77; n = 31) and adjusted HR of 0.62 (95% CI: 0.219, 2.7; n = 27). Conclusions: High levels of tumoral DKK1 expression identify advanced anti-PD/PD-L1/PD-N1 naive GEA pts with the greatest benefit from D + P. Improvements in response/clinical benefit and PFS were observed independent of PD-L1 expression. Tumoral DKKI as a potential predictive biomarker for DKN-01 treated GEA pts will be evaluated in future studies. Overall survival follow-up is ongoing. Clinical trial information: NCT02031545. Research Sponsor: Leap Therapeutics.

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Is splenectomy for dissecting splenic hilar lymph nodes justified in scirrhous type of gastric cancer? First Author: Tsutomu Hayashi, Department of Gastric Surgery, National Cancer Center Hospital, Tokyo, Japan

Background: Splenectomy for dissecting splenic hilar nodes (#10) should be avoided for most gastric cancer considering high morbidity and no survival benefit, while that is often selected in scirrhous type of gastric cancer because this special type frequently invades the whole stomach and the #10 nodes. Splenectomy is necessary for dissecting #10, however, survival benefit of dissecting #10 is unclear. Methods: Patients who had scirrhous gastric cancer and underwent a combination of cytoreduction with splenectomy in National Cancer Center Hospital, Japan, between 2000 to 2011 were retrospectively analyzed. The therapeutic value index was calculated by multiplying the metastatic rate of each nodal station and the 5-year survival of patients who had metastasis to each node. Results: In total, 144 patients were eligible for the present study. The most frequent metastatic site was the nodes along the lesser curvature (#3, 57%), followed by the nodes along the right gastro-epiploic artery (#4d, 45%), the right nodes located at the cardiaca (#1, 34%), the nodes along the left gastro-epiploic artery (#4b, 23%), the inferior nodes at the pyloric ring (#6, 22%), the nodes along the left gastric artery (#7, 21%), the nodes along the short gastric artery (#4sa, 18%), the nodes along the cardiac branched artery (#2, 15%), the nodes along the splenic artery (#1d, 15%), the proximal nodes along the splenic artery (#1tp, 13%), the nodes around the celiac artery (#9, 13%), and the nodes along the common hepatic artery (#8a, 10%). These lymph nodes had a metastatic rate of more than 10%. The node with the highest index was #3 (81%), followed by #1 (74.4%), #9 (59.5%), #4d (58.5%), #4b (57.5%), #10 (48.6%), #7 (46.6%), #6d (44.6%), #11p (38.7%), #2 (30.7%), #8a (26.8%), and #9 (13.9%). The index of #10 was exceeded that of #2, #7, #8a, and #9 which are the key nodes dissected in D2. Conclusions: The metastatic rate of splenic hilar nodes was relatively high, and the therapeutic index was the sixth highest in the fifteen regional lymph nodes included in D2 dissection. Splenectomy for dissecting splenic hilar nodes would be justified in scirrhous type of gastric cancer considering its survival benefit. Research Sponsor: None.

A phase II trial of cytoreduction, gastrectomy, and hyperthermic intraperitoneal perfusion with chemotherapy for patients with gastric cancer and stage IV peritoneal disease. First Author: Brian D. Badgwell, University of Texas MD Anderson Cancer Center, Houston, TX

Background: Current national guidelines do not include hyperthermic intraperitoneal chemotherapy (HIPEC) as treatment for gastric cancer, and there are no completed clinical trials of cytoreduction, gastrectomy, and HIPEC from the U.S. However, recent international studies report long-term survival rates of approximately 20% with cytoreduction/gastrectomy/Hipec. Methods: Patients with gastric adenocarcinoma and positive peritoneal cytology or carcinomatosis who had completed systemic chemotherapy and laparoscopic HIPEC underwent cytoreduction, gastrectomy, and HIPEC with 30 mg mitomycin C and 200 mg cisplatin. The primary end point was overall survival (OS), with secondary end points of safety and postoperative complications. Results: We enrolled 20 patients from 9/2016 to 3/2019, with a median age of 58 years (range, 20-75 years). Six patients had positive cytology only at diagnosis of stage IV disease, whereas 14 had carcinomatosis. All patients were treated with systemic chemotherapy with a median of 8 cycles (range, 5-11 cycles) and at least one laparoscopic HIPEC. The median peritoneal carcinomatosis index at cytoreduction/gastrectomy/Hipec was 2 (range, 0-13). After surgery, the 90-day morbidity and mortality rates were 70% and 0%, respectively. Median length of hospital stay was 13 days (range, 7-23 days). Median follow-up was 1.8 years. Median OS from the date of diagnosis of metastatic disease was 2.1 years. Median OS from the date of cytoreduction, gastrectomy, and HIPEC was 1.4 years. One, 2, and 3-year OS rates were 90%, 54%, and 29%. Conclusions: Survival rates for patients with gastric adenocarcinoma and peritoneal disease treated with cytoreduction, gastrectomy, and HIPEC following oncoaging; our early results are similar to those of recent prospective registry studies. Cooperative group trials should be supported and will be required to confirm survival and safety outcomes. Clinical trial information: NCT02691447. Research Sponsor: No Stomach for Cancer Foundation, Holly Clegg Gastric Cancer Fund.

Safety and tolerability of oxaliplatin-based pressurized intraperitoneal aerosol chemotherapy (PIPAC) for patients with peritoneal carcinomatosis: A phase I dose-finding study in Asian patients. First Author: Raghun Sundar, Drug Development Unit-The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, Sutton, United Kingdom

Background: PIPAC is a novel, laparoscopic intraperitoneal chemotherapy delivery technique which aims to improve on hyperthermic intraperitoneal chemotherapy (HIPEC), ameliorating drug distribution and tissue penetration. Thus far, PIPAC has been conducted with oxaliplatin chemotherapy in Europe, at an arbitrary dose of 92mg/m², 150mg/m² was found to be intolerable. We conducted a dose-escalation phase 1 study to establish the safety, tolerability and recommended phase 2 dose (RP2D) for PIPAC in Asian patients. Methods: This phase 1 study of oxaliplatin administered via PIPAC was designed as a traditional 3+3 dose escalation study for patients with pre-dominant peritoneal metastasis from a gastrointestinal primary tumor, after failure of standard therapies. Dose levels were planned at 45, 60, 90 and 120mg/m². Repeat doses of PIPAC were permitted, 6 weeks apart. Dose limiting toxicities (DLT) were defined as any clinically relevant grade 3 adverse event of Tx received and within 28 days after PIPAC. Results: This study included 16 patients (25 PIPAC procedures; 8 gastric, 4 colorectal and 1 gallbladder, pancreas and appendix cancer each). Median age was 62 years, with a median peritoneal carcinomatosis index (PCI) score of 17 (range 1 - 39). Two patients developed papillary cysts (grade 2 and 3) on day 6 and day 7 after PIPAC administration at the dose cohort of 45mg/m², necessitating cohort expansion to 6 patients. One patient was noted to have asymptomatic grade 3 hyperamylasemia (90mg/m² cohort). There were no other DLTs and all 3 patients in the 60mg/m² (2 patients) and 90mg/m² (1 patient) dose cohorts had PIPAC, who underwent a 2nd PIPAC procedure had a decrease in PCI score from 18.4 to 15.5; one patient at 120mg/m² had an improvement in PCI from 30 to 12. Conclusions: The RP2D of PIPAC with oxaliplatin is 120mg/m². Single agent PIPAC is well tolerated, and future studies with PIPAC may support a bidirectional approach with the incorporation of systemic therapy, with either chemotherapy or immunotherapy to improve efficacy. Clinical trial information: NCT03712424. Research Sponsor: National Medical Research Council Singapore.

Enhanced efficacy of anti-VEGFR2/taxane after progression on immune checkpoint inhibition (ICI) in patients (pts) with metastatic gastroesophageal adenocarcinoma (mGEA). First Author: Lionel Aurelien Kankeu Fonkoua, Mayo Clinic, Rochester, MN

Background: Most pts with mGEA do not respond to ICI or ramucirumab/paclitaxel (RAM/TAX). Emerging data suggest that ICI may potentiate subsequent RAM/TAX efficacy of subsequent RAM/TAX in a larger cohort and explored alterations in the tumor microenvironment. Methods: All pts with mGEA at Mayo Clinic (MN, AZ, FL) who received RAM/TAX (2014-19) were included. We compared best response (BR) of RAM/TAX (usually as 2nd line Tx) without radiologic progression vs BR of RAM/TAX as 2nd line Tx in pts with primary resistance to ICI and will be tested prospectively in a new randomized phase 2 trial (NCT04069273). Research Sponsor: None.

In total, 144 patients were eligible for the present study. Survival rates for patients with gastric adenocarcinoma and peri-
The real-world practice of surgery in patients with metastatic gastric cancer (mGC). First Author: Ekaterina Obarevich, Federal State Budgetary Institution “National Medical Research Center of Oncology” of the Ministry of Health of the Russian Federation, Moscow, Russian Federation

Background: According to recent studies the results of treatment patients with initially mGC are still not sufficient, mostly metastatic transformation varies between 6.1 and 12.4 months. The triplet-chemotherapy regimens demonstrate high efficacy and allow to downstage the disease and perform surgical treatment. Conversion treatment in stage IV GC is a modern trend and still an area of ongoing research.

Methods: We analyze the efficacy of first line chemotherapy (6-9 courses) for patients with mGC (n = 55) including the following regimens: 1) mFOLFIRINOX; 2) doublett: oxaliplatin/infotin/celecoxib + fluoropyrimidine; 3) triplet variations: docetaxel, platinum and fluoropyrimidine. 27/55 patients had > 2 metastatic sites, 2/55 patient - 5 metastatic sites. The most common localizations of metastases were peritoneum (n = 34) and retroperitoneal lymph nodes (n = 11). Unlike in REGATTA trial all patients underwent surgical treatment with curative intent followed by complete response of distant metastases after chemotherapy. For patients with ovarian metastases ovariectomy was also performed. Results: Median progression-free survival and median overall survival were 18.5 and 33.27 months, respectively and the 3-year survival rate was 43.5%. Multivariate analysis showed that clinically determined ascites (p = 0.023), limits plastic (p = 0.022), tumor grade 3 (p = 0.014), presence of lymphovascular invasion (p = 0.037), absence of grade III-IV pathomorphosis (p = 0.037) and treatment free interval before surgery < 3.4 month (p = 0.046) were poor independent prognostic factors. Conclusions: Surgery after effective combination chemotherapy may have significant clinical efficacy for selected patients with initially unresectable gastric cancer. According to our data the optimal time for surgery is a 3.4 and more months treatment-free interval in the absence of disease progression. Research Sponsor: None.

Refusal of surgery results in inferior survival in esophageal cancer. First Author: Matthew Parsons, University of Utah, Salt Lake City, UT

Background: Tridimibility therapy with chemoradiation followed by surgery is the standard of care for non-metastatic esophageal cancer. Some patients refuse surgery and this information is captured in the National Cancer Database (NCDB). We sought to understand factors associated with refusal of surgery in these patients and to compare their survival rates with those who undergo surgery. Methods: Data from the NCDB for patients with pathologically proven non-metastatic esophageal cancer from 2006 to 2013 were pooled and screened. Results: Patients with TNM0 disease were excluded. Pearson chi-squared test and multivariate logistic regression analyses were used to assess the distribution of demographic, clinical, and treatment factors. After propensity-score matching with inverse probability of treatment weighting, overall survival (OS) was compared between patients who refused surgery and those who had surgery using Kaplan Meier analyses and doubly-robust estimation with multivariate Cox proportional hazards modeling. Results: We found 890 of 18,942 patients (4.6%) refused surgery. Older patients, females, those with squamous histology, patients insured by Medicare and those who received radiation therapy (RT) were more likely to refuse. Patients who had N1 disease, high incomes, those who received chemotherapy and those who lived farther from care were more likely to have surgery. The initial 6 month OS was not significantly different between patients who refused surgery and those who had surgery (93.5% vs 95.1%; p = 0.064). However, five-year OS was significantly lower in patients who refused (16.4% vs. 38.4%; P < .001). This survival decrement was observed uniquely in patients with both adenocarcinoma and squamous cell carcinoma histology, and in those who refused surgery, the OS decrement was mitigated by increasing RT doses. In those who received over 54 Gy of RT, there was no statistical difference in OS between the groups (HR = 0.84, 95% CI 0.65-1.09). Conclusions: We identified a number of patient characteristics that are related to the refusal of surgery in esophageal cancer. Refusal of surgery was related to a decrease in OS in propensity weighted cohorts. This survival decrement may be mitigated by RT in a dose dependent fashion. Research Sponsor: None.

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Apatinib combined with SOX neoadjuvant therapy for locally advanced gastric cancer: A multicenter, single-armed, prospective study. First Author: Jian-Xian Lin, Department of Gastric Surgery, Fujian Medical University Union Hospital, Fuzhou, China

Background: Molecular targeted therapy has made great progress in the treatment of gastric cancer. In some previous studies, apatinib, an oral small molecular of VEGFR-2 TKI, had been confirmed can improve OS and PFS with an acceptable safety profile in patients with advanced gastric cancer refractory to two or more lines of prior chemotherapy. However, there is limited evidence about the safety and feasibility of apatinib combined with SOX regimen as neoadjuvant therapy for locally advanced gastric cancer (AGC).

Methods: This is a multicenter, single-armed, prospective study. Patients with AGC (CI-N,M,M,) without prior anti-cancer strategies were included. Patients were received 2 to 5 cycles (21 days a cycle) of neoadjuvant therapy using S1 (po, 40-60 mg bid, day1-day5), oxalaplatin(n, 130 mg/m2, day1), and apatinib(0, 500 mg qd). Apatinib was prohibited in the last cycle. The operation should be performed 2 to 4 weeks later of the neoadjuvant therapy. The primary endpoint was RO resection rate. The secondary endpoint included safety, ORR, and DCR.

Results: A total of 56 patients from 10 centers in China were recruited. There were 43 males and 13 females. The median age was 63.04 years (range 41-75 years). There were 43 patients with tumor response evaluation, 29 patients were 43 males and 13 females. The median age was 63.04 years (range 41-75 years). There were 43 patients with tumor response evaluation, 29 patients were 43 males and 13 females. The median age was 63.04 years (range 41-75 years). There were 43 patients with tumor response evaluation, 29 patients were 43 males and 13 females. The median age was 63.04 years (range 41-75 years). There were 43 patients with tumor response evaluation, 29 patients were 43 males and 13 females. The median age was 63.04 years (range 41-75 years). There were 43 patients with tumor response evaluation, 29 patients were 43 males and 13 females. The median age was 63.04 years (range 41-75 years).

There were no significant differences between overall- or recurrence-free survival between the laparoscopic and open: n = 2 (4.0%) vs. n = 1 (4.0%); p = 1.00. No deaths occurred in any group. Although not significant independent risk factor for the OS (hazard ratio = 2.15; 95% confidence interval, 1.25 to 3.68; P = 0.006). A multivariate analysis identified postoperative pneumonia as a significant independent risk factor for the OS (hazard ratio = 2.15; 95% confidence interval, 1.25 to 3.68; P = 0.006).


Association between postoperative pneumonia and prognosis of patients with esophageal cancer. First Author: Yosuke Atsumi, Department of Surgery, Yokohama City University, Yokohama, Japan

Background: We examined the association between postoperative pneumonia and prognosis of patients with esophageal cancer after curative surgery. Methods: We enrolled 122 patients who underwent curative resection for esophageal cancer. Esophageal cancer was staged according to the 7th edition of the AJCC staging manual. Postoperative pneumonia were categorized into the pneumonia group, while those without postoperative pneumonia were classified into the non-pneumonia group. We identified the risk factors for the recurrence-free survival (RFS) and the overall survival (OS). Postoperative pneumonia was defined using the revised Uniform Pneumonia Score. Results: Thirty-four of the 122 patients (27.9%) had postoperative pneumonia. The 5-year OS rate after surgery in the pneumonia group was significantly lower than that in the non-pneumonia group (28.2% versus 55.1%, p = 0.006). Although not significant, the 5-year RFS rate after surgery in the pneumonia group tended to be lower than that in the non-pneumonia group (18.9% versus 49.2%, p = 0.061). A multivariate analysis identified postoperative pneumonia as a significant independent risk factor for the OS (hazard ratio = 2.15; 95% confidence interval, 1.25 to 3.68; p = 0.006).

Conclusions: Our analysis showed postoperative pneumonia was an independent risk factor for worse overall survival in patients who underwent curative resection for esophageal cancer. This finding suggests that we should plan the surgical procedure, perioperative care and surgical strategy to prevent postoperative pneumonia. Research Sponsor: None.

Endoscopic versus surgical resection for mucosal esophageal squamous cell carcinoma: Treatment outcomes and factors affecting survival. First Author: Ga Hee Kim, Asan Medical Center, Seoul, South Korea

Background: Mucosal esophageal squamous cell carcinoma (T1a EC) is treated with endoscopic (ER) or surgical resection (SR). The data regarding prognosis of T1a EC and the associated factors are still lacking. This study aimed to compare the treatment outcomes of T1a EC in ER and SR groups, and to investigate the factors affecting long-term survival. Methods: We retrieved data for 263 patients with T1a EC who underwent ER (n = 200) or SR (n = 63). Relevant clinical and tumor-specific parameters were reviewed. Underlying comorbidity was scored using Charlson co-morbidity index (CCI). Significant factors affecting survival were determined by Cox regression analysis.

Results: The mean age of the patients was 64.5±8.0 years. During a mean follow-up of 54.4±20.4 months, the 5-year overall survival (OS) of all T1a EC patients was 85.7% (86.8% in ER and 82.4% in SR group; p = 0.631). In multivariate analysis, CCI was a significant factor affecting survival (p < 0.001). The 5-year OS was 60.2% in patients with CCI > 2 and 88.2% in patients with CCI ≤2 (p < 0.001). The 5-year cumulative incidence of primary EC recurrence was 1.9% and metachronous EC recurrence was 15.1% in ER group (0% in SR group). Incidence of subsequent second primary cancers was 9% in ER and 9.5% in SR. The 5-year cumulative incidences of all cases of cancer recurrence in ER and SR groups were 27.5% and 10.8%, respectively (p = 0.037). The procedure-related adverse events occurred in 10.0% in ER and 41.3% in SR (p < 0.001). Among the 24 (12.0%) and 10 (15.9%) deaths in ER and SR group, respectively, primary EC-specific death was not reported. The major causes of death were not primary cancers in ER group (75%), and post-operative complications or organ failure in SR group (70%).

Conclusions: Long-term survival was excellent in patients undergoing ER or SR for T1a EC. The prognosis of T1a EC was significantly associated with underlying comorbidity. Attention should be paid to metachronous cancer recurrence in ER group and operation-related adverse events in SR group. Research Sponsor: None.

Short- and long-term outcomes following laparoscopic gastrectomy for advanced gastric cancer compared with open gastrectomy. First Author: Kazuki Shibuya, Hokkaido University, Sapporo, Japan

Background: To investigate the oncological feasibility and technical safety of laparoscopic gastrectomy with D2 lymphadenectomy for advanced gastric cancer. Methods: 186 advanced gastric cancer patients treated by gastrectomy with D2 lymphadenectomy were performed by 14 Japanese surgeons. Postoperative complications were documented and graded according to the Clavien-Dindo classification. The incidence of adverse events (AEs) and grade 3/4 AEs were 84.8% (39/46) and 17.4% (8/46), respectively. The most common AEs were neutropenia (40%), fever (20.4 months, the 5-year overall survival (OS) of all T1a EC patients was 85.7% (86.8% in ER and 82.4% in SR group; p = 0.631). In multivariate analysis, CCI was a significant factor affecting survival (p < 0.001). The 5-year OS was 60.2% in patients with CCI > 2 and 88.2% in patients with CCI ≤2 (p < 0.001). The 5-year cumulative incidence of primary EC recurrence was 1.9% and metachronous EC recurrence was 15.1% in ER group (0% in SR group). Incidence of subsequent second primary cancers was 9% in ER and 9.5% in SR. The 5-year cumulative incidences of all cases of cancer recurrence in ER and SR groups were 27.5% and 10.8%, respectively (p = 0.037). The procedure-related adverse events occurred in 10.0% in ER and 41.3% in SR (p < 0.001). Among the 24 (12.0%) and 10 (15.9%) deaths in ER and SR group, respectively, primary EC-specific death was not reported. The major causes of death were not primary cancers in ER group (75%), and post-operative complications or organ failure in SR group (70%).

Conclusions: Long-term survival was excellent in patients undergoing ER or SR for T1a EC. The prognosis of T1a EC was significantly associated with underlying comorbidity. Attention should be paid to metachronous cancer recurrence in ER group and operation-related adverse events in SR group. Research Sponsor: None.
**Loss of body weight during neoadjuvant chemotherapy with docetaxel, cisplatin, and fluorouracil as predictive of poor survival of patients with esophageal squamous cell carcinoma.** First Author: Munehiro Ito, Department of Gastrointestinal Medical Oncology, National Cancer Center Hospital, Tokyo, Japan

**Background:** Though neoadjuvant chemotherapy with docetaxel/cisplatin/5-fluorouracil (DCF) showed a promising efficacy in patients (pts) with resectable esophageal squamous cell carcinoma (ESCC), grade 3 anorexia during the course and body weight loss (BWL) were frequently experienced. BWL is considered as a factor for poor survival in operable cancer pts, however, there is rarely reported of the relationship of BWL during neoadjuvant therapy and survival. **Methods:** We retrospectively evaluated pts of ESCC with clinical stage I or II, excluding T4, who had received neoadjuvant DCF and esophagectomy (R0 resection) at our institution between April 2010 and December 2018. We define the cut-off level at more than 3% weight reduction (BWL3 group) between before and after first cycle of DCF. **Results:** Among the 77 pts who were selected for this analysis, 13 patients showed BWL > 3% (BWL5 group), and other 64 pts did not (no-BWL group). The median age, proportions of performance status 0, ct3 stage, ct2-3 stage and serum albumin lower than normal level in no-BWL and BWL3 group were 65 and 67.9y, 59 and 77%, 88 and 54%, 75 and 69%, 34 and 31%, respectively. There was no significant difference in histological therapeutic effect (grade 2/3) with 50% in no-BWL, and 62% in BWL3 group (P = 0.549). The incidence of postoperative grade 2 or higher pneumoniasaw same in both group (23% vs 17%, P = 0.695). The median overall survival (OS) was not reached in non-BWL group and 39.5m in BWL3 group (P = 0.048), re- spectively. In multivariate analysis, BWL is independent prognostic factor for OS (hazard ratio [HR] = 11.5, 95%CI: 2.45-53.8, P = 0.002). **Conclusions:** Our exploratory study demonstrated that body weight loss during first course of neoadjuvant DCF therapy for ESCC patients may be a prognostic factor for survival. Research Sponsor: None.

**Induction oxaliplatin capcitabine followed by switch to carboplatin-paclitaxel based RT versus continuing oxaliplatin capcitabine RT in operable esophageal adenocarcinoma: Survival analysis of the randomized phase II neoscope trial.** First Author: Sonnath Mukherjee, University of Oxford, Oxford, United Kingdom

**Background:** Initial results of the NEOSCOPE trial comparing pre-operative CarPac vs OxCap based chemoradiotherapy (CRT) in patients with adenocarcinoma of the oesophagus or oesophagogastric junction showed comparable toxicity and improvement in pathological complete response (pCR) in favour of the CarPacRT. Here we report survival after a median follow-up of 40.7 months (95% CI: 45.1-53.6). **Methods:** NEOSCOPE was an open, randomised, ‘pick a winner’ phase II trial. Patients with resectable oesophageal adenocarcinoma who were ct3 and/or CPS grade 1, 2, then ct3 stage, ct2-3 stage and serum albumin lower than normal level in no-BWL and BWL3 group were 65 and 67.9y, 59 and 77%, 88 and 54%, 75 and 69%, 34 and 31%, respectively. There was no significant difference in histological therapeutic effect (grade 2/3) with 50% in no-BWL, and 62% in BWL3 group (P = 0.549). The incidence of postoperative grade 2 or higher pneumoniasaw same in both group (23% vs 17%, P = 0.695). The median overall survival (OS) was not reached in non-BWL group and 39.5m in BWL3 group (P = 0.048), respectively. In multivariate analysis, BWL is independent prognostic factor for OS (hazard ratio [HR] = 11.5, 95%CI: 2.45-53.8, P = 0.002). **Conclusions:** Our exploratory study demonstrated that body weight loss during first course of neoadjuvant DCF therapy for ESCC patients may be a prognostic factor for survival. Research Sponsor: None.

**An open-label phase II study of nivolumab plus pembrolizumab in patients with advanced gastric cancer (EPOC1706).** First Author: Akihito Kawaeo, National Cancer Center Hospital East, Kashiwa, Japan

**Background:** Pembrolizumab, anti-PD1 antibody, provides response rates of around 15% in patients (pts) with PD-L1-positive advanced gastric cancer (AGC). Lenvatinib, a multikinase inhibitor of VEGF receptors and other receptor tyrosine kinases, substantially decreased the tumor-associated macrophages and increased infiltration of CD8-positive T cells and enhanced anti-tumor activity of PD-1 inhibitors in vivo model. This phase II study has been conducted to evaluate efficacy and safety of the combination of lenvatinib plus pembrolizumab in pts with AGC. **Methods:** Eligible pts were with AGC having measurable lesions according to RECIST ver. 1.1. Pt enrollment was 8 weeks after CRT. Cancer therapy was performed 6-8 weeks after CRT. The primary endpoint was pCR, secondary endpoints were toxicity, PFS and OS. **Results:** Between Oct 2013 and Feb 2015, 85 patients were recruited from 17 UK centres. Median OS was not reached in the CarPacRT group and was 41.72 months (95% CI 19.58-) in the OxCap group (HR 0.526 [95% CI 0.29-1.07]; p=0.079). 3-year and 5-year OS rates were 74% (95% CI 58%-85%) and 54% (95% CI 34%-71%) (CarPacRT), and 52% (95% CI 35%-67) and 39% (95% CI 21%-56%) (OxCapRT). Median PFS (not reached vs 35.3 months, HR=0.61 [95% CI 0.33-1.12]; p=0.31) and metastatic PFS (not reached vs 39.0 months, HR=0.61 [95% CI 0.32-1.41]; p=0.18) both favoured the CarPacRT arm. Local recurrence rate was low (OxCapRT= 10%; CarPacRT= 7%). The OS benefit for CarPacRT was consistent across subgroups but not statistically significant. **Conclusions:** In this longer term analysis there was some evidence that induction OxCap followed by switch to CarPacRT was superior to continuing OxCapRT, with efficacy similar to that seen in other published studies such as ‘CROSS’ and ‘FLONT’. Taken together with the previously published pCR results CarPacRT rather than OxCapRT is recommended in future randomized trials. Funding: Cancer Research UK, Cancer Research UK (C44694/A14164), Clinical trial information: NCT04438329. Research Sponsor: NEOSCOPE.
Continuous fluoropyrimidine (FP) with platinum (P) based chemotherapy (CT) versus maintenance FP after induction therapy in advanced gastric (G) and gastroesophageal (GE) cancer. First Author: Daniel Walden, Mayo Clinic Arizona, Phoenix, AZ

Background: Combination FP with P CT have become the standard of care for advanced G/GE cancer. Clinical trials in conjunction with practice, have adopted induction FP and P CT for 3-4 months (mos). In other GI malignancies, induction CT followed by maintenance CT (MTC) has been shown to improve patient (pt) outcomes compared to observation, with a decrease in treatment (trtm) related toxicities with induction therapy. However a maintenance approach in G/GE has not been investigated in clinical trials. We investigated pt outcomes with metastatic G/GE who received continuous induction (ICTX) versus induction followed by MTC. Methods: A retrospective analysis of pts with metastatic G/GE adenocarcinoma treated with (FP+P) based CT from 2007 to 2017 from three centers of a single institution was performed. Metastatic G/GE cancer pts who achieved at least stable disease after initial induction trtm were included. Pts were categorized into the ICTX group if they received greater than 16 weeks or 8 cycles of combined CT and assigned to the MTC group if they received maintenance FP therapy after 8 or less cycles of combined induction CT. Data was extracted from the medical record to determine progression free survival (PFS), overall survival (OS), and toxicities. Results: Sixty-four pts that met criteria and were evaluated, thirty-four received ICTX and thirty received MTC. No significant difference in PFS (2.1 vs 8.0 mos p = .72; HR=110 95%CI:6.6-183) was observed between the ICTX and MTC groups, additionally there was no significant difference in OS. A significant decrease in trtm related toxicities were observed, with a higher proportion of thrombocytopenia (84.8% vs 50.0% p = .004), and grade 3 neuropathy (39.4% vs 13.8% p = .024) in ICTX pts (Table). Conclusions: ICTX following induction FP/P CT is associated with an improved toxicity profile and appears to be effective compared to ICTX in metastatic G/GE cancer. Future randomized studies confirming its potential benefits compared with continuous induction CT are warranted. Research Sponsor: None.

MTC (n=30) ICTX(n=34)

Grade 3 Neuropathy 4 13
Thrombocytopenia 13 28
Any ≥3 AE 22 18

Hyperprogressive disease during nivolumab chemotherapy in metastatic gastric cancer: Multicenter retrospective study in Japan. First Author: Takeshi Suzuki, Department of Gastroenterology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan

Background: Nivolumab has demonstrated a survival benefit for advanced gastric cancer (AGC). However, hyperprogressive disease (HPD) has been reported in various cancers. Methods: The subjects of this retrospective study were AGC patients with metastable disease who received nivolumab, and their tumors were assessed at least 3 times (during prior therapy, before, and after nivolumab) in 24 institutions. Tumor growth rates (TGR) during nivolumab were compared to those during prior therapy as reported (Champiat S, 2018). HPD was defined as an increase in TGR > 2-fold. Results: 218 patients were identified as the subjects. While 33 (51.5%) partial response (PR) were achieved; 130 patients (59.6%) showed progression disease (PD), 38 of whom were classified as HPD (17.4%) and 2 patients showed pseudo progression (1.0%). The median progression-free survival (PFS) was 19 months (95% CI: 19.2-24.0) and the median overall survival (OS) was 8.5 months (95% CI: 7.1-9.6) in all patients. While patients with PD showed shorter prognosis compared to non-PD patients (median PFS: 1.5 months vs 6.4 months, hazard ratio: 6.0 [95% CI: 4.3-8.4]; p < 0.0001; median OS: 4.7 months vs not reached, hazard ratio: 4.1 [95% CI: 2.8-6.3]; p < 0.0001), there were no differences either in PFS or OS between patients with HPD and those with PD other than HPD (median PFS: 1.5 months vs 1.6 months, hazard ratio: 1.3 [95% CI: 0.9-2.0]; p = 0.1994; median OS: 5.0 months vs 4.6 months, hazard ratio: 1.0 [95% CI: 0.6-1.5]; p = 0.8696). Histological type, liver metastases, carbohydrate antigen 19-9 (CA19-9) level were associated with HPD. Conclusions: HPD was observed 17.4% in AGC patients treated with nivolumab. There were no differences either in PFS or OS between patients with HPD and those with PD other than HPD. Further prospective investigations are warranted.

Laparoscopic versus open total gastrectomy for clinical stage I gastric cancer: Morbidity and mortality results from a prospective randomized multicenter controlled trial (CLASS02). First Author: Fenglin Liu, Zhongshan Hospital, Fudan University, Shanghai, China

Background: The safety of laparoscopic total gastrectomy (LTG) for the treatment of gastric cancer remains lack of clinical evidence. The aim of this study is to compare the safety of LTG for clinical stage I gastric cancer with the conventional open total gastrectomy (OTG). Methods: From January 2017 to September 2018, a total of 227 patients with clinical stage T1NO/1/2NOMO gastric cancer were enrolled in this clinical trial and randomly assigned to Laparoscopic Gastrectomy group (LG, n=105) or Open Gastrectomy group (OG, n=122). The morbidity and mortality with 30 days following surgery, the recovery course, and the postoperative stay between LG group (n=105) and OG group (n=109) were compared. Clavien-Dindo classification system was used to stratify surgical complications. Results: The overall morbidity rate was not significantly different in each group (LG group: 19.05%; OG group: 20.18%; Rate difference (RD): -1.14%, 95%CI: -11.75%-9.58%). Intraoperative complications occurred in 3 (2.86%) patients in LG group and 4 (3.67%) patients in OG group (RD: -0.81%, 95%CI: 6.52%-4.85%). In addition, there was no significant difference in the overall post-operative complication rate of 18.10% in LG group and 17.43% in OG group (RD: 0.66%, 95%CI: -9.61%-1.01%). Each subtypes of postoperative complication were not significantly different between groups. One patient in LG group died of intra-abdominal bleeding from splenic artery, and there was a significant difference in mortality between LG group and OG group (RD: 0.95%, 95%CI: -2.54%-5.20%). The distribution of severity was similar between the two groups. Conclusions: Laparoscopic surgery can safely perform LTG with lymphadenectomy for clinical stage I gastric cancer. Clinical trial information: NCT03007550. Research Sponsor: Clinical Trial Fund of Zhongshan Hospital Fudan University (2016ZSLC13), Pharmaceutical/Biotech Company.
Comparing five-weekly S-1 plus cisplatin with tri-weekly capcitabine plus cisplatin in patients with HER2-negative recurrent gastric cancer after S-1 adjuvant therapy or chemotherapy naïve advanced gastric cancer: A pooled analysis of HERBS-2 (OSSG 1103) and HERBS-4A (OSSG 1105) trials. First Author: Jin Matsuyama, Department of Gastroenterological Surgery, Higashiosaka City Medical Center, Higashiosaka, Japan

Background: HERBS-2 trial was a phase II trial where S-1 plus cisplatin (SP) were compared in recurrent HER2 negative gastric cancer (GC) patients with recurrence free interval (RFI) by S-1-containing adjuvant of 6 months. We performed pooled analyses of HERBS-2 and HERBS-4A trials where SP and XP were compared in chemotherapy-naïve HER2 negative gastric cancer (GC) patients as these trials being identical.

Methods: Both HERBS-2 and 4A trials, patients were randomly assigned to receive either SP (S1 at 40-60 mg twice daily for 21 days plus cisplatin at 60 mg/ m²/day on day 8, every 5 weeks) or XP (capecitabine 1,000 mg/m² twice daily for 14 days plus cisplatin 80 mg/m² on day 1, every 3 weeks). Results: In HERBS-2 which was closed early due to poor accrual, SP (N=10) tended to confer a better overall survival (OS) compared with XP (N=9)(18.7% (95%CI, 2.8 - NR months) vs.13.4% (95% CI, 5.2 - 31.3) months, hazard ratio (HR), 0.443 (95% CI, 0.156 - 1.258))p<.117). In pooled analyses with HERBS-2 and 4A, SP (N=50) vs. XP (N=51) showed longer progression free survival (6.4 vs.5.1 months; HR, 0.666; P= .621), OS (14.8 vs. 10.6 months; HR, 0.695)(p<.099), time to treatment failure (4.6 vs. 3.6 months; HR, 0.668; (P=.045), and higher disease control rate (86.4% vs. 68.1%, P=.149). Subgroup analysis revealed that OS benefit in SP arm compared to XP arm was significantly larger if the patient having PS of 0 (HR, 0.554 (95% CI 0.309 to 0.959); interaction p= .035), or the tumor arising from upper area of stomach (HR, 0.266 (95% CI 0.107 to 0.731); interaction p= .012) or harboring differentiated type cancer (HR, 0.433 (95% CI, 0.228 to 0.882); interaction p=.001), respectively. Conclusions: Our data suggest the use of SP in the 1st line setting in HER2 negative advanced or recurrent GC with RFI by S-1 adjuvant of ≥ 6 months.

Surrogate indicators of survival in patients who received neoadjuvant chemotherapy for type 4 and large type 3 gastric cancer in JCOG0501.

First Author: Masanori Terashima, Division of Gastric Surgery, Shizuoka Cancer Center, Shizuoka, Japan

Background: Pathological response grade (pR) is a common endpoint for assessing the efficacy of neo-adjuvant chemotherapy (NAC) in patients with advanced gastric cancer (GC). We report preliminary results of JCOG051, which was a phase II trial comparing chemotherapy plus surgery with NAC for locally advanced GC.

Methods: Patients with type 4 and large type 3 resectable GC were randomized either surgery plus adjuvant S-1 (arm A) or NAC (S-1 plus cisplatin) plus surgery plus S-1 (arm B) in JCOG051. Histological type (sig vs non-sig) was evaluated using preparative biopsy specimen. Cox proportional hazards model was utilized to assess the effects of covariates for overall survival (OS). Pathological response was defined as Grade1b-3 according to the Japanese Gastric Cancer Association grading.

Results: Among 286 (147 in arm A and 139 in arm B) patients who underwent surgery, 132 patients with complete pathological data in arm B were evaluated. Macroscopic tumor response (pR) was observed in 70 patients (36%) and 62 patients (46%) in arm A and B, respectively. As shown in the table, pathological response was significantly better after adjusting other factors (HR, 0.51 (95% CI 0.30-0.87), p = 0.014). Conclusions: pR may be used as a surrogate endpoint for future clinical trials in type 4 and large type 3 GC. Clinical trial information: COJ0000073 Research Sponsor: National Cancer Center Research and Development Funds.Grant-in-Aid for Clinical Cancer Research from the Ministry of Health, Labour and Welfare of Japan.

Palliative systemic chemotherapy with or without pressurized intraperitoneal aerosol chemotherapy with cisplatin and doxorubicin (PIPAC C/D) for gastric cancer with peritoneal metastasis: A propensity score analysis. First Author: Vladimir Khramokov, P.A. Hertsen Moscow Research Oncological Institute-National Medical Research Centre of Radiology, Moscow, Russian Federation

Background: Gastric cancer (GC) with peritoneal metastasis (PM) has a dismal prognosis. Palliative systemic chemotherapy (SC), usually double combinations of platinum and fluoropyrimidines, is the standard care. Pressurized IntraPeritoneal Aerosol Chemotherapy with Cisplatin and Doxorubicin (PIPAC C/D) yields promising results. Here we aimed to compare overall survival (OS) between SC + PIPAC C/D vs. SC alone in patients with PM from GC.

Methods: Prospective cohort of 95 consecutive patients with PM from GC treated in palliative intent at our institution from 2010 to 2018. Of these patients, 69 received SC + PIPAC C/D (“PIPAC”), 26 SC alone (“control”). Choice of treatment was not dictated by medical criteria, but by (non-) availability of the single-use medical devices needed for PIPAC in Russia. All patients received double or triple chemotherapy with platinum together with fluoropyrimidines or capcitabina. Cox proportional hazard model based on propensity score (PS) was used to assess the effect of PIPAC on OS and account for confounding factors.

Results: The HR adjusted for PS for PIPAC vs. control was 0.396 (CI 95% 0.224-0.700, p-value 0.001). In the simple (unadjusted) Kaplan-Meier, median survival in the control group was 7.0 months (CI: 4.51 - 9.49) and in the PIPAC group 14.0 months (CI: 11.46-16.54). In the control group, all 26 patients died after 12.5 months. In the PIPAC group, 36 of 69 patients died after 4 to 20 months. The longest observed survival time in the PIPAC group was 27 months. Significance for the log-rank test after Mantel-Cox (not adjusted) was p < 0.001. Conclusions: Compared with SC, PIPAC as intensified chemotherapy combining PIPAC C/D and SC doubled OS. These promising results need to be confirmed in a randomized trial. Research Sponsor: None.

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A phase III study of nivolumab (Nivo) in previously treated advanced gastric or gastroesophageal junction cancer (G/GEJ) (ATTRACTION-2): Three-year update data. First Author: Li-Tzong Chen, National Health Research Institutes, Taiwan, Taiwan

Background: Nivo is the first immune checkpoint inhibitor (ICI) to show efficacy and tolerability in G/GEJ cancer patients refractory to or intolerant of standard chemotherapy. Although Nivo has demonstrated durable efficacy in several cancer types, no long-term efficacy data in G/GEJ cancer has been reported to date. Here, we report the 3-year survival data of Nivo in G/GEJ cancer.

Methods: A total of 493 patients with unresectable advanced or recurrent G/GEJ cancer after the failure of two or more chemotherapy regimens were randomized in a 2:1 ratio to receive 3 mg/kg Nivo (N = 330) or placebo (N = 163) until disease progression or unacceptable toxicity. The primary endpoint was overall survival (OS). Updated results of the efficacy and safety were based on ≥ 3 years of follow-up after last patient enrollment. In subgroup analysis, we evaluated OS by BOR and incidence of select treatment-related adverse events (TRAEs).

Results: As of data cut-off in February 2019, 3 years after last patient enrollment, the hazard ratios of OS and PFS in the Nivo group compared with the placebo group remained 0.62 and 0.60, respectively. The 36-month OS rates of Nivo and placebo were 5.6% and 12.2%, and the 36-month PFS rates were 2.4% and 0%, respectively. In the OS subgroup analysis by BOR, the median OS and 3-year OS rate in CR/PR patients with Nivo were 26.7 months and 25.5%, respectively. The incidence rate and severity of TRAEs were comparable with those of the 2-year cut-off. In the OS subgroup analysis based on the presence or absence of select TRAEs, the hazard ratio in patients with select TRAEs was 0.46 compared to those without select TRAEs. We are analyzing the baseline characteristics that are associated with long-term survival with Nivo.

Cost-effectiveness analysis of pressurized intraperitoneal aerosol chemotherapy (PIPAC C/D) in patients with gastric cancer and peritoneal metastasis. First Author: Mehdi Jawanbakht, Optimax Access UK Ltd, Market Access Consultancy, Southampton, United Kingdom

Background: The efficacy of systemic chemotherapy is still highly unsatisfactory for patients with gastric cancer and peritoneal metastases. The aim of this study was to assess the costs effectiveness of pressurized intraperitoneal aerosol chemotherapy with low-dose cisplatin and doxorubicin (PIPAC C/D) for advanced gastric cancer. Methods: We developed a state transition Markov model to estimate the costs and effectiveness of the use of PIPAC C/D versus palliative chemotherapy. Intervention was assessed in two different levels including upfront therapy (PIPAC C/D plus XELOX chemotherapy versus first-line chemotherapy alone) and second line therapy (PIPAC C/D only versus second-line chemotherapy (ramucirumab monotherapy)). Data from multiple sources such as published literature and UK-based databases were used to inform the economic model. Deterministic and probabilistic sensitivity analyses were conducted to explore the impact of key parameter variation on the results. Results: For the upfront therapy the estimated total costs in the intervention and comparator arms were £33,875 (SD: £2,394) and £71,477 (£927) respectively. PIPAC C/D plus XELOX led to an increase of 0.56 in QALYs. Incremental cost per quality adjusted life years (QALYs) was £28,879. Result from probabilistic sensitivity analysis showed that PIPAC C/D plus XELOX is cost effective in more than 50% of Monte Carlo simulations at £30,000 threshold. For the second-line therapy, the total costs for PIPAC C/D was £15,985 (£1,399) and for the second-line palliative chemotherapy was £36,319 (£3,673). PIPAC C/D led to an increase of 0.21 in QALYs and £20,022 reduction in costs, meaning the intervention is dominant strategy in the second line therapy as it is less costly and more effective.

Conclusions: The cost effectiveness results for the upfront therapy indicate that PIPAC C/D plus chemotherapy intervention is more costly and more effective than the second-line chemotherapy. PIPAC C/D only intervention has the potential to reduce costs and improve clinical outcomes for patients with advanced gastric cancer with peritoneal metastasis and therefore a dominant strategy. Research Sponsor: Capnomed GmbH, Zimmern, Germany.

Treatment efficacy of ramucirumab-based chemotherapy in patients with alpha-fetoprotein producing gastric cancer (AFPGC). First Author: Daisaku Kamiyamabepu, Cancer Institute Hospital of JFCR, Tokyo, Japan

Background: AFPGC is an aggressive subgroup of gastric cancer and is associated with a worsened survival because of a high incidence of liver metastasis. Ramucirumab-based chemotherapy is the standard treatment as a second line in advanced gastric cancer. The efficacy of ramucirumab may have compensated for disadvantage in survival. Considering the generally poor prognosis of AFPGC, it is speculated that ramucirumab may have compensated for disadvantage in survival. Research Sponsor: None.

Methods: We retrospectively assessed 283 patients who received paclitaxel or nab-paclitaxel combined with ramucirumab between July 2015 and December 2018. AFPGC was defined when serum AFP levels were normal during treatment. Non-AFPGC was defined when serum AFP levels were normal when diagnosed. Other patients were excluded. Patients’ demographics, progression-free survival (PFS), overall survival (OS) and objective response rates (ORR) were compared between the two groups. Results: Among the 283 patients, 24 patients were AFPGC and 189 patients were non-AFPGC. AFPGC was associated with high incidences of intestinal histology (46%) and liver metastasis (63%), while AFPGC was associated with a low incidence of peritoneal metastasis (21%), compared with non-AFPGC. There was no significant difference in PFS and OS between the two groups. Median PFS were 5.4 (95%CI 3.6-6.7) months in AFPGC and 4.1 (3.7-5.1) months in non-AFPGC (HR 0.93 95%CI 0.60-1.46, p = 0.788), respectively. Median OS were 19.0 (95%CI 13.2-NA) months in AFPGC and 19.3 (17.9-20.3) months in non-AFPGC (HR 1.2195%CI 1.070-2.10, p = 0.494), respectively. Regarding with ORR, AFPGC showed higher ORR with 52.6% (95%CI 30.2-75.1), while 37.3% (95%CI 26.4-48.3) in non-AFPGC (p = 0.236), although this was not statistically significant. Conclusions: Ramucirumab showed comparable survival and higher ORR in AFPGC than in non-AFPGC. Considering the generally poor prognosis of AFPGC, it is speculated that ramucirumab may have compensated for disadvantage in survival. Research Sponsor: None.

Real-world efficacy and biomarker of nivolumab for advanced gastric cancer. First Author: Ryohye Kawabata, Department of Surgery, Osaka Rosai Hospital, Sakai, Japan

Background: Although nivolumab demonstrated survival benefit and a manageable safety profile in previously-treated advanced gastric cancer in a phase III trial (ATTRACTION-2), the efficacy of nivolumab in real-world and predictive factors of responses to nivolumab for advanced gastric cancer remain unclear. We evaluated the efficacy of nivolumab and compared clinicopathological characteristics with responses to nivolumab and long-term survivors in patients with gastric cancer. Methods: 205 patients with unresectable or recurrent gastric cancer who were treated with nivolumab as 3rd or more line treatment were enrolled from 23 institutions. Tissue specimens were collected in 199 patients, PD-L1 expression of tumor specimens defined as tumor positive score (TPS) and combined positive score (CPS) and mismatch repair (MMR) were analyzed by immunohistochemistry. Tumor responses were assessed according to RECIST version 1.1. Hyper progressive disease (HPD) was defined as ≥two folds increase in tumor growth rate. Results: 138 out of 205 enrolled patients had measurable lesions. Response rate and HPD rate were 16.7% (23/138) and 22.0% (29/132), respectively. Response rate was significantly higher in patients with performance status (PS) 0-1, non-peritoneal diseases, CPS ≥10, and MMR deficient patients. On the other hand, PS 2-3 and liver metastases were predictive factors of HPD. Patients with CPS ≥10 and MMR deficiency showed significantly better progression-free (P = 0.005, P = 0.001) and overall survivals (P = 0.005, P = 0.002). CPS showed no significant association with any outcomes. Conclusions: Real-world efficacy of nivolumab was shown in previously-treated advanced gastric cancer. CPS and MMR could be the useful biomarkers for the efficacy of nivolumab treatment as well as PS and metastasis site. Clinical trial information: UMIN000032164.

Long-term survival in patients with peritoneal metastasized gastric cancer treated with cytoreductive surgery and HIPEC: A multi-institutional cohort from PSOGI. First Author: Andreas Brandt, Champalimaud Foundation, Lisbon, Portugal

Background: Peritoneal metastasis of gastric cancer is relatively common (17%) and is associated with poor survival. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is still controversially discussed, as it has proven an increase in median survival in selected patients, but only a small subgroup reached long-term survival. The aim of this study was to collect and analyze a worldwide cohort of patients treated with CRS and HIPEC with long-term survival in order to explore relevant patient characteristics. Methods: We conducted a questionnaire, which was distributed to all collaborators of the Peritoneal Surface Oncology Group International (PSOGI). Inclusion criteria were: histopathologic proven peritoneal metastasis of gastric cancer, treated with CRS and HIPEC, and overall survival >5 years. Patient, tumor, and therapeutic details were collected and analyzed. Results: A total of 29 patients with a mean age of 52.5 years and a mean PCI of 3.2 were included. The overall median survival was 11.0 years (min 5.0; max 27.9). The predictors completeness of cytoreduction (CC-0) and low PCI (PCI < 6) were present in 23/29 patients. 13/29 patients developed at a median of 82.2 months tumor recurrence. Tumor recurrence was associated with inferior median overall survival compared to patients without tumor recurrence (8.8 years vs. not reached, p = 0.002). Conclusions: Long-term survival and even cure are possible in patients with peritoneal metastasis of gastric cancer treated with CRS and HIPEC. Completeness of cytoreduction (CC-0) and low PCI seemed to be crucial. Further studies are needed in order to improve existing selection criteria. Research Sponsor: None.
Hospital Score (RMH score), modified Glasgow prognostic score (mGPS), and immune related adverse event (iRAE) in Good Group, and 18% in Poor Group.

Median progression free survival was 61 days and 180 days in Good Group and 36 days and 85 days in Poor Group. Overall survival (OS) was significantly shorter in Poor group (180 days vs 85 days, p = 0.0255). Disease control rate was 23% in Good group and 9% in Poor group. 33% patients were experienced immune related adverse event (IARE) in Good Group, and 18% in Poor Group.

We investigated prognostic factor of OS in Poor Group such as Royal Marsden Score (RMS score), modified Glasgow prognostic score (mGPS), and Japanese Clinical Oncology Group (JCOG) prognostic index. RMS score and JCOG prognostic index good or moderate group was significantly longer overall survival than poor group (93 days vs 35 days (p = 0.0214)). JCOG prognostic index was most correlated with OS among these tools. Conclusions: This study suggested that nivolumab has a modest effect and is feasible as third-line or later line for AGC patients. JCOG prognostic index was suggested to be effective in predicting prognosis in AGC patients who received nivolumab.

Research Sponsor: None.

ESOPHAGEAL AND GASTRIC CANCER

Preliminary analysis of total neoadjuvant therapy for patients with locally advanced gastric (G) and gastroesophageal (GE) adenocarcinoma. First Author: Eric Roeland, Massachusetts General Hospital Cancer Center, Boston, MA

Background: Nearly half of patients with G/GE cancer do not receive or complete post-operative chemotherapy and/or chemoradiation (CRT). Total neoadjuvant therapy (TNT) is an emerging alternative treatment strategy. We have previously reported a 28% pCR with FOLFOXIRI followed by CRT. However, TNT outcomes with FLOT or FOLFOX followed by CRT are lacking.

Methods: We retrospectively analyzed patients after resection of locally advanced G/GE after receiving TNT. Patient received neoadjuvant FOLFOX or FLOT x 8 cycles, CRT (45 Gy, GE 50.4 Gy) with concurrent chemotherapy (5FU, carboplatin/paclitaxel). The primary aim was to update TNT completion rates. Secondary aims included pCR and toxicity. We performed descriptive statistics, t-test, chi-squared, and Fisher’s exact tests as appropriate.

Results: From 12/2015 to 09/2019, 173 patients underwent TNT and resection (15.7% active treatment, 23-79) and 73% male. Tumor locations included 57.5% G, 30.0% GE, and 12.5% GEJ. Median age was 66.0 (range: 27-79) and 73% male. Tumor locations included 57.5% G, 30.0% GE, and 12.5% GEJ. Median age was 66.0 (range: 27-79) and 73% male. Tumor locations included 57.5% G, 30.0% GE, and 12.5% GEJ. Median age was 66.0 (range: 27-79) and 73% male. Tumor locations included 57.5% G, 30.0% GE, and 12.5% GEJ.

Conclusions: TNT outcomes with FLOT or FOLFOX followed by CRT are lacking. We reported TNT outcomes with 22.2% pCR (n, %) 2 (22.2) 8 (25.8) 1.00 overall. We found a 25% pCR without significant differences between type of neoadjuvant chemotherapy. Conclusions: TNT followed by resection is feasible with acceptable rates of treatment completion and toxicity. Notable limitations include the retrospective analysis, small sample size, and heterogenous treatment. The pCR rate is promising and warrants further prospective study to optimize TNT approaches. Research Sponsor: None.

Duration of TNT, months (mean) 17 (4.24.2) 15 (4.17.9) 0.13

NEUROPATHY (n, %)

Weight loss (%)

-5.86 (-12.4-0.6) 0.0 (4.4-12.6) 0.21

Neuropathy (n, %)

1 (7.8) 8 (26.7) 0.01

Oncolyisis (n, %)

2 (2.2) 3 (9.6) 0.31

RO resection (n)

8 (88.9) 30 (96.8) 0.34

pCR (n, %)

2 (22.2) 8 (25.8) 0.10

ESOPHAGEAL AND GASTRIC CANCER

Preliminary analysis of total neoadjuvant therapy for patients with locally advanced gastric (G) and gastroesophageal (GE) adenocarcinoma. First Author: Eric Roeland, Massachusetts General Hospital Cancer Center, Boston, MA

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ESOPHAGEAL AND GASTRIC CANCER

Preliminary analysis of total neoadjuvant therapy for patients with locally advanced gastric (G) and gastroesophageal (GE) adenocarcinoma. First Author: Eric Roeland, Massachusetts General Hospital Cancer Center, Boston, MA

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Results: From 12/2015 to 09/2019, 173 patients underwent TNT and resection (15.7% active treatment, 23-79) and 73% male. Tumor locations included 57.5% G, 30.0% GE, and 12.5% GEJ. Median age was 66.0 (range: 27-79) and 73% male. Tumor locations included 57.5% G, 30.0% GE, and 12.5% GEJ.

Conclusions: TNT outcomes with FLOT or FOLFOX followed by CRT are lacking. We reported TNT outcomes with 22.2% pCR (n, %) 2 (22.2) 8 (25.8) 1.00 overall. We found a 25% pCR without significant differences between type of neoadjuvant chemotherapy. Conclusions: TNT followed by resection is feasible with acceptable rates of treatment completion and toxicity. Notable limitations include the retrospective analysis, small sample size, and heterogenous treatment. The pCR rate is promising and warrants further prospective study to optimize TNT approaches. Research Sponsor: None.
Concurrent versus sequential neoadjuvant chemoradiation therapy for esophageal and gastroesophageal junction adenocarcinoma. First Author: Robert J. Torphy, University of Colorado School of Medicine, Aurora, CO

Background: Neoadjuvant therapy is the standard of care for locally advanced esophageal and gastroesophageal junction (GEJ) adenocarcinoma, with most patients receiving neoadjuvant chemoradiation (CRT). CRT can be delivered concurrently or sequentially after induction chemotherapy. The purpose of this study was to evaluate pathologic complete response (pCR) and overall survival (OS) among patients who received concurrent versus sequential CRT in the National Cancer Database (NCDB).

Methods: Patients who received neoadjuvant CRT and underwent curative intent esophagectomy for esophageal or GEJ adenocarcinoma from 2006-2015 were included. Patients with clinical T4 or metastatic disease were excluded. Concurrent CRT was defined as radiation treatment starting within 6 weeks of chemotherapy start. Sequential CRT was defined as radiation treatment starting within 6 weeks after chemotherapy start. Propensity weighting was conducted to balance patient, disease, and facility covariates between groups. Results: 12,460 patients met inclusion criteria. 11,880 (95%) patients received concurrent CRT and 580 (5%) patients received sequential CRT. Patients who received sequential CRT were significantly younger (mean age: 60.7 vs 62.2 years), had higher clinical nodal stage (N2-3: 14.7% vs 10.1%), and were more often treated at academic/research hospitals (67.1 vs 55.5) (all p < 0.001). pCR was achieved in 16.2% of patients who received sequential CRT and in 14.0% of patients who received concurrent CRT (p = 0.13). Following propensity weighting, OS was significantly improved among patients who received sequential versus concurrent CRT (HR 0.82; 95% CI 0.74-0.92; p < 0.001) with a median OS for the sequential cohort of 41.4 months versus 29.4 months for those who received concurrent CRT. Conclusions: In this retrospective study from a large national database of patients who received neoadjuvant CRT for esophageal and GEJ adenocarcinoma, sequential CRT is associated with a significant OS benefit. These results merit consideration of a well-powered prospective multi-institutional randomized clinical trial to further evaluate this observed difference.

Research Sponsor: None.

Efficacy and safety of nivolumab and irinotecan as third-line chemotherapy for advanced gastric cancer: A multi-institutional retrospective study. First Author: Ryosuke Kumanishi, Aichi Cancer Center Hospital, Nagoya City, Japan

Background: Although nivolumab (NIVO) and irinotecan (IRI) are currently used as third- or later-line therapy for advanced gastric cancer (AGC), few direct comparisons between them have been available. The present study therefore aims to compare the efficacy and safety of NIVO with IRI and explore clinical factors that predict efficacy. Methods: Patients with AGC who underwent NIVO or IRI treatment between November 2016 and June 2018 at three institution were retrospectively examined. Subsequent chemotherapy after treatment failure was not allowed. Cox proportional hazard regression analysis was used to compare the survival rates (HR, progression-free survival (PFS), overall survival (OS), and adverse events (AEs). The main inclusion criteria were patients pretreated with fluoropyrimidines and taxanes, Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0-2, and no previous NIVO or IRI treatment. Results: A total of 71 and 61 patients received NIVO and IRI, respectively, with both groups having similar baseline characteristics, except for gender. Efficacies were as follows (NIVO/IRI): RR, 20%/6% (p = 0.17); median PFS, 1.6 months (m)/8.8 m (HR 0.93, p = 0.67); median OS, 6.4 m/6.4 m (HR 0.91, p = 0.61); 1-year survival rate, 24.9%/19.3% (p = 0.61). Interaction analysis found no significant interaction between drugs and various factors such as ECOG PS (p = 0.59) and neutrophil/lymphocyte ratio (p = 0.33) relative to OS. Subsequent chemotherapy agents were administered to 32 patients (45%) in the NIVO group (17 patients out of them received IRI) and 36 patients (59%) in the IRI group (23 patients out of them received NIVO) (p = 0.12). IRI tended to have lower grade 3 or more AEs than IRI, especially neutropenia (3% vs. 28%, respectively; p = 0.01) and febrile neutropenia (1% vs. 8%, respectively; p = 0.09), as well as neutropenia, nausea, diarrhea, constipation, fatigue, and anorexia of any grade. Five patients developed immune-related adverse events in the NIVO group: pneumonitis (n = 1) and rash (n = 4). Conclusions: Although no remarkable differences in efficacy were found between NIVO and IRI for AGC, NIVO had a better safety profile compared to IRI. This study found no clinical factors that predicted efficacy.

Research Sponsor: None.

Safety of perioperative atezolizumab in combination with FLOT versus FLOT alone in patients with resectable esophagogastric adenocarcinoma: An interim safety analysis of the DANTE, a randomized, open-label phase II trial of the German Gastric Group at the AIO and the SAKK. First Author: Salah-Eddin Al-Batran, Institute of Clinical Research (iKyF) at Krankenhaus Nordwest, UCT-University Cancer Center, Frankfurt, Germany

Background: The DANTE study evaluates atezolizumab in the perioperative setting of locally advanced potentially resectable gastric or esophagogastric adenocarcinoma in combination with perioperative FLOT. Here, we report the protocol-defined interim safety analysis. Methods: DANTE is a large, multi-national, prospective, multicenter, randomized, investigator-initiated, open-label phase II trial. Patients (pts) with locally advanced, potentially resectable adenocarcinoma of the stomach or GEJ (cT2 and/or N-positive) without cardiac involvement were enrolled. 395 pts were randomized 1:1 to 4 preoperative-2-week cycles (8 weeks) of FLOT followed by surgery and 4 additional cycles of FLOT plus atezolizumab at 840 mg every 2 weeks. The 3 additional cycles of atezolizumab at 1200 mg every 3 weeks as monotherapy (arm A) or FLOT alone (arm B). Primary endpoint is time to disease progression or relapse after surgery (PFS/DFS). Results: Recruitment started in Sept 2016; by September 2019, a total of 122 pts have been randomized. This analysis is based on the first 40 pts (20 pts in each arm). The pts had a median age of 62 y and 75% of pts had an ECOG PS of 0 in both arms. The cohort was well balanced in terms of tumor location and clinical stage. 90% of pts enrolled completed all preoperative cycles in each arm. 3 of 45 patients had grade 3-4 adverse events with relation to study treatment was 154 in arm A and 148 in arm B. Total number of serious adverse events (SAE; related or not) was 16 in Arm A and 14 in arm B. 20% of pts in each arm had an SAE due to perioperative morbidity. No surgical mortality was observed. 18 and 19 pts proceeded to surgery in arms A and B, respectively. Premature treatment discontinuation occurred in 2 pts in each arm: disease progression (1) and deterioration of general health condition (1) in arm A; and pts’ wish (1) and death (1) in arm B. Median hospitalization time was 15 days in arm A and 16 days in arm B. Conclusions: perioperative atezolizumab plus FLOT is feasible and safe. The study continued recruitment. Clinical trial information: NCT03421288. Research Sponsor: Roche Pharma.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Multicenter phase II study of neoadjuvant chemotherapy with S-1 and oxaliplatin for locally advanced gastric cancer (Neo-G-SSOX II). First Author: Masato Kondo, Kobe City Medical Center General Hospital, Kobe, Japan

Background: Prognosis for locally advanced gastric cancer (LAGC), such as clinical T4 disease, bulky nodal metastases, type 4 and large type 3 gastric cancer, was not improved even by D2 gastrectomy followed by adjuvant chemotherapy. Neoadjuvant chemotherapy is another promising approach, therefore, we have conducted a phase II study to evaluate the efficacy and safety of the neoadjuvant chemotherapy of S-1 and oxaliplatin (G-SSOX) followed by gastrectomy and D2/3 lymph node dissection for LAGC, and the primary endpoint of curative resection rate was met (Miki A, ESMO 2019). We show longer follow-up data from this study. Methods: Patients with adenocarcinoma of the stomach; clinical T4; clinically resectable gastric cancer of type 4 or large type 3; bulky nodal involvement around major branched arteries to the stomach were enrolled. Patients receive two cycles of neoadjuvant chemotherapy with S-1 (80 mg/m2, p.o., days 1-14 followed by 1 week rest) and oxaliplatin (130 mg/m2 at day 1), followed by D2 or higher surgery with no residual disease. Patients with pathological R0/R1 resection received S-1 (80 mg/m2, p.o., days 1-28 followed by 2 week rest) for 1 year as adjuvant chemotherapy. Primary endpoint was curative resection rate. Results: Between August 2015 and March 2017, forty-one patients were enrolled. Of the patients, 39 patients (95%) completed the two courses of neoadjuvant chemotherapy of G-SSOX, 37 (90%) received gastrectomy, and 36 (87.8%) received curative resection (R0/R1). Grade 3 or higher toxicities during neoadjuvant chemotherapy of G-SSOX were neutropenia (7%), fatigue (7%), diarrhea (5%) and thrombocytopenia (2%). No treatment related deaths were observed. Surgical complications including postoperative complications were observed in 13 patients (35%). Pathological response rate after neoadjuvant G-SSOX was 40%. With a median follow-up period of 33.8 months, 3-year-relapse free survival and 3-year overall survival was 54.3% and 73.3%, respectively. Conclusions: An update analysis confirmed that neoadjuvant chemotherapy of G-SSOX is a feasible and might be one of the promising strategies for patients with LAGC. Clinical trial information: UMIN00001866. Research Sponsor: None.

Poster Session (Board #F10), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Efficacy of palliative liquid nitrogen spray cryotherapy in curbing progression of dysphagia in esophageal cancer. First Author: Swathi Eluri, University of North Carolina School of Medicine, Chapel Hill, NC

Background: Progressive dysphagia in locally advanced esophageal cancer worsens quality of life (QoL). Endoscopic cryobiolysis may effectively palliate dysphagia. Aim: To study the effect of palliative cryobiolysis with truFreeze Spray Cryotherapy (SCT) in patients with esophageal cancer. Methods: This is an interim analysis of a multi-center prospective study of esophageal cancer patients who are non-surgical candidates, not on active systemic therapy, without esophageal stents, or prior SCT. SCT is an endoscopic ablation modality using liquid nitrogen (LN2) delivered by catheter. SCT occurred at 6 week intervals or as indicated at a dose of 2x30 or 3x30 sec/treatment site. Dysphagia and esophageal symptoms were assessed at baseline and after treatment with a 5-point Dysphagia score and the EORTC-QOL-OES18 (higher score = more symptoms). Results: 39 subjects (mean age 74.1 ± 12.2; 87% men; Table) had 182 treatment sessions over a median follow-up of 206.9 days, and received a median 3 SCT sessions with an average dose of 90 (3x30 sec/site). There was 1 procedure related SAE (2.6% of patients and 0.5% procedures). Mean follow-up dysphagia score was 16 ± 0.8 and 90% had same or improved dysphagia score after SCT treatment, p < 0.001. On average, treated patients maintained the same or improved levels of dysphagia for 117 days. Esophageal QoL was maintained with improvement in “eating problems” (2.4 before treatment to 1.82 after, p < 0.01). Only 4 subjects needed a difference in stent size (m) or gastrostomy tube size (m) for nutrition. Conclusions: SCT for palliation of esophageal cancer was effective in limiting progression of dysphagia, while maintaining esophageal QoL. Only 10% required either esophageal stenting or feeding tube at >6 month follow-up. Clinical trial information: NCT03243734. Research Sponsor: CSA Medical, Inc.

Poster Session (Board #F11), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

A hybrid of the prone and left lateral decubitus positions for thoracoscopic esophagectomy with extended LN dissection for esophageal squamous cell carcinoma. First Author: Hirofumi Kawakubo, Keio University School of Medicine, Tokyo, Japan

Background: We first performed thoracoscopic esophagectomy (TE) as a minimally invasive procedure with the left decubitus position in 1996. In 2009 we developed a hybrid of the prone and left lateral decubitus positions for TE with extended LN dissection (Extensive-TE). The patient is fixed with the semi-prone position and we can easily change patient positions from the left lateral decubitus position to the prone position using rotation system of the operation table. The upper mediastinal procedure including lymphadenectomy along the right and left recurrent laryngeal nerve (RLN) is performed with the patient in the left lateral decubitus position, while the middle and lower mediastinal procedures are performed with the patient in the prone position with artificial pneumothorax. Methods: ESCC patients who underwent Extensive-TE between January 2016 and December 2016, were retrospectively reviewed. The patients’ background, surgical outcomes, postoperative complications and recurrence-free survival (RFS) were studied. Results: Primary tumor was located in Cervical esophagus for 2 (1%), the upper-thoracic esophagus for 28 (15%), the mid-thoracic esophagus for 104 (54%) and the lower-thoracic esophagus for 57 (30%). The number of patients classified with pre-treatment clinical stage of 1/2/3/4 was 94(49%)/42(22%)/46(24%)/95(5%), respectively. Eight patients were evaluated as having cM disease due to supraclavicular LN metastasis. The number of patients classified with postoperative pathological stage of 0/1/2/3/4 was 5(3%)/70(37%)/48(26%)/49(27%)/97(9%), respectively. The average total operation time was 542±110. The blood loss was 274±110. The incidence of postoperative pneumonia, anastomotic leakage, chylothorax, and recurrent nerve palsy was 11%, 14%, 2%, and 7% respectively. One patient died postoperatively within 90 days after surgery. Three years RFS with clinical stage of 1/2/3+4 was 91.5%/54.8%/51.9%, respectively. Conclusions: The magnifying effect of thoracoscopic enables us to perform more precise surgery and preserve normal lung. The use of the hybrid position is thought to be feasible and effective methods. Research Sponsor: None.

Poster Session (Board #F13), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Surgical approach to gastric cancer with hepatic metastases. First Author: Maria Bencivenga, Upper GI Surgery University of Verona, Verona, Italy

Background: Surgical approach to gastric cancer patients with extra-hepatic metastases is becoming more and more accepted but few information exist concerning the surgical management of gastric cancer with extra-hepatic metastases. With this retrospective study we evaluated if the prognosis is influenced by different metastatic sites and we looked for the presence of prognostic factors. Methods: We analysed 282 patients with gastric cancer and synchronous metastatic sites and we looked for the presence of prognostic factors. Results: Median overall survival was 10.9 months. We found no survival differences according to the site of metastases: median survival was of 11.2, 16.9, 21.4, 7.0 months for peritoneal, hepatic, lymph-nodal, and haematogenous metastases, respectively (p = 0.797). In all subgroups we observed an interesting number of long-term survivors (peritoneal 14.3% ≥36 months, 7.6% ≥60 months; hepatic 13.6% ≥36 months, 2.2% ≥60 months; lymph nodes 12.5% ≥36 months, 3.1% ≥60 months; > 1 site 18.7% ≥36 months, 1.6% ≥60 months). At multivariate analysis the factors that influenced survival were: number of resected lymph-nodes (p = 0.033), extension of lymphadenectomy (p < 0.001), pTNM (p = 0.003), curvature (p = 0.032) and histology (p = 0.028). Conclusions: We showed that no differences in overall survival according to site of metastases exist and we suggest that patients in whom a curative resection is possible, should be treated by resection of both gastric cancer and metastases. Research Sponsor: None.

Poster Session (Board #F14), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

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Tumor treating fields (TTFields; 150 kHz) and FOLF OX combination treatment effects on gastric cancer in vitro. First Author: Einav Zeevi, Novocure Ltd, Haifa, Israel

Background: Gastric cancer is the third most common cause of cancer mortality worldwide, yet long-term survival in gastric cancer remains poor despite systemic therapeutic advances. FOLFOX (oxaliplatin, fluorouracil [5-FU], and leucovorin) is an approved chemotherapy regimen for gastric cancer treatment. Tumor Treating Fields (TTFields) are an antimitic, loco-regional anticancer treatment delivered via non-invasive application of low intensity (1-3V/cm), intermediate frequency (100-500 kHz), alternating electrical fields. TTFields targets rapidly dividing cancer cells by disrupting microtubules leading to mitotic catastrophe, abnormal chromosome segregation, and apoptosis induction. We investigated the potential use of TTFields alone and in combination with FOLFOX for gastric carcinomas.

Methods: TTFields (150 kHz) and FOLFOX treatment was performed in AGS (50%) and KATO III (50%) gastric cancer cell lines. AGS and KATO III cells were treated for 72 hours with TTFields (1.1 and 1.7 V/cm, respectively) at frequencies of 100-400 kHz using the inovitro system. Efficacy of TTFields and FOLFOX was also tested in combination by applying both TTFields and FOLFOX over the optimal frequency in combination with various drug concentrations. Cell counts, apoptosis induction, clonogenic potential, and overall effect were determined. Results: The optimal TTFields frequency that led to the greatest cell count reduction (AGS, 55%; KATO III, 52%) was 150 kHz. The clonogenic potential was reduced by >70% in both cell lines. TTFields combined with each FOLFOX component (oxaliplatin, 5-FU, or leucovorin) led to a significant reduction in AGS and KATO III cell survival (2-way ANOVA, P < 0.001 for each cell line) versus each treatment alone. In AGS, TTFields plus FOLFOX combination treatment led to a further reduction in the overall effect (cytotoxic and clonogenic; 79%) versus TTFields alone (65%) and FOLFOX alone (34%). Similar results were observed in KATO III cells.

Conclusions: These results suggest that TTFields (150 kHz; optimal frequency) are an effective gastric cancer treatment; and combining TTFields with FOLFOX may further enhance efficacy. There is a strong rationale to continue exploring the use of TTFields in combination with standard care for gastric cancer treatment in the clinical settings. Research Sponsor: Novocure.

Poster Session (Board #F15), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM and Poster Walks, Thu, 5:00 PM-5:45 PM

Safety and efficacy of durvalumab following multimodality therapy for locally advanced esophageal and GEJ adenocarcinoma: Two-year follow-up results from Big Ten Cancer Research Consortium study. First Author: Hirva Mandani, Karmanos Cancer Institute, Detroit, MI

Background: Concurrent chemoradiation(CRT) followed by esophagectomy is a standard care for locally advanced esophageal cancer. Treatment failure of LA-EAC and GEJ adenocarcinoma. Approximately 50% of patients(pts) experience disease recurrence 2 yrs after treatment(tx) completion. No adjuvant tx has been shown to improve survival in pts. Immune checkpoint inhibitors have activity in metastatic PD-L1 positive EAC. Preclinical studies have shown radiation +/- chemotherapy upregulate PD-1/PD-L1 pathway.

Methods: We conducted a phase II trial evaluating safety and efficacy of durvalumab(durva) in pts with LA-EAC and GEJ adenocarcinoma who have residual disease in surgical specimen after neoadjuvant CRT and R0 resection. Pts received durva 1500mg IV every 4 weeks for up to 1yr. Results: 24 pts were enrolled from 4/2016-1/2018; median age: 60yrs (range, 43-70), 18 received carbo/paclitaxel and 6 received cis/5-FU concurrently with radiation. Staging at diagnosis: T2N0(n = 3, 12.5%), T2N2(n = 3, 12.5%),T3N0(n = 6, 25%), T3N2(n = 4, 17%), T3N3(n = 1, 4%), T3N3(n = 1, 4%). 19 pts (79%) had positive lymph nodes(LNs) at the time of surgery following CRT. 12 pts completed 1yr of tx, 12 came off tx because of relapse(6), AE(5), and consent withdrawal(1). At median follow up of 21.9mo(range, 22.9-28.1), 11 pts have relapsed: 9 distant and 2 locoregional. Two of 3 pts with grade 3 irAEs are alive and disease free at 17 and 23 mo respectively. 1-yr RFS and OS were 79.2% and 95.5%, respectively.

Conclusions: Adjuvant durvalumab following multimodality therapy for LA-EAC and GEJ adenocarcinoma is safe and improves outcome compared to historical rate of 50%. Rx of 20.6% at 26 months. Evaluation of predictive biomarkers of RT is underway. Clinical trial information: NCT02639065. Research Sponsor: AstraZeneca.

Poster Session (Board #F16), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Propensity score regression analysis of esophageal cancer treatment with surgery alone or neoadjuvant chemotherapy. First Author: Wyn Griffith Lewis, University Hospital Wales, Cardiff, United Kingdom

Background: The aim of this study was to examine the outcomes of oesophageal adenocarcinoma (OC) treatment with either surgery alone (S), or with neoadjuvant chemotherapy (NAC) followed by surgery (Sx). The propensity score (PS) regression analysis, in order to examine whether the benefits reported in the MRC OEO2 trial were reproducible in UK cancer network clinical practice. Methods: Consecutive patients undergoing potentially curative treatment for OC in a regional cancer network were studied. Multiple regression models, including PS, were used to account for confounding factors and the primary outcome measure was disease-free (DFS) and overall survival (OS). Results: A cohort of 440 patients was included in a regression analysis controlling for confounders (176 S, 264 NACS). NACS was associated with positive margin status (NAXS vs. S, 42.4% vs. 26.7%, p<0.05), poor 5-year DFS (32.1% vs. 56.9, p<0.001), and poor 5-year OS (27.5% vs. 47.3%, p<0.001). On regression adjustment based on propensity scores, NACS was not associated with DFS (hazard ratio (HR) 0.220) or OS (p=0.431). Mandard tumour regression grade (TRG) was significantly associated with DFS (hazard ratio (HR) 0.2195% CI 0.07-0.70) and OS (HR 0.27, 95% CI 13-0.59). Five-year DFS and OS related to TRG was 63.6 and 61.5% vs. 8.0 and 8.6% (p<0.001) for good and poor responders respectively.

Conclusions: Prescribing NAC to all OC patients risks delay in effective treatment of patients who are relatively chemo-resistant. Given the variability in pathological response, identifying OC patients who derive the most NAC benefit should be the focus. Research Sponsor: None.

Poster Session (Board #F17), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Poster Session (Board #F18), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

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ESOPHAGEAL AND GASTRIC CANCER

Neoadjuvant chemotherapy (TPF regimen) followed with robotic surgery and its impact on outcome in management of esophageal cancers: Indian experience. First Author: S.P. Somashekkar, Manipal Comprehensive Cancer Center, Bangalore, India

Background: Neoadjuvant chemotherapy coupled with robotic three stage esophagectomy have shown promising results in esophageal cancer. Methods: 136 patients diagnosed with squamous cell cancer esophageus were included to analyze the benefit of NACT with TPF (docetaxel 75mg/m² day 1, cisplatin 75mg/m² day 1, 5-FU 750mg/m² per day 1-4) regimen 3 cycles followed by three stage robotic esophagectomy. Esophagus, assessed by EUS and PET-CT scan, pre-chemo and post-chemo, in biopsy proven Squamous cell Carcinoma 97.6% pathological results were prospectively maintained in a data base. Results: Median age 62.7 years, male to female 5.9:4.1, T2 4%, T3 90% & T4 6%. N0 10% & N+90%. Post NACT, Partial response of 50.8%, and a complete pathological response of 27.6% was observed with response rate of 66.3% 20 pts. had mucositis, but none had grade 3 toxicity, neutropenia in 24 pts. and febrile neutropenia in 7 pt., vomiting and fatigue in 35 pts. Mean blood loss 256.5±85.8mL, duration of surgery 322.4±28.4min, ICU stay 15±0.8-day, hospital stay 10.5±2.1 day. Proximal and distal margin was negative for all whereas only 2 patients had a positive CRM. Mean Lymph node yield was 22.4±3.5 nodes. All patients had complete robotic surgery with no conversions and major intraoperative complication. Post-operatively Minor complication was noted in 5 patients temporary vocal cord paralysis, 10 delayed gastric emptying, wound infection in 3 and minor lung infection 9. Major complication in form of leak (3), stenosis (5), chylous leak (4) was noted. 30-day mortality 4.5%. With the longest follow up of 50 months, 3 year DFS and OS was 75.4% & 68% respectively.

Conclusions: Neoadjuvant chemotherapy with TPF regimen showed excellent response rates with minimal G3 toxicity and is well tolerated in Indian patients. Combination of NACT with robotic esophagectomy has excellent outcome with low morbidity & mortality. Research Sponsor: None.
Potency of CD8+ T-cell mediated antitumor immunity from intratumoral immunotherapy with STING agonist, ADU-S100, in an esophageal adenocarcinoma model. First Author: Laila Babiar, The Esophageal and Lung Institute, Allegheny Health Network, Pittsburgh, PA

Background: Esophageal adenocarcinoma (EAC) is a deadly disease with poor prognosis due to limited treatment options. STING is a transmembrane protein that activates the transcription of type I IFN genes, resulting in the stimulation of APCs and enhanced CD8+ T-cell infiltration. Recently, STING agonists have demonstrated durable antitumor activity in solid tumors when used alone and in combination with either chemotherapy, radiation or immunotherapy. In this study we evaluated the efficacy and immunomodulatory effects of STING agonist +/- radiation in an established EAC model.

Methods: Esophagojejunostomy was performed on rats to induce reflux leading to the development EAC. At 32 weeks post operatively, rats received either STING (ADU-S100) or placebo (PBS), +/- 16Gy radiation. Tumor regression was evaluated by pre- and post - treatment MRI, serial biopsies, histology and RT-PCR. Additionally, immunofluorescence was performed using CD8 and PD-L1 antibodies.

Results: A comparison of MRIs in the study groups between 32 and 40 weeks demonstrated a mean increase in percentage tumor volume of 76.7 % and 152.4 % in the P and P+R arms and a decrease of 30.1 % and 50.8 % in the S and S+R arms, respectively (ANOVA test p < 0.0001). Overall, the S+R group demonstrated the best results with maximum mean volume reduction with all cases responding. Downstream gene expression, pre, on, and post- treatment demonstrated significant upregulation of IFNγ, TNFa, IL-6 and CCL-2 in the treatment groups compared with placebo. On and post treatment, radiation alone, ADU-S100 alone and ADU-S100 + radiation groups demonstrated enhanced PD-L1 expression, induced by higher densities of IFNγ producing CD8+ T-cells (p < 0.01).

Conclusions: ADU-S100 +/- radiation exhibits potent anti-tumor efficacy and a promising immunomodulatory profile in a de novo EAC model providing the rationale for clinical testing, likely concurrenly in combination with immune checkpoint inhibitors. Research Sponsor: None.

Cytoreductive surgery in selected patients with metastatic gastric cancer treated with systemic chemotherapy. First Author: Yaniv Berger, University of Chicago, Chicago, IL

Background: Cytoreductive surgery (CRS - gastrectomy combined with metastasectomy) for non-palliative indications is controversial for patients with metastatic gastric adenocarcinoma (MGA). We hypothesized that CRS in addition to systemic chemotherapy is associated with an improved survival when compared to patients with MGA receiving chemotherapy alone. Methods: Patients with MGA who received systemic chemotherapy between 2004-2016 were identified using the National Cancer Database (NCDB). Nearest neighbor 1 propensity score matching of demographic, tumor-related and treatment-related factors was used to create comparable groups. Overall survival (OS) was compared between subgroups using Kaplan-Meier analyses. Immortal bias analysis was performed among those that survived at least 90 days. Results: We identified 29,728 chemotherapy-treated patients who were divided into 4 subgroups: No surgery (NS, n = 25,690), metastasectomy alone (n = 1707), gastrectomy alone (n = 2248) and CRS (n = 620) with a median OS of 8.6, 10.9, 14.8 and 16.3 months, respectively (p < 0.001). OS for propensity matched patients who underwent CRS (n = 490) was longer than NS (16.3 vs. 8.8 months, p = 0.001), including those with clinical MI stage (n = 203) in both unmatched and propensity matched (median OS 19.7 vs. 8.6 months, p < 0.001) cohorts. On Cox regression model using the matched data, the hazard ratio for CRS vs. NS was 0.80 (95%CI 0.76-0.84). In the immortal matched cohort, the corresponding median OS was 16.7 vs. 9.7 months, p < 0.001. Conclusions: CRS in addition to systemic chemotherapy may be associated with an OS benefit in a selected group of patients with metastatic gastric adenocarcinoma. Suboptimal matching for tumor burden is our major limitation. In contrast to studies that focus on gastrectomy alone in the setting of MGA, this study highlights the role of CRS among patients receiving systemic chemotherapy. Research Sponsor: None.

Regulation of gastric carcinoma development in gastric adenoma/dysplasia by crebfz inhibition via miRNA-421. First Author: Yu Jin Kim, Department of Gastroenterology, Hallym Medical Center, Hallym University College of Medicine, Seoul, South Korea

Background: In our previous study, we identified three miRNAs (hsa-miR-421, hsa-miR-29b-15p, and hsa-miR-27b-5p) with two miRNAs (FBXO11 and CREBFZ) that might play an important role in the development of gastric adenocarcinoma (GAC) from premalignant adenomas. However, the expression and function of these miRNAs have not been well characterized. Methods: We investigated the roles of CREBFZ and miRNAs as potential biomarkers for the progression of gastric cancer (GC) in low/high-grade dysplasia and early gastric cancer patients using immunohistochemical staining and miRNA in situ hybridization. Considering that targets can modulate in GC, we analyzed the CREBFZ expression in gastric cancer cell lines by RT-PCR and western blot analysis.

Results: We observed lower expression of CREBFZ with increasing miRNAs in the MKN74 gastric cancer cells compared to that in SNJU-NCC-19. Next, the role of CREBFZ in MKN74 gastric cancer cells was investigated via cell viability and the MKN-74 gastric cancer cells compared to that in SNU-NCC-19. Next, the role of CREBFZ inhibition via miRNA-421.

Conclusions: This study suggests that increased CREBFZ by hsa-miR-421/hsa-miR-29b-15p inhibition may be important to prevent the progression of gastric cancer in its early stage. Research Sponsor: National Research Foundation of Korea (NRF-20141A1A3050247).

LIN-1 hypo-methylation as a distinct phenotype in non-EBV/non-MSI-H esophagogastric junction adenocarcinoma. First Author: Yu Imamura, Department of Gastroenterological Surgery, Cancer Institute Hospital of the Japanese Foundation for Cancer Research, Koto-Ku, Tokyo, Japan

Background: Most esophagogastric junction (EGJ) adenocarcinoma exhibits chromosomal instability (CIN) type with wide range of CpG site methylation. However, it is still uncertain if epigenetic alteration is a distinct phenotype in non-EBV/non-MSI-H EGJ adenocarcinoma. The aim of this is to examine clinicopathological and molecular characteristics of LINE-1 methylation, and its prognostic role, in non-EBV/non-MSI-H EGJ adenocarcinoma. Methods: After removing EBV-associated or MSI-H tumors, which are the distinct molecular subtype with hyper methylation, a total 335 cases of chemo-naïve non-EBV/non-MSI-H EGJ adenocarcinoma from four academic institutions in Japan, were eligible. LINE-1 methylation was examined by Pyrosequencing. Results: LINE-1 methylation level was successfully sequenced in 319 cases (95.3%). LINE-1 methylation level is representative of genome-wide methylation status. The aim of this is to examine clinicopathological and molecular characteristics of LINE-1 methylation, and its prognostic role, in non-EBV/non-MSI-H EGJ adenocarcinoma. Methods: After removing EBV-associated or MSI-H tumors, which are the distinct molecular subtype with hyper methylation, a total 335 cases of chemo-naïve non-EBV/non-MSI-H EGJ adenocarcinoma from four academic institutions in Japan, were eligible. LINE-1 methylation was examined by Pyrosequencing. Results: LINE-1 methylation level was successfully sequenced in 319 cases (95.3%). LINE-1 methylation level is representative of genome-wide methylation status. The aim of this is to examine clinicopathological and molecular characteristics of LINE-1 methylation, and its prognostic role, in non-EBV/non-MSI-H EGJ adenocarcinoma. Methods: After removing EBV-associated or MSI-H tumors, which are the distinct molecular subtype with hyper methylation, a total 335 cases of chemo-naïve non-EBV/non-MSI-H EGJ adenocarcinoma from four academic institutions in Japan, were eligible. LINE-1 methylation was examined by Pyrosequencing. Results: LINE-1 methylation level was successfully sequenced in 319 cases (95.3%).
Significance of intratumoral tertiary lymphoid structure (TLS) as predictive factors of nivolumab therapy after conversion surgery for unresectable gastric cancer: A retrospective study. First Author: Hiraoki Tanaka, Department of Gastroenterological Surgery, Osaka City University Graduate School of Medicine, Osaka, Japan

**Background:** Conversion surgery for unresectable advanced gastric cancer has been increasing with the development of chemotherapy. Adjuvant chemotherapy regimens after conversion surgery have not been standardized. The main mechanism of nivolumab is augmentation of antitumor immune response of tumor infiltrating cytotoxic T cells (CTL) to cancer cells, and it has recently been reported that nivolumab therapy before and after chemotherapy is effective in other carcinomas. We previously reported that tertiary lymphoid architecture (TLS) correlates with tumor-infiltrating T cells and is associated with a better prognosis in untreated patients. The purpose of this study was to investigate the relationship between the presence of TLS in the primary tumor and prognosis in patients with gastric cancer who underwent conversion therapy. **Methods:** We evaluated 52 patients with advanced gastric cancer including 17 patients underwent conversion surgery and 35 patients underwent palliative surgery without prior chemotherapy in our department from 2009 to 2017. The local immune environment and presence of TLS was evaluated by immunohistochemical staining. **Results:** Intratumoral TLS occurred in 20% of patients with advanced cancer who did not receive chemotherapy before surgery and in 52% of patients who received conversion surgery. And the prognosis of patients with the presence of TLS was better than no TLS. Intratumoral CDF T-cell infiltration was slightly associated presence of TLS. We had a case in which nivolumab was highly effective and converted to conversion surgery. Intratumoral CD8 T-cell infiltration was slightly associated presence of TLS. The patients with higher tumor mutation load have a better tendency for OS and PFS, among AGC patients who received Nivo and Ram combination therapy. Clinical trial information: NCT02999295. Research Sponsor: Ono Pharmaceutical Co. Ltd.

**Conclusions:** The patients with higher tumor mutation load have a better tendency for OS and PFS, among AGC patients who received nivolumab and ramucirumab combination therapy. Nivolumab (Nivo) plus ramucirumab (Ram) showed promising efficacy with ORR (40.0% vs 20.0%), PFS (5.3 vs 2.3 months) and OS (18.1 vs 10.6 months). 6-month PFS rate was better in TML higher group (48%) compared to TML lower group (18%). In multivariate analysis, higher TML showed 2.030 of hazard ratio (95% CI; 0.849-4.855, P=0.12) for PFS and 1.915 (95% CI; 0.578-6.343, p=0.287) for OS. The patients with higher tumor mutation load have a better tendency for OS and PFS, among AGC patients who received Nivo and Ram combination therapy. Clinical trial information: NCT02999295. Research Sponsor: Ono Pharmaceutical Co. Ltd.

**Table 1:**

<table>
<thead>
<tr>
<th>TML Group</th>
<th>ORR (%)</th>
<th>PFS (months)</th>
<th>OS (months)</th>
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<tbody>
<tr>
<td>Lower</td>
<td>20.0</td>
<td>2.3</td>
<td>10.6</td>
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<tr>
<td>Higher</td>
<td>48.0</td>
<td>4.8</td>
<td>18.1</td>
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**Results:** By the data cut off of December 15, 2018, the median follow up duration on therapy was 13.7 month. Thirty AGC pts who obtained tissue sample were analyzed. Median tumor mutation load (TML) was 6.755 mutation/Mb (range 0.84-19.67). Higher TML (cut-off median) related to better tendency of efficacy with ORR (40.0% vs 20.0%), PFS (5.3 vs 2.3 months) and OS (18.1 vs 10.6 months). 6-month PFS rate was better in TML higher group (48%) compared to TML lower group (18%). In multivariate analysis, higher TML showed 2.030 of hazard ratio (95% CI; 0.849-4.855, P=0.12) for PFS and 1.915 (95% CI; 0.578-6.343, p=0.287) for OS. The patients with higher tumor mutation load have a better tendency for OS and PFS, among AGC patients who received Nivo and Ram combination therapy. Clinical trial information: NCT02999295. Research Sponsor: Ono Pharmaceutical Co. Ltd.

**Conclusions:** The patients with higher tumor mutation load have a better tendency for OS and PFS, among AGC patients who received nivolumab and ramucirumab combination therapy. Nivolumab (Nivo) plus ramucirumab (Ram) showed promising efficacy with ORR (40.0% vs 20.0%), PFS (5.3 vs 2.3 months) and OS (18.1 vs 10.6 months). 6-month PFS rate was better in TML higher group (48%) compared to TML lower group (18%). In multivariate analysis, higher TML showed 2.030 of hazard ratio (95% CI; 0.849-4.855, P=0.12) for PFS and 1.915 (95% CI; 0.578-6.343, p=0.287) for OS. The patients with higher tumor mutation load have a better tendency for OS and PFS, among AGC patients who received Nivo and Ram combination therapy. Clinical trial information: NCT02999295. Research Sponsor: Ono Pharmaceutical Co. Ltd.
416 Poster Session (Board #G5), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Transcriptional profile of immune microenvironment and their prediction role for the prognosis of esophageal squamous cell carcinoma. First Author: Jianji Guo, Department of Cardio-Thoracic Surgery, The First Affiliated Hospital of Guangxi Medical University, Nanning, China

Background: Esophageal squamous cell carcinoma (ESCC) is one of the most common cancer types in China. The genetic characteristics and biomarkers have already been described in many studies, but the immune microenvironment features were seldom reported. Our study was aimed to explore the relationship between the immune profile in stage IIa ESCC and patients’ prognosis.

Methods: 20 eligible patients withIIIa ESCC and completed chemoradiotherapy (9 with and 1 without radiotherapy) were divided into two groups based on the median expression values of 395 genes. The univariate analyses showed 20 genes were significantly associated with overall survival (OS). Unsupervised hierarchical cluster analysis using 20 gene expression data revealed two distinct clusters (cluster 1 and 2). The cluster patterns showed the expression of Progesterone receptor was positively correlated with the maximal standardized uptake values (SUVmax). The least absolute shrinkage and selection operator (LASSO) method was used to select variables (preliminarily subject to optimal coding using HR smoothed curves for OS) with the highest prognostic value. Selected variables were then analysed in a multivariate Cox Regression Model and used to build a GIPI nomogram.

Results: NLR and CRP taken as continuous variables and ALB categorized as < vs > 150 IU/L were found as the most meaningful independent predictors of OS (HR 1.30 (95%CI 1.02-1.65), 2.00 (95%CI 1.09-3.66), 2.62 (95%CI 1.29-6.20) and p values 0.04, 0.01, 0.02, respectively) and used to build the GIPI nomogram. Nomogram-based predicted OS for 10 patients as an external validation set (Spearman r = 0.82, p-value = 0.03). The rates of OS for the external validation set were 100% for cluster 1 and 15% for cluster 2. The 5-year survival rate for cluster 2 patients had significantly longer OS than cluster 1. Moreover, the cluster2 patients expressed higher NOS2, IL15, IKZF2, KITLG, RELA, REL, RAD50, MCM5, and N corresponded to the patients with favorable prognosis. The scores of GIPI for all patients were significantly lower for cluster 2 patients than cluster 1 patients (P < 0.001).

Conclusions: We found that the PDXs could recapitulate FDG avidity of those parental tumors between 15 Patient-PDX pairs (Spearman r = 0.54, p-value = 0.04). The prediction model with the identified five genes (PLS, PYY, HBOQ1, SLCG6AS1, N736) provided excellent prediction values compared with actual SUVmax for 15 patients as a validation set (Spearman r = 0.56, p-value = 0.03) and for 8 patients as a test set (Spearman r = 0.90, p-value = 0.005). The PredictionScore showed significant positive correlation with the actual SUVmax for 7 patients as an external validation set (Spearman r = 0.82, p-value = 0.03). PXD can be used to develop a gene panel for the PET positivity prediction in GC. Our results showed that the scoring system can be clinically applicable for developing a predicted stratification model. Future studies will aim to evaluate the panel for a higher number of PET-confirmed GC patients to establish a rational patient selection for PET scan in clinical settings. Research Sponsor: Development of standard personalized medicine platform integrating clinical genomics with PD-1/Ligation models.
The FGFR-inhibitor derazantinib (DZB) is active in PDX-models of GI-cancer with specific aberrations in FGFR. First Author: Paul McSheehy, Basilea Pharmaceutica International Ltd., Basel, NJ, Switzerland

Background: DZB is an oral small-molecule Fibroblast Growth Factor Receptor 1/2/3 inhibitor (FGFRi) with clinical activity in FGFR2-fusion-positive cholangiocarcinoma. DZB was screened for activity in gastrointestinal cancer (GIC), by using a panel of GIC cell-lines, human tumor xenographs and 30 GIC patient-derived xenograph (PDX) models. Methods: DZB anti-proliferative potency was determined in 26 GIC cell lines to determine the GI50. The GIC cell-line, SNU-16 was grown s.c. in nude mice and treated daily for 3 weeks with DZB at the MTD of 75 mg/kg, p.o. Plasma and tumor were removed and analyzed for drug-levels and PD biomarkers to assess pathway inhibition. DZB (MTD) was tested in the PDX-screen (15 biliary, 13 gastric and 2 colorectal cancer; n=3/group) using models with FGFR-fusions, FGFR-mutations and/or differing FGFR copy-number (CN)/RNA-seq expression levels. Efficacy and tolerability were quantified as a dT/C (treated/control).

Results: Cellular GI50s ranged from 0.02-20 μM; the most sensitive (GI50<0.5 μM) had FGFR-fusions or high-expression. In mice, DZB induced stasis of SNU-16 tumors (dT/C ~0.0) and was well tolerated (dT/C >1.0); the plasma PK was dose-dependent with a Cmax of 2 μM (4 hr), a Cmin of 0.5 μM. DZB induced dose- and time-dependent changes in the MAPK-pathway and expression of downstream genes, consistent with its mode of action. In PDX-models, efficacy varied from no-response to 100% regression. Known driver-mutations were associated with partial-responses (best dT/C = 0.42), but models with FGFR-fusions, especially FGFR2-fusions, were very sensitive leading to stasis or strong-regression, particularly in gastric cancer. High-expression of FGFR2 was also associated with strong responses. There was no direct correlation between CN and high RNA-seq values suggesting amplification was not always a predictor of high expression. Endpoint PD-analyses of the PDX-models is ongoing to identify other potential stratifiers and PD-markers of response. Conclusions: DZB showed convincing activity in GIC-models with FGFR-fusions and/or high expression. A clinical trial is planned in patients with gastric cancer to investigate DZB as mono- and combination-therapy. Research Sponsor: Basilea Pharmaceutica International Ltd.

Gene mutations distinguishing gastric from colorectal and esophageal adenocarcinomas. First Author: Tuyen Hoang, UCI Institute of Clinical and Translational Science, Irvine, CA

Background: Genetic analysis of gastrointestinal malignancies shows a great number of mutations. Most mutations found in gastric tumors are found in colorectal and esophageal tumors, and vice versa. The challenge remains to identify mutations that distinguish gastric cancer from colorectal and esophageal cancers. Using open-access cancer genomics data, we sought to identify mutations that accounted for the unique phenotypic features of gastric tumors. Methods: Thirteen cancer genomics datasets with demographic, clinical, and molecular characterization of tissues from 61 patients with metastatic gastric and/or colorectal cancer were analyzed. Each subject was flagged with or without a mutated gene. For each anatomical location, pathologic stage and metastatic site may contribute the further understanding of cancer immunity in advanced GC. Research Sponsor: Grant-in-Aid for Scientific Research.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Slug overexpression and association with clinicopathological features in gastric cancer. First Author: Jouki Kim, Seoul St Mary's Hospital, Seoul, South Korea

Background: Slug is a suppressive transcriptional factor of E-cadherin, acting as an activator of epithelial-mesenchymal transition (EMT). Its clinical relevance in gastric cancer (GC) is not fully known. Methods: Our study evaluated the expression patterns of EMT and cancer stem cell markers in GC patients who had clinical stage 2-3, underwent gastrectomy, D2 lymph node dissection (LND), adjuvant chemotherapy, Immunohistochemistry of E-cadherin, vimentin, CD133, ABCG2, NEDD9, SMAD4, XB130, Slug. Slug was investigated from 200 gastric cancer samples using tissue microarrays. The correlation between markers expressed and the association with clinicopathological factors were analyzed. Results: Slug expression was more frequent in stage 3 than stage 2 (p=0.000), advanced T (p=0.007) and N stage (p=0.000), while histologic type did not make difference. Slug expression correlated with the expression of cancer stem cell marker CD133 (r=0.180, p=0.015) and CD33 expression was also related with ABCG2 (r=0.412, p=0.000). High Slug group showed shorter overall survival, compared to low Slug group (median OS 134 vs 124 months, p=0.044). The 2-year and 5-year disease-free (DF) rate for patients with high Slug and low Slug was 87.1% and 79.8%, 68.1% and 79.8%, respectively (p=0.038). The DFS curve reached an earlier plateau at 11-month in low Slug group, while in high Slug group took as long as 99 months. A multivariate analysis using the Cox proportional hazards regression model demonstrated Slug to be an independent prognostic factor for overall survival; hazard ratio 0.504 (95% CI 0.278-0.916) (p=0.025). Conclusions: In stage 2-3 GC patients who underwent gastrectomy with D2 LND and adjuvant chemotherapy, high Slug expression is associated with better disease-free and overall survival. Patients may benefit by testing Slug immunohistochemistry to predict prognosis after gastrectomy. Research Sponsor: None.

ESOPHAGEAL AND GASTRIC CANCER

The clinical prognostic significance of lymphovascular invasion in gastric cancer. First Author: Hirohito Fujikawa, Department of Gastrointestinal Surgery, Kanagawa Cancer Center, Yokohama, Japan

Background: Lymphovascular invasion (LVI) of malignant tumor is regarded as an initial state of metastasis, including the lymph nodes, and therefore may be a prognostic factor in many malignancies. However, in gastric cancer, according to the current Japanese guidelines, LVI is not clinically useful information, except for in predicting the curability of endoscopic resection, and its clinicopathological characteristics and biological behavior remain unclear. The present study explored the histopathological significance of LVI in gastric cancer and clarified its correlation with the prognosis. Methods: From January 2000 to December 2013, a total of 2090 cases of gastric cancer undergoing radical gastrectomy were enrolled in this study. The correlation of LVI and other histopathological factors with the prognosis was evaluated. Lymphatic vessel invasion (LVI) and venous invasion (Vi) were diagnosed following the current Japanese classification. LVI positivity (LVI+) and LVI negativity (LVI−) were defined as the presence of lymphatic vessel and/or venous invasion and the absence of LVI, respectively. Results: LVI+ was noted in 894 cases (42.8%). The age (p<0.001), negativity (LVI−) were defined as the presence of lymphatic vessel and/or venous invasion, and the 5-year overall survival rates in LVIP cases were lower than those in LVIN (60.9% [95% confidence interval: 56.3-65.3] vs. 76.7% [95% confidence interval 65.2-84.8], p=0.005). Conclusions: LVI in gastric cancer is an independent factor, and its effect tends to be more significant in advanced cancer with lymph node metastasis. These patients may therefore require more effective adjuvant therapy. Research Sponsor: None.

Correlation of radiomics of metastatic lesions in gastroesophageal adenocarcinoma (GEA) with tumoral DKK1 mRNA expression and other immune biomarkers in patients (pts) treated with DKN-01. First Author: Cynthia A. Sirard, Heathcare Pharmaceuticals, Inc., Cambridge, MA

Background: Dickkopf-1 (DKK1) modulates Wnt and PI3K/AKT signaling pathways and is a suppressive transcriptional factor of E-cadherin, acting as an initial state of metastasis, including the lymph nodes, and therefore may be a prognostic factor in many malignancies. However, in gastric cancer, according to the current Japanese guidelines, LVI is not clinically useful information, except for in predicting the curability of endoscopic resection, and its clinicopathological characteristics and biological behavior remain unclear. The present study explored the histopathological significance of LVI in gastric cancer and clarified its correlation with the prognosis. Methods: From January 2000 to December 2013, a total of 2090 cases of gastric cancer undergoing radical gastrectomy were enrolled in this study. The correlation of LVI and other histopathological factors with the prognosis was evaluated. Lymphatic vessel invasion (LVI) and venous invasion (Vi) were diagnosed following the current Japanese classification. LVI positivity (LVI+) and LVI negativity (LVI−) were defined as the presence of lymphatic vessel and/or venous invasion, and the 5-year overall survival rates in LVIP cases were lower than those in LVIN (60.9% [95% confidence interval: 56.3-65.3] vs. 76.7% [95% confidence interval 65.2-84.8], p=0.005). Conclusions: LVI in gastric cancer is an independent factor, and its effect tends to be more significant in advanced cancer with lymph node metastasis. These patients may therefore require more effective adjuvant therapy. Research Sponsor: None.

Poster Session (Board #G15), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Efficacy of pembrolizumab (pembro) monotherapy versus chemotherapy for PD-L1-positive (CPS ≥10) advanced G/GEJ cancer in the phase II KEYNOTE-059 (cohort I) and phase III KEYNOTE-061 and KEYNOTE-062 studies. First Author: Zev A. Wainsberg, David Geffen School of Medicine at UCLA, Los Angeles, CA

Background: Pts with advanced gastric/gastroesophageal junction (G/GEJ) cancer receiving monotherapy (CPS >0, CPS ≥10 in cohort I) with KEYNOTE-059 (NCT02335441), 2L in KEYNOTE-061 (NCT02370498), or 1L in KEYNOTE-062 (NCT02494583). We present efficacy data for patients with PD-L1 combined positive score (CPS) ≥10 tumors in these trials. Methods: In study 059, 49 pts in cohort I with CPS ≥10 received pembro (n=53) or chemotherapy (chemo, n=55). In study 062, 82 pts with CPS ≥10 received pembro (n=92) or placebo + chemo (n=90). PD-L1 endpoints included overall survival (OS), progression-free survival (PFS), objective response rate (ORR), and duration of response (DOR). Results: Median follow-up in study 059 was 5.6 mo. Median OS with pembro was 7.9 mo (95% CI 5.8-11), and 12 mo OS was 32.6%. PFS at 6 mo was 17.4%, ORR was 17.4%, and median DOR was 20.9 mo (2.8+ to 34.9+). In study 062, after a median follow-up of 8.8 mo, pembro prolonged OS vs chemo (median 10.4 vs 8.0 mo; HR, 0.64; 95% CI, 0.41-1.02); 12-mo OS was 45.3% for pembro and 23.6% for chemo. Median PFS was 2.7 mo for pembro and 3.4 mo for chemo (HR, 0.86; 95% CI, 0.56-1.33). ORR was 24.5% vs 9.1%, and median DOR was NR (41.26+ mo) and 6.9 mo (2.6-6.9) for pembro vs chemo. Median OS following cohort I was 17.4 mo for pembro and 10.8 mo for chemo. Pembro prolonged OS vs chemo (median 17.4 vs 10.8 mo; HR, 0.69; 95% CI, 0.49-0.97); 12-mo OS was 56.5% vs 46.7%. Median PFS was 2.9 mo vs 1.6 mo (HR, 1.09; 95% CI, 0.79-1.49). ORR was 25.0% vs 37.8%, and median DOR was 19.3 mo (1.4 to 33.6 mo) vs 6.8 mo (15.3 to 30.4 mo) for pembro vs chemo, respectively. Conclusions: Collectively, these data indicate that 1L, 2L, and 3L+ pembro monotherapy is clinically meaningful efficacy in patients with CPS ≥10, with a more durable response than chemotherapy. Clinical trial information: NCT02335441, NCT02370498, and NCT02494583. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Poster Session (Board #G16), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Pembrolizumab (pembro) in microsatellite instability-high (MSI-H) advanced gastric/gastroesophageal junction (G/GJE) cancer by line of therapy. First Author: Joseph Chao, City of Hope Comprehensive Cancer Center, Duarte, CA

Background: Pembrolizumab has demonstrated promising antitumor activity in patients (pts) with advanced G/GJE cancer with PD-L1 CPS ≥1 and CPS ≥10 irrespective of MSI-H status. Here, we examine the antitumor activity of pembrolizumab monotherapy vs pembrolizumab + chemotherapy (CT) in pts with MS-H advanced G/GJE cancer in KEYNOTE (KN)-059 (NCT02335441), KN061 (NCT02370498), and KN062 (NCT02494583).

Methods: Eligible pts with advanced G/GJE cancer with ≥2 prior therapies (KN-059 cohort 1; KN061; or no prior therapy (KN062)) were enrolled. In KN059 cohort 1, pts received pembrolizumab only. In KN061 pts were randomized to pembrolizumab or placebo (chemo), and in KN062 to pembrolizumab + cisplatin+5-FU/cape (chemo), or placebo. Pts received pembrolizumab 200 mg Q3W for up to 2 y. MSI-H status was determined centrally by PCR. Endpoints included OS, PFS, ORR, and safety. Data cutoff dates were Aug 8, 2018 (KN059), Oct 26, 2017 (KN061), and Mar 26, 2019 (KN062).

Results: At data cutoff, 259 pts (n = 7 [3%] MSI-H) had enrolled in KN059 cohort 1 (3L+); 592 (27% [5%] MSI-H) in KN061 (2L), and 763 (50% [7%] MSI-H) in KN062 (IL). Median follow-up was 5.6 mo, 7.9 mo, and 11.3 mo, respectively. For the overall study populations, median OS was 5.5 mo for pembrolizumab (3L+), 6.7 mo vs 8.3 mo for pembrolizumab vs chemo (2L), and 10.6 mo vs 11.0 mo for pembrolizumab vs chemo (IL). Median PFS was 2.0 mo (3L+), 1.5 mo vs 4.1 mo (2L), and 2.0 vs 6.4 mo (IL). ORR was 11.6% (3L+), 11.7% vs 12.5% (2L), and 14.8% vs 37.2% (IL), with median DOR of 16.1 mo, 18.0 vs 5.5 mo, and 13.7 vs 6.8 mo. In pts with MSI-H tumors, OS and PFS were prolonged with pembrolizumab vs chemo, with higher ORR (Table). Conclusions: As with PD-L1 expressers, MSI-H status is a predictive biomarker for pembrolizumab monotherapy in advanced G/GJE cancer with >2 prior therapies. Clinical trial information: (KN)-059 (NCT02335441), KN061 (NCT02370498), and KN062 (NCT02494583).

Research Sponsor: Merck & Co., Inc., Kenilworth, NJ, USA.

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m, median; NR, not reached; *Only pembro monotherapy & chemo alone arms included.

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Gastric Cancer Registry: A comprehensive patient-reported resource for multidisciplinary and translational genomic approaches to gastric cancer. First Author: Alison Figueroa Almeda, Stanford University School of Medicine, Stanford, CA

Background: Gastric cancer (GC) is the fifth leading cancer diagnosis and third frequent cause of cancer death globally. GC results from a cascade of clonal neoantigens, microbiome, and immune cell populations. Saliva will be analyzed with linked reads sequencing to unearth germline mutations not analyzed with whole exome sequencing datasets to construct a complete molecular landscape of GC. Early analysis of GC tissue includes whole exome sequencing (WES) to identify mutations, whole genome sequencing (WGS) for copy number variation, and RNA sequencing (RNAseq) for expression profiling. Results are used to inform colorectal cancer genomics with molecular biology, statistics, and bioinformatics to build a platform for discovery and the development of tools that will ultimately improve prevention, treatment, and prevention of GC. Research Sponsor: Gastric Cancer Foundation.

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Poster Session (Board #G22), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

MT-5111: A novel HER2 targeting engineered toxin body in clinical development. First Author: Roger J. Waltzman, Molecular Templates, Inc. Ste. 100, Austin, TX

Background: Engineered toxin bodies (ETBs) are comprised of a proprietary engineered Shiga-like Toxin A subunit genetically fused to antibody-like binding domains. MT-5111 is a de-immunized ETB targeting HER2 for solid tumors. MT-5111 works through a novel mechanism of direct cell-kill, via endosomal protein and may have improved tumor penetration capability in solid tumor settings. MT-5111 binds an epitope on HER2 distinct from trastuzumab or pertuzumab, that may provide for mechanisms that exist for TKI, ADC, or antibody modalities. MT-5111 is a de-immunized ETB targeting HER2 for solid tumors. MT-5111 works through a novel mechanism of direct cell-kill, via endosomal penetration and may have improved tumor penetration capability in solid tumor settings. MT-5111 expression activity and MT-5111 expression activity of MT-5111 was measured in non-HER2+ tissue sites in a large-scale prospective analysis. Seven patients who had no standard therapy could access exploratory new drug on targetable agents through this study. Clinical trial information: 163380. Research Sponsor: Daiichi Sankyo.
Utility of PET-CT CMR after neoadjuvant chemotherapy with DCF for esophageal cancer as a predictive factor of recurrence. First Author: Suzuki Kosuke, Department of Gastroenterological and Pediatric Surgery, Oita University Faculty of Medicine, Oita, Japan

Background: PET-CT is considered as standard modality for evaluating metastasis of esophageal cancer before treatment. On the other hand, it is unclear whether PET-CT CMR (complete metabolic response) could be useful for assessment after neoadjuvant chemotherapy. To clarify the utility of PET-CT CMR as an adequate modality for prediction for recurrence after neoadjuvant chemotherapy with DCF for esophageal cancer. Methods: Fifty-eight cases of esophageal cancer (cStageII/III) who achieved the esophagomyotomy with neoadjuvant chemotherapy of DCF since June 2013 in Oita University. We evaluated the clinicopathological factors, DFS and OS between CMR group (n=22, 38%) and non-CMR group (n=36, 62%). Results: In the clinical stage before chemotheraphy, T-factor was higher in the non-CMR group (p = 0.044), but there were no significant differences of lymph node metastasis (p = 0.27) and stage (p = 0.94) between the two groups. There was no significant difference of the SUV max (16.4 ± 6.5 vs 15.7 ± 6.5, p = 0.18) of the main lesion before chemotheraphy and the FDG accumulation rate of lymph node (94 cases (63.6%) vs 25 cases (58.3%), p = 0.69) between the two groups. There were no significant differences of the surgical procedure, lymph node dissection area, number of harvested lymph nodes, amount of bleeding, operation time, curability, and intra/post-operative complications between the two groups. There were 5 cases (15%) with postoperative recurrence in the CMR group (lung 1 case, extra-regional lymph nodes 3 cases, bone 1 case), 17 cases (47%) in the non-CMR group (local 4 cases, lung 3 cases, liver 5 cases, extra-regional lymph nodes 6 cases, bone 4 cases, pleura 2 cases), but there was no significant difference between the two groups (p = 0.062). There were significant differences between the two groups for 3-year DFS (81.3 vs 65.3 months, p=0.021) and 3-year OS (93.9 vs 61.6 months, p=0.01). Conclusions: PET-CT CR CMR could not predict recurrence at present. PET-CR CMR cases had better prognosis compared to non-CMR cases in terms of 3-year DFS and 3-years OS. Research Sponsor: None.

A clinical scoring system for survival prediction in advanced gastric cancer. First Author: Jinchul Kim, Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Seoul, South Korea

Background: We established a scoring system using easily approachable clinical characteristics at the timing of initiating palliative chemotherapy to achieve accurate overall survival prediction to first-line treatment consisting of fluoropyrimidines in patients with advanced gastric cancer. Methods: A total of 1,733 patients were included in the study. The dataset was split into a training set (n=1,156, 67%) and validation set (n=577, 33%). Top-ranked variables were identified using the Random Forest for Survival algorithm and analyzed into a Cox regression model, thereby constructing the scoring system for predicting overall survival of advanced gastric cancer. Results: Five variables were finally included in the scoring system: serum neutrophil-lymphocyte ratio, alkaline phosphatase, albumin level, performance status, and histologic differentiation. The scoring system determined four distinct risk groups in validation dataset with median overall survival of 19.0 months (95% confidence interval [CI] = 16.0 to 21.5 months), 15.7 month (95% CI = 13.6 to 17.7 months), 12.9 month (95% CI = 11.4 to 14.6 month), 8.1 month (95% CI = 5.3 to 12.3 month), and 3.9 month (95% CI = 1.5 to 8.2 month), respectively. AUC to estimate discrimination performance of the scoring system was 66.1 for one-year overall survival. Conclusions: We developed a simple and clinically useful predictive scoring model in a relatively homogenous population who initiate fluoropyrimidine-containing chemotherapy in advanced gastric cancer. Generalized application of the scoring model will require additional independent validation. Research Sponsor: None.

Effect of proton pump inhibitors on the occurrence and development of gastric cancer and the polarization of macrophages in the microenvironment to M2-type. First Author: Xia-Qing Lu, Breast Surgery, the Second Hospital of Shanxi Medical University, Taiyuan, China

Background: Long-term use of Proton pump inhibitors was associated with an increased gastric cancer(GC) risk in subjects even after HP eradication therapy. In contrast some basic research showed that PPI inhibited the growth of GC. In the tumor-microenvironment (TME), macrophages that are recruited around the tumor are activated to form the tumor-associated macrophages (TAMs), which are the most abundant mononuclear cells in the tumor infiltrating leukocytes. Many studies have shown that TAMs are associated with poor prognosis of tumors. Methods: Immunohistochemistry was used to detect the phenotype of macrophages in patients with gastric cancer treated with PPI or without PPI. Transcriptomics sequencing analyzed the signal pathways that were highly expressed in PPI-treated gastric cancer for further exploring the mechanism of PPI's main role in gastric cancer cells. In vitro, explore the effects of PPI on gastric cancer cells and the next step on macrophages. The effects of PPI on the growth of gastric cancer and the degree of infiltration and phenotype transformation of macrophages were verified by in vivo experiments. Results: In the gastric cancer tissues treated with PPI, the macrophage phenotype is mostly M2 type, thereby exerting a cancer promoting effects. Transcriptomics results showed high expression of genes associated with endoplasmic reticulum stress in gastric cancer tissues after PPI treatment, compared with patients who were not treated with PPI. Among them, GRP78 is a classic marker of endoplasmic reticulum stress. It was not only highly expressed in gastric cancer treated by PPI, but also acted on macrophages through exosomes secreted by gastric cancer cells, and caused macrophage to polarize to M2. Conclusions: PPI caused GC cells to over-express GRP78 which secrete into the microenvironment through exosomes, thereby transforming macrophages into M2 type under the action of GRP78. Finally M2 type macrophages promoted the progression of gastric cancer. Research Sponsor: None.
Neutrophil-to-lymphocyte ratio as a prognostic factor and its relationship to patient (pt) outcomes in the RAINBOW trial. First Author: Kei Muro, Department of Clinical Oncology, Cancer Center Hospital, Nagoya, Japan

Background: Neutrophil-to-lymphocyte ratio (NLR/N) reflects underlying levels of systemic inflammation and has prognostic value in advanced gastric cancer (GGE). We investigated the relationship between pretreatment NLR and clinical outcomes in the RAINBOW study of ramucirumab (R) with paclitaxel (P) in GGE. Methods: NLR is defined as the ratio of absolute neutrophil count and absolute lymphocyte count from peripheral blood. Pls in ITT population with baseline NLR were analyzed. As no clear NLR cutoff is established in GGE, multiple cutoffs (4, 5, 6) were evaluated and relationships between baseline NLR and efficacy endpoints examined. Median OS, PFS were estimated using Kaplan Meier method; prognostic effects on OS/PFS of baseline NLR subgroups (sg) and treatment effects on OS/PFS within each baseline NLR sg were evaluated using univariate Cox PH models. Results: Baseline characteristics were generally balanced between high NLR sg. Higher baseline NLR groups were associated with worse outcomes regardless of cutoff [MOS N < 4 vs > 4: 9.2 (8.1, 10.3) vs 5.6 (4.8, 6.6), HR = 0.61 (0.49, 0.75); N < 5 vs > 5: 8.6 (7.8, 9.6) vs 5.3 (4.5, 6.5), HR = 0.59 (0.47, 0.75); N = 6 vs > 6: 8.6 (7.8, 9.6) vs 4.7 (4.2, 5.9), HR = 0.55 (0.43, 0.70)]. Consistent treatment benefits (R+P vs Placebo (PB)+P) were observed within high baseline NLR sg (Table). No new safety signals were observed. Conclusions: In this exploratory analysis of RAINBOW, pretreatment NLR (< 4, 5, 6) were independent prognostic factors of improved survival. Treatment benefits with R+P was preserved within high baseline NLR levels defined by different cutoffs and was consistent with ITT results. Clinical trial information: NCT01706633. Research Sponsor: Eli Lilly and Company.

440 Poster Session (Board #H7), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Epstein-Barr virus associated gastric carcinoma at the United States-Mexico border: A single institution study. First Author: Sumit Gaur, Texas Tech Univ, Health Sci Ctr El Paso TX, El Paso, TX

Background: Globally, gastric cancer (GC) is the fourth most prevalent cancer, and the second leading cause of cancer related deaths. Epstein-Barr virus is implicated in the pathogenesis of 5-10% of gastric cancers. Based upon the results obtained from well studied tumors in Asia, EBV related GC is characterized by promoter hypermethylation, PIK3CA mutations (80%) and increased expression of PD-1 and PD-L1, making it an attractive target for molecularly targeted therapy and immunotherapeutic options. As such, a case can be made for routine testing for EBV in all GC patients. University Hospital, El Paso is a tax payer funded safety net health system in El Paso county, TX. We conducted a pilot study to characterize the prevalence of EBV associated gastric cancer seen at this facility. Methods: After obtaining institutional review board (IRB) approval, we identified cases of GC that were diagnosed between January 1, 2008- and December 31-2017. A total of 104 cases were identified of which 17 samples were randomly selected. Pathology specimens were reviewed to identify grade, subtype (intestinal vs diffuse), degree of lymphocytic infiltration and presence/absence of H. pylori. Representative sections from archived tumors were used to perform in-situ hybridization to look for the presence of Epstein-Barr early RNA. Samples were analyzed using the Rembrandt In situ Hybridization and Detection Universal BACP kit. Results: The median age of the 17 patients is 63 years with 59% being males. 95% self identified as Hispanic. 41% were smokers, 18% used alcohol. The mean BMI was 27.3. Forty one percent of gastric cancer cases were found in the body, 29% in the antrum, 12% in the cardia, and 6% in the fundus. Forty one percent of cases were Stage IV, 24% stage II, 17% Stage III and 17% Stage I. 95% of cases were high grade, 53% of them had signet ring features. 18% of samples were H. pylori positive. None of the seventeen samples tested positive for EBV. Conclusions: This study seems to contribute significantly to the understanding of the role of EBV in the pathogenesis of gastric cancer in our local population. As such routine testing for EBV in all gastric cancer patients may not be a cost effective utilization of resources at our hospital. Research Sponsor: Institutional intramural grant.

441 Poster Session (Board #H8), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Genomic correlates of extreme pathologic response following neoadjuvant chemotherapy in locally advanced gastric cancer to reveal distinct vulnerabilities. First Author: Jashdeep Datta, University of Miami Miller School of Medicine, Miami, FL

Background: Clinical factors associated with pathologic response (PR) following neoadjuvant chemotherapy (NCT) in locally advanced gastric cancer (NCT) have not been previously investigated. Methods: Validable pre-NCT tumor samples from patients with LAGC who underwent resection and demonstrated extreme pathologic response (EPR; ≥10% PR; n = 30) were analyzed using the commercial dNCR platform (dNCR Oncology Corp, USA) for pathway and gene expression signatures association with EPR. Results: Of 40 patients, a majority had ≥CT2/N+ disease and were treated with predominantly platinum (98%) or 5-FU (88%) based NCT regimens. Two patients with MSI-high tumors had ≥10% PR and were excluded from analysis. The EPR cohorts did not differ significantly in clinical (i.e., tumor location, ct/N status, NCT regimen), extent of gastrectomy, number of lymph nodes examined, or margin status characteristics. Although EPR cohorts did not differ with respect to tumor differentiation grade, Lauren classification, proportions of TCGA consensus CN or GS subtypes, tumors with ≥10% PR were more likely to have vascular (P < 0.001) and perineural (P = 0.007) invasion. At median follow-up of 34 months (IQR 25,77), ≥10% PR was associated with improved DSS compared with ≤10% PR (median NR vs. 27m, P = 0.03). Our results suggest that a larger cohort size and prospective validation are warranted to further elucidate the role of tumor biology in predicting EPR. Conclusions: Our analysis supports the hypothesis that a subset of patients with advanced GEA may benefit from checkpoint blockade in advanced gastric cancer, with demonstrated response to PD-1/PD-L1, as well as the possibility of targeting the molecular alterations associated with extreme pathologic response. Research Sponsor: None.
The relevance of neuropilin-1 expression with prognosis according to the histology of gastric cancer. First Author: Ho Seok Seo, Division of Gastrointestinal Surgery, Department of Surgery, College of Medicine, The Catholic University of Korea, Seoul, South Korea

Background: Neuropilin-1 (NRP-1) is known to be related with various types of cancer and considered a biomarker for treatable and targeted therapies. The aim of the study is to identify the clinical implication of NRP-1 expression in terms of prognosis in gastric cancer. Methods: A total of 265 patients who underwent radical gastrectomy for the treatment of gastric cancer from 2008 to 2018 were included. NRP-1 expression of tumors was determined by immunohistochemistry. Patients' clinicopathologic characteristics, operation details, and long-term outcomes were retrospectively analyzed. Results: 181 (68.3%) patients showed NRP-1 expression. There was no survival difference according to the NRP-1 expression in all patients. The patients were divided into gland formation (GF) type and no gland formation (nGF) type according to histologic type. NRP-1 expression rates were 65.6% (84/128) and 70.8% (97/137), respectively. In the group of GF, NRP-1 expression was not independent prognostic factor, although patients with NRP-1 expression had better survival outcome. In contrast, patients with NRP-1 expression had worse 5-year survival rate in the group of nGF (p = 0.027) and it was an independent prognostic factor multivariate analysis (HR, 192: 95% CI, 1.041 - 3.551). Conclusions: NRP-1 expression in the nGF type gastric cancer predicts a poor prognosis. Research Sponsor: National Research Foundation of Korea.

Predictive role of mismatch repair deficiency (MMR-D) in patients receiving first-line fluoropyrimidine and platinum (F-P) doublet chemotherapy for metastatic and locally advanced unresectable gastric cancers (GC). First Author: Heejung Chae, Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

Background: Although adjuvant chemotherapy has been known to have a detrimental effect on MMR-D patients (pts) with resectable GC, it is unclear whether palliative chemotherapy for advanced GC would also adversely affect the survival outcome of MMR-D pts. Immune-checkpoint inhibitor (ICI) monotherapy was approved as a standard treatment for 3rd line of advanced GC and also showed a remarkable efficacy in MMR-D pts regardless of line of therapy.ICI is now being investigated in combination with 1st-line cytotoxic chemotherapy. Hence, we aim to evaluate the prognostic impact of MMR on cytotoxic chemotherapy in advanced GC. Methods: We reviewed our prospective database to identify pts with initially metastatic, recurrent and locally advanced unresectable GC who had received 1st-line F-P doublet from 2015 to 2018. MMR status was assessed by immunohistochemistry with previously-collected tumor tissue and correlated with clinical characteristics and survival outcomes. Results: Out of 892 pts identified from the database, 543 underwent MMR test (382 initially metastatic (70.3%); 127 recurrent (23.3%); 32 locally advanced unresectable (6.3%)). Median age was 58 years (range, 24-86) with male comprising 64.0%. MMR-D was found in 4.4% (n = 24) and associated with age ≥ 65 (50% vs 29.9%, P = 0.037), antrum-origin (62.5% vs 34.1%, P = 0.004) and well/moderately-differentiated histology (41.7% vs 25.8%, P = 0.110). According to our prognostic model (Koo DH et al, 2019), MMR-D pts were less likely to be classified into poor-risk group (4.2% vs 16.8%, P = 0.102). In good-risk group, MMR-D pts had significantly shorter PFS (6.0 vs 9.0 months, P = 0.045) and OS (10.1 vs 20.9 months, P = 0.047), while pts in moderate and poor risk group showed no difference in survival depending on MMR status. Conclusions: MMR-D GC showed significantly shorter PFS and OS on F-P doublet in good-risk pts and further investigation is needed to determine underlying molecular mechanisms. With the negative impact of MMR-D on the effect of cytotoxic chemotherapy, exclusion of MMR-D status should be considered in future trials of ICI and cytotoxic chemotherapy combination. Research Sponsor: None.

Association of ascitic neutrophil to lymphocyte ratio with prognosis in patients with advanced gastric cancer. First Author: Jae-Joon Kim, Medical Oncology and Hematology, Department of Internal Medicine, Pusan National University Yangsan Hospital, Yangsan, South Korea

Background: Approximately 40% of metastatic gastric cancer patients develop peritoneal carcinomatosis, and this condition leads patients to grave prognosis. Blood neutrophil to lymphocyte ratio (NLR) is associated with prognosis in various solid tumors, such as non-small cell lung cancer, colorectal cancer, and gastric cancer. We performed this study to investigate the prognostic significance of NLR of ascitic fluid. Methods: This is a retrospective study. Patients were consecutive included if they: 1) had historically confirmed gastric adenocarcinoma, poorly cohesive carcinoma, or poorly differentiated carcinoma, 2) were relapsed after curative resection or initially metastatic, 3) had ascites due to peritoneal metastases of gastric cancer, 4) had received paracentesis at least once and the result of ascites exam is available. Patients with clinically active infection in the time of paracentesis is excluded. If multiple times of paracentesis was done, we used initial result. Results: From March 2012 to August 2018, total 157 patients who were visited at Pusan National University Yangsan Hospital met the inclusion criteria. Median age was 58 (29-86) years and male patients was 63% (n = 99). In 38.9% (n = 61) patients, gastric cancer was diagnosed in primary site and in ascites synchronously. At the time of first paracentesis, 47.1% (n = 74) of patients had already been received palliative chemotherapy due to metastatic gastric cancer. In the ascites, mean and median NLR is 2.2:6.8 and 0.3 (0-65). All except 3 patients were expired, and the median survival time form para- centesis was 47 (95% confidence interval 38.6-54.5) days. In the Kaplan-Meier survival analysis, patients with higher NLR (≥ 4) have shorter survival from paracentesis (39 days, 95% CI 31.5-45.4) in compared to lower NLR (< 0.33) (61 days, 95% CI 29.4-92.6, log-rank p = 0.011). In the additional analyses, higher neutrophil count (41 vs 72 days, p = 0.045) and lower protein level (32 vs 61 days, p = 019) of ascites are also poor prognostic factor. Conclusions: High NLR of malignant ascites is poor prognostic factor in patients with gastric cancer. The role of neutrophil in the malignant ascites should be evaluated in future research. Research Sponsor: None.

A novel gene signature for predicting response to chemoradiotherapy in esophageal adenocarcinoma. First Author: Souvik Ghatak, Department of Molecular Diagnostics and Experimental Therapeutics, Beckman Research Institute of City of Hope, Biomedical Research Center, Monrovia, CA

Background: While neoadjuvant chemoradiotherapy (CRT) has emerged as an important treatment modality in patients with locally advanced esophageal adenocarcinoma (EAC), ~60%-70% of patients do not respond to such treatments; but are exposed to their toxicity nonetheless. This highlights the clinical need for the development of biomarkers that can robustly predict response to CRT and spare others from the toxicity and expense associated with these treatments. Herein, we systematically identified a biomarker signature that predicts response to CRT in EAC patients. Methods: Using a clinical-trial driven cohort of 25 EAC patients treated with 5-fluorouracil plus carboplatin and concurrent radiation therapy, we performed whole-exome sequencing (WES) in 8 EAC patients with chemoresistance and 17 patients with response to CRT. In total, we analyzed 84 paired tumor and normal DNA samples. After WES data pre-processing, we identified a panel of immune-related genes (TIM3, LAG3, IDO1 and CXCL9) in these patients, and evaluated their relationships with clinical outcomes. We next developed a statistical model using these genes that robustly predicts response to CRT in EAC patients and has a significant potential for personalized management of EAC patients. Research Sponsor: U.S. National Institutes of Health.
Abdominal obesity and risk for esophageal cancer: A nationwide population-based cohort study of South Korea. First Author: Dong Ho Lee, Seoul National University Bundang Hospital, Seongnam-Si, South Korea

Background: The relationship between overall obesity, as measured by body mass index (BMI), and risk of esophageal squamous cell carcinoma (ESCC) has been reported, and it has a negative correlation. However, the relationship with abdominal obesity, as measured by waist circumference, may be different. We investigated the association between abdominal obesity and ESCC.

Methods: Retrospective cohort study with 22,809,722 individuals who had undergone regular health check-ups provided by the National Health Insurance Corporation between 2009 and 2012 (median follow-up period was 6.4 years) in South Korea. Abdominal obesity was defined as a waist circumference over 90 cm for men and 85 cm for women. We estimated hazard ratios (HRs) and 95% confidence intervals (CIs) using Chi-squared test and Cox proportional hazard model adjusted for confounding factors. Primary outcome was newly developed esophageal cancer.

Results: After adjusting for BMI, abdominal obesity increased the risk of ESCC (HR 1.29, 95% CI 1.23–1.36). Waist circumference is associated with increased risk of ESCC in a dose-dependent manner (p for trend < 0.0001). We analyzed individuals divided into five categories of BMI. Among individuals with overweight (BMI 23–24.9 kg/m²) and obese (BMI 25–29.9 kg/m²), abdominal obesity was a risk factor associated with developing ESCC (HR 1.22, 95% CI 1.11–1.34; HR 1.28, 95% CI 1.18–1.39, respectively).

Conclusions: Abdominal obesity, not BMI itself, is associated with an increased risk for ESCC. Therefore, reducing abdominal obesity may affect decreasing the development of ESCC. Research Sponsor: None.

Tissue levels of steroid hormones and their receptors, prolactin, and SHBG in patients with gastric cancer. First Author: Oleg Ivanovich Kit, Rostov Research Institute of Oncology, Rostov-on-Don, Russian Federation

Background: Hormones and their receptors are important effectors providing interconnection between the primary tumor and metastatic niche. The aim of the study was to determine levels of steroid hormones and their receptors, prolactin (PRL) and sex hormone-binding globulin (SHBG) in tissues of gastric cancer (GC), omentum and peritoneum. Methods: Levels of steroid hormones and their receptors, PRL, and SHBG were determined by ELISA in tissues of primary tumors, omentum and peritoneum in patients with gastric cancer (GC) T3-4aN0-3M1 and in the stomach, omentum and peritoneum of non-cancer patients (n = 17).

Results: In GC (M0), estradiol was reduced in primary tumors, omentum and peritoneum by 4.2, 4.0 and 8.6 times, respectively; increased levels of free testosterone (by 1.8 times), PRL (by 3.5 times) and SHBG (by 1.4 times) were observed (p < 0.05). GC (M1) was characterized by high levels of estrogen receptors (ER) α by 1.2 times (p < 0.05), progesterone (PR) by 3.5 times and SHBG by 1.4 times (p < 0.05). Tissues of the omentum and peritoneum showed increased levels of ERα by 2.4 and 3.9 times, ERβ by 1.5 (p < 0.05) and 2.5 times, PR by 2.2 and 1.5 times (p < 0.05). GC (M0) had low ERα levels. Conclusions: Decreased levels of estradiol, together with elevated levels of free testosterone and prolactin, in tumor tissues can be considered marking for perilone metastases. Correlation between the content of these hormones in the omentum and peritoneum and the presence of metastasis in the organs confirms the “seed and soil” principle. Research Sponsor: None.

Levels of oncofetal proteins in pathological tissues of patients with gastric cancer. First Author: Oleg Ivanovich Kit, Rostov Research Institute of Oncology, Rostov-on-Don, Russian Federation

Background: Spread to the peritoneal cavity and lymphatic system is the most important factor of gastric cancer prognosis. Successful implantation of cancer cells in a distant place is possible only when cancer cells accept a special kind of molecular invitation sent by some organs. Our purpose was to study levels of CA-19.9, CA-125, CA-72.4, and mSIS (albmin, albumin, lymphocyte–monocyte ratio) in tissues of tumors, omentum and peritoneum in patients with gastric cancer (GC) T3-4aN0-3M0 and T3-4aN0-3M1.

Methods: Levels of CA-19.9, CA-125, CA-72.4 were determined by ELISA in primary tumors, the omentum and peritoneum of patients from main groups 1 (M0) – GC T3-4aN0-3M0 (n = 21) and 2 (M1) – GC T3-4aN0-3M1 (n = 21); in tissues of the stomach, omentum and peritoneum in non-cancer patients (n = 17).

Results: CA-19.9, CA-125 and CA-72.4 were increased, compared to control values, in all studied samples from 1.6 times (CA-72.4) to 180.1 times (CA-19.9). Only CA-19.9 levels differed depending on the metastatic spread: 1.8 times (p = 0.05) higher in T3-4aN0-3M1 than in T3-4aN0-3M0. CA-19.9 levels in T3-4aN0-3M0 exceeded the control values by 20 times; in 20 patients with T3-4aN0-3M0 the value was only 4.1 times higher than in controls and 4.8 times lower than in T3-4aN0-3M1, while in 4 patients it did not differ significantly from the value in T3-4aN0-3M0. In the peritoneal tissues, CA-19.9 levels in T3-4aN0-3M0 exceeded the control values by 19.2 times; in 21 patients with T3-4aN0-3M0 the value was only 2.2 times higher than in controls and 8.5 times lower than in T3-4aN0-3M1. CA-125 and CA-72.4 were increased in the omentum and peritoneum in non-cancer controls (n = 17).

Conclusions: CA-19.9 is an independent prognostic factor (hazard ratio 2.63, 95% confidence interval 1.33–5.27, p = 0.005). In most patient subgroups, the mSIS was associated with greater risk of disease-specific death. A stepwise increase in the prevalence of hematogenous recurrences was directly proportional to the mSIS. When patients were subdivided by mSIS before adjuvant treatment, there were no significant differences in disease-specific survival. Our findings demonstrate that the preoperative mSIS may serve as a powerful prognosticator of ESCC that definitively stratifies clinical outcomes as well as a tool for selecting treatment strategies. Research Sponsor: None.
Conversion surgery for advanced gastric cancer with peritoneal metastasis. 

First Author: Masaki Nakamura, Second Department of Surgery, Wakayama Medical University, School of Medicine, Wakayama, Japan

Background: Patients with peritoneal metastasis have significantly poor prognosis. We have performed pretherapeutic staging laparoscopy (SL) to diagnose peritoneal metastasis for patients with large type 3, type 4 or severe invasive gastric cancer. When peritoneal metastasis disappears by chemotherapy for patients with positive peritoneal cytology (CY1) or peritoneal dissemination (PI), we perform the conversion surgery (CS).

Methods: We retrospectively analyzed clinical outcomes of 134 patients with advanced gastric cancer who underwent SL between 2005 from 2016. We examined safety and usefulness of CS for patients with CY1 or PI. Results: CYPO, CYIP and PI were found in 67, 28 and 39 patients, respectively. The median survival time (MST) of patients with CYPO, CYIP and PI were 39, 21 and 11 months (CYPO vs CYIP, p = 0.029; CYIP vs PI; p < 0.001; CYIP vs PI; p < 0.001). In patients with CYPO, 20 of 26 patients who received chemotherapy underwent the second look SL, and 14 patients (54%) underwent CS (RO) as peritoneal cytology turned negative. These regimens of chemotherapy were S1/CDP (n = 9), Doxetaxel/CDDP/S1 (n = 2), SOX (n = 2) and S1/Doxetaxel (n = 1) and the median number of treatment courses was 3.86 courses. The MTS of patients with or without CS were 40 months and 11 months (p = 0.001). Then, there was no difference in overall survival between patients with CS and patients with CYPO at the first SL (p = 0.866). All patients with Pfrecebe chemotheraphy, and 11 of these patients underwent the second look SL. As peritoneal metastasis of 7 patients (8%) disappeared by chemotherapy, they underwent CS (RO). The MTS of patients with and without CS were 31 months and 9 months (p = 0.026). Regarding complications after CS, surgical-site infection and interstitial pneumonia each occurred in one patient (grade II), and intestinal obstruction (grade IIIa) occurred in one patient. There was no difference in overall survival between patients with CS and PET-NR, ypT0-2 29 (13) Ectopic 14 (11) Equivocal 10 (10) Treatment regimens of chemotherapy were PTh1/R 34 (25%) patients achieved down staging or cytoreductive surgery. 7 patients (52%) had pre- and post-induction PETs; 232 pts proceeded to surgery and were included for analysis. Treatment regimens comprised of CROSS (22%) and FL/OT (4%). Median age was 66 (IQR 57-72), 85% male, 91% ECOG O/F, 62% GEJ involvement, and 89% adenocarcinoma histology. Characteristics and treatment regimens were balanced between the PET-R and PET-NR groups (all p > 0.05). Median time from end of treatment to PET was 30 days (IQR 22-36); 67% were PET-R, Pathologic complete response (CR) rates were similar for PET-R vs. PET-NR (14% vs. 13%, p = 0.08). The discordance rate between PET vs. pathologic response was 34% (Table). Aborted surgery rate was higher in the PET-NR group (8% vs. 3%, p = 0.03); 70% of aborted cases were due to peritoneal involvement. Median overall survival was similar between the two groups (PET-R 31.5 mo vs. PET-NR 36.1 mo, p = 0.62). Conclusions: In our population-based cohort, PET response did not demonstrate prognostic utility and was associated with a significant pathology discordance rate. The role of PET/CT is evolving and the use of post-induction PET/CT response assessment and prognostic value may be questionable. Research Sponsor: None.

Relationship between PET response and pathological response in distal esophageal/gastroesophageal junction (DE/GEJ) cancers. 

First Author: Irene S. Yu, BC Cancer, Vancouver, BC, Canada

Background: The utility of PET scans (PETs) to predict outcomes after neoadjuvant treatment of DE/GEJ cancers is unclear. We aimed to explore the relationship between PET response and pathologic/clinical outcomes in a real-world setting.

Methods: We conducted a retrospective study to evaluate clinical outcomes of 134 patients with advanced gastric cancer who underwent SL between 2010-2017. Medical Electronic Health Records and California Cancer Registry of demographic and clinical data were collected for pts with nmGA who underwent surgery with curative intent from 2010-2017. Medical chart reviews were conducted to validate outcomes. We used multivariate Cox regression to determine prognostic factors for cancer recurrence and overall survival.

Results: Demographics of study cohort (n = 406): mean age 65 years; 71% male, 58% Caucasian, 26% Asian, 13% Latino. There was an even distribution between pts with locoregionally advanced (defined as pT4 or pN+) vs. localized (pT1-3, pN0) disease. Tumor histology: 49% intestinal, 19% diffuse, 13% mixed, 19% unknown. Type of surgery: 27% open gastrectomy, 59% laparoscopic, 14% unknown. Multimodality therapy: 29% received peroperative systemic rx alone (48% adjuvant only, 52% neoadjuvant +/- adjuvant), 35% received peroperative systemic rx plus radiation (40% adjuvant only, 60% neoadjuvant +/- adjuvant), 36% underwent surgery only. With median f/u time after surgery of 5 years, 21% of pts developed cancer recurrence and 43% had died. Weight loss prior to diagnosis, locoregional stage, and positive resection margins were a/w recurrence (HR = 1.6-2.5, p < .05). Only locoregional stage was prognostic for worse survival (HR = 2.7, p < .0001). Positive resection margins were seen in 6% of pts and were a/w diffuse histology (HR = 2.9-8.8, p < .02). Multimodality therapy was not a/w recurrence but was a/w longer survival after adjusting for stage (HR = 0.3, p < .0001). Addition of radiation to systemic rx did not confer further improvements in either recurrence or survival. Conclusions: This study highlights surgicopathology practice patterns for pts with nmGA and demonstrates a survival benefit with multimodality rx. Additional data are being gathered from other UC medical centers to confirm these findings and explore differences across institutions and ethnicities. Research Sponsor: None.

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Preoperative muscle strength as a predictor of complications after esophagectomy. First Author: Madison Colcord, Levine Cancer Institute, Charlotte, NC

**Background:** Sarcopenia has been associated with post-operative complications and length of stay (LOS) in patients undergoing esophagectomy. A variety of methods exist to measure muscle mass and strength, with few comparisons between methods. We compared hand-grip strength (HGS), muscle mass and intramuscular adipose tissue as predictors of post-operative outcomes.**Methods:** Patients with esophageal cancer undergoing esophagectomy were identified between January 2015 – June 2019 at Levine Cancer Institute. Skeletal muscle index (SMI) and skeletal muscle density (SMD), a measure of intramuscular adipose tissue, were derived from CT. HGS was measured using a dynamometer. Uni- and multivariable GLM analyses were performed. **Results:** 115 patients (100 male, 15 female) underwent esophagectomy with an average age of 64.3 +/- 9.8. The analysis was stratified by sex due to significant differences in HGS, SMI, and SMD. Among men, univariable analysis revealed a significant association between pre-operative HGS < 25 kg and increased risk of post-operative pneumonia (p=0.002), ventilation >48h (p=0.002), LOS (p=0.002), discharge home (p=0.000), and one-year mortality (p=0.005). All associations except discharge home remained significant in multivariable analyses (Table). Among women, no factors analyzed were significantly associated with postoperative outcomes. Conclusion: HGS is a more powerful predictor of postoperative complications and LOS than either muscle mass or intramuscular adipose tissue among men undergoing esophagectomy. HGS is cost-effective and easily incorporated into routine clinical care, allowing for preoperative intervention to optimize patients for esophagectomy. To better understand the implications in women, additional research with a larger cohort is needed. Research Sponsor: None.

<table>
<thead>
<tr>
<th>Multivariable post-esophagectomy outcomes for men.</th>
<th>Variable</th>
<th>Odds Ratio</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Painness</td>
<td>Age</td>
<td>1.03</td>
<td>0.0175</td>
</tr>
<tr>
<td>Ventilation &gt;48h</td>
<td>White Race</td>
<td>0.46</td>
<td>0.0475</td>
</tr>
<tr>
<td>Discharge to Home</td>
<td>Age</td>
<td>0.76</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mortality 1yr</td>
<td>Prop Feeding Tube</td>
<td>0.39</td>
<td>0.0395</td>
</tr>
<tr>
<td>Length of Stay*</td>
<td>SMD &lt;25g</td>
<td>0.009</td>
<td>NS</td>
</tr>
<tr>
<td>Pre-Op SMD &lt;25g</td>
<td></td>
<td>0.040</td>
<td>NS</td>
</tr>
</tbody>
</table>

*One-transformed

Effect of age on swallowing dysfunction after esophagectomy. First Author: Della Mann, Levine Cancer Institute, Charlotte, NC

**Background:** Patients undergoing esophagectomy frequently experience malnutrition, which in combination with the catabolic effects of surgery can result in loss of muscle mass and function. Safe swallowing requires the preservation of muscle mass. Modified barium swallow (MBS) enables assessment of postoperative swallowing impairments. We assessed the incidence and risk factors of swallowing dysfunction post-esophagectomy. **Methods:** Patients with a MBS post-esophagectomy were identified between January 2015-June 2019 at Levine Cancer Institute at Carolinas Medical Center. Swallowing was evaluated with the Penetration Aspiration Scale. Muscle loss was evaluated with pre-operative hand-grip strength (HGS) and skeletal muscle index (SMI) and skeletal muscle density (SMD) from axial CT images. Uni- and multivariable GLM analyses were performed. **Results:** 91 patients (79 men, 12 women) underwent esophagectomy with an average age of 64.0 +/- 10.1. Pre-operative HGS, SMI, and SMD all decreased with age. Significant differences existed between sexes in HGS, SMI, and SMD, so the cohort was stratified by sex for analysis. Univariable analysis of male patients revealed older age, lower body mass index (BMI), smoking history, prior feeding tube, and lower pre-operative HGS and SMI were associated with aspiration or penetration on MBS. Among women, no factors analyzed were significantly associated with swallowing dysfunction. Conclusions: Swallowing dysfunction after esophagectomy is correlated with increased age and lower BMI. The role of muscle loss in the risk of aspiration after esophagectomy is not clear. Further research is needed to determine the relationship between these factors with the goal of enabling preoperative physiologic optimization and patient selection. Research Sponsor: None.

Factors associated with aspiration on MBS among men post-esophagectomy.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate Odds Ratio</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skeletal Mass Index</td>
<td>0.96 (0.91-1.01)</td>
<td>0.078</td>
</tr>
<tr>
<td>Prior Feeding Tube</td>
<td>2.48 (1.97-3.17)</td>
<td>0.059</td>
</tr>
<tr>
<td>Age</td>
<td>1.11 (1.04-1.17)</td>
<td>0.001</td>
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<tr>
<td>Smoking Ht</td>
<td>2.67 (1.05-6.80)</td>
<td>0.039</td>
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<tr>
<td>BMI</td>
<td>0.89 (0.80-0.98)</td>
<td>0.005</td>
</tr>
<tr>
<td>HGS &lt;25kg</td>
<td>2.46 (1.48-4.16)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

NS: Not significant

A prediction model for pathological findings after neoadjuvant chemoradiation therapy for resectable locally advanced esophageal cancer based on PET images using radiomics and machine-learning. First Author: Yuji Murakami, Hiroshima University Hospital, Hiroshima, Japan

**Background:** The pathologic complete response (PCR) rate by neoadjuvant chemoradiotherapy (NCRT) for resectable locally advanced esophageal squamous cell carcinoma (ESCC) is about 40%. If we could predict a PCR from pre-treatment image data, it might be possible to select patients who can be cured by organ-preserving CRT. The purpose of this study is to construct a predictive model for PCR by NCRT in patients with locally advanced ESCC using radiomics and machine-learning. **Methods:** We used data of 98 ESCC patients who underwent NCRT and surgery from 2003 to 2016. Firstly, we fused the radiotherapy treatment planning CT images and PET images scanned before treatment. Then using target delineations on planning CT images, we created eight kinds of target regions on PET images. Secondly, we generated a total of 69,688 features per outcome. We input values, and the information of these target regions that were preprocessed by radiomics technique. Among them, we extracted the optimal features for machine-learning using the least square support vector machine (LASSO) logistic regression. Thirdly, artificial neural networks were used as a machine-learning method to create a predictive model. The extracted radiomics features were used as input values, and the output of “PCR” or “not PCR” was used as output values. We used data of randomly selected 58 patients for training and constructed a predictive model. Then we used data of 15 patients to validate the models and created the optimal model. Finally, we evaluated the predictive model using the test data of 25 patients. **Results:** By the LASSO analysis, 32 radiomics features were extracted for machine-learning classification. This predictive model predicted pathological findings after NCRT in 24 of 25 test data. The accuracy, specificity and sensitivity in the prediction of PCR after NCRT by this predictive model were 96.0%, 93.8%, and 100%, respectively. **Conclusions:** A prediction model based on PET images using radiomics and machine-learning could predict pathological findings after NCRT for patients who can be cured by organ-preserving CRT. Research Sponsor: Rakuten Medical, Inc.

TPS547 - Trials in Progress Poster Session (Board #L1), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

A phase Ib study of near infrared photomunotherapy (NIR-PI-T) using ASP-1929 in combination with nivolumab for patients with advanced gastric or esophageal cancer (GE-PI-T study, EPOCH1901). First Author: Tomohiro Kadota, Department of Gastroenterology and Endoscopy, National Cancer Center Hospital East, Kashiwa, Japan

**Background:** Near Infrared Photomunotherapy (NIR-PI-T) is a newly developed, molecular targeted cancer therapy based on conjugating a near infrared silica-phthalocyanine dye to a monoclonal antibody, which result in necrotic cell death of targeted cancer cell immediately after exposure to near infrared light. Phase Ia trial of NIR-PI-T with RM-1929 (anti-EGFR antibody cetuximab conjugated to IRDye 700DX) showed a 43% objective response rate (ORR) for recurrent head and neck squamous cell carcinoma (Cognetti DM, et al. ASCO 2019 abstr 6014). Meanwhile, PD-1 blockade reverses adaptive immune resistance, resulting in activation of tumor infiltrating lymphocyte after NIR-PI-T in syngeneic mouse models (Nagaya T, et al. Cancer immunology research. 2019). The objective of this study is to investigate the safety and efficacy of the NIR-PI-T using ASP-1929 (analogous to RM-1929) in combination with nivolumab for advanced gastric or esophageal cancer. **Methods:** The study is an open-label, single-arm, single-center, Phase Ib clinical trial. Eligible patients are with unresectable esophagogastric squamous cell carcinoma or EGFR positive adenocarcinoma after standard chemotherapy. Dose escalation cohort is designed to determine the recommended dose of laser irradiation energy density in a “+3” design (50, 75, and 100 J/cm²). Nivolumab of 240 mg on Day 1 and ASP-1929 of 640 mg/m² on Day 8 is administered, and laser irradiation is performed under endoscopy using the laser PIIT unit on Day 9. In expansion cohort, approximately 20 patients will be enrolled. The primary endpoint is proportion of incidence of dose-limiting toxicity, and the secondary endpoints are proportion of incidence of adverse events, ORR, local complete response rate, progression-free survival (PFS), local PFS, overall survival, and proportion of incidence of device malfunction. We also investigate several biomarkers using pre- and post-treatment biopsied samples. First patient will be enrolled in December 2019. Clinical trial information: JapCITI-1949669. Research Sponsor: Rakuten Medical, Inc.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
**TPS458**

Trials in Progress Poster Session (Board #L2), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Tislelizumab plus chemotherapy versus placebo plus chemotherapy as first-line therapy in patients with locally advanced or metastatic gastric or gastroesophageal junction (G/GEJ) adenocarcinoma. Adult patients (n=720) from >160 centers will be randomized 1:1 to receive tislelizumab (200 mg IV Q3W) or placebo in combination with chemotherapy. Oxaliplatin (130 mg/m² IV Q3W) + capecitabine (1000 mg/m² orally BID for 2 weeks) or cisplatin (80 mg/m² IV Q3W) + 5-fluorouracil (800 mg/m² IV Q3W/days 1-14) will be used as a backbone chemotherapy on an individual basis. Chemotherapy will be administered for up to 6 cycles; capecitabine maintenance therapy is optional for patients who received capecitabine and oxaliplatin. Progression-free and overall survival are primary endpoints of the study. Secondary endpoints will include overall response rate, quality-of-life outcomes, and the safety/tolerability profile of combination therapy. Exploratory endpoints include disease control rate, time to response, and an analysis of potential predictive biomarkers including PD-L1 expression; the VENTANA PD-L1 SP263 assay will be used for PD-L1 expression analysis. This study is actively enrolling. Clinical trial information: NCT03777657. Research Sponsor: BeiGene, Co., Ltd.

**TPS459**

Trials in Progress Poster Session (Board #L3), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

A global phase II trial in-progress with pembrolizumab plus pembrolizumab in patients with advanced gastric or gastroesophageal cancer. First Author: Jeeyun Lee, Samsung Medical Center Sungkyunkwan University School of Medicine, Seoul, South Korea

Background: The majority of gastric cancer (GC) patients fail to derive sufficient benefit from currently available therapies. Pembrolizumab received accelerated approval in 2017 as a third-line therapy in PD-L1 positive GC patients with an ORR of 13.3%. Further studies in second- and third-line GC patients showed comparable outcomes when pembrolizumab was combined with chemotherapy. Pembrolizumab, a humanized antibody designed to inhibit the immunosuppressive effects of phosphatidyserine (PS), is being evaluated in combination with pembrolizumab in patients with advanced gastric and gastroesophageal junction (GEJ) cancer. Pembrolizumab binds in a high-affinity complex with 2-glycoprotein and PS to reverse immunological nonresponsiveness and activate multiple immune cell receptors, including TIM3 and TAMS. Data from the Phase III Sunrise second-line lung cancer study indicated that patients who progressed on study treatment with pembrolizumab plus docetaxel and continued with a checkpoint inhibitor showed significantly improved overall survival. Cumulative data suggest that pembrolizumab may potentiate pembrolizumab-mediated checkpoint inhibition, potentially increasing overall clinical benefit. Methods: This phase 2, multicenter, open-label, single-arm global study is designed to assess the safety, tolerability, and clinical efficacy of pembrolizumab in combination with pembrolizumab in advanced gastric or GEJ adenocarcinoma patients, regardless of PD-L1 status, who have progressed on or after at least one prior standard therapy. Patients must be treatment naive for checkpoint inhibitors. The study, started in August 2019, consists of an initial 3+3 dose escalation safety cohort to confirm the expansion cohort dose. A total of 80 patients will be enrolled. Primary endpoints will assess antitumor activity of the treatment combination on objective response rate using RECIST1.1 and safety/tolerability. Secondary objectives will evaluate antitumor characteristics, pharmacokinetics, and immunogenicity. Exploratory objectives include the evaluation of a novel biomarker signature panel and its relationship to efficacy outcomes. Research Sponsor: Oncology, Inc.

**TPS460**

Trials in Progress Poster Session (Board #L4), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

A phase II trial of [fam]-trastuzumab desuxtucetax (T-Dx, DS-8201a) in subjects with HER2-positive, unresectable, or metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma. First Author: Charles S. Fuchs, Yale Cancer Center, Smilow Cancer Hospital, New Haven, CT

Background: Despite attempts, no HER2-directed therapies have been approved for gastric or GEJ cancer after disease progression on trastuzumab. [Fam] trastuzumab desuxtucetax (T-Dx, DS-8201a) is a novel HER2-directed antibody-drug conjugate composed of a humanized monoclonal antibody specifically targeting HER2, a cleavable tetrapeptide-based linker (drug-to-antibody ratio of ~8), and a potent topoisomerase I inhibitor payload. In a phase I study, T-Dx (5.4 or 6.4 mg/kg) showed promising antitumor activity inHER2+ advanced/intrinsicallyHER2+ tumors, including a confirmed objective response rate (ORR) of 43% among subjects with extensively pretreated HER2-positive gastric cancer (Shitara et al. Lancet Oncol. 2019;20(6):827-836). Here we describe the phase 2 trial evaluating the efficacy and safety of T-Dx in subjects with HER2-positive gastric/G/EJ cancer previously treated with trastuzumab (NCT04040705). Methods: This is a single-arm, open-label, multicenter, phase 2 study in patients with centrally confirmed, HER2-positive (immunohistochemistry [IHC] 3+ or IHC 2+/in situ hybridization positive), unresectable or metastatic gastric/GEJ cancer that progressed on or after first-line therapy with a trastuzumab-containing regimen. HER2 status will be confirmed by a fresh biopsy before enrollment. Subjects are excluded if they received anticancer therapy after a first-line trastuzumab-containing regimen. The study began in August 2019 and will recruit ~72 subjects from 25 to 30 sites in North America and Europe. T-Dx at 6.4 mg/kg will be administered intravenously once every 3 weeks until disease progression. The primary efficacy endpoint is confirmed ORR by independent central review (ICR) using RECIST v1.1 criteria. Secondary endpoints include duration of response and progression-free survival by ICR and investigator assessment. ORR by investigator assessment, and overall survival. Additional endpoints include safety, disease control rate, and pharmacokinetic analyses. Health-related quality of life will also be measured in a clinical trial interview. NCT04040705. Research Sponsor: Daichi Sankyo.

**TPS461**

Trials in Progress Poster Session (Board #L5), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM and Poster Walks, Thu, 5:00 PM-5:45 PM

Phase II study of the combination of abemaciclib and pembrolizumab in locally advanced unresectable or metastatic gastroesophageal adenocarcinoma: Big Ten Cancer Research Consortium BTCTRC-G18-149. First Author: Nataliya Volodymyrivna Uboha, University of Wisconsin, Carbone Cancer Center, Madison, WI

Background: Metastatic gastroesophageal adenocarcinoma (GEA) has poor prognosis. Overall survival (OS) remains around 12 months (mo) with current first-line therapies. Pembrolizumab is approved for advanced GEA that has progressed on at least 2 prior lines of systemic therapy. However, the majority of patients progress on this treatment, and less than 15% of patients experience objective response (OR). This study will evaluate efficacy of pembrolizumab in combination with cyclin-dependent kinase 4/6 (CDK4/6) inhibitors. Abemaciclib will augment response to pembrolizumab in GEA. Methods: This is a multi-institutional, single arm, open label, phase II study of abemaciclib in combination with pembrolizumab in patients with advanced GEA who have progressed or were intolerant to at least 2 prior lines of therapy. Patients previously treated with immune checkpoint inhibitors or with microsatellite unstable tumors will be excluded. Treatments will be given on a 21 day cycle until disease progression or intolerable toxicities. Pembrolizumab, 200 mg intravenously, will be given on day 1, and abemaciclib, 150 mg, will be taken orally twice a day on days 2-21. Primary endpoint is progression free survival (PFS). Secondary endpoints include PFS rate at 6 mo, disease control rate, OS and OR rate. Correlative endpoints will examine relationship between PDL1 status, genomic signature and treatment response. Saliva samples will be collected for microbiome analysis. Archival tumor tissue and blood samples will be banked for future studies. A total of 31 evaluable subjects will be enrolled to detect a anticipated increase in the median PFS from 2 months (null hypothesis) to 4 months with 80% power at the one-sided 0.05 significance level. The trial is open to enrollment. Clinical trial information: NCT03997448. Research Sponsor: Eli Lilly.
Trials in Progress Poster Session (Board #L6), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Tislelizumab plus chemotherapy as first-line treatment for unresectable, locally advanced recurrent/metastatic esophageal squamous cell carcinoma. First Author: Harry Y. Yoon, Mayo Clinic, Rochester, MN

Background: Esophageal squamous cell carcinoma (ESCC) is the predominant histological subtype of esophageal cancer, particularly in Asian countries. Inhibition of the PD-1/PD-L1 axis has demonstrated antitumor activity in patients with advanced unresectable or metastatic ESCC. Tislelizumab, an investigational humanized IgG4 monoclonal antibody with high affinity and binding specificity for PD-L1, was engineered to minimize binding to FcγRe on macrophages in order to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy. Results from early phase clinical studies suggest tislelizumab, as a single agent or in combination with chemotherapy, was generally well tolerated and had antitumor activity in patients with solid tumors, including ESCC. Methods: This global phase 3, randomized, placebo-controlled, double-blind study (NCT03783442) is designed to evaluate the efficacy and safety of tislelizumab plus chemotherapy as first-line treatment of unresectable, locally advanced recurrent or metastatic ESCC. Adult patients with histologically confirmed unresectable ESCC, or locally advanced recurrent/metastatic disease with a ≥6 month treatment-free interval, are eligible; palliative radiation administered > 4 weeks from study initiation is allowed. Patients who received prior anti-PD-L1, anti-PD-L2, or first-line therapy are ineligible. Patients (n=480) will be randomized 1:1 to receive tislelizumab 200 mg IV every 3 weeks (Q3W) plus investigator-chosen chemotherapy (IC) or placebo plus IC. IC options include: platinum (cisplatin 60-80 mg/m² or oxaliplatin 130 mg/m² IV Q3W) + 5-FU 750-800 mg/m² by continuous IV infusion over 24 hours for 5Q3W; or cisplatin + paclitaxel 1000 mg/m² orally BID for 14Q3W; or cisplatin + paclitaxel 175 mg/m² IV Q3W. Progression-free and overall survival are primary endpoints; secondary endpoints include objective response rate, duration of response, and health-related quality of life. Safety will be assessed by monitoring adverse events, physical examinations, vital signs, and electrocardiograms. This study is actively enrolling. Clinical trial information: NCT03783442. Research Sponsor: BeGene, Co., Ltd.

Trials in Progress Poster Session (Board #L8), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Phase II study of trifluridine/tipiracil (FTD/TPI) and oxaliplatin as induction chemotherapy (IC) in resectable esophageal and gastroesophageal junction adenocarcinoma (EGAC). First Author: Sarbatk Mukherjee, Roswell Park Comprehensive Cancer Center, Buffalo, NY

Background: Neoadjuvant chemoradiation (CRT) followed by surgery is a standard approach for localized EGAC. Despite multimodality treatment, 5-year overall survival (OS) is less than 50%, with pathologic complete response (pCR) rates of 20%. Achievement of pCR is associated with improved OS. We propose to use a novel combination of FTD/TPI and oxaliplatin as IC. We hypothesize that IC before CRT will increase the pCR rate in localized EGAC. Methods: This is an open-label, multicenter phase II trial. Patients (pts) with potentially resectable loco-regional EGAC are eligible. Pts. should have adequate organ function, ECOG performance status of 0–1, age < 76 years, and endoscopic ultrasound-determined node-positive disease with any T-stage, or T3–T4a with any N stage. Pts. will then undergo concurrent CRT (standard radiation dose of 50.4 Gy will be utilized) with weekly Carboplatin (AUC 2) and Paclitaxel (50 mg/m²) for 6 weeks followed by surgery. Our primary objective is to evaluate the pCR rate. The secondary objectives include evaluation of 2-year disease-free survival (DFS), 2-year OS, and assessment of toxicities of the IC. As a correlative endpoint, circulating tumor DNA level will be correlated with disease recurrence and metabolic response on PET CT. Assuming a historic pCR rate of 20% with standard CRT, 41 pts (enrollment of up to 45 pts accounting for non-evaluable pts) are needed to show a 15% increase in pCR with IC with 80% power at one-sided 0.05 significance level. In stage 1, n=12 evaluable pts will be enrolled. If there is 5 or more pCRs, an additional n=19 pts will be enrolled in stage 2. If 12 or more pCRs are observed in the total n = 41 evaluable pts, then the proposed treatment regimen will be considered promising for further study. The study duration is 2 years with a follow-up period of 3 years. Clinical trial information: NCT040997028. Research Sponsor: National Comprehensive Cancer Network (NCCN); Oncology Research Program.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
TPS466 - Trials in Progress Poster Session (Board #L10), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

A phase Ib study of alofanib, an allosteric FGFR2 inhibitor, in patients with advanced or metastatic gastric cancer. First Author: Galina Statsenko, Omsk Regional Cancer Center, Omsk, Russian Federation

Background: Fibroblast growth factor receptor 2 (FGFR2) is amplified or overexpressed in 3% to 6% of patients with gastric cancer and associated with a poor prognosis. Targeted inhibition of FGFR2 development promise to multikinase inhibitors. Besides, resistance to monoclonal antibodies depends on the type of FGFR2 isoforms IIc or IIb expressed by cancer cells. Alofanib (RPT835) is a novel selective allosteric inhibitor of FGFR2. Alofanib could bind to both active and quiescent forms of FGFR (extracellular domain and had an inhibitory effect on FGFR2-induced phosphorylation of FRS2a. On preclinical models no severe organ and function tests were observed. Based on these results, alofanib has advanced into clinical evaluation. Methods: RPT835GCIB is a Phase Ib study, being conducted in at least four sites in Russia, evaluating the safety and preliminary efficacy of alofanib in patients with advanced and metastatic gastric adenocarcinoma pretreated with ≥ 1 previous lines of therapy. This trial consists of two parts. The standard dose-escalation part (design 3+3) aims to establish the maximum tolerated dose (MTD) or recommended phase 2 dose (RP2D) as a primary endpoint. The first part of the study includes a 28-day period when alofanib is administered daily intravenously for 5-days followed by a 2-day interval (rest). There are five dose levels: 50, 100, 165, 250, and 350 mg/m2. The dose-expansion phase accrues additional 20 patients, where comprehensive information to be collected. Secondary endpoints include pharmacokinetic parameters, rate of adverse events, progression-free survival, overall survival, and objective response rate. All patients will receive alofanib until disease progression or unacceptable toxicity. FGFR2 amplification, fusion, and overexpression will be assessed as well. Clinical trial information: NCT04071184.

Research Sponsor: Skolkovo Foundation, Ruspharmtech.

TPS467 - Trials in Progress Poster Session (Board #L11), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

EORTC 1707 VESTIGE: Adjuvant immunotherapy in patients with resected gastric cancer following preoperative chemotherapy with high risk for recurrence (ypN+ and/or R1): An open-label randomized controlled phase II study. First Author: Elizabeth Catherine Smyth, Cambridge University Hospital NHS Foundation Trust, Cambridge, United Kingdom

Background: Gastroesophageal adenocarcinoma patients with metastatic lymph nodes (ypN+) or a microscopically incomplete surgical resection (R1) following neoadjuvant chemotherapy are at high risk of disease recurrence. Current practice is to continue with the same perioperative chemotherapy used prior to surgery, despite these suboptimal outcomes. Immune checkpoint blockade with nivolumab and ipilimumab has demonstrated activity in advanced gastroesophageal adenocarcinoma. We hypothesise that high risk (ypN+ and/or R1) post resection gastroesophageal adenocarcinoma patients who are treated with nivolumab plus ipilimumab will have better disease free survival than patients who continue with standard post-operative chemotheraphy. Methods: VESTIGE is an ongoing, international, open label ranomized phase II study designed to evaluate the efficacy of adjuvant nivolumab plus ipilimumab versus standard post-operative chemotherapy in high risk (ypN+ and/or R1) post resection gastroesophageal adenocarcinoma patients. Eligible patients (n=240) will be randomised 1:1 to receivepost-operative adjuvant chemotherapy (identical regimen as pre-operatively) or nivolumab 3mg/kg IV q2w plus ipilimumab 1mg/kg IV q6w x 1 year. Key inclusion criteria include ypN+ and/or R1 status following neoadjuvant chemotherapy plus surgery and an adequate pre-specified surgical resection. The primary endpoint of the study is disease free survival, with secondary endpoints of overall survival, safety, toxicity and quality of life. The trial will recruit 240 patients at 24 number of sites across 8 countries, including the United States, Israel, Norway, Poland, Portugal, Spain, and United Kingdom. Recruitment commenced July 2019 and is anticipated to take 30 months. The VESTIGE translational research programme includes collection of pre-treatment bioprices, post-chemotherapy biopsies and/or specimen blocks for additional on treatment to explore biomarkers predictive of immune checkpoint blockade efficacy. Clinical trial information: NCT03443856.

Research Sponsor: BMS.

TPS468 - Trials in Progress Poster Session (Board #L2), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Margetuximab (M) combined with anti-PD-1 (MGD012) or anti-PD-1/LAG-3 (MGD013) +/- chemotherapy (CTX) in first-line therapy of advanced/metastatic HER2+ gastroesophageal junction (GEJ) or gastric cancer (GC). First Author: Daniel V.T. Catenacci, University of Chicago Medical Center and Biological Sciences, Chicago, IL

Background: Trastuzumab (T), a monoclonal antibody (mAb) targeting HER2, is standard of care palliative 1st-line therapy for advanced HER2+ GC/GE patients (pts). M, an Fc-engineered anti-HER2 mAb, targets the same HER2 epitope but with higher affinity for both ISBV (high binding) and ISBF (low binding) alleles of activating Fc receptor CD16A. M coordinately enhanced both innate and adaptive immunity, including antigen-specific T-cell responses to HER2, PD-L1 and LAG-3. T-cell checkpoint molecules that suppress T-cell function. MGA012 (INCMA000012) is a humanized, hinge-stabilized, IgG4 x anti-PD-1 mAb blocking binding of PD-L1 or PD-L2 to PD-1. MGD013 is a humanized Fc-bearing bispecific tetravalent protein that binds to both PD-1 and LAG-3, depending on their relative ligand binding. We previously reported that a CTX-free regimen of M+PD1-blockade was well tolerated in GEJ/GC pts, and induced a 30% objective response rate (ORR). This was 2-3 fold greater than in historical controls with checkpoint inhibitors alone. This registration-directed trial assesses efficacy, safety, and tolerability of M-checkpoint inhibition CTX in metastatic/locally advanced, treatment-naïve, HER2+ GE/ GC pts.

Methods: This is a 2:1, adaptive open-label phase 2/3 study. The first single arm, CTX-free cohort A evaluates M+MGD012 in HER2+ (immunohistochemistry [IHC] 3+) or PD-L1+ (excluding microsatellite instability high) pts. After 40 pts are evaluated for response/safety, 60 more will be enrolled if the threshold for continuation is met. In randomized cohort B, HER2+ (IHC 3+ or 2+/fluorescent in situ hybridization+) pts are enrolled irrespective of PD-L1 status. Pt 1 randomizes pts to 1 of 3 arms (50 pts each): control arm (T+CTX) or 1 experimental arm (M+CTX; M+CTX+MGD012; M+CTX+MGD013). CTX is investigator’s choice XELORO or mFOLFOX6. Part 2 consists of control (T+CTX) vs experimental arm (M+CTX) or either MGA012 or MGD013. Results from part 1 of 30 pts each. The primary endpoint is a probability of success approach to determine futility criteria. Study objectives include objective response rate (primary); safety and tolerability, disease control rate, duration of response, progression-free and overall survival, and pharmacodynamics and immunologic biomarker assessment. Study enrollment is ongoing in North America. Pts will also enroll in Europe and Asia. Clinical trial information: NCT04032704.

Research Sponsor: Seattle Genetics, Inc.
**TPS470** Trials in Progress Poster Session (Board #L14), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

A phase II study of futibatinib (TAS-120) in patients (pts) with advanced (adv) solid tumors harboring fibroblast growth factor receptor (FGFR) genomic aberrations. First Author: Antoine Hollebecque, Gustave Roussy Cancer Campus, Villejuif, France

**Background:** FGFR genomic aberrations are known to drive oncogenesis in multiple tumor types via FGFR signaling pathways dysregulation. Future trials, in an oral, highly selective, irreversible FGFR-4 inhibitor that has shown potent antiproliferative activity against FGFR-deregulated tumors of diverse tissue origins in preclinical studies. In a phase 1 dose-escalation/expansion study, futibatinib showed promising antitumor activity and tolerability in previously treated pts with tumors harboring FGFR aberrations. This phase 2 study was designed to evaluate the efficacy and safety of futibatinib in pts with tumors harboring FGFR aberrations. The study will enroll pts in multiple cohorts based on diagnosis and FGFR aberration status; cohorts enrolling pts with adv solid tumors are reported here. **Methods:** In this global, open-label, phase 2 study, pts (≥18 years; Eastern Cooperative Oncology Group performance status of 0 or 1) will be enrolled in cohort A (~60 pts with metastatic/localy adv solid tumors, except primary brain tumors or intrahepatic cholangiocarcinoma, harboring FGFR4 amplifications and with ≥2 prior therapies). Key exclusion criteria are clinically significant alterations in calcium-phosphorus homeostasis, ectopic mineralization/calcification, and prior FGFR inhibitor treatment. Pts will receive 20 mg futibatinib once daily in a continuous 28-day cycle until disease progression, unacceptable toxicity, or other discontinuation criteria are met. The primary endpoint is objective response rate (ORR) per Independent Review (IR). Secondary endpoints include ORR per Investigator, disease control rate, duration of response, progression-free survival, overall survival, and safety. The anticipated start date is in April 2020. Research Sponsor: Taiho Oncology.

**TPS472** Trials in Progress Poster Session (Board #L16), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

A phase II study evaluating safety and efficacy of niraparib in patients with previously treated homologous recombination (HR) defective or loss of heterozygosity (LOH) high-metastatic esophageal/GEJ/proximal gastric adenocarcinoma: A Big Ten Cancer Research Consortium study. First Author: Hirva Mamdani, Karmanos Cancer Institute, Detroit, MI

**Background:** Adenocarcinoma of esophagus (EAC) and GEJ is the fastest rising cancer in the US. The outcomes are extremely poor with median overall survival (OS) being 12 mo in review. FGFR1, 2, 3, 4 and FGFR5 gene amplifications and with ≥2 prior therapies. Key exclusion criteria are clinically significant alterations in calcium-phosphorus homeostasis, ectopic mineralization/calcification, and prior FGFR inhibitor treatment. Pts will receive 20 mg futibatinib once daily in a continuous 28-day cycle until disease progression, unacceptable toxicity, or other discontinuation criteria are met. The primary endpoint is objective response rate (ORR) per Independent Review (IR). Secondary endpoints include ORR per Investigator, disease control rate, duration of response, progression-free survival, overall survival, and safety. The anticipated start date is in April 2020. Research Sponsor: Taiho Oncology.

**TPS473** Trials in Progress Poster Session (Board #L17), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

A pilot study of avelumab in Epstein-Barr virus-associated gastric cancer. First Author: Ronan Andrew Mc Laughlin, Mater Hospital Dublin, Buncrana, Ireland

**Background:** Gastric Cancer (GC) is the third most common cause of cancer related deaths worldwide. The median overall survival of patients with stage 4 disease is approximately 1 year. Current accepted treatment approach with chemotherapy is applied without consideration for genetic or biologic heterogeneity. Whilst immune-based approaches in GC look promising it is clear that single-agent PDI/PD1L1 inhibition benefit a minority. We must clarify a means of identifying prospectively those patients who may benefit from this treatment. A recent phase II study explored the hypothesis that administering anti-PD1/PD1L1 therapy with first-line chemotherapy (FOLFOX) followed by anti-PD1/PD1L1 therapy in patients who achieve a RECIST partial response will result in improved outcomes. The anticipated frequency of PD1/PD1L1 positive tumors is 20%, we will screen 100 patients to accrue the 30% needed to complete the trial. The primary endpoint is overall survival. Tumor samples will be screened for PD1/PD1L1 expression and its correlation with response and resistance to therapy. Type II error rate is 0.09, power = 0.9, 30 patients must be recruited if the null hypothesis is true. The trial opened to recruitment in May 2017 and will recruit up to 50 patients over 3 years. Clinical trial information: NCT03289345. Research Sponsor: AstraZeneca, The study is sponsored by The Royal Marsden Hospital.
A multicenter phase II trial of tumor treating fields plus chemotherapy for first-line treatment of gastric adenocarcinoma. First Author: Jin Li, Department of Medical Oncology, Fudan University Shanghai Cancer Center; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China

Background: Gastric carcinoma (GC) is the third leading cause of death in China (299,000 deaths in 2015). Current therapies include surgery, chemotherapy, radiotherapy and targeted therapy, which prolong PFS and OS to 6 months and 8-14 months, respectively. Tumor Treating Fields (TTFields) are non-invasive, regional antimitotic treatment modality approved by the FDA for glioblastoma and malignant pleural mesothelioma. TTFields at specific frequency (100-500 kHz) are delivered via transducer arrays placed on the skin of the upper abdomen, back, right and left hypochondriac regions where the primary tumor lesion is located. TTFields were effective in preclinical models of gastric cancer and there are several ongoing Phase 3 trials of TTFields in multiple solid tumors. In this phase 2, single arm, open-label, multicenter study, we will investigate for the first time the efficacy and safety of TTFields concomitant with XELOX (oxaliplatin/capecitabine) as the first-line treatment of GC.

Methods: Patients (N = 50) with histologically confirmed unresectable, locally advanced or metastatic Gastric Esophageal Junction (GEJ) or Gastric Adenocarcinoma (GC), aged ≥ 18 years, ECOG PS 0-1, who had no previous systemic treatment for the recurrent or metastatic disease will be enrolled. Patients will receive TTFields (50 kHz via the NovoTTF-100L (P) medical device for average monthly use of 18 hrs/day) plus XELOX chemotherapy (Oxaliplatin: 130 mg/m² on day 1 every 3 weeks; Capecitabine: 1000 mg/m², PO, BID on day 1-14 every 3 weeks). For HER-2 positive patients, therapy (Oxaliplatin: 130 mg/m² on day 1 every 3 weeks; Capecitabine: 135 mg/m² IV Q3W) and radiotherapy at a total dose of 50.4 Gy. An Independent Data Monitoring Committee will be established to assess the safety/tolerability of tislelizumab plus cCRT in the first 20 enrolled pts; Progression-free survival (PFS), assessed by a Blinded Independent Review Committee per RECIST v1.1, is the primary endpoint. Secondary efficacy endpoints include overall response rate, duration of response, and overall survival. Incidence and severity of adverse events (CTCAE V5.0) and HRQoL monitoring across the study will occur at regular intervals thereafter. A dependent Data Monitoring Committee will be established to assess the safety/tolerability of tislelizumab in the first 20 enrolled pts; Progressive-free survival (PFS), assessed by a Blinded Independent Review Committee per RECIST v1.1, is the primary endpoint. Secondary efficacy endpoints include overall response rate, duration of response, and overall survival. Incidence and severity of adverse events (CTCAE v5.0) are additional secondary endpoints. Exploratory endpoints include PFS rate at Years 1 and 2, pharmacokinetic profile, and predictive biomarker analyses. Clinical trial information: NCT039957590. Research Sponsor: BeiGene, Ltd.
747 Oral Abstract Session, Fri, 1:30 PM-3:00 PM

Ramucirumab (RAM) or merestinib (MER) or placebo (PL) plus gemcitabine (GEM) and cisplatin (CIS) as first-line treatment for advanced or meta-
static biliary tract cancer (BTC): A randomized, double-blind, phase II
study. First Author: Juan W. Valle, The Christie NHS Foundation Trust,
Manchester, United Kingdom

Background: We assessed RAM or MER plus standard of care GEM+CIS as
first-line treatment for BTC. Methods: Patients (pts) with BTC, ECOG PS 0/1,
and measurable and re-segmented were randomized 2:1:1 to oral MER 80 mg QD, oral
PL, or IV RAM 8 mg/kg days 1 and 8 and Q3W or IV PL days 1 and 8 Q3W. Pts
also received up to 8 cycles IV GEM 1000 mg/m² + CIS 25 mg/m² days 1 and 8 Q3W.
RAM, MER, or PL could continue until disease progression. Primary endpoint:
progression-free survival (PFS). Secondary endpoints: overall survival (OS),
objective response rate (ORR), and safety. PFS and hazard ratios (HRs) were
compared using stratified log-rank tests and Cox regression models, re-
spectively. NCT02711553. Results: 309 pts were randomized to RAM (106),
MER (104), or PL (101). Median OS was not reached in either arm. Efficacy
endpoints are in Table. Fewer pts received post-discontinuation systemic therapy in
the RAM group (37.5%, MER 50.0%, PL 52.0%). The most common grade ≥3 treatment-emergent adverse events were: RAM vs PL: neuropenia (49.0% vs 33.0%), thrombo-
cytopenia (34.6% vs 17.0%), and anemia (26.9% vs 19.0%); MER vs PL: neu-
ropenia (47.1% vs 33.0%), thrombocytopenia (18.6% vs 17.0%), and alanine
aminotransferase increased (10.8% vs 5.0%). Conclusions: PFS, OS, and ORR
were not improved with the addition of RAM or MER to GEM+CIS. Treatment was
well-tolerated, with safety profiles consistent with known profiles for RAM, MER,
and GEM+CIS. Translational studies are ongoing. Clinical trial information:

Effectiveness

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>RAM vs CIS</th>
<th>MER vs CIS</th>
<th>PL vs CIS</th>
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<tbody>
<tr>
<td>HR (95% CI)</td>
<td>1.153 (0.959 1.376)</td>
<td>1.342 (1.086 1.648)</td>
<td>1.399 (1.140 1.703)</td>
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<td>Median OS, mo (95% CI)</td>
<td>15.31 (11.94 – 18.70)</td>
<td>12.92 (11.34 – 14.49)</td>
<td>11.68 (10.81 – 13.13)</td>
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<tr>
<td>HR (95% CI)</td>
<td>0.530 (0.456 0.616)</td>
<td>0.722 (0.607 0.858)</td>
<td>0.807 (0.692 0.941)</td>
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<tr>
<td>Median progression-free survival, mo (95% CI)</td>
<td>7.13 (6.48 – 7.77)</td>
<td>6.97 (6.21 – 7.73)</td>
<td>6.49 (5.65 – 7.32)</td>
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<tr>
<td>Odds ratio vs PL (95% CI)</td>
<td>0.0870 0.7599</td>
<td>0.1020 0.7111</td>
<td>0.1040 0.6836</td>
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746 Oral Abstract Session, Fri, 1:30 PM-3:00 PM

Patient-reported outcomes (PROs) from the Phase III IMbrave150 trial of
atezolizumab (atezo) + bevocizumab (bev) vs sorafenib (sor) as first-line
treatment (tx) for patients (pts) with unresectable hepatocellular carci-
noma (HCC). First Author: Peter R. Galie, University Medical Center Mainz,
Mainz, Germany

Background: Atezo + bev in pts with unresectable HCC who had not received
prior systemic therapy has shown statistically significant and clinically
meaningful improvement in OS and PFS per independent review facility-
assessed RECIST 1.1 vs sor in the Phase III IMbrave150 study (Cheng ESMO
Asia 2019). Here, we report PRO data from this trial to show pt perspectives on
the overall clinical benefit of atezo + bev. Methods: Pts were randomized 2:1
to receive either atezo 1200 mg IV Q3W + bev 15 mg/kg IV Q3W or sor 400 mg
PO BID until loss of clinical benefit or unacceptable toxicity. Pts completed the
EORTC QLQ-C30 and EORTC QLQ-HCC18 questionnaires before tx, every 3 wk
(EORTC QLQ-C30 and EORTC QLQ-HCC18 questionnaires before tx, every 3 wk
and every 3 mo after tx). Progression of disease was defined as a ≥10-point
decrease from baseline for 2 consecutive assessments or 1 assessment
followed by death within 3 wk of pt-reported quality of life (QOL), physiological,
functioning, and role functioning. Pre-specified exploratory analyses included
TTO and of proportion of pts with a clinically meaningful change (< 10 points
from baseline) in key pt-reported symptoms. Results: Questionnaire com-
pletion rates were ≥92% in both arms from baseline through most of the tx
period. Compared with sor, atezo + bev delayed TTD of pt-reported QOL,
median TTD (19.2 vs 3.6 mo; HR, 0.63 [95% CI: 0.46, 0.85]), physical functioning
(median TTD, 131 vs 4.9 mo; HR, 0.53 [95% CI: 0.39, 0.73]), and role functioning
(median TTD, 91.3 vs 3.6 mo; HR, 0.62 [95% CI: 0.46, 0.84]). Atezo + bev also
delayed TTD in pt-reported appetite loss, fatigue, pain, and diarrhea vs sor; a
lower proportion of pts on atezo + bev experienced clinically meaningful de-
terioration in each of these symptoms vs sor. Conclusions: High-quality PRO
results from IMbrave150 showed large and consistent benefits in key aspects of
the pt experience with atezo + bev, further supporting its overall clinical benefit
in pts with unresectable HCC who have not received
prior systemic therapy. Clinical trial information: NCT03434379. Research Sponsor:
F. Hoffmann-La Roche, Ltd.

748 Rapid Abstract Session, Fri, 7:00 AM-7:45 AM and Poster Session
(Board #A1), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Nivolumab (NIVO) + ipilimumab (IPI) + cabozantinib (CABO) combination
therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC):
Results from CheckMate 040. First Author: Thomas Yue, The University at
Hong Kong, Hong Kong, China

Background: The programmed death-1 inhibitor NIVO had durable responses
and a manageable safety profile in pts with aHCC in CheckMate 040
(NCT01658878; Eichhouri et al. Lancet 2017) and is approved in the United States,
Canada, and Elsewhere, and in combination with ipilimumab (IPI)-treated pts
with advanced HCC (GEM) and cisplatin (CIS) as first-line treatment to aHCC. In
another CheckMate 040 cohort, NIVO + IPI combination therapy had
durable responses in SOR-treated pts with aHCC, with objective response rates
(ORR) >30% in each dosing arm (Yau et al. J Clin Oncol 2019). CABO is also
being studied in combination with IPI-treatment as first-line or second-line
standard of care treatment (median overall survival of OS) of 10.2 mo (Abou-Alfa et
al. N Engl J Med 2018). This is the first report of efficacy and safety of NIVO + CABO
+ IPI (doublet and triplet) combinations in pts with aHCC. Methods: SOR-naïve or
experienced pts with aHCC were randomized to 2 arms: 1) NIVO 3 mg/kg Q2W +
CABO 40 mg daily or (2) NIVO 3 mg/kg Q2W + IPI 15 mg/kg Q6W + CABO 40 mg daily.
Treatment continued until intolerable toxicity or disease progression. Primary endpoints
included ORR (investigator assessed using RECIST v1.1) and safety/tolerability.
Data cutoff was January 2019. Results: 71 pts were randomized to NIVO +
CABO (n = 36) or NIVO + IPI + CABO (n = 35). Investigator-assessed ORR was 17% (6 pts
with partial response [PR]) in the NIVO + CABO arm and 26% (9 pts with PR) in
the NIVO + IPI + CABO arm. Disease control rate was 86% for the NIVO +
CABO arm and 83% for the NIVO + IPI + CABO arm; median progression-free survival
was 5.5 mo for the NIVO + CABO arm and 6.8 mo for the NIVO + IPI + CABO arm.
Median OS was not reached in either arm. Grade 3-4 treatment-related adverse
events (TRAEs) were reported in 15 pts (42%) in the NIVO + CABO arm and 25
pts (71%) in the NIVO + IPI + CABO arm and led to discontinuation in 1 (3%) and
7 (20%) pts, respectively. No new safety signals were observed in either arm.
Updated data describing the efficacy and safety of the combinations will be
shown. Conclusions: In pts with aHCC, NIVO + CABO + IPI combination therapy
showed clinically meaningful responses, although the triplet had a higher
treatment rate of TRAEs observed than the doublet regimen, the majority of AEs were
manageable and reversible. Clinical trial information: NCT01658878. Research Sponsor:
Bristol-Myers Squibb.
Immune checkpoint blockade (ICB) response evaluation with MRI/MR elastography (MRE) in surgical and nonsurgical patients with HCC. First Author: Aliya Qayum, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Currently, there is a lack of imaging biomarkers of immunotherapy outcome in hepatocellular carcinoma (HCC). The study aim was to determine IHC enhancement on MRI and stiffness change measured by magnetic resonance elastography (MRE) can predict immunotherapy response. Methods: This was a prospective, Institutional Review Board approved study of 38 patients with HCC treated with immune checkpoint blockade (ICB) therapy. All patients had liver MRI/MRE and HCC biopsy at baseline, and MRI/MRE with biopsy or resection after 6 weeks therapy. HCC stiffness (kPa) was measured on MRE elastograms (liver stiffness maps). HCC enhancement and change in stiffness were compared with treatment response to ICB in 11/25 (44%) patients (pembrolizumab), and 2) surgical patients (nivolumab + ipilimumab). For non-surgical patients, treatment response was defined as overall survival >1 year. For surgical patients, treatment response was defined as <50% viable tumor at time of resection. Analysis was performed using descriptive statistics and Spearman correlation; p-value < 0.05 was considered statistically significant. Results: Twenty-five patients were evaluable. Median age was 67 years (32, 78). Etiology of liver disease was NASH (n = 8), HCV (n = 8), HBV (n = 2) and unknown (n = 7). Treatment response occurred in 11/25 (44%) patients. Median HCC size and change in size were 4.7 cm (1.2, 14.0) and -2.2 cm (1.5, 10.2), respectively. Median baseline HCC stiffness and change in stiffness were 5 kPa (2.2, 12.4) and -0.1 kPa (-2.2, 1.5), respectively. Median change in HCC size for responders and non-responders was -1.2 cm (-6.8, 0.4) and 0 cm (-1.5, 1.1), respectively (p = 0.02). Treatment response was associated with absence of portal venous phase capsular enhancement and increase in HCC stiffness, (p = 0.001). Conclusions: Capsular enhancement and MRE stiffness change may be useful biomarkers of immune cell activated response to ICB therapy. Research Sponsor: None.

The comparisons of the outcomes between surgical resection and proton beam therapy for single primary hepatocellular carcinoma. First Author: Shunsuke Tamura, Division of Hepato-Biliary-Pancreatic Surgery, Shizuoka Cancer Center Hospital, Shizuoka, Japan

Background: There are many treatment choices for hepatocellular carcinoma (HCC). Proton beam therapy (PBT) is considered a treatment option for HCC. The purpose of this study was to compare surgical resection (SR) and PBT in order to clarify the prognostic factors for operable HCC based on a single institution’s database. Methods: Patients with single primary nodular HCC ≤ 100 mm without vessel invasion on pretreatment imaging were divided into the SR group and PBT group. In the PBT group, the patients with unresectable HCC due to their liver function and/or performance status (PS) were excluded. Results: There were 314 and 31 patients who underwent SR and PBT, respectively. The median survival time in the SR group was significantly better than in the PBT group (104.1 vs. 64.6 months, p = 0.008). Regarding the relapse-free survival (RFS), there was no significant difference between the SR and PBT groups (31.8 vs. 14.0 months, p = 0.099). Conclusions: In RFS, the PBT group and the SR group were comparable. However, the PBT group was significantly worse than SR group in overall survival. SR may therefore be favorable as an initial treatment for HCC compared to PBT. Clinical trial information: 1856. Research Sponsor: None.

Clinical predictors of progression of a hepatic lesion from Li-RADS (LR) 3 to LR5 among patients (pts) at risk of hepatocellular carcinoma (HCC). First Author: Lindsay Marie Hannan, University of Washington/Fred Hutchinson Cancer Center, Seattle, WA

Background: We sought to identify predictors of progression of LR3 lesions (i.e. indeterminate for HCC) to LR5 lesions (i.e. definitely HCC) on follow-up imaging among cirrhotic pts. Methods: Imaging reports with LR assignments were identified among pts seen at the University of Washington, 2013-2017. Cirrhotic pts with a LR3 lesion and follow-up scan within 1 year (yr) of LR3 lesion date were included (n = 313). Clinical data were abstracted from chart review. Survival analyses employing interval censoring were performed. Variables as potentially predictive of LR3 progression were identified in univariate analyses, with backwards elimination done (p < 0.05) to obtain the final multivariate model. Results: 20.4% of LR3 lesions progressed to LR5 within 1 yr; 73% were still LR3, 8% progressed to LR4. The population was predominantly male (68%), Caucasian (7%), older than 55 (63%). The most common cirrhotic etiologies were HCV (46.7%), alcohol (32.6%), and NASH (12.8%), not mutually exclusive. AFP at the time of LR3 scan was low if available (39% with AFP < 5, 16% 5-10, 28% unknown). 22.7% had impaired liver function (ALBI grade 3). 19.5% lacked data to calculate ALBI grade. CT scan was the most common exam (56%). Multiple LR3 lesions were seen on 51% of scans. Most LR3 lesions were right sided (75%), < 3 cm (31%), 7% of lesions were > 3 cm. Men (HR 2.0, p = 0.02), earlier scan yr (HR 1.04 per yr, p < 0.0001), older age (HR 1.42 per 15 yr, p = 0.047), lesion size (HR 1.21 per 2 cm, global p = 0.02) appeared as independent predictors of LR3 to LR5 progression based on the final model. Of 16 variables examined, men were more likely to have chronic HCV, history of alcohol use and less likely to have alcoholic hepatitis. No other differences were seen. In an exploratory analysis, risk of male sex (HR 1.99, p = 0.03) persisted despite control for HCV, alcohol, age, race, scan yr, lesion size, and number of lesions. Conclusions: Identification of clinical factors associated with LR3 progression may allow for risk modeling tools that may assist in determining imaging frequency and timing of intervention. The increased risk among men vs women is not explained by clinical or radiographic features listed above. Research Sponsor: None.

CheckMate 459: Health-related quality of life (HRQoL) in a randomized, multicenter phase III study of nivolumab (NIVO) versus sorafenib (SOR) as first-line (IL) treatment in patients (pts) with advanced hepatocellular carcinoma (aHCC). First Author:Julien Edeline, Medical Oncology, Centre Eugene Marquis, Rennes, France

Background: SOR is approved as IL therapy for pts with aHCC, but there is still an unmet need to help improve or maintain HRQoL. This phase 3 study compared HRQoL of NIVO vs SOR as IL therapy in pts with aHCC as an exploratory endpoint. Methods: FACT-Hep was administered cycle 1, day 1 and every other cycle. The effect of NIVO vs SOR on HRQoL using FACT-Hep was assessed via repeated measures mixed models (MRRM); Kaplan-Meier curves and Cox proportional-hazards models determined, between-baseline differences in time to first and time until definitive deterioration (TTD/TUDD) based on prespecified thresholds for minimally important differences. The GPS item from FACT-Hep was used to assess the burden associated with treatment side effects. p = 0.05. 473 pts with aHCC were randomized to NIVO (n = 371) or SOR (n = 372). Median OS was 16.4 mo for NIVO, 14.7 mo for SOR (HR 0.85 [95% CI 0.72-1.02]; p = 0.0752). ORR was 15% for NIVO, 7% for SOR (OR 2.41 [95% CI 1.84-3.92]). HRQoL scores were completed at baseline by 94.6% and 92.5% of participants, respectively, and were similar (FACT-Hep total: NIVO 140.7 [SD 21.5] and SOR 140.6 [SD 19.1]). Questionnaire compliance rates exceeded 70% at most visits. MRRM analyses yielded clinically meaningful and statistically significant least squares means differences favoring NIVO on FACT-Hep total (10.1 [95% CI 7.3-13.0]), physical well-being (PWB; 2.0 [95% CI 1.4-2.6]), and functional well-being (FWB; 2.5 [95% CI 1.7-3.2]); scores. No sub-scales favored sorafenib. TTD was significantly delayed in NIVO for FACT-Hep total (HR 0.62 [95% CI 0.51-0.74]), PWB (HR 0.62 [95% CI 0.52-0.74]), FWB (HR 0.73 [95% CI 0.61-0.88]), and hepatobiliary cancer subscale (HR 0.57 [95% CI 0.48-0.69]). TUDD results were consistent with TTD. A greater proportion of NIVO pts did not experience increased burden of side effects (50%-67.7%) compared with SOR (26.8%-45%) based on the GPS item. Conclusions: These patient-reported findings demonstrate that pts taking NIVO had superior HRQoL and reduced side effect burden, further supporting clinical data showing a treatment benefit for IL NIVO in aHCC. Clinical trial information: NCT02576509. Research Sponsor: Bristol-Myers Squibb.
Effect of baseline medications on response to immunotherapy in hepatocellular carcinoma.

**First Author:** Tomi Jun, Icahn School of Medicine at Mount Sinai, New York, NY

**Background:** Immunotherapy (IO) response rates in advanced hepatocellular carcinoma (HCC) are less than 20%. The microbiome has been shown to mediate IO response in animal and models, and clinical studies have observed that antibiotics, especially prior to IO initiation, are associated with reduced IO response. We reasoned that commonly prescribed antibiotic medications, such as proton pump inhibitors (PPIs) and histamine receptor antagonists (H2RAs), which are known to influence the microbiome, may also influence IO response.

**Methods:** This is a retrospective chart-review based study of 95 patients with advanced HCC treated with IO at a single academic medical center. The primary outcome was overall survival (OS). The secondary outcome was overall response rate (ORR). The primary predictors were antibiotic or antacid exposure in the 60 days prior to IO. A secondary predictor was antibiotic or antacid exposure in the 30 days prior to IO.

**Results:** The cohort was predominantly male (84%), was racially diverse (31% White, 23% Black, 23% Asian, 13% Hispanic), and had a median age of 65 years. There were 49 deaths with a median follow-up of 0.96 years. The most common underlying liver diseases were HCV (49%), HBV (31%), and NASH (19%). The majority of patients had cirrhosis (80%), with a median Child Pugh score of 6. Within 60 days before IO, 25 patients received antibiotics, 40 received PPIs and 5 received H2RAs. Most patients receiving antibiotics also received a PPI (92%). The median duration of antibiotics was 5 days. Neither antibiotic nor antacid exposure within 60 or 30 days prior to IO was significantly correlated with OS in univariate or multivariate analyses, nor were they correlated with ORR.

**Conclusions:** No significant associations between baseline exposure to antibiotics and antibiotics and OS or ORR were identified in this single-institution study. Larger observational studies or mechanistic studies are needed to clarify interactions between medications, the microbiome, and IO response.

**Research Sponsor:** None.

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IGF-1 Child-Turcotte-Pugh score as a predictor of overall survival to therapy in CTP-A, BCLC stage C patients with advanced hepatocellular carcinoma. *First Author: Yehia I. Abugabal, University of Texas MD Anderson Cancer Center, Houston, TX

**Background:** Child-Turcotte-Pugh (CTP) A is the standard population for active HCC therapy. The IGF-1 CTP score, comprises levels of type 1 insulin-like growth factor (IGF-1), bilirubin, INR, and albumin, significantly improved the prediction of overall survival (OS) in recently published studies. Our current study aimed to investigate the accuracy of the IGF-1 CTP score in predicting OS in HCC Child-Pugh A patients (pts) treated with local and/or systemic therapies (tx). The overall hypothesis is that the IGF-1 CTP score can further distinguish CTP-A pts in terms of overall survival, PFS. **Methods:** Between 2014 and 2018, a total of 274 pts with newly diagnosed HCC at Texas Medical Center were included in this retrospective enrolled. Clinicopathologic features and treatment history were collected. We calculated IGF-1 CTP scores, used Kaplan-Meier method and log rank test to estimate and compare to time to event outcomes between subgroups of patients. **Results:** 198 pts were CTP Class A, 209 patient underwent systemic tx, 65 underwent local tx (see table); 161 were re-classified as CTP-A with a median OS of 16.09 months (95% CI = 13.06 to 23.29 months) (p <0.0001), whereas 37 patients were reclassified as intermediate risk (IGF-CTP-B) and had significantly shorter OS of 10.66 months (95% CI = 5.49 to 26.51) (p <0.0001). **Conclusions:** The results of this study support our biologically-driven hypothesis that IGF-1 CTP score is predictive of overall survival to therapy in advanced HCC treated with local and/or systemic therapy. Among HCC pts with CTP-A, some are reclassified as CTP-B/C and were found to have significantly poorer prognosis in terms of shorter OS. Future validation of the predictive ability of our IGF-1 score may lead to adopting it as a stratification tool in clinical trials as well as to predict HCC outcome and guide therapy decision in routine practice. **Research Sponsor:** U.S. National Institutes of Health.

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Efficacy and safety of lenvatinib (LEN) in Korean patients (pts) with advanced hepatocellular carcinoma (aHCC): Multicenter retrospective analysis. *First Author: Jaekyung Cheon, Division of Hematology and Oncology, Department of Internal Medicine, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, South Korea

**Background:** LEN has demonstrated the efficacy and safety in pts with aHCC as first-line treatment in the pivotal REFLECT trial. Further evaluation in real-world setting is necessary to measure the clinical outcomes of LEN in daily practice. **Methods:** This is a multicenter retrospective analysis from 3 Korean referral cancer institutions. Between September 2018 and August 2019, a total of 74 pts received LEN for the management of BCLC B or C aHCC, and 66 pts who had at least one follow-up visit after the start of LEN were included in this analysis. **Results:** Median age was 58 years (range, 19-81), and 46 pts (69.7%) were male. Baseline characteristics were as follows; Child-Pugh class A/B/C in 46 (69.7%)/14 (21.2%)/6 (9.1%), BCLC B/C/D in 11 (5.5%)/2 (3.0%), prior systemic therapy was 25 (37.9%) including 14 (21.2%) with prior immune checkpoint inhibitors (ICIs). LEN was used as first-second/third to fourth lines of therapy in 41 (62.1%)/13 (19.7%)/12 (18.2%) pts, and 27 (40.9%) had extensive disease extent excluded in the REFLECT trial. With a median follow-up duration of 4.8 months (95% CI, 3.4-6.1), the median PFS and OS were 4.6 (95% CI, 3.2-6.0) and 7.5 months (mo) (95% CI, 3.7-11.2), respectively, in overall pts: first-line setting, 4.2 (95% CI, 3.2-5.2) and 6.5 mo (95% CI, 5.0-8.1), respectively; >= second-line setting, 6.1 mo (95% CI, 3.6-8.5) and not reached, respectively, in pts with prior ICIs, median PFS was 6.1 mo (95% CI, 5.1-8.8) and median OS was not reached. According to the RECIST v 1.1, response rates and disease control rate were 12.1% and 71.2%, respectively, in overall pts. The most common grade 3-4 toxicities were hyperbilirubinemia (n=9, 13.6%), AST elevation (n=7, 55.6%), diarrhea (n=4, 6.1%) at fatigue (n=4, 6.1%)

**Conclusions:** LEN was effective and well tolerated in pts with aHCC in Korean real-life setting. **Research Sponsor:** None.
Biliary tract cancer (BTC) in the elderly: A real-world tertiary cancer center experience. First Author: Massimiliano Salati, PhD Program in Clinical and Experimental Medicine, University of Modena and Reggio Emilia, Modena, Italy

**Background:** Although BTC is mostly a disease of the elderly, only limited data are available on the optimal management of this patient (pt) population. In fact, older pts are underrepresented in clinical trials and results are seldom reported by age group. In this study, we aimed at evaluating pattern of care and treatment outcome in BTC aged ≥70 years and comparing them with their younger counterparts. **Methods:** Medical records of BTC followed at the Modena Cancer Centre from 2007 and 2019 were retrospectively reviewed. Overall survival (OS) was estimated with the Kaplan-Meier curves and compared by log-rank test. Differences between categorical variables were assessed using the chi square test. Univariate and multivariate analyses were performed to assess the impact of covariates on survival. **Results:** A total of 120 BTC patients (49%) ≥70 were included in the analysis, 54% (64) were female, 47% (56) had ICCa, 41% (49) GBC, and 12% (15) eCCA. 68% (81) had unresectable locally advanced or metastatic disease. 32% (39) underwent surgical resection, 60% (72) were treated with first-line chemotherapy. Duration of treatment on to receive second-line (2L) did not differ between early or late responders. In the advanced disease setting, median OS was 8 months and was significantly worse than that of the younger counterparts (p=0.001). Older patients were less likely to receive 1L (p<0.001) and 2L (p=0.001) chemotherapy and doublet regimens (p=0.001). Female gender (p=0.031), ECOG PS 0 (p<0.001), stage III (p<0.001) and NLR>3 (p=0.001) were independently associated with a better prognosis in BTC. In the current AJCC staging, which significantly decreased survival in patients older than 70 years, even after adjusting for other factors (C+LND (OR:0.60; CI:0.44-0.81), RC (OR:0.52; CI:0.31-0.92)), the decreasing rate of metastasis-free survival (MFS) was 3.04-19.65 (p<0.001) and NLR (p<0.001). There was no significant difference between OS and baseline myopenia (p=0.4), ALBI grade (p=0.2), BCLC stage (p=0.5), up to 7 in or out (p=0.35), previous TKI treatment (p=0.15), metastasis (p=0.91), or vascular invasion (p=0.12). However, the patients who had decreased SMI had significantly poorer prognosis (p=0.028). In both groups, there was a significant difference in patients with SMI decreasing or without decreasing of SMI, such as baseline myopenia (p=0.7), ALBI grade (p=0.4), BCLC stage (p=1.0), Child Pugh score (p=0.8), age (p=0.6), sex (p=0.3), up to 7 in or out (p=0.1), previous TKI treatment (p=0.3), and relative dose intensity at 4 weeks (p=0.9). Conclusions: There was no significant correlation between baseline myopenia and OS. However, chronological decreasing of SMI for 8 weeks was a prognostic factor of BTC patients treated with lenvatinib (LEN). Therefore, monitoring and preventing of decreasing of skeletal muscle mass may be important. Research Sponsor: None.

Clinical outcome associated with neoadjuvant chemoradiation and orthotopic liver transplantation versus definitive chemoradiation in 49 patients with unresectable, hilar, or extrahepatic cholangiocarcinoma. First Author: Brady S. Laughlin, Mayo Clinic Arizona, Phoenix, AZ

**Background:** Our aim was to compare survival between patients receiving neoadjuvant chemoradiation and orthotopic liver transplantation (OLT group) versus definitive chemoradiation (CRT group) for extrahepatic hilar cholangiocarcinoma. Methods: 49 patients ≥70 in OLT group vs. 20 in CRT group with unresectable hilar/extrahepatic cholangiocarcinoma were treated at Mayo Clinic Arizona between Feb. 1998-Sept. 2019. Treatment included external beam radiation therapy (median 4500cGy) and boost (median 900cGy) with 5-fluorouracil (dose range 180-225 mg/m2) or capetcitabine (dose range 825-1000 mg/m2 BID) prior to or without OLT. Radiation boosts were delivered with EBRT or bile duct brachytherapy. Patients were between 27.9-94.3 years (median 64.3) at diagnosis. 18 patients had previous diagnosis of PSC. Rejection (IL 1L, while 29% (21) of the were on to receive second-line (2L). No differences in terms of both chance to receive surgery (p=0.59) and survival (p=0.25) were recorded compared to youngers. In the advanced disease setting, median OS was 8 months and was significantly worse than that of the younger counterparts (p<0.001). Older patients were less likely to receive 1L (p<0.001) and 2L (p=0.001) chemotherapy and doublet regimens (p=0.001). Female gender (p=0.031), ECOG PS 0 (p<0.001), stage III (p<0.001) and NLR>3 (p=0.001) were independently associated with a better prognosis in BTC. In the current AJCC staging, which significantly decreased survival in patients older than 70 years, even after adjusting for other factors (C+LND (OR:0.60; CI:0.44-0.81), RC (OR:0.52; CI:0.31-0.92)), the decreasing rate of metastasis-free survival (MFS) was 3.04-19.65 (p<0.001) and NLR (p<0.001). There was no significant difference between OS and baseline myopenia (p=0.4), ALBI grade (p=0.2), BCLC stage (p=0.5), up to 7 in or out (p=0.35), previous TKI treatment (p=0.15), metastasis (p=0.91), or vascular invasion (p=0.12). However, the patients who had decreased SMI had significantly poorer prognosis (p=0.028). In both groups, there was a significant difference in patients with SMI decreasing or without decreasing of SMI, such as baseline myopenia (p=0.7), ALBI grade (p=0.4), BCLC stage (p=1.0), Child Pugh score (p=0.8), age (p=0.6), sex (p=0.3), up to 7 in or out (p=0.1), previous TKI treatment (p=0.3), and relative dose intensity at 4 weeks (p=0.9). Conclusions: There was no significant correlation between baseline myopenia and OS. However, chronological decreasing of SMI for 8 weeks was a prognostic factor of BTC patients treated with lenvatinib (LEN). Therefore, monitoring and preventing of decreasing of skeletal muscle mass may be important. Research Sponsor: None.

Clinical outcome associated with neoadjuvant chemoradiation and orthotopic liver transplantation versus definitive chemoradiation in 49 patients with unresectable, hilar, or extrahepatic cholangiocarcinoma. First Author: Brady S. Laughlin, Mayo Clinic Arizona, Phoenix, AZ

**Background:** Our aim was to compare survival between patients receiving neoadjuvant chemoradiation and orthotopic liver transplantation (OLT group) versus definitive chemoradiation (CRT group) for extrahepatic hilar cholangiocarcinoma. Methods: 49 patients ≥70 in OLT group vs. 20 in CRT group with unresectable hilar/extrahepatic cholangiocarcinoma were treated at Mayo Clinic Arizona between Feb. 1998-Sept. 2019. Treatment included external beam radiation therapy (median 4500cGy) and boost (median 900cGy) with 5-fluorouracil (dose range 180-225 mg/m2) or capetcitabine (dose range 825-1000 mg/m2 BID) prior to or without OLT. Radiation boosts were delivered with EBRT or bile duct brachytherapy. Patients were between 27.9-94.3 years (median 64.3) at diagnosis. 18 patients had previous diagnosis of PSC. Rejection (IL 1L, while 29% (21) of the were on to receive second-line (2L). No differences in terms of both chance to receive surgery (p=0.59) and survival (p=0.25) were recorded compared to youngers. In the advanced disease setting, median OS was 8 months and was significantly worse than that of the younger counterparts (p<0.001). Older patients were less likely to receive 1L (p<0.001) and 2L (p=0.001) chemotherapy and doublet regimens (p=0.001). Female gender (p=0.031), ECOG PS 0 (p<0.001), stage III (p<0.001) and NLR>3 (p=0.001) were independently associated with a better prognosis in BTC. In the current AJCC staging, which significantly decreased survival in patients older than 70 years, even after adjusting for other factors (C+LND (OR:0.60; CI:0.44-0.81), RC (OR:0.52; CI:0.31-0.92)), the decreasing rate of metastasis-free survival (MFS) was 3.04-19.65 (p<0.001) and NLR (p<0.001). There was no significant difference between OS and baseline myopenia (p=0.4), ALBI grade (p=0.2), BCLC stage (p=0.5), up to 7 in or out (p=0.35), previous TKI treatment (p=0.15), metastasis (p=0.91), or vascular invasion (p=0.12). However, the patients who had decreased SMI had significantly poorer prognosis (p=0.028). In both groups, there was a significant difference in patients with SMI decreasing or without decreasing of SMI, such as baseline myopenia (p=0.7), ALBI grade (p=0.4), BCLC stage (p=1.0), Child Pugh score (p=0.8), age (p=0.6), sex (p=0.3), up to 7 in or out (p=0.1), previous TKI treatment (p=0.3), and relative dose intensity at 4 weeks (p=0.9). Conclusions: There was no significant correlation between baseline myopenia and OS. However, chronological decreasing of SMI for 8 weeks was a prognostic factor of BTC patients treated with lenvatinib (LEN). Therefore, monitoring and preventing of decreasing of skeletal muscle mass may be important. Research Sponsor: None.
The adherence to AASLD guidelines in treating patients with hepatocellular carcinoma: institutional experience. 
First Author: Ashish Manne, Medical Oncology, Mitchell Cancer Institute, The University of South Alabama, Mobile, AL

Background: The American Association for the Study of Liver Disease (AASLD) guidelines outline an algorithm for managing the treatment modality of choice for patients with hepatocellular carcinoma (HCC) based on Barcelona Clinic Liver Cancer (BCLC) stage. The AASLD guidelines have several limitations and the adherence rate has been reported to be low. The adherence to AASLD guidelines in treating patients with HCC was explored in this study.

Methods: Between 2017 and 2019, 106 patients with HCC were identified. In our cohort, 70 patients (66%) were discussed in the multidisciplinary tumor board (MTDB) and their first-line treatment modality was selected based on consensus recommendations from the MTDB team members. The adherence rate of MTDB recommendations to AASLD guidelines was calculated. Results: Median age was 65 (range 42-90). Males represented 84% while females represented 16%. Caucasians, African Americans and Asians represented 69%, 30% and 1%, respectively. BCLC stage 0, A, B, C and D represented 7%, 32%, 23%, 27% and 11%, respectively. First-line treatment modality of choice recommended by MTDB is summarized in Table 1. The overall adherence rate of MTDB recommendations to AASLD guidelines is 60%. For BCLC stage 0, A, B, C and D, the adherence rate was 60%, 86%, 44%, 58% and 25% respectively. Conclusions: Our MTDB recommendations adherence rate to AASLD guidelines was 60%. The reported low adherence rate to the guidelines suggest that AASLD guidelines would benefit from refinement and periodic update. Research Sponsor: None.

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<th>Systemic therapy BSC</th>
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Primary liver angiosarcoma and factors associated with improved outcomes: An analysis of the National Cancer Database. First Author: Prantesh Jain, Department of Hospital Medicine, Cleveland Clinic, OH, Cleveland, OH

Background: Primary liver angiosarcoma (LAS) is a rare and aggressive tumor of the liver. In this analysis of the national cancer database (NCDB) we sought the risk of mortality and factors associated with survival amongst patient diagnosed with LAS. Methods: Patients diagnosed with hepatocellular carcinoma (HCC) or LAS from 2004 - 2014 were identified in the NCDB. The Kaplan-Meier method with the log-rank test was used to calculate survival for HCC and LAS patients. Additional analyses were performed on the cohort with LAS to assess the impact of surgery, chemotherapy, radiation therapy (RT), and site type on overall survival (OS). Multivariable analyses using Cox proportional methods, adjusted for age, sex, Charlson/Deyo score, race, ethnicity, insurance status, facility location and type, surgery status, and chemotherapy status were performed to obtain adjusted hazard ratio (aHR).

Results: Total of 118,066 patients with HCC and 346 patients with LAS were identified in the database. Median survival for HCC patients was 11.9 months (95% CI:11.7-12.2) and 2.0 months for LAS patients (95% CI: 1.8 - 2.4). Risk of mortality was higher for patients with LAS compared to those with HCC (aHR: 95% CI: 2.33 (1.97 - 2.53), p < .0001). Among the LAS patients, those who received surgery had a median survival of 8.6 months (95% CI: 5.6 - 17.3), and 1.8 months for those who did not (95% CI: 1.48 - 1.94),| 4.13)| then those treated at a non-academic center (1.5 months, 95% CI: 1.2 - 1.8). Though, there was no significant difference in OS (aHR (95% CI): 0.48 (0.21 - 1.10), p = 0.082). A very small number of patients received chemotherapy or RT to conduct a meaningful analysis. Conclusions: Patients diagnosed with primary LAS have a worse OS compared to those with HCC. Amongst patients with primary LAS, surgical resection was associated with better OS overall. Treatment at an academic center is associated with better median survival, although OS did not reach statistical significance in our analysis. Research Sponsor: None.

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502 Poster Session (Board #B5), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Association of socioeconomic disparities with underutilization of palliative care in patients with metastatic foregut cancer. First Author: Michelle Ju, UT Southwestern, Dallas, TX

Background: Metastatic foregut cancers (MFC) are frequently associated with debilitating symptoms that have significant negative impact on patients’ quality of life. Palliative care (PC) is effective in mitigating disease-, psychological-, and treatment-related effects. However, PC remains heavily underutilized. The aim of our study was to characterize the rate of PC utilization in MFC and determine the impact of various clinicopathologic and socioeconomic factors associated with the receipt of PC. Methods: We conducted a retrospective review of 277,957 National Cancer Database patients diagnosed with MFC between 2004-2013. Chi-squared tests were used to analyze differences between groups. Logistic regression was performed to assess the impact of factors on the likelihood of receiving PC. Results: PC utilization increased among all groups over time (23.3% in 2004 vs. 14.7% in 2007-2010 vs. 16.4% in 2011-2013 for all cancers). Female sex, Medicaid, median income < $46,000/year, higher education level, higher Charlson/Deyo Score, and pancreatic or biliary cancers were associated with increased likelihood of PC interventions. Additionally, patients treated at an academic center or integrated network cancer program were more likely to receive PC than patients treated in the community setting. When receipt of PC was stratified by race, Hispanics were significantly less likely to have undergone palliative interventions compared to non-Hispanic Whites (OR 0.70). Patients with Medicare or private insurance were less likely to receive PC than those with Medicaid or uninsured patients or public insurance (44.7% vs 38.7% vs 7.2% respectively). Conclusions: Our study shows the discrepancies in survival between patients with differing insurance statuses. Of all insurance groups, those privately insured had the largest median survival. Research Sponsor: None.

503 Poster Session (Board #B6), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Sociodemographic characteristics as predictors of outcomes in hepatocellular carcinoma: A retrospective cohort study. First Author: Bryce David Beutler, University of Nevada, Reno School of Medicine-Department of Internal Medicine, Reno, NV

Background: There has been a rise of cholangiocarcinoma though the cause is unclear. Cholangiocarcinoma is more often than not incurable at diagnosis and associated with a high mortality rate. Our goal was to compare survival of patients with differing insurance types diagnosed with cholangiocarcinoma identified in the National Cancer Database (NCDB). Methods: We identified 5,638 patients with cholangiocarcinoma in the NCDB diagnosed between 2004-2014. Patients included were categorized as having no insurance, private insurance, Medicare, or Medicaid were included. Between-insurance survival differences were estimated by the Kaplan-Meier method and associated log-rank tests. Tukey-Kramer adjusted p < 0.05 indicated statistical significance. Results: Statistically significant survival differences were indicated between all insurance groups (all adjusted p < 0.05), such that privately insured patients had the highest median survival. The discrepancy in survival between uninsured and privately insured patients was the largest (65.6 months vs 13.1 months, respectively). Medicaid patients on average had a survival of 7.5 months, while Medicare patients had a median survival of 7.8 months. 28.8% of uninsured patients presented with stage I cholangiocarcinoma, whereas 34.5% of privately insured patients presented with stage I cholangiocarcinoma. More Medicare patients were treated at community cancer programs compared to privately insured patients (56.2% vs 30.7%, respectively). Likewise, more Medicare patients were treated at academic/research programs compared to those with private insurance, Medicaid, or those who were uninsured (44.7% vs 38.7% vs 7.2% vs 3.7%, respectively). Conclusions: Our study shows the discrepancies in survival between patients with differing insurance statuses. Of all insurance groups, those privately insured had the largest median survival. Research Sponsor: None.
504 Poster Session (Board #87), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

**Hepatobiliary Cancer**

**Impact of facility type, insurance status, and income on use of single agent chemotherapy (SACT) for advanced hepatocellular carcinoma (HCC): Analysis of National Cancer Database (NCDB). First Author: Richard T. Lee, The University of Texas MD Anderson Cancer Center, Houston, TX**

**Background:** This study analyzes the pattern of use of SACT in the treatment and survival of AHCC before and after sorafenib was FDA approved in late 2007.

**Methods:** Adult patients diagnosed with HCC and treated with only chemotherapy (CT) from 2004 - 2014 were identified in NCDB database. Patients were analyzed during 3 time frames: 2004-2006 (pre-sorafenib (PS)), 2007-2011 (early sorafenib (ES) and 2012-2014 (late sorafenib (LS)). Cox proportional hazards models and Kaplan-Meier method were used for analyses. **Results:** The NCDB contained 31,107 patients with HCC diagnosed from 2004-2014 and treated with CT alone. Patients were generally men (77.3%), >50 years of age (92.5%), and with a variety of T-stages - T1 (41.2%), T2 (23.9%), T3 (28.3%), and T4 (16.9%). The use of SACT was only 6.2% in the PS period, increased to 15.5% in the ES period, and to 22.3% in the LS period (p<0.0001). During this later period, the highest proportion of SACT is among academic and integrated network facilities (23.4%) as compared to community facilities (16.4%, p<0.0001). The MS of patients with HCC treated only with CT has improved significantly over the study periods from 10 months (95% CI: 9.5-10.6) to 12.5 months (12.0-12.9) to 15.6 months (15.6-16.4) to 19.9 months (19.2-20.5) (p<0.0001). Significant differences in MS were found between facility types in all time frames (Table). Multivariate analysis indicates worse outcomes for patients treated at community cancer programs (HR 1.66, 1.53-1.79) as compared to academic programs as well as for no insurance (HR 1.13, 1.05-1.22) and estimated household income of <36,000 (HR 1.61, 1.53-1.79) compared to ≥36,000.

**Conclusions:** Despite an overall improvement in survival for AHCC patients treated with only CT, significant differences in the utilization of SACT and survival exist by facility type, insurance status, and income. **Research Sponsor:** None.

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505 Poster Session (Board #88), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

**Early nutritional risk assessment by NRS 2002 to predict survival in patients with advanced biliary tract cancer. First Author: Se Eung Oh, Gangnam Severance Hospital, Seoul, South Korea**

**Background:** Biliary tract cancer (BTC) has heterogeneous disease with dismal prognosis. We investigated the predictors of overall survival (OS) among Korean patients with BTC according to their baseline nutritional risks estimated by Nutritional Risk Screening (NRS) 2002 score. **Methods:** From September 2006 to July 2017, we retrospectively reviewed the data of 601 patients with BTC. Data on demographic and clinical parameters were collected from electronic medical records, and overall survival (OS) and progression-free survival (PFS) was estimated using the Kaplan-Meier method. Stepwise Cox regression analysis was used to determine the factors associated with survival. **Results:** Patients with a NRS 2002 score ≤2 were classified as “no-risk,” those with a score of 3 were classified as “moderate-risk,” and those with a score of ≥4 were classified as “high-risk.” Survival analysis showed significant differences in the median OS according to the NRS 2002 groups: “no-risk” group: 12.6 months (95% CI: 11.5-13.7); “moderate-risk” group: 6.1 months (95% CI: 4.3-8.0); and “high-risk” group: 3.9 months (95% CI: 3.2-4.6) (p<0.0001). On the Cox’s regression analysis, NRS 2002 score came out as the most independent factor for OS (for “moderate-risk” HR 1.61, 95% CI 1.288-2.027, p<0.0001; for “high-risk”, HR 2.122, 95% CI 1.728-2.612, p<0.0001), compared with other prognostic factors including liver metastasis, peritoneal seeding, white blood cell count, platelet count, neutrophil-to-lymphocyte ratio, cholesterol, CEA, and CA19-9. **Conclusions:** Our study demonstrated OS of advanced BTC was strongly related to their baseline nutritional status assessed by NRS 2002. Constitutional nutritional assessment can help to improve patient prognosis through proactive and individualized nutritional intervention. Baseline nutritional status should be integrated for implementing prognostic scoring system, which can provide more sophisticated risk stratification of patients with metastatic BTC. **Research Sponsor:** None.

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506 Poster Session (Board #89), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

**Determination of quality of care for patients with hepatocellular carcinoma in Nova Scotia. First Author: Cathie Ouellet, University of Laval, Québec, QC, Canada**

**Background:** Hepatocellular carcinoma (HCC) is the most common primary malignancy found in the liver. Little is known about the outcomes of HCC patients in the province of Nova Scotia (NS). There is suggestion that closer proximity to tertiary care center provides better outcomes for HCC patients. We hypothesized that cancer care for HCC patients differs based on a patient’s accessibility to an academic cancer care center. **Methods:** A retrospective chart review of HCC patients diagnosed from 2015 to 2017, looking at referrals patterns, treatments and wait time was undertaken. Patients who live within the urban area of Halifax, NS (N = 97), where the academic cancer center is, was compared to patients who live outside Halifax (rural, N = 70). **Results:** 167 patients were identified with a diagnosis of HCC, which included 159 males and 28 females with median age of 68 years old at HCC diagnosis. During that period, only 35.3% of patients diagnosed with HCC had a tissue diagnosis and 67.7% had a baseline AFP (16% had an AFP > 400). Just over 76% were diagnosed based on clinical features. Surgical intervention occurred in 15.6% and local treatments including radiation and TACE occurred in 35.9% of patients. Referral rate to Medical Oncology (MO) was 73%, of which 34.1% of patients had seen a MO at the time of data cut off (09-15-2019). 22 patients were eligible for systemic therapy but only 14 patients received systemic treatment (sorafenib n = 14). **Conclusions:** Initial data suggests patients who live in Halifax appear to have better outcomes than those outside. Further analysis is required to identify what differs between the urban and rural centers accounting for the seen difference in survival. **Research Sponsor:** None.

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507 Poster Session (Board #810), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

**Comparison of the frequency of adverse events requiring interventions determined by telephonic follow up in hepatocellular carcinoma patients treated with sorafenib and lenvatinib. First Author: Koki Morishita, Department of Pharmacy,National Cancer Center Hospital East, Kashiwa, Japan**

**Background:** The REFLECT trial demonstrated that lenvatinib is non-inferior to sorafenib for first-line treatment of unresectable hepatocellular carcinoma (HCC). However, no comparison of the frequency of adverse events (AE) occurring requiring interventions has been reported yet between uHCC patients receiving sorafenib and those receiving lenvatinib. At the National Cancer Center Hospital East, Japan, pharmacists conduct telephone follow-up (TF) during the first month after the start of treatment with sorafenib or lenvatinib in uHCC patients, for the purpose of detecting and treating AE early. The aim of this study was to reveal the frequency of AEs requiring interventions between patients receiving sorafenib and those receiving lenvatinib, based on TF. **Methods:** The characteristics, AEs and contents of intervention by TF of 56 uHCC patients who had been started on treatment with sorafenib or lenvatinib were reviewed retrospectively. The study subjects were 33 patients initiated on lenvatinib treatment and monitored by TF from March 2017 to March 2018 (Group S) and 23 patients initiated on lenvatinib treatment and monitored by TF from March 2018 to March 2019 (Group L). **Results:** The total numbers of TFs in Group S and Group L were 91 and 48, respectively. The rate of AEs requiring interventions was significantly higher in Group S as compared to Group L (22/33 vs. 17/48; p = 0.032). The frequencies of the interventions, including use of supportive treatments (A), withdrawal of sorafenib or lenvatinib (B), and medical examination (C), differed between the two groups (A+B+C: Group S, 85/3 times vs. Group L, 2/0/0 times). The most frequently observed AE that necessitated intervention in Group S was the hand-foot syndrome (HFS) (75.0%, 12/16). **Conclusions:** The frequency of interventions for AEs appears to be higher in uHCC patients receiving sorafenib than in those receiving lenvatinib. Although a great number of patients taking sorafenib had HFS early detection of the symptoms through TF contributed to prevention of treatment withdrawal on account of AEs. **Research Sponsor:** None.

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Hepatic adverse events during treatment with immune checkpoint inhibitors (ICI) in cancer patients: A territory-wide patient cohort study.

First Author: Stephen Lam Chan, Department of Clinical Oncology, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, China

Background: Hepatic adverse events (AEs) are commonly encountered during ICI treatment in cancer. We evaluated the incidence and impact of hepatic AEs in a territory-wide cohort of 1509 patients who received ICI for cancer treatment.

Methods: This is a territory-wide retrospective observational cohort study in Hong Kong. We identified patients through the regional hospital database (CDBMR), based on the drug record of ICI from 1 January 2014 to 30 October 2018. All liver functions before, during, and at 3-month after ICI, were retrieved. Hepatic AEs were graded according to CTCAE 4.0. Results: The mean age was 60 years and 65.4% were male with the commonest malignancies being lung cancer (37.0%), liver cancer (17.0%) and gastrointestinal (GI) cancer (8.4%). Grade 1-2 and grade 3-4 hepatic AE occurred 39.8% and 23.3% of patients, respectively, during or within 3 months after ICI. During ICI, 39.5% developed grade 1-2 and 13.0% had grade 3-4 hepatic AE. The most common manifestations of hepatic AE occurred as elevation of ALT/AST (grade 1-2: 38.7%; grade 3-4: 10.3%). The median time of duration from ICI 1st dose to hepatic ≥ Grade 3 AE was 54 days (IQR: 22-124).

Patients with liver cancer were more likely to develop hepatic ICI (grade 1: 27.4%; grade 3-4: 55.5%). In all patients and cancer subgroup, patients with grade 3-4 hepatic AE had worse OS than grade 1-2 hepatic AE. (Table). Conclusions: Hepatic AEs occur in more than half of the patients receiving ICI, with over 20% being grade 3-4 AE. Regardless of tumor types, development of hepatic AE during ICI is associated with poor prognosis. Research Sponsor: None.

12-month overall survival rate.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Without hepatic AE</th>
<th>With hepatic AE</th>
<th>P value#</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1-2</td>
<td>48.9% (42.3%-55.5%)</td>
<td>38.9%</td>
<td>0.001</td>
</tr>
<tr>
<td>Grade 3-4</td>
<td>27.4% (24.0%-30.8%)</td>
<td>18.3%</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Grade 1-2 | Grade 3-4 | P value# |
<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>48.9%</td>
<td>27.4%</td>
</tr>
<tr>
<td>Liver cancer</td>
<td>39.6%</td>
<td>18.3%</td>
</tr>
<tr>
<td>GI cancer</td>
<td>24.2%</td>
<td>23.3%</td>
</tr>
</tbody>
</table>

Effect of neoadjuvant immunotherapy and targeted therapies on surgical resection in patients with solid tumours: A systematic review and meta-analysis.

First Author: Pablo Emilio Serrano Ayar, McMaster University, Department of Surgery, Division of General Surgery, Hamilton, ON, Canada

Background: Neoadjuvant immunotherapy with anti-programmed cell death protein-1 (PD-1) or anti-programmed cell death ligand-1 (PD-L1) and tyrosine kinase inhibitor (TKI) therapy is currently being used to treat certain solid tumours to delay surgical resection. Results suggested that patients obtained celecoxib, parecoxib or oxycodone once every 12 hours can have the same level of analgesic effect during each time period of 4-30 minutes.

Results: The results suggested that patients obtained celecoxib, parecoxib or oxycodone once every 12 hours can have the same level of analgesic effect during each time period of 4-30 minutes. The pooled proportion of patients undergoing TACE was 62% (95% CI 0.02 to 0.32) in the PD-1 therapy group and 29% (95% CI -0.10 to 1.03) in the TKI group. The pooled serious adverse events rate was 17% (95% CI 0.02 to 0.32) in the PD1-PD1 immunotherapy or TKI therapy. Random-effects model was used to estimate the pooled proportion of patients undergoing planned resection, and weights were estimated using inverse variance method. Statistical heterogeneity test was calculated using the I² and chi-squared test.

Results: From 368 relevant articles, eleven studies with a total of 382 patients receiving neoadjuvant PD1 immunotherapy (n = 234) or neoadjuvant TKI therapy (n = 148) were analyzed. The types of tumours included hepatic, colorectal carcinoma (1 study), renal cell carcinoma (8 studies), bladder carcinoma (1 study) or non-small cell lung cancer (1 study). The pooled proportion of patients who completed planned surgical resection after neoadjuvant therapy was 95% (95% CI 0.92 to 0.99). The overall partial response rate prior to surgery was 12% (95% CI 0.07 to 0.16) in the PD1 therapy group and 46% (95% CI 0.12 to 0.70) in the TKI group. The pooled serious adverse events was 17% (95% CI 0.02 to 0.32) in the PD1 therapy group and 29% (95% CI -0.10 to 0.68) in the TKI group. For all patients receiving neoadjuvant therapy, the pooled median overall survival was 23.41 months (95% CI 16.21 to 30.62) and median progression free survival was 7.74 months (95% CI 4.41 to 10.51).

Conclusions: Neoadjuvant PD1 or TKI therapy prior to surgery for solid tumours is safe, does not delay surgical resection and can result in a partial radiological response prior to surgery. Research Sponsor: None.

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Nivolumab (NIVO) + ipilimumab (IPI) combination therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC): Subgroup analyses from CheckMate 040. First Author: Aiwi Ruth He, Georgetown University Hospital, Washington, DC

Background: NIVO monotherapy is approved in the United States and other countries for pts with HCC treated with sorafenib (SOR) based on CheckMate 040 (NCT01658878) results, which reported 14% objective response rate (ORR) and 16-month median overall survival (mOS; E+Khoueiry et al. Lancet 2017). Primary efficacy and safety of NIVO + IPI in pts with aHCC previously treated with SOR were presented recently (Yau et al. J Clin Oncol 2019). Here, we will present subgroup analyses from this study. Methods: Pts were randomized to 3 arms: (A) NIVO 1 mg/kg + IPI 3 mg/kg Q3W (4 doses) or (B) NIVO 3 mg/kg + IPI 1 mg/kg Q3W (4 doses), each followed by NIVO 240 mg Q2W, or (C) NIVO 3 mg/kg Q4W. Treatment continued until intolerable toxicity or disease progression. Primary endpoints included safety/tolerability, ORR, and duration of response (DOR; investigator assessment per RECIST v1.1). Key secondary endpoints included disease control rate (DCR), OS, and progression-free survival (PFS; blinded independent central review [BICR] per RECIST v1.1); key exploratory endpoints included ORR (BICR per RECIST v1.1). Dose cut-off was January 2019. Results: A total of 148 pts were randomized. Minimum OS follow-up from last pt randomization date to data cutoff was 28 months. At baseline, 34% of all pts had vascular invasion; 82% had extrahepatic spread; and 91% had Barcelona Clinic Liver Cancer stage C. 84% discontinued SOR because of disease progression and 14% because of toxicity. For all treated pts, ORR was 39% (7% had complete response), with median DOR of 17 months; DCR was 49%; the 30-month OS rate was 37%. NIVO + IPI was well tolerated; 38% of pts had grade 4 treatment-related adverse events (TRAEs) most common any grade: pruritus and rash; most common grade 3-4: aspartate aminotransferase increase and lipase increase; 5% had grade 3-4 TRAEs leading to discontinuation. Subgroup analyses based on duration of prior SOR therapy and other pt characteristics will be presented. Conclusions: NIVO + IPI led to meaningful benefit with manageable safety profile in pts previously treated with SOR. NIVO + IPI may provide a new treatment option for these pts. Clinical trial information: NCT01658878. Research Sponsor: Bristol-Myers Squibb.

Effect of postoperative apatinib treatment after resection of hepatocellular carcinoma with portal vein invasion: A phase II study. First Author: Hui-Chuan Sun, Liver Cancer Institute and Zhongshan Hospital, Fudan University, Shanghai, China

Background: Adjuvant therapy for hepatocellular carcinoma (HCC) is an unmet need. Apatinib, a VEGFR2 inhibitor, showed antitumor activity and tolerability for HCC pts in a phase Ia study. We aimed to explore the safety and efficacy of apatinib in adjuvant settings after resection of HCC with portal vein tumor thrombosis (PVTT). Methods: This was a single-center single-arm phase 2 study. The key inclusion criteria were: (1) pathologically confirmed HCC; (2) underwent liver resection with curative intention within 4-6 wk before recruitment; (3) PVTT and genomic variables and OS were assessed using uni- and multivariable Cox model for OS. Estimated using the Kaplan-Meier method. The association between clinical endpoints included ORR (BICR per RECIST v1.1). Here, we will present subgroup analyses from this study. Methods: Pts were randomized to 3 arms: (A) NIVO 1 mg/kg + IPI 3 mg/kg Q3W (4 doses) or (B) NIVO 3 mg/kg + IPI 1 mg/kg Q3W (4 doses), each followed by NIVO 240 mg Q2W, or (C) NIVO 3 mg/kg Q4W. Treatment continued until intolerable toxicity or disease progression. Primary endpoints included safety/tolerability, ORR, and duration of response (DOR; investigator assessment per RECIST v1.1). Key secondary endpoints included disease control rate (DCR), OS, and progression-free survival (PFS; blinded independent central review [BICR] per RECIST v1.1); key exploratory endpoints included ORR (BICR per RECIST v1.1). Dose cut-off was January 2019. Results: A total of 148 pts were randomized. Minimum OS follow-up from last pt randomization date to data cutoff was 28 months. At baseline, 34% of all pts had vascular invasion; 82% had extrahepatic spread; and 91% had Barcelona Clinic Liver Cancer stage C. 84% discontinued SOR because of disease progression and 14% because of toxicity. For all treated pts, ORR was 39% (7% had complete response), with median DOR of 17 months; DCR was 49%; the 30-month OS rate was 37%. NIVO + IPI was well tolerated; 38% of pts had grade 4 treatment-related adverse events (TRAEs) most common any grade: pruritus and rash; most common grade 3-4: aspartate aminotransferase increase and lipase increase; 5% had grade 3-4 TRAEs leading to discontinuation. Subgroup analyses based on duration of prior SOR therapy and other pt characteristics will be presented. Conclusions: NIVO + IPI led to meaningful benefit with manageable safety profile in pts previously treated with SOR. NIVO + IPI may provide a new treatment option for these pts. Clinical trial information: NCT01658878. Research Sponsor: Bristol-Myers Squibb.

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Grade 3 or 4 adverse events a

<table>
<thead>
<tr>
<th>Parameter, n (%)</th>
<th>Part 1 (n=4)</th>
<th>Part 2 (n=24)</th>
<th>Overall (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best Overall Response a</td>
<td>0</td>
<td>4 (16.7)</td>
<td>4 (14.3)</td>
</tr>
<tr>
<td>Complete response (CR)</td>
<td>0</td>
<td>1 (4.2)</td>
<td>1 (3.6)</td>
</tr>
<tr>
<td>Partial response (PR)</td>
<td>0</td>
<td>3 (12.5)</td>
<td>3 (10.7)</td>
</tr>
<tr>
<td>Stable disease (SD)</td>
<td>6</td>
<td>18 (75.0)</td>
<td>24 (85.7)</td>
</tr>
<tr>
<td>Progression (PD)</td>
<td>1</td>
<td>4 (16.7)</td>
<td>5 (17.9)</td>
</tr>
<tr>
<td>OrR* a, %</td>
<td>4 (14.3)</td>
<td>22 (91.7)</td>
<td>26 (92.9)</td>
</tr>
<tr>
<td>VAP, Gy</td>
<td>92</td>
<td>92</td>
<td>92</td>
</tr>
</tbody>
</table>

a Not evaluable

Conclusions: Median follow-up was 12.6 months. Median age was 61.3 years and 57% were male. The most common primary site was colorectal (42%), followed by pancreas (25%) and non-small cell lung cancer (10%). 42% had colorectal adenocarcinoma, 46% had other adenocarcinoma, and 12% had other histology. A BRAF/RAS family mutation, extra-hepatic metastases, exclusion of liver metastases from RT fields, lower BED, and concurrent radiosensitizing chemotherapy were associated with worse OS. This may inform patient selection and RT delivery for aggressive local therapy for liver metastases. Research Sponsor: None.

Clinical and genomic factors associated with outcome following ablative radiotherapy for oligometastatic and oligoprogressive liver tumors. First Author: Danielle Sara Bitterman, Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA

Background: There is increasing use of ablative radiotherapy (RT) for oligometastatic and/or oligoprogressive cancer, but the population who may benefit from this more aggressive treatment remains poorly defined. We hypothesized that the identified factors associated with improved outcomes following ablative RT for oligometastatic/oligoprogressive liver tumors. Methods: We retrospectively analyzed 106 patients who had tumor genomic profiling and received a 5, 6, or 15-fraction course of ablative RT for liver metastases from aHCC. The interval of the ablative treatment was calculated from the last dose of chemotherapy for patients who did not continue treatment through RT. Overall survival (OS) was estimated using the Kaplan-Meier method. The association between clinical and genomic variables and OS were assessed using uni- and multivariable Cox regression analyses. Results: Median follow-up was 12.6 months. Median age was 61.3 years and 57% were male. The most common primary site was colorectal (42%), followed by pancreas (25%) and non-small cell lung cancer (10%). 42% had colorectal adenocarcinoma, 46% had other adenocarcinoma, and 12% had other histology. A BRAF/RAS family mutation, extra-hepatic metastases, exclusion of liver metastases from RT fields, lower BED, and concurrent radiosensitizing chemotherapy were associated with worse OS. This may inform patient selection and RT delivery for aggressive local therapy for liver metastases. Research Sponsor: None.
516 Poster Session (Board #B19), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM
Major impact of personalized dosimetry using 90Y loaded glass microspheres SIRT in HCC: Final overall survival analysis of a multicenter randomized phase II study (DOSISPHERE-OI), First Author: Etienne Garin, Cancer Institute Eugène Marquis, Rennes, France
Background: 90Y loaded microsphere SIRT (radioembolization) is a treatment option for advanced HCC. However, personalized dosimetric endpoints are currently used. The goal of this study was to compare the efficacy of 90Y loaded glass microsphere SIRT in HCC using a standard versus a personalized dosimetric approach. Methods: DOSISPHERE-OI was a multicenter, randomized phase 2 trial in unresectable HCC patients with at least one tumor ≥7cm. Treatment arm was randomly assigned (t) to standard dosimetry arm (SDA), with a goal to deliver 120±20Gy to the treated volume or to personalized dosimetry arm (PDA) with a goal to deliver at least 205Gy to the index lesion. The primary endpoint was the response rate (RR) of the index lesion according to EASL criteria. Secondary endpoints included dose response evaluation, safety and overall survival (OS). Results: Sixty HCC patients were randomized (PDA: 31, SDA: 29, intent to treat population=ITTP), and 56 treated (28 in each arm). RR was significantly increased in the PDA versus the SDA, in the ITTP, respectively 64.5% versus 31% (p=0.0095) as in the安全性 population (SP), treatment effectiveness was received, personalized 35, standard 21, respectively 74.3% versus 14.3% (p<0.0001). Median OS was significantly increased in the PDA versus the SDA, in the ITTP, respectively 26.7m (CI 95%:17.7- NR) versus 10.6m (CI 95%:6.18, p=0.0096, HR=0.42 (95%CI:0.25, 0.826), n=56, as in the SP treatment effectiveness received, personalized 35, standard 21, respectively 26.7 (95%CI:17.7- NR) versus 9.5m (CI 95%:4.8-14.9), p=0.015, HR=0.342 (95%CI:0.171-0.683), p=0.0023. Median OS was 26.7m (CI 95%:13.5- NR) versus 6.0m (CI 95%:3.8-14.9) for the patients who received a tumor dose ≥200Gy in the DOR respectively, as in the ITTP, p=0.0015, HR=0.354 (95%CI:0.171- 0.735), p=0.0063. Treatment-related clinically relevant hepatic grade 3 AEs were observed in 5.7% and 14.2% of the patients of the PDA and SDA arms, respectively, (p=n.s.). Conclusions: MAIA SPECT/CT based personalized dosimetry is safe and dramatically increased RR and OS of HCC patients. These results question the interpretation of all phase 3 trials of SIRT designed without per- ersonalized dosimetry in HCC. Clinical trial information: 2015-A00894-45. Search Sponsor: BTG UK Ltd.

518 Poster Session (Board #B21), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM
Updated efficacy and safety of KEYNOTE-224: A phase II study of pembrolizumab (pembro) in patients with advanced hepatocellular carci- nomia (HCC), First Author: Masatoshi Kudo, Kindai University Faculty of Medicine, Osaka, Japan
Background: Pembrolizumab (pembro) in patients with advanced hepatocellular carcinoma (HCC). Results: Of a 2 y follow-up analysis of the efficacy and safety of pembrolizumab, this study is presented here. Eligible patients had histologically confirmed HCC, radiographic progression on/intolerance to sorafenib and disease not amenable to curative treatment, Child Pugh A, ECOG PS 0-1 and BCLC stage C or B. Pts received pembrol 200 mg iv Q3W for 2 y or until disease progression, un- acceptable toxicity, consent withdrawal or investigator decision. Results: Individuals assessed were 99 99.9% patients data were evaluat- ed for AEs because a total of 224 patients in all pembrolizumab arms were evaluable for AEs. Median OS was 17.0 mo (95%CI:11.4-27.1) and was similar across subgroups. Median DOR was 30.8% (95% CI 21.0-39.8) and was similar across subgroups. Median OS was 17.0 mo (95%CI:11.4-27.1) and was similar across subgroups.

519 Poster Session (Board #B22), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM
Real-world treatment patterns and survival in patients (pts) with hepato- cellular carcinoma in the United States, First Author: Michael Morse, Duke University Medical Center, Durham, NC
Background: Outcomes in pts with hepatocellular carcinoma (HCC) vary by epidemiology, degree of hepatic dysfunction and tx. We analyzed the relationship between tx patterns and outcomes to help characterize emerging clinical data in the context of contemporary disease management. Methods: Retrospective observational study of the Flatiron Health de-identified electronic health record-derived database to analyze the relationship between first recorded tx (1tx) and overall survival (OS) in pts diagnosed with HCC (any stage) Jan 2011 to Nov 2018. Tx categories included transplant, resection/SBRT/ RFA. TACE/TARE/TAE, tyrosine kinase inhibitor (TKI), cancer immunotherapy (CIT), and others. Descriptive statistics were used to summarize tx distribution and pt characteristics. Results: A total of 2343 pts with HCC were categorized by 1tx: transplant (n = 35), resection/SBRT/RFA (n = 408), TACE/TARE/TAE (n = 830), TKI (n = 75), and CIT (n = 20). Pt demographics were generally similar across txs (Table). Overall, pts with HCC had a median OS of 16.6 mo; varying from 71.5 mo in pts receiving systemic tx for HCC to < 12 mo (TKI, CIT, and others). Discussion: We found that pts with advanced HCC receiving systemic tx for HCC have poor prognoses in clinical practice. Despite the limitations of data availability, this study showed a substantial unmet need for more effective HCC tx options. Search Sponsor: F. Hoffmann-La Roche, Ltd.
Optimal timing of radiotherapy for incomplete transarterial chemoembolization in BCLC stage B hepatocellular carcinoma. First Author: Hwa Kyung Byun, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea

Background: Numerous studies have reported on the efficacy of radiotherapy (RT) after incomplete transarterial chemoembolization (TACE). However, the optimal timing of RT remains unclear. This study investigated the optimal time of initiating RT for incomplete TACE in patients with BCLC stage B hepatocellular carcinoma (BCLC-B HCC). Methods: Between 2001 and 2016, 116 lesions in 104 patients with BCLC-B HCC were treated with RT after TACE. The time interval between the last session of TACE and initiation of RT was obtained from medical records and analyzed retrospectively. The optimal cut-off time interval that maximized the difference in local failure-free rate (LFFR) was determined using maximally selected rank statistics. Results: The median duration between TACE and RT was 26 (range: 2-165) days. Median number of TACE treatments on the target lesion before RT was 2; median tumor size was 7 cm. At a median follow-up of 18 (range: 3-160) months, the median overall survival was 18 months. The probability of local control increased as the time interval between TACE and RT decreased. The optimal cut-off value of the time interval was 5 weeks. With the cut-off of 5 weeks, 65 and 39 patients were classified into early and late RT groups, respectively. The early RT group had significantly poorer Child-Pugh class and higher alpha-fetoprotein levels. Most characteristics including tumor size (7 cm vs. 6 cm; P = .344) were not significantly different between the groups. One-year LFFR was significantly higher in the early RT group (94.6% vs. 70.8%; P = .005). On multivariate analysis, early RT was an independent predictor of favorable LFFR (hazard ratio: 3.82, 95% confidence interval: 1.64-8.88, P = .002). Conclusions: The optimal time for the administration of RT for incomplete TACE is within 5 weeks following TACE. Early administration of RT within 5 weeks after TACE was associated with better local control. Research Sponsor: None.

Optimal timing of radiotherapy for incomplete transarterial chemoembolization in BCLC stage B hepatocellular carcinoma. First Author: Hwa Kyung Byun, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea

Background: Numerous studies have reported on the efficacy of radiotherapy (RT) after incomplete transarterial chemoembolization (TACE). However, the optimal timing of RT remains unclear. This study investigated the optimal time of initiating RT for incomplete TACE in patients with BCLC stage B hepatocellular carcinoma (BCLC-B HCC). Methods: Between 2001 and 2016, 116 lesions in 104 patients with BCLC-B HCC were treated with RT after TACE. The time interval between the last session of TACE and initiation of RT was obtained from medical records and analyzed retrospectively. The optimal cut-off time interval that maximized the difference in local failure-free rate (LFFR) was determined using maximally selected rank statistics. Results: The median duration between TACE and RT was 26 (range: 2-165) days. Median number of TACE treatments on the target lesion before RT was 2; median tumor size was 7 cm. At a median follow-up of 18 (range: 3-160) months, the median overall survival was 18 months. The probability of local control increased as the time interval between TACE and RT decreased. The optimal cut-off value of the time interval was 5 weeks. With the cut-off of 5 weeks, 65 and 39 patients were classified into early and late RT groups, respectively. The early RT group had significantly poorer Child-Pugh class and higher alpha-fetoprotein levels. Most characteristics including tumor size (7 cm vs. 6 cm; P = .344) were not significantly different between the groups. One-year LFFR was significantly higher in the early RT group (94.6% vs. 70.8%; P = .005). On multivariate analysis, early RT was an independent predictor of favorable LFFR (hazard ratio: 3.82, 95% confidence interval: 1.64-8.88, P = .002). Conclusions: The optimal time for the administration of RT for incomplete TACE is within 5 weeks following TACE. Early administration of RT within 5 weeks after TACE was associated with better local control. Research Sponsor: None.

Optimal timing of radiotherapy for incomplete transarterial chemoembolization in BCLC stage B hepatocellular carcinoma. First Author: Hwa Kyung Byun, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea

Background: Numerous studies have reported on the efficacy of radiotherapy (RT) after incomplete transarterial chemoembolization (TACE). However, the optimal timing of RT remains unclear. This study investigated the optimal time of initiating RT for incomplete TACE in patients with BCLC stage B hepatocellular carcinoma (BCLC-B HCC). Methods: Between 2001 and 2016, 116 lesions in 104 patients with BCLC-B HCC were treated with RT after TACE. The time interval between the last session of TACE and initiation of RT was obtained from medical records and analyzed retrospectively. The optimal cut-off time interval that maximized the difference in local failure-free rate (LFFR) was determined using maximally selected rank statistics. Results: The median duration between TACE and RT was 26 (range: 2-165) days. Median number of TACE treatments on the target lesion before RT was 2; median tumor size was 7 cm. At a median follow-up of 18 (range: 3-160) months, the median overall survival was 18 months. The probability of local control increased as the time interval between TACE and RT decreased. The optimal cut-off value of the time interval was 5 weeks. With the cut-off of 5 weeks, 65 and 39 patients were classified into early and late RT groups, respectively. The early RT group had significantly poorer Child-Pugh class and higher alpha-fetoprotein levels. Most characteristics including tumor size (7 cm vs. 6 cm; P = .344) were not significantly different between the groups. One-year LFFR was significantly higher in the early RT group (94.6% vs. 70.8%; P = .005). On multivariate analysis, early RT was an independent predictor of favorable LFFR (hazard ratio: 3.82, 95% confidence interval: 1.64-8.88, P = .002). Conclusions: The optimal time for the administration of RT for incomplete TACE is within 5 weeks following TACE. Early administration of RT within 5 weeks after TACE was associated with better local control. Research Sponsor: None.

Optimal timing of radiotherapy for incomplete transarterial chemoembolization in BCLC stage B hepatocellular carcinoma. First Author: Hwa Kyung Byun, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea

Background: Numerous studies have reported on the efficacy of radiotherapy (RT) after incomplete transarterial chemoembolization (TACE). However, the optimal timing of RT remains unclear. This study investigated the optimal time of initiating RT for incomplete TACE in patients with BCLC stage B hepatocellular carcinoma (BCLC-B HCC). Methods: Between 2001 and 2016, 116 lesions in 104 patients with BCLC-B HCC were treated with RT after TACE. The time interval between the last session of TACE and initiation of RT was obtained from medical records and analyzed retrospectively. The optimal cut-off time interval that maximized the difference in local failure-free rate (LFFR) was determined using maximally selected rank statistics. Results: The median duration between TACE and RT was 26 (range: 2-165) days. Median number of TACE treatments on the target lesion before RT was 2; median tumor size was 7 cm. At a median follow-up of 18 (range: 3-160) months, the median overall survival was 18 months. The probability of local control increased as the time interval between TACE and RT decreased. The optimal cut-off value of the time interval was 5 weeks. With the cut-off of 5 weeks, 65 and 39 patients were classified into early and late RT groups, respectively. The early RT group had significantly poorer Child-Pugh class and higher alpha-fetoprotein levels. Most characteristics including tumor size (7 cm vs. 6 cm; P = .344) were not significantly different between the groups. One-year LFFR was significantly higher in the early RT group (94.6% vs. 70.8%; P = .005). On multivariate analysis, early RT was an independent predictor of favorable LFFR (hazard ratio: 3.82, 95% confidence interval: 1.64-8.88, P = .002). Conclusions: The optimal time for the administration of RT for incomplete TACE is within 5 weeks following TACE. Early administration of RT within 5 weeks after TACE was associated with better local control. Research Sponsor: None.
Baseline liver function and outcomes in the phase III REFLECT study in patients with unresectable hepatocellular carcinoma (hHCC). First Author: Arndt Vogel, Hannover Medical School, Hannover, Germany

Background: Lenvatinib (LEN) is approved for first-line treatment of hHCC. Baseline (BL) liver function (Child-Pugh score [CPS] and albumin-bilirubin grade [LABI]) was prognostic in hHCC patients (pts) who received sorafenib (SOR) but has not been assessed with LEN in hHCC. Here, we report post hoc analysis of BL liver function and efficacy/safety outcomes from the phase 3 REFLECT study. Methods: Overall survival (OS), progression-free survival (PFS), objective response rate (ORR), and safety were stratified by BL ALBI or CPS. OS and PFS were estimated by Kaplan-Meier method. Independent radiologic review utilized mRECIST criteria for ORR. Safety was assessed using NCI-CTCAE, version 4.0. Results: Liver function measured by ALBI and CPS seemed to be prognostic for OS and median OS [95% CI]: 13.9 [11.6-16.0] v 10.6 [8.3-13.5] mo; HR: 0.781; 95% CI, 0.611-0.995) in overall cohort and 45% in Asian subgroup and improved PFS v PBO. Safety was consistent with that previously reported in pembro studies. No HBV/HCV flares identified. Conclusions: Pembro reduced risk for death by 22% in overall cohort and 45% in Asian subgroup and improved PFS v PBO. Safety was comparable to that of pembro monotherapy. Results are consistent with KEYNOTE-240 (NCT02702401) and KEYNOTE-224 (NCT02702244) in Asian patients and are licensed in Japan. Pembro may support a favorable risk-benefit balance for second-line pembro in hHCC.

Poster Session (Board #C5), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Nivolumab (NIVO) and drug eluting bead transarterial chemoembolization (deb-TACE): Preliminary results from a phase I study of patients (pts) with liver limited hepatocellular carcinoma (HCC). First Author: James J. Harding, Memorial Sloan Kettering Cancer Center, New York, NY

Background: Regional therapies in HCC impact the immune microenvironment and may augment the effects of systemic checkpoint inhibitors. Methods: This is a multicenter phase 1 study of NIVO and deb-TACE in unresectable HCC pts (BCLC Stage B) and Child Pugh A cirrhosis (NCT03134270). The primary objective is to assess safety. Secondary objectives include response rate by RECIST v1.1, progression-free and overall survival by Kaplan-Meier methodology, and blood/tumor immune correlates. A < 3 design sequentially evaluates 3 cohorts of differing schedules of NIVO relative to deb-TACE. Deb-TACE (75mg of doxorubicin) is administered on Day 0. NIVO is dosed at 240mg IV every 14 days for 1 year (Cohort I; NIVO begins day +14 after deb-TACE; Cohort 2, interrupted NIVO dosing begins at Day 28 but is held on Day 35 and redose on Day 42; Cohort 3, continuous NIVO dosing begins on Day 28 without interruption). Results: As of July 2019, 9 pts have been treated [median 65 years (range: 54-76), male (89%), viral (44%)(HBV, 3 HCV), non- viral (56%) (2 EtOH, 1 NASH, 2 unknown) patients]. Median PFS, ORR, %b

Poster Session (Board #C6), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

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ABSTRACT

WITHDRAWN
Respiratory-gated magnetic resonance image guided radiation therapy for hepatocellular carcinoma: A pilot study, First Author: Hyun- Cheol Kang, Department of Radiation Oncology, Seoul National University Hospital, Seoul, South Korea

Background: Hypofractionated RT has shown encouraging results in hepatocellular carcinoma (HCC) patients. However, HCC adjacent to the gastrointestinal (GI) tract should be carefully treated using the high-precision irradiation technique due to risk of radiation damage. We evaluated the feasibility of a respiratory-gated magnetic resonance image guided radiation therapy (RgMRg-RT) for hepatocellular carcinoma (HCC).

Methods: Forty-three patients with HCC underwent RgMRg-RT in our hospital from 2015 to February 2019, including patients with Child-Pugh A/B7 cirrhosis and unresectable tumors near the gastrointestinal tract. The median radiation dose was 50 Gy (range, 25-60) and median fraction number was 5 (range, 4-15). Gating was performed based on real-time magnetic resonance image without an external surrogate. Results: The median follow-up period was 11.7 months (range, 3.6-37.9 months). The rates of local control of the target tumor at 6 months and 1 year were 90.2 and 86.9%, respectively. The overall survival rates at 6 months, 1, and 2 years were 84.3, 76.3, and 68%, respectively. The median distances from gross tumor to the esophagus, stomach, duodenum and colon were 6.1 (range, 1.9-14.3), 6.4 (0.13-3.4), 3.8 (0.13-5.5) and 4cm (0.3-13), respectively. A total of 15 tumors (45.5%) were located within 2cm of the gastrointestinal tract and 9 tumors (27%) within 1cm. Grades 3 treatment-related bleeding was observed in one patient and one patient had radiation-induced liver disease. Conclusions: Hypofractionated RgMRg-RT was a safe and potentially ablative therapy for HCC. RgMRg-RT is a good alternative treatment for patients with HCCs that are unsuitable for surgical resection or local ablative therapy. Research Sponsor: None.

Immunotherapy versus biologics as second-line therapy in advanced hepatocellular carcinoma (HCC), First Author: Mohammed Al-Jumayli, Kansas University Cancer Center, Kansas, KS

Background: Sorafenib or lenvatinib are the current frontline options for advanced HCC. Multiple biologic agents including multi-Tyrosine Kinase Inhibitors (TKI) cabozantinib & regorafenib have been recently approved for the previously treated population. Immunotherapy (IO) agent Nivolumab have also been approved in the same setting. Due to lack of prospective head to head comparison, there is no standardized way for alternating those agents beyond frontline. Methods: We performed a retrospective review of KU cancer registry. Patients with advanced HCC were divided into 2 groups based on the 2nd line systemic regimen (IO vs non-IO). Kaplan-Meier and Cox proportional hazards models were utilized to evaluate progression free survival (PFS) and overall survival (OS). Results: Between 2016-2019, 98 patients were identified, 41 received IO, while 57 received biologics. All patients had sorafenib as 1st line therapy. Most patients have ECOG 0-1 and Child-Pugh class A or B. 55% had hepatitis C, 6% hepatitis B and 27% have history of alcohol misuse. Almost 50% of patients have received prior liver directed therapy. Comparing IO vs non-IO groups, median PFS was 3.9 months vs 3 months and median OS was 10 months vs 10 months. There was no statistically significant difference in PFS & OS but there was a delay separation in the survival curve favoring IO. Similar outcome was seen in a subgroup analysis of the hepatitis C patients. Conclusions: This retrospective comparative review of current 2nd line regimens is one of the first & largest studies reported. In this study population, IO was not superior to multi-TKI as a 2nd line therapy. The late survival advantage in favoring IO might suggest a delay IO effect in a subgroup of patients. Future studies should define specific biomarkers that could predict response and allow treatment to be optimized depending on patient and tumor characteristics. Furthermore, combining IO plus multi-TKI might be a promising next step in HCC treatment. A number of ongoing trials are testing this strategy including our CAMILLA trial of Cabozantinib plus Durvalumab, currently enrolling patients at the University of Kansas Cancer Center NCT0353982. Research Sponsor: None.

Objective response (OR) by mRECIST to predict overall survival (OS) in patients with hepatocellular carcinoma (HCC) treated with sorafenib in the SILIUS trial, First Author: Masatoshi Kudo, Kindai University Faculty of Medicine, Osaka, Japan

Background: In SILIUS (NCT01243433) trial, combination of sorafenib and hepatic arterial infusion chemotherapy did not significantly improve OS in patients with advanced HCC compared with sorafenib alone (Kudo M, et al. Lancet Gastroenterol Hepatol 2018). In this study, we explored the relationship between OR and OS in the SILIUS trial. Methods: Association between OR and OS in patients treated with sorafenib (n = 102) were analyzed. The median OS of responders was compared with that of non-responders by using Mantel-Cox test to exclude guarantee-time bias. Landmark analyses were performed, as sensitivity analyses, and the effect on OS was evaluated by Cox regression analysis with OR as a time-dependent covariate, with other prognostic factors. Results: 02 of responders (n = 18) was significantly better than that of non-responders (n = 78) (p < 0.0001), where median OS was 27.2 (95% CI, 16.0-Not reached) months for responders and 8.9 (95% CI, 6.5-12.6) months for non-responders. Conclusion: Objective response by mRECIST achieved by sorafenib was an independent predictor of OS based on unstratified Cox regression analyses. Conclusions: In the SILIUS trial, OR achieved by sorafenib per mRECIST is an independent predictor of OS in patients with HCC. Research Sponsor: None.

Multivariable analysis of factors associated with OS.

<table>
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<th>Parameter</th>
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<td>PS (0 vs. 1)</td>
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SHR-1210 combined with GEMOX as first-line treatment in patients with advanced biliary tract cancer, First Author: Xiaofeng Chen, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China

Background: This study aimed to evaluate the efficacy and safety of SHR-1210 (a humanized anti-programmed cell death receptor 1 antibody) plus gemcitabine and oxaliplatin (GEMOX) as first line treatment in patients (pts) with biliary tract cancer (BTC). Methods: This was a single-arm, single-center, open-label, exploratory trial, which included advanced BTC pts. Pts received SHR-1210 (3mg/kg, total dose ≤200mg, ivd, D1/W2) combined with gemcitabine (800mg/m2, ivd, D1/W2) and oxaliplatin (85mg/m2, ivd, D2/W2). Combined chemotherapy lasted for no more than 12 cycles. Once chemotherapy toxicity occurred or at end of 12 cycle combined chemotherapy, pts with stable disease or objective response would continue to take SHR-1210 as single agent until disease progression or intolerable toxicity. The primary endpoint was the 6-month progression free survival (PFS) rate. Results: From February 2018 to April 2019, 37 eligible pts were enrolled. The median age was 64 (range 41-74) years, male/female was 70.3/29.7%, and bile duct cancer/gallbladder cancer was 59.5/40.5%. All 37 pts were included in the safety analysis. The overall AE incidence rate was 97.3%. The incidence of grade ≥3 AEs was 73.0%, which mainly included increased GGT (gammaglutamyltransferase, 18.9%), hypokalemia (18.9%), and fatigue (16.2%). Particularly, the incidence of fever is 73.0%, in which 2 pts experienced grade 3/4 fever. Among 36 evaluable pts, 19 pts got partial response (PR, 52.8%), 14 pts got stable disease (SD, 38.9%), and 3 pts progressive disease (PD, 8.3%) at best. The primary endpoint 6-month PFS rate was 50.0% (95% CI 32.4-65.4), which indicated that the primary endpoint of the study was reached, and mPFS was 6.2 months (95% CI 4.2-7.1). The 12-month overall survival (OS) rate was 50.5% (95% CI 30.6-67.4), and mOS was 121 months (95% CI 8.0-NA). Conclusions: This study has reached the pre-defined primary endpoint with a high response rate. Predictive biomarker analysis was reported in another abstract. Further study is needed to validate the efficacy of this combination. Clinical trial information: NCT0348676. Research Sponsor: None.
**Biomarker exploration for SHR-1210 plus GEMOX as first-line treatment in advanced biliary tract cancer.** First Author: Xiaofeng Chen, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China

**Background:** We conducted a trial to evaluate the efficacy and safety of SHR-1210 (a humanized anti-programmed cell death receptor 1 antibody) plus gemcitabine and oxaliplatin (GEMOX) as in untreated patients (pts) with biliary tract cancer (BTC) (NCT03486678). This study is to explore the predictive biomarkers for efficacy. **Methods:** Baseline lymphocyte count and lactate dehydrogenase (LDH) level were obtained from routine tests. Gene mutation and tumor mutation burden (TMB) from baseline tissue and blood samples were tested by the next generation sequencing (NGS) with a 425-gene panel. The expressions of PD-L1 and markers for lymphocyte, natural killer cells, and macrophages in baseline tumor tissue samples were analyzed by immunohistochemistry (IHC).

**Results:** The median progression free survival (PFS) and overall survival (OS) in this trial was 6.2m and 12.9m, respectively. Firstly, pts with normal LDH level had a better tendency for longer PFS (6.2m vs 5.0m, p = 0.053) and significantly longer OS (p = 12.6m vs 6.8m, p < 0.001) than those with elevated LDH (> 271 U/L). Low baseline lymphocyte count (< 11.1 x 10^9/L) was related to worse OS (12.6m vs 6.9m, p < 0.001) and PFS (6.2m vs 3.9m, p = 0.02). Secondly, baseline tissue and ctDNA gene mutations were detected in 33 and 30 pts, respectively. Tissue analysis showed that pts with STK11 (p = 0.0254), CTNNB1, STK11, and NFI had longer PFS than those with mutations. Pts with ARID1A gene wild type showed a tendency for longer PFS (p = 0.0634) and significantly longer OS (p = 0.0049). Gene mutations from baseline ctDNA revealed that pts with wild type SMARCA4, CTNNB1, STK11, and NFI had longer PFS than those with mutations. Lastly, IHC meant that PD-L1 positivity may be related to longer PFS (TPS > 1% vs 0.08, p = 0.05, > 5% vs 1%, p = 0.05). Besides, pts with CD68+ HLA-DR+ macrophages > 0.09%, CD68+ HLA-DR- macrophages > 2.5%, and CD68+CD56bright+17% and CD68dim > 0.05 also got PFS benefits (all p = 0.05). TM (tumor size) > 7 mm and m (mutation) was not associated with PFS. **Conclusions:** Despite limited sample size, biomarkers from routine blood test, gene mutation and immune microenvironment can be helpful to stratify pts who are sensitive to immunotherapy in advanced BTC. Clinical trial information: NCT03486678. Research Sponsor: None.
Role of para-aortic lymph node sampling for patients with potentially resectable biliary cancer. First Author: Hiromichi Itó, Japanese Foundation for Cancer Research, Tokyo, Japan

Background: While paraaortic lymph node (PALN) metastasis has been known as poor prognostic indicator for patients with biliary cancer and is regarded as distant metastasis in AJCC staging system. However, previous diagnostic criteria of PALN metastasis by current imaging studies is not accurate and the incidence of PALN metastasis among patients with potentially resectable biliary cancer and its impact on their long-term outcomes remain unclear.

Methods: The patients who underwent exploratory laparotomy with PALN sampling for potentially resectable biliary cancer at our institution from 2006 through 2018 were included. All patients were appropriately staged preoperatively with CT/MRI and patients with suspected PALN metastasis preoperatively were not considered resectable disease, and thus, such patients were not included. The incidence of PALN metastasis and long-term outcomes (recurrence-free and overall survivals [RFS, OS]) for patients with/without PALN metastasis were compared. Results: Total 383 patients with three types of biliary cancers (164 perihilar cholangiocarcinoma [PHCC], 150 distal cholangiocarcinoma [DCC] and 104 gallbladder cancer [GBCA]) were included. The median age was 71 years and 65% were male. Majority of them (362 patients [95%]) completed planned resection and 9 patients (2%) died of post-operative complications. PALN metastasis was confirmed on 33 patients (9%) among the entire cohort; the yield of positive PALN sampling was the highest in the patients with GBCA (14%), followed by 9% in those with PHCC and 4% in those with DCC. Among 33 patients with positive PALN, 20 underwent tumor resection. Median RFS and OS following resection for the patients with PALN metastasis were 11 months and 22 months, respectively, compared to 46 months and 56 months for those without, respectively (p < 0.001 for both RFS and OS). There were no survivors beyond 5-years among those with PALN metastasis.

Conclusions: The yield of routine intraoperative PALN sampling is not small even among patients with potentially resectable biliary cancer and positive PALN indicates poor long-term outcomes. This procedure can provide the opportunity to avoid morbid operation for patients who unlikely benefit. Research Sponsor: None.

Regorafenib in patients with unresectable hepatocellular carcinoma (uHCC) in routine clinical practice: Interim analysis of the prospective, observational REFINE trial. First Author: Ho Yeong Lim, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea

Background: Regorafenib significantly improved overall survival (OS) versus placebo in patients (pts) with uHCC who progressed on prior sorafenib therapy in the phase 3 RESORCE trial. The multicenter, international REFINE trial was placebo in patients (pts) with uHCC who progressed on prior sorafenib therapy. Regorafenib significantly improved overall survival (OS) versus placebo in patients (pts) with uHCC who progressed on prior sorafenib therapy in the phase 3 RESORCE trial. However, progression-free survival (PFS) and overall survival (OS) were 11 months and 22 months, respectively, compared to 46 months and 56 months for those without, respectively (p < 0.001 for both RFS and OS). There were no survivors beyond 5-years among those with PALN metastasis. Among 33 patients with positive PALN, 20 underwent tumor resection. Median RFS and OS following resection for the patients with PALN metastasis were 11 months and 22 months, respectively, compared to 46 months and 56 months for those without, respectively (p < 0.001 for both RFS and OS). There were no survivors beyond 5-years among those with PALN metastasis.

Conclusions: The yield of routine intraoperative PALN sampling is not small even among patients with potentially resectable biliary cancer and positive PALN indicates poor long-term outcomes. This procedure can provide the opportunity to avoid morbid operation for patients who unlikely benefit. Research Sponsor: None.

Irreversible electroporation of the bile duct in swine: A pilot study. First Author: Sang Hyun Kim, Department of Gastroenterology, Korea University Anam Hospital, Seoul, South Korea

Background: Irreversible electroporation (IRE) is a relatively new ablative method. However, the application of IRE ablation has not been attempted for the treatment of biliary disease. Minimally invasive approach using endoscopic retrograde cholangio-pancreatography (ERCP) can be a novel therapeutic modality for IRE ablation. In this study, we investigated the feasibility and effect of endoscopic IRE for biliary tract in animal model. Methods: A new catheter electrode was developed for endoscopic IRE ablation of biliary tract. The electrode for IRE ablation has two band-shaped electrodes on catheter tip. We performed ERCP and endoscopic IRE ablations on normal common bile duct in 6 Yorkshire pigs. Experimental parameters of IRE were 500V/cm, 1000V/cm and 2000V/cm (under 50 pulses, 100 μs length). Animals were sacrificed after 24 hours and ablated bile duct were collected. Histological and immunohistochemistry and western blot were performed. Results: Well-demarcated focal color changes were observed on the mucosa of the common bile duct under all experimental parameters. After IRE ablation, bile duct epithelium was disappeared around ablated area and it showed fibrotic change in H&E stain. Depth of change after IRE was different between each experimental parameters. Apoptotic change of bile duct was localized around mucosa in 500V. Diffuse transmural fibrosis of bile duct was shown after IRE ablation with 2000V. TUNEL immunohistochemistry showed the cell death of bile duct mucosa and submucosa along the electrode. Within 24 hours, no complication was observed in pigs after endoscopic IRE ablation. Conclusions: Endoscopic IRE ablation using ERCP was successfully resection of common bile duct by using catheter-shaped electrode. It can be a potential therapeutic option as minimally invasive ablation for treatment of biliary tumors. Research Sponsor: None.
Pattern of progression in advanced HCC treated with ramucirumab/placebo: Results from two randomized phase III trials (REACH/REACH-2). First Author: Maria Reig, Barcelona Clinic Liver Cancer Group, Liver Unit, Hospital Clinic of Barcelona, IDIBAPS, CIBERHE, Barcelona, Spain

**Background:** REACH (NCT0143347) and REACH-2 (NCT02435433) studied ramucirumab (RAM) in pts with advanced hepatocellular carcinoma (HCC) following sorafenib; REACH-2 enrolled pts with baseline alpha-fetoprotein (AFP) ≥400 ng/mL and met its primary endpoint of overall survival (OS) for RAM vs placebo. This post-hoc analysis examined radiological progression patterns (RPP) incidence every 6 weeks per RECIST v1.1, and if RPP were related to OS and post-progression survival (PPS). **Methods:** Pts with advanced HCC, Child-Pugh A, and ECOG PS 0-1 with prior sorafenib were randomized (REACH 2:1; REACH-2:1) to receive RAM 8 mg/kg or placebo Q2W. Among pts with ≥1 RPP (new extrahepatic lesion [NEW], NEW intrahepatic lesion [INH], extrahepatic growth [EHG], or intrahepatic growth [IHG]), results were analyzed by trial and for pooled individual patient data of REACH-2 and REACH (AFP ≥400 ng/mL). Cox models evaluated treatment effect of RAM on OS, and prognostic implications of RPP on OS (adjusting baseline ECOG PS, AFP, macrovascular invasion, arm) and on PPS (adjusting ECOG PS, AFP at progression). **Results:** RPP incidence in the pooled population was: NEH 39%; NH 24%; EH 39%; IHG 37%. RAM was worse for RPP incidence and OS compared to placebo. NEW in NEH in REACH (HR 2.33, 95% CI 1.51, 3.60), REACH-2 (HR 1.49, 95% CI 0.72, 3.08), and the pooled data (HR 1.75, 95% CI 1.12, 2.74). Use of post-discontinuation therapy may have influenced results. OS was also significantly reduced in those with NEW across studies (Table). RAM provided OS benefit in the pooled population, including pts with NEW (HR 0.56, 95% CI 0.39, 0.80). **Conclusions:** Acknowledging limitations of post-randomization RPP analysis, the emergence of NEW on RAM or placebo may be an independent poor prognostic factor for PFS. The impact of PPS may have varied across all RPP subgroups. Clinical trial information: NCT0143347 and NCT02435433. Research Sponsor: Eli Lilly and Company.

### Pooled data of phase III REACH-2 and REACH trials for HCC patients

<table>
<thead>
<tr>
<th>RPP</th>
<th>REACH (N=414)</th>
<th>REACH-2 (N=211)</th>
<th>Pooled (N=625)</th>
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<tr>
<td>NEH</td>
<td>1.64 (1.24, 2.73)</td>
<td>1.94 (1.05, 3.60)</td>
<td>1.89 (1.27, 2.83)</td>
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<td>NH</td>
<td>1.16 (0.73, 1.84)</td>
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<td>1.24 (0.91, 2.00)</td>
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<tr>
<td>EH</td>
<td>1.68 (0.75, 3.75)</td>
<td>1.31 (0.71, 2.43)</td>
<td>1.32 (0.75, 1.67)</td>
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<tr>
<td>IHG</td>
<td>1.08 (0.75, 1.57)</td>
<td>1.68 (0.75, 3.71)</td>
<td>1.48 (0.93, 2.36)</td>
</tr>
</tbody>
</table>

**Multivariable Cox models 95% (CI) of OS by RPP.**

Hepatic and hematological toxicity associated with selective internal radiation therapy (SIRT): A meta-analysis of randomized clinical trials. First Author: Ashish Manne, Medical Oncology, Mitchell Cancer Institute, The University of South Alabama, Mobile, AL

**Background:** For advanced hepatocellular cancers (HCCs) and colorectal cancers (CRCs) with liver metastasis, the impact of selective internal radiation therapy (SIRT) with yttrium-90 on survival outcomes is not established. A meta-analysis of randomized clinical trials (RCT) was performed to determine the relative risk (RR) of hepatic and hematological toxicities with the use of SIRT, compared to therapies not including SIRT. For patients with advanced HCC or CRC, we assessed the RR of high grade (grades 3 and 4) hyperbilirubinemia, fatigue, leucopenia, thrombocytopenia and elevated liver enzymes (AST and ALT) with use of SIRT.

**Methods:** Citations from PubMed/Medline, clinical trials.gov, package inserts, and abstracts from major conferences were reviewed to identify RCTs comparing arms with or without SIRT. Potential publication bias was assessed using the Egger test for funnel plot asymmetry. There was no publication bias and the trials were of high quality based on Jadad scoring. Patients in control arms received trans-arterial chemo-embolization (TACE) or sorafenib for HCC or FOLFOX for CRC. The proportion and 95% confidence intervals (CIs) for patients with adverse events were derived for each arm of the study and used to calculate the RR. For the meta-analysis, both the fixed-effects model and the random-effects model were considered; the method proposed by DerSimonian and Laird was used to estimate the random-effects model. **Results:** The RR of grade 3/4 leucopenia was consistently high across the use of SIRT across all the studies (RR 2.05, 95% CI (1.22, 3.42), p value 0.027). The risk of hepatic dysfunction and fatigue was higher with SIRT but not statistically significant. **Conclusions:** Since SIRT is associated with increased risk of high-grade leucopenia, caution is advised in selecting patients with HCC’s with underlying decompensated cirrhosis or with CRCs and on cytotoxic therapy. Proper selection of patients would reduce toxicities from SIRT alone or in combination with systemic chemotherapy. Research Sponsor: None.

A pilot study of durvalumab/tremelimumab (durva/treme) and radiation (XRT) for metastatic biliary tract cancer (mBTC): Preliminary safety and efficacy. First Author: Theodore S. Hong, Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA

**Background:** Metastatic biliary tract cancer (mBTC) is a lethal malignancy with median 5 year OS of less than 10%. Immunotherapy, particularly single agent tremelimumab (TREME)-L, has limited efficacy in mBTC with objective response rates of less than 10%. Preclinical data shows responses in metastatic MSS pancreatic or colon cancer with combination anti-PD-1/CTLA-4 and radiation (XRT) to produce systemic response (abscopal effect) (Parikh A, GI ASCO 2019, ASCO 2019.). We evaluate safety and efficacy of dual PD-1/CTLA-4 inhibition with XRT in mBTC patients. **Methods:** A phase 1b study was planned to evaluate safety and radiation-induced toxicity. A phase 1b trial is currently ongoing. **Results:** 15 mBTC patients were enrolled. Eligible patients had histologically-confirmed mBTC, ECOG PS 0-1, and must have had at least 1 site of progressive disease (C2D0 every other day to a single metastatic site. Durva/Treme continued for 4 cycles, followed by 4 cycles of maintenance durva until progressive disease, discontinuation or withdrawal. Endpoints include disease control rate (DCR) (SD+PR+CR)), PFS and OS and safety. Radiological evaluations were done q2 mo. **Conclusions:** 15 mBTC pts enrolled and evaluable from May 2018 to March 2019. Median age 63 years (range 48-75), 47% male. DLTs occurred in 3 patients during the safety run-in. One patient experienced DLT at dose level -1 and subsequent DCR analysis was performed. Median age 63 years (range 48-75), 47% male. DLTs occurred in 3 patients during the safety run-in. One patient experienced DLT at dose level -1 and subsequent DCR analysis was performed. **Results:** 15 mBTC pts enrolled and evaluable from May 2018 to March 2019. Median age 63 years (range 48-75), 47% male. DLTs occurred in 3 patients during the safety run-in. One patient experienced DLT at dose level -1 and subsequent DCR analysis was performed. **Results:** 15 mBTC pts enrolled and evaluable from May 2018 to March 2019. Median age 63 years (range 48-75), 47% male. DLTs occurred in 3 patients during the safety run-in. One patient experienced DLT at dose level -1 and subsequent DCR analysis was performed.
The efficacy and safety of lenvatinib in patients with intermediate-stage hepatocellular carcinoma: A nationwide multicenter study in Japan. First Author: Kaoru Tsuchiya, Department of Internal Medicine III, Division of Gastroenterology and Hepatology, Medical University of Vienna, Vienna, Austria

Background: Lenvatinib (LEN) has been used in patients with unresectable hepatocellular carcinoma (uHCC) since Mar 2018 in Japan. We conducted a nationwide multicenter study and especially focused on the efficacy and safety in the patients with intermediate-stage uHCC. Methods: A total of 240 patients received LEN from March 2018 at 15 sites in Japan was enrolled. Tumor assessments in accordance with modified RECIST were done using dynamic CT or MRI within 4-8 weeks and every 6-8 weeks thereafter. Results: In this study, 88 of 240 (36.7%) patients were BCLC stage B. Among them 76 (86.3%) patients received TACE before LEN and the median number of TACE was 2 (IQR). Only 4 patients were TACE experienced and other 84 (95.5%) patients received LEN as a 1st line therapy. The median pretreatment ALBI score was -2.35 and 75 (85.2%) patients were Child-Pugh A. In this cohort, 73 (83.0%) patients were beyond up-to-seven criteria and the median pretreatment AFP was 38.2 (2-12870) ng/mL. The median observation time was 8.5 months and 165 patients died. The median progression free survival was 8.7 months, and the median overall survival (OS) was not reached. Objective response rate (ORR) and disease control rate (DCR) were 48.5% and 80.3%. AFP decrease (> 20%) after 1 month was observed in 52 (59.0%) patients. Child-Pugh B patients (n = 13) had significantly shorter OS than Child-Pugh A (p = 0.02) and median OS in Child-Pugh B patients was 8.8 months. The patients received > 6 times TACE before LEN had significantly shorter OS than patients received ≤ 6 times TACE (p = 0.02). Additional TACE was performed in 8 patients and The median time of restarting LEN was 19 days. The median ALBI score before additional TACE, Day 1 after TACE and Day 28 after TACE were -2.38, -2.07, and -2.36. There was no severe adverse event associated with additional TACE. The median duration of LEN in patients treated with LEN and additional TACE was 8.5 months. Conclusions: The ORR and DCR of LEN in Child-Pugh A patients with intermediate-stage uHCC were 46.6% and 79.3%. The therapeutic strategies for intermediate-stage HCC should be discussed based on the liver function, tumor stages, and treatment course about TACE. Research Sponsor: None.

Hyperprogressive disease during PD-1 blockade in patients with advanced hepatocellular carcinoma. First Author: Hongiae Chon, CHA Hospital, Seongnam, South Korea

Background: Immune checkpoint blockade with PD-1 inhibitors has shown promising clinical efficacy in patients with hepatocellular carcinoma (HCC). However, emerging evidences show that PD-1 blockade can sometimes lead to a flare-up of tumour growth, known as hyperprogressive disease (HPD). This study aimed to evaluate the incidence and pattern of HPD in a multicenter, real-world cohort of East Asian patients with advanced HCC treated with PD-1 blockade. Methods: We enrolled 148 advanced HCC patients treated with nivolumab between March 2016 and December 2018 in Korea. Clinicopathologic variables, tumor progression dynamic, and treatment outcomes were comprehensively analyzed. Progressive disease was assessed using tumor growth kinetics (TGG), tumor growth rate (TGR), and time to treatment failure (TTF), and patient with HPD were defined as those who met the criteria of progressive disease by both TGG and TGR. Results: In this large cohort of HCC patients, the median age was 60 years and the majority were male (85%) and HBV-infected (72%). The objective response rate was 17.6% including two complete responders (1.4%). Ongoing responses were seen in 46% of responders at data cut-off. The incidence of HPD after PD-1 blockade was 23.9%. HCC patients with HPD had dismal prognosis with worse progression-free survival (PFS) and overall survival (OS) (HR, 1947; 95% CI, 1226-3093 and HR, 1839; 95% CI, 1108-3055, respectively) than progressive disease without HPD. Among various baseline clinicopathologic parameters, elevated neutrophil-to-lymphocyte ratio (NLR) was only significantly associated with HPD. The optimal cut-off value of NLR for HPD prediction was 3.74 determined by ROC curves, and NLR > 3.74 was associated with worse PFS and OS. Conclusions: The real-world efficacy of PD-1 blockade in HCC patients was consistent with previous studies. However, there was also a corresponding risk of HPD as well as a clinical benefit. Therefore, careful patient selection using immunologic biomarkers, such as NLR, could enhance the therapeutic benefit of PD-1 blockade in clinical trials and real-world practice of HCC.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Role of precision medicine for patients with advanced biliary tract cancers. First Author: Antoine Hollebecque, Gustave Roussy Cancer Campus, Villejuif, France

Background: Biliary tract cancers (BTC) are rare and heterogeneous cancers with poor prognosis. Several actionable genomic targets have been described in BTC and data on the efficacy of targeted therapies remain limited. The main objectives of this retrospective study was to evaluate the frequency of actionable genomic alterations among BTC and the impact of targeted therapy. Methods: We performed a retrospective analysis on BTC patients seen at Gustave Roussy from Dec 2011 to Jul 2019. All clinical and genomic reports were reviewed. Results: The study population included 212 patients with the main following characteristics: median age 61 years, female 51%, intrahepatic cholangiocarcinoma 57%, median of 2 previous lines. Of 212 BTC patients, 170 patients had a genomic profile based on archival tissue or a new tumor biopsy (IGR panel n = 120; Foundation One panel n = 92). 124 patients (73%) had at least one genomic alteration and 68 (40%) patients had genomic alteration considered as actionable. The most common actionable targets were FGFR2 rearrangement/mutation (n = 24, 35.3%), HER2/3 mutations (n = 9, 13.2%) and IDH1/2 mutations (n = 7, 10.3%). Of those 68 patients, 58 received the matched targeted therapy: FGFR inhibitor n = 24, HER2/3 inhibitors n = 9, Akt/Pi3KCA/mTOR inhibitors n = 7, IDH1 inhibitor n = 6. In the treated population, the objective response rate was 36.2% and the disease control rate 85.1%. Progression-free survival (PFS) was 6.2 months compared to 2.8 months (p = 0.02) for patients who did not received targeted treatment. Overall survival (OS) was 17.7 months compared to 11.0 months (p = 0.03) for patients who did not received targeted treatment. Conclusions: Actionable targeted therapies resulted in a 36% response rate, a 85% tumor control rate, 17.7 months OS, compared to 11.0 months (p = 0.03) for patients who did not receive targeted treatment. Of those 68 patients, 58 received the matched targeted therapy: FGFR inhibitor n = 24, HER2/3 inhibitors n = 9, Akt/Pi3KCA/mTOR inhibitors n = 7, IDH1 inhibitor n = 6. In the treated population, the objective response rate was 36.2% and the disease control rate 85.1%. Progression-free survival (PFS) was 6.2 months compared to 2.8 months (p = 0.02) for patients who did not received targeted treatment. Overall survival (OS) was 17.7 months compared to 11.0 months (p = 0.03) for patients who did not receive targeted treatment.

First-in-human phase I trial of small activating RNA (saRNA) oligonucleotide MTL-CEBPA in combination with sorafenib in patients with advanced hepatocellular carcinoma (HCC). First Author: Debasish Sarker, King's College London, London, United Kingdom

Background: MTL-CEBPA is the first saRNA to enter clinical trials and targets the transcription factor C/EBPα, a master regulator of myeloid cell differentiation. We have previously reported a favourable safety profile of MTL-CEBPA given as a single agent QW3 every 28 days, in patients with HCC (Sarker D et al. ASCO 2018). After discontinuation of MTL-CEBPA, three out of five patients treated with sorafenib off study have had maintained complete radiological response (CR) of T4 and 8 months duration; 2 patients demonstrated resolution of lung metastases > 1 year. Here we present updated data on phase 1 patients treated with sorafenib off study as well as subsequent combination cohorts. Methods: MTL-CEBPA 130mg/m² QW3 or BIW and sorafenib 400mg bid were administered to patients with HCC using combination or sequential dosing regimens: each cohort received either tyrosine kinase inhibitor naïve or resistant. On treatment liver biopsies evaluated changes in M2 macrophages (CD163). Flow cytometry of peripheral blood determined changes in myeloid cell populations. Results: 12 patients have been treated with MTL-CEBPA co-administered with sorafenib and 14 patients treated with MTL-CEBPA followed by sorafenib (23M/ 3F, median age 65.5years, range 44-83, ECOS PG 0/1/8/8). The most common treatment-related AEs (all grades/grade 3) in this group include facial flushing (4/0), raised AST (3/7), raised ALT (2/1), fatigue (5/0), raised ALP (2/0), and anemia (2/2). diarrhea (3/0), rash (2/0) and anorexia (1/1). 1 TKI naive patient in the co-administration cohort has maintained CR at 7 months and two patients have SD (ongoing at 3 & 4 months both in sequential cohort). IHC in the patient with CR has demonstrated 95% reduction in M2 macrophages with significant decrease in frequency of immature CD45- neutrophils (~85.7%); p = 0.00078). PMN-MDSCs (~49.3%; p = 0.00145) and M-MDSCs (~8.4%; p = 0.0072). All responding patients have undergone HBV or HCV. Conclusions: MTL-CEBPA is a novel saRNA targeting myeloid cells which may result in a significantly enhanced oncological effect in HCC. Updated data on safety and efficacy will be presented. Clinical trial information: NCT02716012. Research Sponsor: Mina Therapeutics.

The impact of inflammatory biomarkers, BMI, and sarcopenia on survival in advanced hepatocellular carcinoma treated with immunotherapy. First Author: Mehmet Akce, Winship Cancer Institute, Atlanta, GA

Background: Sarcopenia and inflammation are independently associated with worse survival in cancer patients. This study aims to determine the impact of inflammatory biomarkers, BMI, and sarcopenia on survival in advanced hepatocellular carcinoma (HCC) patients treated with immunotherapy. Methods: We performed a retrospective review of advanced HCC patients treated with immunotherapy-based therapies at Winship Cancer Institute between 2015 and 2019. Baseline computed tomography and magnetic resonance imaging scans were collected at mid-L3 level, assessed for skeletal muscle density using Sliceromatic (TomoVision, version 5.0) and converted to skeletal muscle index (SMI) by dividing it by height (m^2). Gender-specific sarcopenia was defined by median value of SMI. The optimal cut for continuous inflammation biomarker was determined by bias-adjusted log-rank test. Overall Survival (OS) was set as primary outcome and Cox proportional hazard model was performed. Results: 57 patients were included; 77.2% male, 52.6% Caucasian, 58.5% ECOG PS 0-1, 80.7% Child Pugh A. Treatment was second line and beyond in 71.9%. The median follow-up time was 6 months. Sarcopenia cut-off for males and females was SMI of 43 and 39, respectively. 49.1% of patients had sarcopenia. Median OS was 5 vs. 14.3 months in sarcopenic vs. non-sarcopenic patients (p=0.054). Median OS was 5 and 17.5 months in patients with BMI <25 and BMI ≥25 respectively (p=0.034). Median OS was 3.6 and 14.3 months for patients with neutrophil to lymphocyte ratio (NLR) ≤5 vs. NLR >5.1 (p<0.001). In multivariable Cox regression model, higher baseline NLR was associated with worse OS (HR: 4.17, 1.52-10.30, p=0.003). Gender specific sarcopenia showed a trend of worse OS (HR: 1.71, 0.73-4.00, p=0.215) but was not statistically significant. BMI<25 was associated with worse OS (HR: 2.73, 1.15-6.53, p=0.023). In the association with PFS, neither baseline BMI nor gender specific sarcopenia showed statistical significance. Conclusions: Baseline BMI and NLR may predict OS after immunotherapy treatment. After controlling for baseline Child Pugh Score and NLR, gender specific sarcopenia was not associated with OS significantly. Research Sponsor: None.

Predictors of immunotherapy (IO) response in hepatocellular carcinoma (HCC). First Author: Samantha Ann Armstrong, Indiana University School of Medicine, Indianapolis, IN

Background: Despite advances in understanding the molecular pathways of HCC, therapeutic options are limited and patient survival is dismal. IO is a promising HCC treatment. There are currently no indicators to identify which patients (pts) will have a prolonged response (PR) or durable remission (DR). In this single institutional retrospective analysis, pts received one of five IO containing regimens with nivolumab, pembrolizumab, atezolizumab plus bevacizumab, durvalumab or cemiplimab until disease progression (PD) or unacceptable toxicity. Methods: IO treatments included: 1) IO monotherapy, 2) IO combination therapy with chemotherapy (CTx) or other IO treatments, 3) IO conversion therapy. Baseline characteristics, IO toxicity, vascular invasion (VI), tumor thrombus (TT), multifocal disease, toxicity grade, steroid use for IO mediated toxicities and derived Neutrophil-to Lymphocyte ratio (NLR) were correlated to clinical outcome: progression free survival (PFS), overall survival (OS), response rate (RR), using Pearson’s chi-square test or student’s t-test. Responses were assessed using RECIST v1.1 criteria for stable disease (SD), partial response (PR) and PD were correlated with best response and PFS. OS was calculated by the Kaplan-Meier method. Results: Cohort demographics (n = 76) were: 72% male; 38% African American, 30% Caucasian and 16% Asian; 29% of pts had HBV, 43% had HCV, 1% had both HBV/HCV and 13% had no viral etiology (n = 64). The majority of pts were stage III (43%) or IV (38%). At the start of IO, 32% had VI, 32% had TT and 80% had multifocal or metastatic disease. 65% of pts experienced IO toxicity, 24.3% at grade 3 or higher, and 34% requiring steroids. Best response to IO was SD in 65.7% of pts, PR in 25.7% and PD in 8.6%. Median OS was 13m (95% CI 7.9-18.3) from the start of IO and median PFS of n = 65) was 14m (95% CI 6.8-21.2). Median OS and PFS were significantly improved in pts with PR compared to PD (14 vs 8m, p < 0.0055, PFS 15 vs 3m p = 0.006). Both OS and PFS showed benefits for SD of ≥2 months compared to those with PD (11 vs 8m, p < 0.0005, PFS 5 vs 3m = p < 0.007). VI, TT, stage, viral etiology, toxicity grade and dNLR did not correlate with OS, PFS and RR, however, neutrophil to lymphocyte ratio (NLR) trended toward improved OS, PFS and RR. Conclusions: Baseline BMI and NLR may predict OS after immunotherapy treatment. Absence of steroid use for toxicity trended toward improved IO response. Research Sponsor: None.
Background: First line therapy for advanced cholangiocarcinoma (CCA) is currently gemcitabine and cisplatin. However, survival rarely exceeds one year with this regimen. PI3K/AKT activation has been shown to increase resistance to chemotherapy in CCA; therefore, inhibiting this pathway may improve chemotherapy's efficacy. This phase II study evaluated the safety and efficacy of copanlisib, a potent and reversible pan-class I PI3K inhibitor, with gemcitabine and cisplatin in advanced CCA.

Methods: Between July 2016 and April 2019, pts with histologically confirmed advanced/unresectable CCA received cisplatin (25 mg/m²), gemcitabine (1000mg/m²), and copanlisib 60mg on day 1 and 8, with cisplatin in advanced CCA. Median mean dose to liver minus GTV was 15.0 GyRBE (range, 8.2-23.5). Five pts were treated between 2015-2019 with a 15-fraction regimen using simultaneous-integrated boost and protection (SIB/SIP) technique to escalate tumor dose while sparing of OARs and results in favorable local control. However, additional correlative work is ongoing to identify a possible biomarker for copanlisib. Clinical trial information: NCT02635990. Research Sponsor: Bayer AG.

Results: Twenty-four pts received at least one dose of the study drug (62.5% female, median age 64 years, with 70.8% intrahepatic, 16.7% extrahepatic, and 12.5% gallbladder cancer. For all pts, median OS was 13.9 months (95% CI, 6.8-17.9) and median PFS was 6.2 months (95% CI, 1.3-11.1). PFS at 6 and 12 months was 57.0% and 42.2%, and 6 and 12-month OS was 73.9% and 53.2%, respectively. Only 19 pts were considered evaluable for RR. Five pts were either lost to follow up, withdrew consent, or died before a second scan was done. Significant PFS was 31.5% and 11 (57.9%) pts had grade 3 or higher adverse events (AE) occurring in 75% of pts. The most common grade 3-4 AEs were decreased neutrophil count (40%) and increased lipase (20%). Treated related AEs led to drug discontinuation for 3 pts (12.5%) and dose modification while on study for 7 pts (29.2%).

Conclusions: Gemcitabine, cisplatin, and copanlisib in combination did not meet the primary endpoint of 6-month PFS. However, additional correlative work is ongoing to identify a possible biomarker for copanlisib. Clinical trial information: NCT02635990. Research Sponsor: Bayer AG.

557 Clinical characteristics and outcomes of patients with advanced hepatocellular carcinoma treated with immunotherapy: A real-world retrospective study. First Author: Adel Cherqui, Jacobs Medical Center, Bronx, NY

Background: Advanced HCC is an aggressive malignancy with dismal prognosis. Newer agents, including immunotherapy (IT), have been granted accelerated list approval. Information outside clinical trials is scarce. This study is aimed to describe the clinical characteristics and outcomes of HCC patients treated with IT. Methods: Patients with HCC treated with IT were identified using the institutional data-mining software, Clinical Looking Glass. Patient demographics, clinical, and treatment characteristics were collected. Progression-free survival (PFS) was defined as time from treatment initiation to disease progression or death, and overall-survival (OS) as time from diagnosis of advanced disease to death. PFS and OS were plotted using Kaplan-Meier curves. Results: A total of 52 patients; median age 64 years; male predominance (38, 73.1%) were identified. There were 24 (54.5%) Hispanics, 9 (20.5%) Non-Hispanic Blacks, 7 (15.9%) Non-Hispanic White and 4 (9.1%) Asians. Cirrhosis was seen in 41 (82.7%), and median MELD score was 8 (IQR: 7-10). Hepatitis B and C infection were encountered in 12 (24.5%) and 22 (44%) patients, respectively. Imaging evidence of intravascular invasion was seen in 16 (34.8%) and extrahepatic metastases in 7 (14.9%) cases. Local treatment was provided to 29 (59.2%) and radiation treatment to 14 (28.6%) patients. Nivolumab was used in all the cases, as first-line treatment in 17 (32.7%) and as second line in 35 (67.3%). The median PFS was 6.2 (1.3-10.6) months and was similar in first-line and second line treatment (8 vs 5.9 months, p=0.90). The median OS was 24.2 (18-28) months; there was a tendency towards higher survival rates in patients that were treated in second line (16.8 vs 25.2 months, 0.017) Conclusions: In this multiethnic cohort, the “real world” experience of the benefit of IT in HCC is encouraging, with a median OS exceeding two years. Expanded data may elucidate the differences if any, between use of IT as front- vs. second-line therapy, in PFS and OS. Research Sponsor: None.

558 Real-world efficacy and safety of immune checkpoint inhibitors in advanced hepatocellular carcinoma: Experience of a tertiary Asian center. First Author: Kennedy Ng, National Cancer Centre Singapore, Singapore, Singapore

Background: Immune checkpoint inhibitor (ICI) use in advanced hepatocellular carcinoma (HCC) is increasing. Real-world data on efficacy and safety however is lacking, more so when used in patients who fall out of standard clinical trial criteria. Methods: We conducted a retrospective review of all patients with advanced HCC seen at our centre who received at least one dose of an ICI between May 2015 - June 2018. Data cutoff was 31 Dec 2018. Responses were evaluated using RECIST v1 criteria. Results: 114 patients fulfilled inclusion criteria. Median age 66 years and 88.6% were male. 45.6% had an ECOG PS of 0 - 1. 64.9% received an ICI within a clinical trial setting. 62.3% received monotherapy. 19.6% of patients had Child-Pugh B disease on initiation of ICI, and 69.3% had an ALBI Grade of 2, 50.0% were known to have hepatitis B and 11.4% had hepatitis C. Baseline HBV VL ranged from undetectable to 620000 IU/mL. 30.7% received prior systemic treatment, most commonly sorafenib (82.9%). Over a median follow-up duration of 5.7 months (0.03 - 42.4), ORR was 18.4%, and disease control rate (DCR) was 51.8%. Median PFS was 2.6 months (1.7 - 3.9), and median OS was 13.9 months (7.0 - 16.2). 5 patients (23.8%) had response duration of more than 18 months. 35.1% received further systemic therapy after ICI. On multivariable analyses, age ≥ 65 years, higher albumin level and lower bilirubin level were associated with increased OS. 60.0% of patients experienced adverse events (AEs) of any grade, 12.0% of these being grade 3 - 4. No grade 5 adverse events were observed. Use of antiviral therapy was associated with a lower risk of hepatic AEs (p = 0.04) whilst baseline HBV VL was not associated with an increased risk of reactivation or hepatic AEs. Conclusions: Two real world settings, responses and adverse event profiles to ICI use are comparable to those observed in clinical trials despite a more heterogeneous population base. The expansion of indications for ICI use in advanced HCC beyond current approvals warrants further study. Research Sponsor: None.

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HEPATOBILIARY CANCER

560 Poster Session (Board #D21), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM
Clinical outcomes of hepatocellular carcinoma patients with Child-Pugh class B treated with stereotactic body radiation therapy. First Author: J Nicholyn Bcaclay, Stanford University, Stanford, CA

Background: Caution is usually employed in the treatment of patients with hepatocellular carcinoma (HCC) due to the inherent liver radiosensitivity, especially in patients with Child-Pugh C (P) and B classes. This study aims to review the outcomes of patients treated with SBRT for CP class B with HCC.

Methods: Medical records of all patients with HCC and compromised liver function (CP class B) treated with SBRT between 2003 and 2018 were reviewed. After institutional review board approval. Clinical, laboratory, and treatment-related data were collected and analyzed for their correlation to toxicity and survival. Liver function was assessed prior to SBRT and at 1, 3, and 6 months after treatment using the CP score classification. Patients were censored for toxicity after extensive tumor progression in the liver, new liver-directed therapies, or liver transplant. Time-to-events were calculated from date of SBRT.

Results: A total of 22 patients were identified, but 3 were excluded for incomplete follow-up. Median follow-up time was 33 months (range: 11-95 months). At baseline, 13 (68%) patients had a CP score of 7, and 6 (32%) had a CP score of 8. The median PTV volume was 94 cc (range: 14-710 cc). The median prescribed dose was in 5 fractions (range: 35-45 Gy in 3-5 fractions). After SBRT, 8 (42%) patients presented with worsening in CP score, with a mean increase of 1.5 points (95% CI, 0.6-2.5; p = 0.005) at the first month of follow-up, but followed by recovery in liver function with change in CP score not statistically different from baseline at 3- or 6-month follow-up times (p = 0.35 and p = 0.13, respectively). Eight patients (42%) presented with acute hepatobiliary toxicity, with six of those presenting with grade 2 toxicity. Patients with CP score change ≥2 points (n = 6) showed a significantly higher incidence of acute grade 2 or higher hepatobiliary toxicity (p = 0.001) with a trend toward worse overall survival (33 vs. 51 months, p = 0.45).

Conclusions: In our cohort, SBRT demonstrated to be safe for patients with Child-Pugh Class B liver function. Research Sponsor: None.

561 Poster Session (Board #D22), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM
Proteomic features of HCC tumors reveal clinically distinct subtypes independent of somatic mutations. First Author: Sun Young Yim, Korea University Medical Center, Seoul, South Korea

Background: Recent massive sequencing studies of HCC genomes revealed many new genetic alterations that might be accountable for HCC development and provided comprehensive view of malignant disease. However, genomic profiling of tumors is limited by a loose correlation between genetic alterations and their functional products such as proteins and metabolites. To overcome current limitation, we generated genomic and proteomic data to further dissect HCC tumors and performed integrated analysis of both data sets.

Methods: We analyzed proteomic data and genomic data such as somatic mutations, mRNA expression, miRNA expression, and copy number alterations from 300 HCC tumors to uncover most correlated genomic alterations with proteins. Clinical significance of identified key protein features were validated in multiple independent cohorts in HCC patients. Gene network analysis with integrated genomic and proteomic data further revealed association of subtypes with currently available treatments of HCC such as sorafenib and immunotherapy. In addition, multiple in-depth analysis was performed with integrated proteomic and genomic data to identify novel therapeutic targets for each subtype. Functional validation with cell lines demonstrated that some of candidates are essential for survival of HCC cells. Conclusions: HCC is classified into three subtypes by integrating genomic and proteomic data. These analyses have identified potential therapeutic targets as well as biomarkers associated with therapeutic targets. Our study demonstrated merit of integrated analysis of proteomic data with genomic data to uncover potential driver genes of HCC development. Research Sponsor: MD Anderson Cancer Center.

562 Poster Session (Board #E1), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM
Exploring the genomic landscape of hepatobiliary cancers to establish a novel molecular subtype classification. First Author: Anthony Joseph Scholer, John Wayne Cancer Institute at Providence St. John’s Health Center, Santa Monica, CA

Background: The current understanding of the genomic landscape of hepatobiliary cancer (HBC) is limited. Recent genomic and epigenomic studies have demonstrated that various cancers of different tissue origins can have similar molecular phenotypes. Therefore, the aim of this study is to evaluate the genomic alterations of HBCs as a first step towards creating a novel molecular subtype classification.

Methods: The genomic landscape of hepatobiliary cancers was explored using a multi-omics approach. WGS and targeted panels were used to analyze tumors from patients with cholangiocarcinoma (CCA), and gallbladder carcinoma (GBC). From 61 gene mutation platforms, we found 42 genes common to all HBC cases. Associations between histomolecular characteristics of HBCs (hepatocellular (HCC), cholangiocarcinoma (CCA), and gallbladder carcinoma (GBC)) with gene mutations (classified by COSMIC CENSUS) were analyzed using Pearson’s χ2 test. A total of 1,017 alterations were identified in 61 genes (516 missense variant, 157 gene amplifications, 101 inactivating mutations, 106 truncating mutations, 84 up-stream gene variants, 37 gene homozygous deletions, 16 gene rearrangements) in 329 patients: 115 (35%) CCA, 87 (26.4%) GBC, and 127 (38.6%) HCC. The majority 77.8% (256) of tumors harbored at least two mutations and 38.9% (128) had at least one alteration, with GBC having a higher average number of alterations (3.08±1.41) than HCC (2.73±1.32) and CCA (2.49±1.44) However, HCCs had the highest maximum number of alterations compared to CCA and GBC (p < 0.05). The ten genes most frequently altered across all the HBCs were TP53, TERT, CTNNB1, KRAS, ARID1A, CDKN2A, IDH1, PIK3CA, MYC, and SMARCA4 with disparities in the distribution of alterations (3.23±1.32 HCC vs. 2.23 CCA and 2.87 GBC) (p < 0.001). IDH1 mutations were associated with CCA, CTNNB1 and TERT mutations with HCC, and TPS3 mutations with both HCC and GBC. Conclusions: HCC subtypes appear to have unique mutational landscapes, but also significant overlaps with generally independent genomic and epigenomic research is needed to develop a histomolecular classification algorithm that can be used for prognostic and therapeutic stratification of these cancers. Research Sponsor: None.

563 Poster Session (Board #E2), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM
Apurinic/apyrimidinic endonuclease-1 and hepatocellular carcinoma. First Author: Nicholas James Skill, Indiana University, Indianapolis, IN

Background: The enzyme apurinic/apyrimidinic endonuclease-1 (APE1) is associated with protection against DNA damage and oxidative damage concomitant with cancer. The purpose of this study is to investigate hepatic APE1 levels in association with hepatocellular carcinoma (HCC) in order to better stratify patients with underlying liver disease for the development of HCC and to identify novel targets for therapy. Methods: Hepatic APE1 levels were determined by immunohistochemistry staining and ELISA within liver and tumor samples from patients with HepC and HCC. Hepatic APE1 staining was semi-quantitated using a scale of 0-100. Serum APE1 levels were determined by ELISA. In addition, APE1 staining was quantified in hepatic paraffin embedded sections from MDR2 /+ mice with HCC and within MDR2 /− mice controls that do not develop HCC. Results: Hepatocyte APE1 staining was lower in livers of patients with HepC and HCC when compared to patients with HepC without HCC. In a similar manner, hepatic APE1 levels were significantly lower in patients with HepC and HCC patients when compared to HepC controls. In contrast, serum APE1 level was greater in patients with HepC and HCC when compared to patients with HepC and no HCC. Moreover, APE1 levels were greater in HCC tumors when compared to non-malignant liver tissue. Hepatocyte APE1 staining in MDR2 /− mice with HCC was lower when compared to MDR2 /− mice that do not develop HCC. In addition, cytosolic APE1 staining was increased in HCC tumor of MDR2 /− mice when compared to controls. Conclusions: Increased APE1 is a potential biomarker of HCC risk in patients with underlying liver disease and is a novel target for therapy in patients with underlying liver disease whom have a higher risk of developing HCC. Consequently, targeted APE1 inhibition may increase chemotherapy response by reducing tolerance to DNA damage. Additional studies are required to better understand the role of APE1 inhibition in HCC in the face of reduced background hepatic APE1 levels. Research Sponsor: None.
Phase Ib study of regorafenib (REG) plus pembrolizumab (PEMBRO) for first-line treatment of advanced hepatocellular carcinoma (HCC). First Author: Anthony B. El-Khoueiry, University of Southern California, Norris Comprehensive Cancer Center, Los Angeles, CA

Background: REG is a multikinase inhibitor with immunomodulatory activity and PEMBRO is an anti-PD-1 monoclonal antibody. Mutations in the FGFR2 gene are observed monotherapy for patients (pts) with HCC previously treated with sorafenib. Based on their potential synergistic effects, we conducted a phase Ib study of REG plus PEMBRO for first-line treatment of advanced HCC.

Methods: This is an ongoing, open-label, dose-escalation study in pts with advanced HCC who had no prior systemic therapy. In the first cohort, pts received REG 120 mg daily PO for 3 weeks on/1 week off plus PEMBRO 200 mg IV q 3 weeks. In later cohorts, the REG dose could be escalated (160 mg) or reduced (80 mg) based on the modified toxicity probability interval design; the PEMBRO dose is fixed. The primary objective is safety and tolerability. Secondary objectives are to define the maximum tolerated dose (MTD) and recommended phase 2 dose, and to assess antitumor activity. Results: As of August 23, 2019, 29 pts have been treated at the REG 120 mg level. Median age is 65 years (range 32-81); 41%/55%/5% of pts are BCLC stage B/C, 100% are Child-Pugh A; ECOG status 0/1 is 72%/28%. Dose-limiting toxicities occurred in 4/78% 5/32% for grade 3 and 3/4 patients increased ALT/AST with 2 increased bilirubin (n = 2); Gr 3 rash (n = 2). The MTD of REG in the combination was 120 mg. Most common Gr 3 or 4 treatment-emergent adverse events (AEs) are shown in n (%)<29. There were no Gr 5 AEs. 59%/31% of pts had REG/PEMBRO-related Gr 3 or 4 AEs. Dose modifications (reductions or interruptions) of REG/PEMBRO for drug-related AEs occurred in 59%/31% of pts. Of 23 evaluable pts, 7 (30%) had a partial response (PR) and 14 (61%) had stable disease (RD1211; additional pt had PR by mRECIST. Conclusions: The combination of REG plus PEMBRO for first-line treatment of advanced HCC showed no unexpected safety signals and encouraging antitumor activity. Accrual is continuing at REG 120 mg dose and an expansion cohort evaluating REG 80 mg plus PEMBRO is planned. Clinical trial information: NCT03347292. Research Sponsor: Bayer.

TAEAs (or 3/4 w/28% pts, n (%))

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<th>Grade</th>
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ALT increased | 7 (28)
Hypertension | 5 (18)
ALT increased | 3 (11)
Bilirubin raised | 4 (14)
Lipase increased | 4 (14)
Hypertension | 3 (11)
Hypomagnesemia | 3 (11)
CD205 viii.1.3; CTCAE v4.03 grade

Survival outcomes according to the tumor mutation burden and PD-L1 expression in hepatobiliary tumors. First Author: Jorge Sánchez-García, Intermountain Medical Center, Murray, UT

Background: Hepatobiliary (HB) tumors are aggressive tumors with emerging evidence for increasing sensitivity to immune checkpoint inhibitors (ICI). Tumor mutation burden (TMB) was found to be a quantitative biomarker associated with production of neoantigens in the tumor and predict the sensitivity to immune therapy. Herein, we explore the TMB, microsatellite instability (MSI) and PD-L1 expression as a potential biomarker of response to immune therapy in HB tumors.

Methods: We retrospectively assessed all patients with hepatobiliary malignancies who have undergone next generation sequencing (NGS) between October 2009 and June 2019. We then analysed the tumor mutation burden and PD-L1 of these tumors and also identified frequency of patients with no clinically actionable mutations. Results: In our total 61 patients with HB tumors pre-dominantly were male (62.3%) with mean age of 63 years. Thirty-four patients had hepatocellular carcinoma, 22 patients had cholangiocarcinoma and 5 patients had gallbladder carcinoma. The most common risk factors were smoking status, cirrhosis, alcohol consumption and hepatitis C virus. The mean TMB reported was 3.2 (1.16 – 7.35). MSI was identified in 13 patients and one was indeterminate. Only 17 patients had PD-L1 positive. At least, 37 patients had one clinically actionable mutation while 24 patients had no clinically actionable mutations. Mean overall survival was 16.6 months, but no statistically significant difference was found with high PD-L1 (3 vs 3.7 months, p=0.3) expression. Conclusions: Our data suggests the TMB in HB tumors is low in general irrespective of their underlying risk factors. We also noted more than half had microsatellite stable tumors and PD-L1 expression. Future larger studies are needed to evaluate TMB, MSI and PD-L1 as a potential biomarker in hepatobiliary tumors to help select patients that will benefit from immune therapy. Research Sponsor: None.

Poster Session (Board #E3), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Association of CXCR2+ granulocytic myeloid derived suppressor cells with the development of cholangiocarcinoma: A possible target for intervention. First Author: Nicholas A. Ullman, University of Rochester Medical Center, Rochester, NY

Background: Cholangiocarcinoma (CCA) is the second most common primary liver malignancy, with increasing incidence. Currently, surgical resection offers the only chance for cure, however the prognosis remains poor in part due to high rates of unresectability, recurrence, and poor response to conventional therapy. Thus, new systemic therapies represent an unmet medical need. Few preclinical models exist for identifying and testing new targeted or immune based therapies. Here we present our findings of the immune infiltrate in human CCA tumor microenvironment (TME) and a spontaneous murine model that faithfully recapitulates human disease. Methods: Histology and immunohistochemistry (IHC) staining was performed on human CCA and adjacent normal liver, Mice with targeted hepatic Kras activation and loss of p53 (KPPC) spontaneously develop CCA. KPPC hepatic tumors and normal livers from littermate controls underwent histological and gene expression studies. Flow cytometric analysis was performed on bone marrow, spleen, peripheral blood, CCA tumors and normal littermate livers. Results: Digital IHC quantification of archival human CCA specimens demonstrated elevated levels of CD56"CXCR2" granulocytic myeloid derived suppressor cells (G-MDSC) compared to adjacent normal liver (p = 0.005). In addition, the CXCR2 ligand, CXL5, was significantly elevated in CCA tumors compared to adjacent normal liver. In KPPC mice, flow cytometric analysis of hepatic tumors showed an abundance of CD45" leukocytes comprised of immunosuppressive G-MDSC vs normal littermate controls (p = 0.0007) which recapitulates human disease. qRT-PCR demonstrated significantly increased expression of Cxcl1, Cxcl2, Cxcl3, Cxcl2, and Cxcl9 in CCA tumors compared to normal livers. Accordingly, granulocytes in KPPC mice were elevated in both the bone marrow and blood compared to normal littermate controls. Conclusions: These data suggest CCA co-opts the CXCR2/CXCL2 axis to mobilize and recruit immunosuppressive G-MDSC to the TME. Targeted therapy against tumor infiltrating neutrophils can be tested in this pre-clinical model to inform clinical translation. Research Sponsor: URMC Department of Surgery.

Poster Session (Board #E4), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Therapeutic targeting of extracellular FGFR2 activating mutations in intra-hepatic cholangiocarcinoma. First Author: James M. Cleary, Dana-Farber Cancer Institute, Boston, MA

Background: Fibroblast growth factor receptor (FGFR) pathway alterations have been identified in approximately 20% of patients (pts) with intrahepatic cholangiocarcinoma (iHCC), most commonly by FGFR2 fusions. Early phase clinical trials have demonstrated encouraging efficacy and testing new targeted or immune based therapies with FGFR2-translocated cholangiocarcinoma, but efficacy in pts with other FGFR2 activating alterations is less clear. Methods: Pts with cholangiocarcinoma underwent CLIA-certified next generation DNA sequencing (NGS) to identify actionable alterations. FGFR2 fusions and other FGFR2 genomic events were assessed, with genomic characterization performed before and after treatment with FGFR inhibitors in appropriate pts. Novel extracellular domain in-frame deletions (INDELS) of FGFR2 and apparent resistance mutations were investigated for oncogenic activity and inhibitor resistance in vitro and in vivo. Results: Cholangiocarcinomas from 284 pts (136 male, 148 female; median age, 64 [20-89], including 139 iHCCs, were sequenced. Among the iHCCs, 16 (11.5%) had FGFR2 fusions, with 9 different gene partners. Surprisingly, 5 (3.6%) iHCCs harbored extracellular domain FGFR2 INDELS. Two of these iHCCs harbored an exon 5 deletion FGFR2 p.H167_N173del. Expression of FGFR2 p.H167_N173del in 3T3 cells resulted in oncogenic transformation. In the clinic, two pts with FGFR2 p.H167_N173del were treated with Debio1347, an oral FGFR1/2/3 inhibitor. Both patients achieved a durable partial response (PR) of 11 months, with one of the pts still on active treatment with Debio1347. The patient who developed acquired resistance underwent repeat biopsy, and NGS identified a secondary mutation (FGFR2 p.L617F) in the kinase domain. In vitro studies demonstrated that this mutation confers resistance to Debio1347. This patient was subsequently treated with another FGFR inhibitor and again experienced a PR lasting 17 months. A third biopsy after disease progression demonstrated a previously unidentified FGFR2 BRAF fusion, with an amino acid loss in the extracellular domain deletions are a novel genomic alteration in iHCC that are transforming and predict clinical sensitivity to FGFR inhibitors. Research Sponsor: Target Cancer Foundation Pharmaceutical/Biotech Company.
Total skeletal, psoas, and rectus abdominis muscle mass as prognostic factors for patients with advanced hepatocellular carcinoma. First Author: Yu Yun Shao, Department of Oncology, National Taiwan University Hospital, Taipei, Taiwan

Background: We investigated whether low skeletal muscle mass (LSMM) defined according to different muscle groups on computed tomography (CT) scans could predict progression of advanced hepatocellular carcinoma (HCC). Methods: We analyzed patients who received first-line sorafenib treatment for advanced HCC in a prospective patient cohort between 2007 and 2012. The muscle masses of total skeletal muscle mass (TSM), paraspinal muscle mass (PS), psoas muscle (PM), rectus abdominis (RA), and abdominal wall (AW) were evaluated using a single CT slice at the third lumbar vertebrae before treatment. LSMM was determined according to the TSM, PS, PM, RA and AW indices, which was calculated as the parameters divided by the square of the body height. Results: We enrolled 137 patients, with a mean age of 57.5 years; 122 were male and 17 were female. Liver disease etiology was hepatitis B virus in 94 (68.6%) patients and hepatitis C virus in 28 (20.4%) patients. All patients had Child-Pugh class A liver reserve. Women had significantly lower TSM index than men did (p = 0.001). Among men, the optimal cut-off points of the TSM, PS, psoas and RA indices for LSMM diagnosis were 39.1, 8.3 and 2.9 cm^2/m^2, respectively. Patients with LSMM exhibited poorer overall survival than patients without LSMM, whether LSMM was defined by TSM index (median 5.8 vs. 11.0 months, p = 0.001), or RA index (median 7.2 vs. 8.1 months, p = 0.003). After adjusting for clinical variables including underweight, age, tumor extent, and performance status, LSMM defined by TSM index (hazards ratio [HR]: 2.12, 95% confidence interval [CI]: 1.12-4.010, p = 0.020), or PM index (HR: 1.650, 95% CI: 1.004-2.710, p = 0.048) remained independent predictors for poor OS. Conclusions: LSMM defined by TSM, PM, RA and AW indices are independent predictors for poor prognosis of advanced HCC, even after adjusted for body weight. Research Sponsor: Ministry of Science and Technology, Taiwan.

Impact of baseline hepatitis B viremia and management on outcomes in patients (Pts) with advanced hepatocellular carcinoma (HCC) and elevated alpha-fetoprotein (AFP): Outcomes from REACH-2. First Author: Peter R. Gale, University Medical Center, Mainz, Germany

Background: REACH (NCT01403437) and REACH2 (NCT02435433) were global, randomized, blinded, placebo (PL)-controlled, phase 3 trials of ramucirumab (RAM) in pts with advanced HCC following sorafenib. REACH-2 limited enrollment to pts with AFP ≥400 ng/mL, and met its primary OS endpoint, consistent with the prespecified REACH subgroup with baseline AFP ≥400 ng/mL. Analysis of pooled individual patient data from REACH1 and REACH2 showed improved OS with RAM vs PL for pts with hepatitis B virus (HBV) etiology (7.7 vs 4.5 mos; HR 0.74, 95% CI 0.55, 0.99). Here we investigate survival and liver function in REACH-2 pts with HBV etiology tested for serum HBV DNA. Methods: Pts had advanced HCC, Child-Pugh A, ECOG PS 0/1, AFP ≥400 ng/mL, and received first-line sorafenib treatment, and were randomized to receive RAM 8 mg/kg or PL Q2W. Pretreatment serum HBV DNA was quantified by HBV-specific PCR (Roche) by a central lab. HBV DNA > 15 IU/mL were detectable (HBV DNA+), ≤ 15 IU/mL were undetectable (HBV DNA-). OS was used to compare progression-free survival (PFS, primary endpoint) and overall proportional hazards model. Liver function was assessed at baseline and before each cycle with the ALB/Lin predictor. Outcomes were assessed by concomitant antiviral therapy. Adverse events (AEs) were graded by NCI-CTCAE v4.0. Pts with available PCR samples and were included in a pooled analysis (70 RAM and 36 PL pts). 48 pts were HBV DNA+ and 58 pts were HBV DNA-. HBV DNA+ pts had lower median OS vs HBV DNA- pts (5.3 vs 10.1 mos, unstratified HR 1.45 95% CI: 1.03-2.02). HBV DNA+ pts had higher concomitant and the risk of recurrence > HCC numerically improved OS compared with those without (n = 12) (5.8 vs 4.0 mos). No difference in OS was noted for HBV DNA+ pts by antiviral therapy use (n = 39 antiviral; n = 19 no antiviral) (10.2 vs 9.7 mos for yes vs no antiviral). In pts taking antiviral therapy, regardless of HBV DNA status, OS was not improved and liver injury/failure related AEs were less frequent. Conclusions: Our data reinforce the use of antiviral therapy to improve outcomes in pts with advanced HBV-associated HCC and elevated AFP. Clinical trial information: NCT02435433. Research Sponsor: Eli Lilly and Company.
Circulating levels of soluble urokinase plasminogen activator receptor (suPAR) to predict outcome after resection of biliary tract cancer. First Author: Sven H Loosen, University Hospital RWTH Aachen, Aachen, Germany

Background: Surgical resection is the only curatively intended therapy for patients with biliary tract cancer (BTC), but 5-year survival rates after tumor resection have remained below 30%, corroborating the need for better pre-operative stratification tools to identify the ideal surgical candidates. The soluble urokinase plasminogen activator receptor (suPAR) represents a mediator of inflammation and has recently been associated with cancer. In this study, we evaluated a potential role of suPAR as a novel biomarker in patients undergoing resection of BTC.

Methods: Tumor expression of uPAR, the membrane bound source of suPAR, was analyzed by IHC in 108 BTC samples. Serum levels of suPAR were analyzed by ELISA in a training and validation cohort comprising a total of 117 BTC patients and 76 healthy controls. Results: A high tumoral uPAR expression was associated with an adverse outcome after BTC resection. In line, circulating levels of suPAR were significantly elevated in BTC patients compared to healthy controls and patients with primary sclerosing cholangitis (PSC). Using a small training set, we established an optimal prognostic suPAR cut-off value of 3.72ng/ml for BTC patients. Importantly, preoperative suPAR serum levels above this cut-off value were associated with significantly impaired overall survival in both the training and validation cohort. Multivariate Cox-regression analysis including clinicopathological parameters such as the tumor stage, markers of systemic inflammation or organ dysfunction and established tumor markers revealed suPAR as an independent prognostic marker following BTC resection. Finally, high preoperative suPAR levels were indicative for acute kidney injury after resection.

Conclusions: Circulating suPAR levels represent a previously unrecognized biomarker in patients with resectable BTC, which might be useful to preoperatively identify the ideal candidates for tumor resection. Research Sponsor: German Research Foundation.

NTRK gene fusions in biliary tract cancers. First Author: Anne Demolis, CUB Hôpital Erasme, Bruxelles, Belgium

Background: Gene fusions involving one of the 3 neurotrophic tyrosine receptor kinases (NTRK) have been identified in approximately 1% of solid tumors and inhibitors of TRK (e.g. larotrectinib) have been shown to have anti-tumor activity regardless of tumor type. NTRK gene fusions have been previously reported in biliary-pancreatic cancers. It is of interest therefore to determine the incidence and molecular characteristics of NTRK gene fusions in patients with bilo-pancreatic cancers. Methods: Formalin-fixed paraffin-embedded archival blocks from surgical resections, biopsies or cytological samples of biliary tract tumors including intra-hepatic cholangiocarcinoma (IH), extra-hepatic cholangiocarcinoma (EH), perihilar cholangiocarcinoma (PH) and gallbladder tumors (G) were selected/retrieved from the tumor bank of the CUB Hôpital Erasme between January 2010 and July 2019. A two-step diagnostic method incorporating immunohistochemistry (IHC) screening followed by NGS analysis was used. Pan-TRK IHC (monoclonal antibody clone EPR17341, AbCam, Cambridge, MA) was used for the screening method. Staining intensity (negative, weak, moderate or strong) and localization (cytoplasmic or nuclear) were evaluated. The presence of at least weak staining tumor cells led to testing by a RNA-based NGS panel (Oncomine Focus Assay, Thermofisher scientific).

Results: 145 archival tumors samples (81 surgical resections, 48 biopsies and 16 cytology) have been selected, including 61 IH, 32 PH, 26 EH and 26 G (67 female and 78 male). 134 samples were suitable to perform IHC. 17 samples were IHC positive. Intensity of staining was weak in 16 samples and moderate in one. Staining location was cytoplasmic (14/17), nuclear (2/17), and nuclear+cytoplasmic (1/17). NGS testing of the 17 IHC positive samples revealed a single NTRK3 gene fusion (ETV6(4)/NTRK3(14)). In this case (female patient with a poorly differentiated PH, deceased), IHC had a weak focal cytoplasmic and nuclear staining. Overall, in the patients screened by IHC and confirmed by NGS, the percentage of NTRK fusions was 0.75%.

Conclusions: NTRK gene fusions are rare in biliary cancer but this finding is of high interest due to the possible treatment with specific TRK inhibitors. Research Sponsor: Bayer Healthcare.

Role of Wnt5a in suppressing invasiveness of hepatocellular carcinoma via epithelial mesenchymal transition. First Author: Kazuki Wakizaka, Department of Gastroenterological Surgery I, Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Background: Wnt signaling pathway includes canonical pathway and non-canonical pathway. Wnt/β-Catenin pathway is known to be associated with the promotion of tumor development while Wnt5a may be associated with the development of hepatocellular carcinoma (HCC). On the other hand, the association between aberrant activation of non-canonical pathway activated by Wnt5a and tumor progression of HCC is not well-known. We investigated the significance of the expression of Wnt5a in HCC.

Methods: Immunohistochemical staining of Wnt5a was performed on the specimen of 243 patients who underwent hepatic resection for HCC. We investigated whether the expression of Wnt5a correlated with the clinicopathological factors, survival, and recurrence in HCC patients. The expression of Wnt5a in human HCC cell lines HLE, HLF, HepG2 and Huh7 was investigated by western blotting. The effects of overexpression or knockdown of Wnt5a on cell lines were evaluated by proliferation assay and invasion assay and changes in epithelial mesenchymal transition (EMT) related molecules were studied by western blotting.

Results: The Wnt5a expression was positive in 63 patients (25.9%) and negative in 180 patients (74.1%). Wnt5a negative was significantly associated with poorly differentiation (P = 0.003) and vascular invasion positive (P = 0.046). By univariate analysis, Wnt5a negative (P = 0.020) was identified as a significant prognostic factor of OS. Multivariate analysis revealed that Wnt5a negative (HR 1.959, 95% CI 1.053-3.409, P = 0.033) was identified as an independent prognostic factor. In the HCC cell lines, the Wnt5a expression was lower in HLE and HLF than in HepG2 and Huh7. Knockdown of Wnt5a by shRNA increased the proliferation and invasiveness in Huh7 with high expression of Wnt5a. As a result, the expression of E-cadherin decreased. In HLF with low expression of Wnt5a, overexpression of Wnt5a inhibited the invasiveness and the expression of vimentin decreased.

Conclusions: Wnt5a negative was associated with poorly differentiation and vascular invasion, and was independent prognostic factor in HCC patients. Wnt5a may be a tumor suppressor involved in EMT mediated changes of invasiveness. Research Sponsor: None.

Genomic characterization of HBV-infected hepatocellular carcinoma patients using circulating tumor DNA. First Author: Daniel Lin, Thomas Jefferson University, Philadelphia, PA

Background: Hepatocellular carcinoma (HCC) is a leading cause of mortality, with Hepatitis B virus (HBV) infection as a dominant etiology. Surgery or ablation may be curative for early-stage HCC. Thus, effective detection and early intervention are needed. Whether circulating genomic alterations in circulating tumor DNA (ctDNA) as a potential diagnostic marker of HCC in HBV-infected patients. Methods: We identified early stage (BCLC 0-1) HCC cases (n = 21) and cancer-free controls (n = 15) from a cohort of Asian patients with HBV, undergoing surveillance at Thomas Jefferson University Hospital between 2013-2017. Blood samples were collected. Circulating cell-free DNA was isolated from plasma and assayed by capture-based next-generation sequencing of a targeted panel of 23 genes implicated in HCC pathogenesis. Sequencing data analysis and somatic mutation identification were conducted using a computational pipeline. Using area under the curve (AUC) in receiver operating characteristic analysis, we evaluated gene alterations and clinical factors (age, gender, cirrhosis) in an exploratory early detection HCC model.

Results: Mutant ARID1A, ATM, CDKN2A, CTNNB1, ERBB2, TP53 genes were increased in HCC cases relative to non-cancer patients (85.7% vs 53.3%, P = 0.058; 42.9% vs 6.7%, P = 0.025; 38.1% vs 6.7%, P = 0.051; 42.9% vs 0%, P = 0.005; 52.4% vs 13.3%, P = 0.016; 100% vs 66.7%, P = 0.008, respectively). HCC patients had higher prevalence of cirrhosis than controls (90.5% vs. 60%, P = 0.046). Using the 6 mutant genes alone, the AUC for discriminating HCC from non-cancer patients was 0.827 (95% confidence interval [CI]: 0.707-0.953), which was greater than the AUC for discriminating cirrhosis from non-cirrhosis (0.531). When the 6 mutant genes were combined with clinical factors, the AUC of the exploratory HCC detection model increased to 0.914 (P = 0.045).

Conclusions: We identified 6 genomic aberrations in ctDNA that were more prevalent in HCC patients compared with non-cancer patients. These 6 gene alterations along with clinical factors were useful for discriminating HBV-infected patients at an early stage. These findings warrant further validation in future studies. Research Sponsor: American Cancer Society Institutional Grant.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
HEPATOBLIARY CANCER

Poster Session (Board #E16), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Gamma-synuclein as a potential novel prognostic marker promoting tumor cell migration in biliary tract carcinoma. First Author: Yusuke Takemura, Department of Surgery, Keio University School of Medicine, Tokyo, Japan

Background: Biliary tract carcinoma (BTC) is a highly malignant tumor, but the detailed pathological mechanism of its development and progression remain ill-defined. Gamma-synuclein (SNCG) promotes invasive behavior in pancreatic cancer and a range of other cancers, and SNCG expression is reportedly a prognostic factor. However, the role of SNCG in BTC remains unknown. Consequently, we investigated the clinicopathological significance and function of SNCG in BTC.

Methods: Using surgically resected BTC specimens from 149 patients with adenocarcinoma (extrahepatic cholangiocarcinoma (ECC) (n = 98); intrahepatic cholangiocarcinoma (ICC) (n = 51)), we immunohistochemically evaluated SNCG positivity and checked for correlations with clinicopathological factors and outcomes. Furthermore, cell lines with high expressions of SNCG were selected from 17 BTC cell lines by using immunohistochemistry and qPCR. Cell proliferation and migration assays were then performed in the presence and absence of SNCG (silenced using). Results: SNCG expression was found in 32 of 149 (21.4%) BTC patients. SNCG expression was significantly correlated with poorly differentiated tumor (P = 0.001) and lymph node metastases (P = 0.001). SNCG positivity was also correlated with poorly differentiated tumor in both ECC and ICC (P = 0.008 and P = 0.03, respectively), but was correlated with lymph node metastases only in ECC (P = 0.003). Multivariate analyses identified SNCG expression as an independent prognostic factor of poor overall survival (P = 0.008) and poor recurrence-free survival (RFS) (P = 0.006). SNCG expression in both ECC and ICC was significantly associated with poor prognosis in univariate analysis, and multivariate analysis identified SNCG as an independent prognostic factor of poor RFS for ECC (P = 0.03). High SNCG expression was found in 3 BTC cell lines (NCC-BDI, NCC-B03, and NCC-CC6-1). Functional analysis revealed that SNCG silencing by siRNA suppressed cell migration significantly in NCC-BDI and NCC-CC6-1 and downregulated cell proliferation in NCC-CC6-1. Conclusions: Our results suggest that SNCG may promote tumor cell activity and is potentially a novel prognostic marker in BTC. Research Sponsor: JSPS KAKENHI grant No. 16K10609.

Poster Session (Board #E17), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Primary versus metastatic intrahepatic cholangiocarcinoma: A comparative comprehensive genomic profiling (CGP) study. First Author: Jeffrey S. Ross, Foundation Medicine, Cambridge, MA

Background: Genomic alterations (GA) characteristic of IHCC are well known. We queried whether the GA of IHCC from primary tumor biopsies (p-bx) would differ from IHCC metastasis biopsies (m-bx).

Methods: CGP was performed on 1,268 cases of advanced stage IHCC using p-bx in 1,048 cases and the GA of IHCC from primary tumor biopsies (p-bx) would differ from IHCC metastasis biopsies (m-bx).

The GA of IHCC from primary tumor biopsies (p-bx) would differ from IHCC metastasis biopsies (m-bx).

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Poster Session (Board #E18), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Circulating free DNA (cfDNA) and tissue next-generation sequencing analysis in a phase II study of infigratinib (BGJ398) for cholangiocarcinoma with FGFR2 fusions. First Author: Shalini Makawita, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Fibroblast growth factor receptor 2 (FGFR2) alterations occur in 11% of cholangiocarcinomas, 85% of which are fusions. A multicenter, open-label, phase II study is currently evaluating the efficacy of infigratinib, a selective FGFR1-3 tyrosine kinase inhibitor, in patients with previously treated advanced cholangiocarcinoma containing FGFR2 fusions. We report detailed biomarker analyses from this study. Methods: Patients with advanced or metastatic cholangiocarcinoma containing FGFR2 fusions whose disease had progressed following cisplatin- or gemcitabine-based therapy were eligible. Patients received oral infigratinib 125 mg once daily on days 1-21 every 28 days. Comprehensive genomic profiling (CGP) was performed on tumor tissue and cfDNA collected prior to the start of therapy. The primary endpoint was investigator-assessed overall response rate (ORR) [RECIST version 1.1]. Data cut-off (prespecified): August 8, 2018. Trial registration: NCT02150967. Results: At data cut-off, 71 patients with FGFR2 fusions were included (62% women; median age 53 years; 55% received ≥2 prior lines of therapy). Median duration of treatment was 5.5 months. ORR (confirmed and unconfirmed) was 31.0% (95% CI 20.5-43.1%) and confirmed ORR was 26.9% (95% CI 16.8-39.1%). 33 unique FGFR2 fusion genes were identified in 71 enrolled patients. The most common fusion gene partner was BICC1 (32%; 23/71). Pathogenic variants in 9 other druggable genes were identified in 32% of patients (13/37) that underwent CGP. FGFR2 fusions were concordant in 67% (8/12) of patients with tumor tissue and cfDNA at screening. Conclusions: The large assortment of FGFR2 fusion genes identified in this study underscores the diversity of FGFR2 rearrangements that may drive cholangiocarcinoma. Although cfDNA analysis was performed in a minority, these preliminary data suggest that cfDNA analysis may be valuable for the identification of FGFR2 fusions and to study intratumoral heterogeneity. Clinical trial information: NCT02150967. Research Sponsor: QED Therapeutics.
Comparison of the clinical features, treatment patterns, and tumor mutations of patients with intrahepatic (ICC) and extrahepatic (ECC) cholangiocarcinoma. First Author: Leon Pappas, Massachusetts General Hospital, Boston, MA

Background: Though studies indicate that the genomic profiles of ICC and ECC are distinct, the molecular features that differentiate them still need to be well characterized. The purpose of this study was to further analyze these differences and patient treatment patterns in a multi-center cohort. Methods: A retrospective chart review was performed at 8 institutions on patients (pts) with ICC or ECC diagnosed after June 2009. Data on demographics, risk factors, treatments, pathology and overall survival (OS) were collected. Tumor genotyping results from CLIA-certified tissue assays were analyzed. Fisher’s exact, Wilcoxon rank sum and log-rank tests were used to compare subgroups. Results: In a database of 737 pts with cholangiocarcinoma, 530(73%) had ICC and 207(27%) had ECC. Pts with ICC more often presented in later stages, had tumors >5cm at resection (p<0.0001) and had metastases to the liver, lymph nodes, lung and/or bone (p<0.01). Pts with ICC more often received liver directed therapy, targeted therapy and multiple lines of systemic therapy and they more often enrolled in a clinical trial (p<0.001). Pts with ECC were more likely to be male, undergo surgery, receive adjuvant chemotherapy and/or chemoradiation (all p<0.05). Mutation profiling performed in 381(52%) pts (ICC/ECC = 301/80) showed that pts with ICC were more likely to have DHH mutations and FGFR2 fusions, whereas pts with ECC were more likely to have KRAS, APC, SMAD4, WNT, TGFb and TPS3 mutations (all <0.05). Factors that did not differ significantly between pts with ICC and ECC include race, rates of primary sclerosing cholangitis, median diagnosis age(9) and 1st resolved rate. Median OS from diagnosis was 19.9 months in ICC and 17.3 months in ECC (p=0.8471). Conclusions: While pts with ICC and ECC have some similarities in their clinical features, differences in metastases patterns and molecular profiling significantly impact their management such that pts with ICC receive more liver-directed therapy, targeted therapy and more lines of systemic therapy. Further prospective studies are needed as referral patterns to tertiary care centers may have impacted these results. Research Sponsor: None.

Hepatocyte-derived intrahepatic cholangiocarcinoma requires Yap and Sox9: A clinical and preclinical analysis. First Author: Sadatdarh Monga, University of Pittsburgh Medical Center, Pittsburgh, PA

Background: Intrahepatic cholangiocarcinoma (ICC) is a liver tumor of increasing incidence and devastating prognosis. WGS and WES have identified numerous molecular pathways and fusions in ICC. Recent studies have also suggested a hepatocellular cell source in ICC associated with chronic liver insult such as non-alcoholic steatohepatitis (NASH) or primary sclerosing cholangitis (PSC). Methods: Since co-expression of myristoylated AKT (myrAKT) & Notch intracellular domain (NICD) in hepatocytes using sleeping beauty transposon/transposase and hydrodynamic tail vein injection (SB-HTVI) lead to ICC, we initiated a comprehensive analysis of co-expression of myrAKT+NICD leading to hepatocyte-derived ICC, conditional deletion of either Yap or Sox9 significantly delayed and almost completely abrogated ICC development. While Yap deletion impaired the initial HC-to-BEC fate conversion, Sox9 elimination had no such effect on reprogramming. Interestingly, following deletion of either Yap or Sox9 we observed a few AKT/NICD-driven ICC tumors expressing either Sox9 or Yap but not both. This also occurred in a small subset of human CC tumors which may be Sox9+/Yap- (4%) or Sox9-/Yap+ (3.7%), showing that deletion of Yap or Sox9 is not sufficient to completely abrogate ICC development. We finally demonstrated that conditional deletion of both Yap & Sox9 completely blocked development of ICC tumors in the myrAKT+NICD model. Conclusion: Thus, we show that cholangiocyte injury or NASH in humans and mice induces hepatocyte-to-cholangiocyte reprogramming to increase the risk of ICC development. We also provided evidence for distinct roles of Yap and Sox9 in ICC development and demonstrate the therapeutic potential of targeting these factors for treatment of subsets of ICC. Research Sponsor: U.S. National Institutes of Health Intramural Endowed Chair.

Poster Session (Board #E19), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Poster Session (Board #E20), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Patient-derived organoids for personalized drug screening in intrahepatic cholangiocarcinoma. First Author: Ricardo J. Antonia, University of California San Francisco, San Francisco, CA

Background: Despite standard treatment with gemcitabine and cisplatin, median survival for unresectable Intrahepatic Cholangiocarcinoma (ICC) is <1 year. Clearly, novel therapeutic strategies are urgently needed. The paucity of targetable mutations in ICC and the as yet unproven benefit of genetically targeted drugs led us to ask whether a reliable clinical benefit may be revealed by patient-specific therapeutic testing in novel models of ICC. Here we describe our ability to establish patient-derived three-dimensional organoid cultures (PDO) that enable individualized identification of active single agents or drug combinations in surrogate models of ICC. Methods: To model patient-specific drug responses, we used the freshly resected ICCs from small samples of single patient tumors to generate PDXs and PDOs, small spheroidal clusters of tumor cells grown in vitro. We have employed a high-throughput drug screening platform using Al-enhanced robotics (Yamaha Motor Corporation) to identify and distribute single, uniformly sized PDOs into 384-well ultra-adherent plates. This is coupled with a TECAN D300e drug dispenser that rapidly delivers nanoliter volumes of a 34-drug panel, thereby facilitating rapid, reliable drug response analyses. Results: Our data show that PDOs retain characteristic genomic and histological features of the patients’ tumors. Drug responses were specific to each patient tumor, but PDXs from all patients responded to a greater or lesser degree of mTOR inhibition, suggesting that this pathway is important in ICC. The response of PDO to the mTOR inhibitor Sapanisertib (INK128), was recapitated in the same patient’s PDX. Further, INK128 was synergistic with standard chemotherapy agents such as carboplatin in PDOs from patients with advanced disease. Conclusions: This approach has the potential to identify personalized treatments. The establishment of PDO may allow economical patient-specific, high throughput drug screens that could ultimately inform clinical practice. Research Sponsor: University of Pittsburgh Medical Center, Pittsburgh, PA

Poster Session (Board #E21), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Beta-catenin mutations in hepatocellular cancer, tumor cell metabolism, and the response of these tumors to mTOR inhibition. First Author: Sadatdarsh Monga, University of Pittsburgh Medical Center, Pittsburgh, PA

Background: Hepatocellular cancer (HCC) continues to grow in incidence despite approval of many new therapies including immune checkpoint inhibitors (ICIs) and TKIs. Genomic landscape of HCC is becoming apparent through WGS and WES. One major driver of HCC is the canonical Wnt/b-catenin pathway. Mutations in CTNNB1, which encodes for b-catenin, are evident in 26-37% of all human HCCs. However, expression of mutant-b-catenin in liver in mice is insufficient for HCC development. Indeed, analysis of HCC cases has revealed CTNNB1 mutations in 30% of HCC cases with missense changes with activation/overexpression of Met and Myc and mutations in TERT promoter or mutations in NFE2L2/KEAP1, APOB and ARID2. Methods: Using sleeping beauty transposon/transposase and hydrodynamic tail vein injection, we co-expressed mutant-CTNNB1 (S545Y, S337 or T41A) and one clinically relevant co-occurrence to study significance and biology of HCC. Any novel findings in the preclinical model were validated in HCC patient cohorts. Results: Co-expression of mutant-CTNNB1 and one relevant co-occurrence led to development of HCC in mice in 6-70x weeks. All HCC in these models showed a dramatic increase in glutamine synthetase (GS), encoded by Gli1, a known target of the Wnt/b-catenin signaling pathway in the liver. This led to an increase in glutamine levels in the tumor-bearing liver. Increased glutamine in the tumors in turn led to increased levels of phospho-mTOR-S2448, a marker of mTORC1 activation. In fact, examination of ~400 patient HCCs showed a significant correlation between positive GS and p-mTOR-S2448 staining. Treatment of Met-b-catenin model with Rapamycin led to notable and significant decrease in HCC burden. Conclusions: Our study demonstrates b-catenin/mutated HCC to be positive for both GS and in turn mTORC1 activation. This provided a novel opportunity for personalized medicine in HCC and CTNNB1-mutated HCCs may be therapeutically targeted by mTOR and more specifically, mTORC1 inhibitors. Research Sponsor: U.S. National Institutes of Health Intramural Endowed Chair.

Poster Session (Board #E22), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

HEPATOBLIARY CANCER
Novel therapeutic avenues for cholangiocarcinoma treatment: A meta-analysis. First Author: Nabeel Aljabban, Penn State School of Medicine, Hershey, PA

Background: Cholangiocarcinoma (CCA) is a rare cancer of the bile ducts but has been increasing in incidence. The mainstay of treatment of CCA is resection or chemoradiation for more advanced disease, with immunotherapy being an evolving field in treatment. A better understanding of CCA pathology will pave new avenues for treatment. Methods: We employed our STARGEO platform to conduct a meta-analysis of public data from NCBI's Gene Expression Omnibus. We performed meta-analysis with 259 CCA tumor samples against 16 normal intrahepatic duct samples as a control. We then analyzed the signature in Ingenuity Pathway Analysis. Results: Our analysis revealed FXR/RXR and LXR/RXR activation as top canonical pathways. Top upstream regulators identified included HNF1A (with predicted inhibition) and ERBB2 (with predicted activation). The most upregulated genes included several extracellular matrix proteins implicated in cancer including COL1A1, LAMC2 (correlated with poor prognosis in CCA), KRT17 (a keratin implicated in various malignancies but not well described in CCA), and LAMB3 (exerts tumorigenesis through PI3K/Akt signaling). Additionally, we found strong upregulation of the immunophilin FKBP1A, which is involved in mTOR activation. We also noted upregulation of ubiquitin-associated gene UBASH3B, which inhibits endocytosis in EGFR and has been described in breast cancer but not CCA. From our investigation of immune checkpoint inhibitors, we found upregulation of classical described inhibitors such as CTLA4, TIGIT, and BTLA. In addition, we found upregulation of SIGLEC7, which has been recently shown to suppress immune function by binding to terminal sialic acid on glycans on the surface of immune cells. Conclusions: Our analysis highlights the possible role of ERBB2 and several extracellular genes in the pathogenesis of CCA. We also identify the role of genes not previously described in CCA such as FKBP1A and UBASH3B. Lastly, our results promote the promise of immunotherapy in CCA treatment. Research Sponsor: None.

Background: EASL guidelines for management of HCC recommends assessing tumor response according to mRECIST at all stages of the disease (EASL guidelines, J Hep 2018). Several studies have reported that objective response by mRECIST predicted overall survival (OS) but definitive data are still lacking. Methods: The PubMed database and ASCO meeting library were searched for full reports of randomized trials in patients with advanced HCC treated by systemic therapy up to August 31, 2018. We search strategy used the following terms: HCC, mRECIST, OS and objective response rate (ORR). We assess the association between ORR and OS in a meta-analysis of pooled data by using random effects model comparing patients achieving objective response (complete or partial response) versus non responders (stable disease, progressive disease, and displayed the results as per hazard ratio (HR, 95% CI). Results: Among 14 articles assessing response by mRECIST to systemic therapies in randomized studies in advanced HCC, 4 studies (5 trials) including 1,463 patients were considered eligible. Systemic therapies tested included lenvatinib, sorafenib, brivanib and nintedanib. Overall, ORR as per mRECIST ranged from 11.5% to 18.8%, being the median OS for responders of 11.5 to 27.2 mo (as opposed 8.9 to 11.4 for non-responders). As per random effects model, the HR for overall survival (responders versus non responders) was 0.47 (95% confidence interval 0.34-0.66, p<0.001). Conclusions: Objective response by mRECIST to systemic therapies in patients with advanced HCC is significantly and strongly associated to OS. Patients achieving an objective response can expect a significantly longer OS. Research Sponsor: None.

Association of objective response by mRECIST with better overall survival (OS) in patients with advanced hepatocellular carcinoma (HCC) treated with systemic therapies: A systematic review and meta-analysis of randomized controlled trials. First Author: Masatoshi Kudo, Kindai University Faculty of Medicine, Osaka, Japan

Background: EASL guidelines for management of HCC recommends assessing tumor response according to mRECIST at all stages of the disease (EASL guidelines, J Hep 2018). Several studies have reported that objective response by mRECIST predicted overall survival (OS) but definitive data are still lacking. Methods: The PubMed database and ASCO meeting library were searched for full reports of randomized trials in patients with advanced HCC treated by systemic therapy up to August 31, 2018. We search strategy used the following terms: HCC, mRECIST, OS and objective response rate (ORR). We assess the association between ORR and OS in a meta-analysis of pooled data by using random effects model comparing patients achieving objective response (complete or partial response) versus non responders (stable disease, progressive disease, and displayed the results as per hazard ratio (HR, 95% CI). Results: Among 14 articles assessing response by mRECIST to systemic therapies in randomized studies in advanced HCC, 4 studies (5 trials) including 1,463 patients were considered eligible. Systemic therapies tested included lenvatinib, sorafenib, brivanib and nintedanib. Overall, ORR as per mRECIST ranged from 11.5% to 18.8%, being the median OS for responders of 11.5 to 27.2 mo (as opposed 8.9 to 11.4 for non-responders). As per random effects model, the HR for overall survival (responders versus non responders) was 0.47 (95% confidence interval 0.34-0.66, p<0.001). Conclusions: Objective response by mRECIST to systemic therapies in patients with advanced HCC is significantly and strongly associated to OS. Patients achieving an objective response can expect a significantly longer OS. Research Sponsor: None.

Pancreaticobiliary maljunction (PBM) is known to be a unique entity closely related to biliary carcinogenesis. We herein report update analysis of PBM focusing on biliary cancer as third report of Japan nationwide survey. From 2010 to 2015, 3,419 patients with PBM were registered at 141 medical institutions in Japan, 3,289 (94.5%) pediatric and 1945 adult patients) out of 3,419 patients were fully investigated, according to presence of bile duct dilatation (BDD), age (pediatric or adult), etc. Results: In pediatric patients only 3 cases with BDO (0.3%) had bile duct cancer. On the other hand, in adults, biliary cancer incidence was 2.1% in patients with BDD and 43.5% in patients without BDD. The rates were extremely high in comparison with 0.0174% of Japanese prevalence of biliary cancer 2013. The cancer incidence of bile duct, gallbladder and both in adults with BDD/without BDD were 6.7%/4.1%, 13.0%/37.3%, and 1.4%/21.1%, respectively. In patients without associated biliary cancers, extrabiliary bile duct resection (EHDBRx) combined with cholecystectomy was performed in 85.5% of adults with BDD, while, in only 31.2% adults without BDD. Regarding the new biliary cancer occurrence of patients having follow-up data, the rate was 0.3% in 354 patients with BDD who underwent EHDBRx, while that was 4.0% in 75 patients without BDD who underwent simple cholecystectomy. In patients without BDD, cancer incidence (6.7%) in the late period (2010 to 2015) was higher than those (3.3% and 3.5%) in early and middle period (1990 to 1999, and 2000 to 2009). Conclusions: This updated nationwide survey of PBM revealed characteristics of associated and newly occurred biliary cancers, and could be widely used as a reference data for diagnosis and treatment of PBM. Research Sponsor: None.
**589**

**Poster Session (Board #F6)**

Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

 Increased frequency of PD-1+CD57+Siglec-7 dysfunctional NK cells in patients with nonalcoholic fatty liver disease. First Author: Yuzuru Sakamoto, Department of Gastroenterological Surgery I, Hokkaido University Graduate School of Medicine, Sapporo, Japan

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**Background:**

The proportion of non-alcoholic fatty liver disease (NAFLD) has been increasing as a cause of hepatocellular carcinoma (HCC) worldwide. Natural killer (NK) cells are involved in the first line of immune defense against cancer. NK cell function is regulated by activating and inhibitory NK cell receptors. However, the role of NK cells in the pathogenesis of NAFLD and NAFLD-HCC is still largely unknown. In this study, we aimed to clarify the phenotypic and functional features of NK cells in NAFLD and NAFLD-HCC.

**Methods:**

We performed mass cytometry (CyTOF) and flow cytometry analysis of NK cells in 33 NAFLD patients (22 chronic hepatitis (CH), 8 liver cirrhosis (LC), 3 with HCC), and 9 healthy donors (HDs). We compared surface markers of NK cells in cancerous and non-cancerous intraparenchymal lymphocytes (IHLs). We also measured NK cell function in the presence of IL-12 and IL-18.

**Results:**

The frequency of NK cells was lower in NAFLD patients compared to HDs. PD-1, CD57, ILT2 were highly expressed, and co-stimulatory markers (CD4+ and CD8+ T cells) were reduced in NAFLD patients compared to HDs. In NAFLD patients, Siglec-7 levels on NK cells were negatively correlated with PD-1 and CD57, and positively correlated with NKP30 and NKP46. The other inhibitory markers (NKLG2A, KIR3DL1, and KIR2DL3), activating markers (CD69 and NKDR2D), and NK cell receptors (Tim-3 and TIGIT) were comparable between NAFLD patients and HDs. PD-1 and CD57 expression levels on NK cells were also significantly upregulated in NAFLD-HCC patients than those in HCs. CD57 was rarely expressed on NK cells in non-cancerous NHLs, on the other hand, highly expressed in cancerous NHLs. The IFNy production and CD107a expression on NK cells were also decreased in NAFLD patients. PD-1+CD57+Siglec-7 NK cells were observed in NAFLD patients, rarely in HCs. PD-1+CD57+Siglec-7 NK cells were functionally impaired compared to other NK subsets. In patients with NAFLD, NK cells, NKp30, NKP46, NKP30, NKP46. The other inhibitory markers (NKLG2A, KIR3DL1, and KIR2DL3), activating markers (CD69 and NKDR2D), and NK cell receptors (Tim-3 and TIGIT) were comparable between NAFLD patients and HDs. PD-1 and CD57 expression levels on NK cells were also significantly upregulated in NAFLD-HCC patients than those in HCs. CD57 was rarely expressed on NK cells in non-cancerous NHLs, on the other hand, highly expressed in cancerous NHLs. The IFNy production and CD107a expression on NK cells were also decreased in NAFLD patients. PD-1+CD57+Siglec-7 NK cells were observed in NAFLD patients, rarely in HCs. PD-1+CD57+Siglec-7 NK cells were functionally impaired compared to other NK subsets. In patients with NAFLD, NK cells, NKp30, NKP46, NKP30, NKP46.

**Conclusions:**

Increased proportion of dysfunctional PD-1+CD57+ Siglec-7 NK cells, and dysfunctional NK cells might be related to impairment of surveillance for HCC. Research Sponsor: None.

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**588**

**Poster Session (Board #F5)**

Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Progression-free survival in patients with cholangiocarcinoma with FGFR2 fusions or rearrangements: An exploration of response to systemic therapy. First Author: Kristen Bibeau, Incyte Corporation, Wilmington, DE

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**Background:**

First Author: Shinichiro Yamada, Tokushima University, Tokushima, Japan

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**Significance of frailty in prognosis after hepatectomy in older patients with hepatocellular carcinoma.**

First Author: Shinnichiro Yamada, Tokushima University, Tokushima, Japan

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**Methods:**

Eighty-one patients over 75 years who underwent hepatectomy for HCC between 2007 and 2018 were enrolled in this study. Frailty was diagnosed as CFS. We compared clinical and pathologic parameters, such as age, gender, preoperative comorbidity, and liver function between 2 groups.

**Results:**

Significantly worse in frailty group (p = 0.03). In univariate analysis for overall survival, lymphocyte ratio (NLR, p = 0.14). Frailty group also showed tendency of high neutrophil-lymphocyte ratio (NLR, p = 0.04) and tendency of high neutrophil-lymphocyte ratio (NLR, p = 0.04).

**Conclusions:**

Frailty is an independent prognostic factor for HCC patients who underwent hepatectomy. Research Sponsor: None.
**TPS592**

**Trials in Progress Poster Session (Board #5P), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

**FIGHT-302: Phase III study of first-line (IL) pemigatinib (PEM) versus gemcitabine (GEM) plus cisplatin (CIS) for cholangiocarcinoma (CCA) with FGFR2 mutations or rearrangements.** First Author: Tanios S. Bekaii-Saab, Mayo Clinic, Phoenix, AZ

**Background:** For advanced CCA, standard of care 1L systemic treatment is GEM + CIS. Given the lack of intrahepatic CCA provide potential therapeutic targets. Fibroblast growth factor receptor (FGFR) 2 gene rearrangements driving CCA tumorigenesis were identified almost exclusively in intrahepatic CCA patients (pts) (incidence, 10-16%). In phase 2, PEM (INCB054828), a selective, potent, oral FGFR1-3 inhibitor elicited an objective response rate (ORR) of 35.5% and median progression-free survival (PFS) of 6.9 months (mo) in previously treated, locally advanced or metastatic CCA with FGFR2 rearrangements (NCT02924376). FIGHT-302, a randomized, open-label, phase 3 study will evaluate efficacy and safety of IL PEM vs GEM + CIS in unresectable/metastatic CCA with FGFR2 mutations or rearrangements. Exclusions include clinically significant neurotoxicity or disorder; history of chemotherapy or hormone therapy in disorder or systemic imbalance with oncotic soft tissue calcification; untreated CNS metastases or history of uncontrolled seizures; Pts will be randomized (1:1) stratified by region and tumor burden) to PEM (13.5 mg QD on a 21-day [d] cycle or GEM (1000 mg/m²) on D1 and D8 of 21-d cycles (max 8). Crossover to PEM allowed after confirmed progression. PEM titration to 18 mg from cycle 2 allowed for pts without hyperphosphatemia (serum phosphate >5.5 mg/dL) and Grade ≥2 treatment-related adverse events during cycle 1. Hyperphosphatemia will be managed with diet modifications, phosphate binders, diuretics, or dose adjustments. Treatment will continue until progression or unacceptable toxicity. Primary endpoint is PFS (by investigator review). Secondary endpoints are OS, ORR, duration of response, disease control rate, safety, and quality of life. Four pts (target N = 432) are enrolled as of Sep 25, 2019. Clinical trial information: NCT03656536. Research Sponsor: Incyte Corporation.

**TPS593**

**Trials in Progress Poster Session (Board #6P), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

**Phase II study of fluorouracil (FU), leucovorin (LV), and lapatinib (LAP) in previously treated advanced biliary tract cancer (NAPOLI-2).** First Author: Benjamin Adam Weinberg, Ruesch Center for the Cure of Gastrointestinal Cancers, Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC

**Background:** Biliary tract cancers (BTCs) are rare and aggressive malignancies. The current standard of care for advanced BTC is gemcitabine (GEM) plus cisplatin. Although there is no established second-line treatment, regimens such as FOLFOX, XELOX, FOLFIRI, XELIRI, GEM, and capcetabine have activity. Na-IRI contains IRI free base encapsulated in liposome nanoparticles which shelter IRI from conversion to its active metabolite (SN-38) and increase intratumoral levels of SN-38 compared with IRI. FU/LV/Na-IRI has shown overall survival benefit and acceptable toxicity in patients (pts) with metastatic pancreatic adenocarcinoma following GEM-based therapy in the NAPOLI-1 trial. Methods: This is a single-arm, open label, multicenter phase II study of pts with advanced BTC previously treated with gemcitabine plus platinum chemotherapy. Pts will receive NA-IRI 70 mg/m² IV over 90 minutes, LV 400 mg/m² IV over 30 minutes, and FU 2400 mg/m² over 46 hours, every 14 days. The primary objective is to determine progression-free survival (PFS) rate at 4 months (mo) using RECIST v. 1 criteria and central radiology review. Response assessments will occur using imaging every 8 weeks. All pts who receive at least 1 dose of the study treatment will be eligible for the primary analysis. We will substitute pts who screen fail or do not begin treatment. Median PFS reported for pts receiving second-line 5FU doublet chemotherapy is 3 months with a PFS₅₀ of 30%. FU/LV/na-IRI would be of interest if it could increase the PFS₅₀ to 50% or higher. We will use a 2-stage Simon Minimax design. Using a 1-sided α of 0.05 and 80% power, 39 pts will be required to detect a difference in PFS₅₀ between 30% and 50%. Assuming a dropout rate of 10%, 44 pts will be enrolled across the 5 study sites. Enrollment began in Q2 2019. Clinical trial information: NCT04005339. Research Sponsor: Ipsen.

**TPS594**

**Trials in Progress Poster Session (Board #7P), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

**Phase II trial of trifluoridine/tipiracil and irinotecan for the treatment of advanced refractory biliary tract cancer.** First Author: Hao Xie, Mayo Clinic, Rochester, MN

**Background:** Effective treatment options are very limited for patients with advanced refractory biliary tract cancer (BTC). Fluoropyrimidine-based chemotherapy regimen such as 5-fluorouracil and irinotecan are frequently used as the first-line therapy with at least some activity in fluoropyrimidine-sensitive and resistant tumors due to its unique mechanisms of action. Given early toxicity and efficacy data from our previous single-arm phase II trial of trifluoridine/tipiracil (FTD/TPI) and irinotecan in advanced refractory BTC, key eligibility criteria include historically confirmed advanced, unresectable BTC who have progressed on at least one line of systemic therapy and have measurable disease per RECIST v1.0. Target accrual is 25. Treatment includes trifluoridine/tipiracil (FTD/TPI) 25 mg/m² on days 1 and 15 and irinotecan 180 mg/m² on day 1 in 14-day cycles. Patients will be evaluated for response every 4 cycles and in the absence of disease progression, therapy may be given up to 2 years. The primary endpoint is the progression-free survival rate at 16 weeks. Secondary endpoints include overall response rate, disease control rate, progression-free survival, overall survival, and incidence of adverse events. Correlative biomarker studies include evaluations of circulating tumor DNA and circulating tumor cells at baseline, after 4 cycles and at progression; and development of patient-derived tumor organoids from pre-treatment biopsies for parallel treatments. This study was approved and funded in part by the National Comprehensive Cancer Network (NCCN) Oncology Research Program from general research support provided by Taiho Oncology, Inc. Clinical trial information: NCT04072445. Research Sponsor: Taiho Oncology, Inc National Comprehensive Cancer Network (NCCN).

**TPS595**

**Trials in Progress Poster Session (Board #8P), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

**Phase I study of a new concept cancer vaccine composed artificial intelligence (AI)-designed shared-antigen peptides plus combined synergistically activating antigen-specific CTL reaction (CYTOO1) in patients with advanced hepatocellular carcinoma (CRESCENT 1).** First Author: Sadahisa Ogasawara, Department of Gastroenterology, Graduate School of Medicine, Chiba University, Chiba, Japan

**Background:** CYTOO1 (CYTLIMIC Inc.) is a novel cancer vaccine involving artificial intelligence (AI)-designed shared-antigen peptides on a one-sided α + 0.5 and 80% power, 39 pts will be required to detect a difference in PFS₅₀ between 30% and 50%. Assuming a dropout rate of 10%, 44 pts will be enrolled across the 5 study sites. Enrollment began in Q2 2019. Clinical trial information: NCT04005339. Research Sponsor: Ipsen.

**Methods:** This is a single-center, phase 1, open-label, single-arm, investigator-initiated clinical trial of CYTOO1 for advanced HCC patients with no eligible standard systemic therapy, Child-Pugh A or B and ECOG PS 0-1 who have progressed on at least one line of systemic therapy and have measurable disease per RECIST v1.1; ECOG PS ≤1; documented FGFR2 mutations or rearrangements. Exclusion criteria include prior radiotherapy or chemotherapy, history of malignancy, or history of uncontrolled Bronchiolitis obliterans syndrome; ECOG PS >1; unstable medical condition; prior participation in another clinical trial of an investigational agent or investigational device within 4 weeks or 5 half-life of prior systemic therapy; period of prior systemic therapy for advanced disease (≤6 mo before enrollment; radiographically measurable/evaluable disease (per RECIST v1.1); EGOG PS ≤1; documented FGFR2 mutations or rearrangements. Exclusion criteria include clinically significant neurotoxicity or disorder; history of chemotherapy or hormone therapy in disorder or systemic imbalance with oncotic soft tissue calcification; untreated CNS metastases or history of uncontrolled seizures; Pts will be randomized (1:1) stratified by region and tumor burden) to PEM (13.5 mg QD on a 21-day [d] cycle or GEM (1000 mg/m²) on D1 and D8 of 21-d cycles (max 8). Crossover to PEM allowed after confirmed progression. PEM titration to 18 mg from cycle 2 allowed for pts without hyperphosphatemia (serum phosphate >5.5 mg/dL) and Grade ≥2 treatment-related adverse events during cycle 1. Hyperphosphatemia will be managed with diet modifications, phosphate binders, diuretics, or dose adjustments. Treatment will continue until progression or unacceptable toxicity. Primary endpoint is PFS (by investigator review). Secondary endpoints are OS, ORR, duration of response, disease control rate, safety, and quality of life. Four pts (target N = 432) are enrolled as of Sep 25, 2019. Clinical trial information: NCT03656536. Research Sponsor: Incyte Corporation.

**TPS596**

**Methods:** This is a single arm, open label, multicenter phase II trial of trifluoridine/tipiracil (FTD/TPI) 25 mg/m² on days 1-5 and irinotecan 180 mg/m² on day 1 in 14-day cycles. Patients will be evaluated for response every 4 cycles and in the absence of disease progression, therapy may be given up to 2 years. The primary endpoint is the progression-free survival rate at 16 weeks. Secondary endpoints include overall response rate, disease control rate, progression-free survival, overall survival, and incidence of adverse events. Correlative biomarker studies include evaluations of circulating tumor DNA and circulating tumor cells at baseline, after 4 cycles and at progression; and development of patient-derived tumor organoids from pre-treatment biopsies for parallel treatments. This study was approved and funded in part by the National Comprehensive Cancer Network (NCCN) Oncology Research Program from general research support provided by Taiho Oncology, Inc. Clinical trial information: NCT04072445. Research Sponsor: Taiho Oncology, Inc National Comprehensive Cancer Network (NCCN).
Phase Ib/II study of sorafenib (SOR) and pembrolizumab (PEMB) in advanced hepatocellular cancer (HCC). First Author: Rohit Gosain, Roswell Park Comprehensive Cancer Center, Buffalo, NY

Background: SOR has been the backbone of advanced HCC therapy with poor outcome. Anti-PD-1 therapy is approved as a second-line treatment option in HCC due to its promising efficacy and safety. Preclinical work showed that SOR is immunomodulatory and may be synergistic when combined with anti-PD-1 therapy. Guided by this data, we initiated this multicenter study of SOR and PEM in advanced HCC patients (pts). Methods: Pts who have Child-Pugh Class A, ECOG PS of 0, biopsy-proven measurable HCC that is unresectable or metastatic, are included. Pts must not receive either SOR or anti-PD-1 therapy before. A total of 27 pts will be enrolled from 2 sites. Pts must have the following lab values: ANC $ 1.500/μL; Hgb $ 8.5 g/dL; Pts $75,000/μL; serum total bilirubin $ 2.0 mg/dL; AST/ALT $ 5 X ULN; serum creatinine $ 1.5 X ULN. Pts with active hep B must be on antiviral therapy. Pts would be on a 4-week run-in of SOR alone at 400mg BID to ensure tolerability and stable dose (minimum 200 BID) before beginning PEM 200mg IV q3 weeks. Both drugs would be administered until progression or unacceptable toxicity with response assessment q6 weeks by RECIST 1.1 criteria. Primary endpoint: response rate. Secondary endpoints: safety, overall survival, and progression-free survival. Correlative Endpoints: Pre-treatment levels of immunosuppressive cells and the functional activity of effector T cells would be compared to post-treatment blood and tumor samples. The first 6 pts who completed 4 weeks of SOR-only treatment and began the combination therapy (addition of PEM at a fixed dose of 200 mg q3w) would comprise the safety lead-in. Pts who withdrew before initiation of combination therapy (for reasons other than DLT) would be replaced. Dose-Limiting toxicity was defined as any grade 3 clinically significant toxicity, which is deemed possibly treatment-related and occurs within the first cycle of combination therapy. Toxicity would be assessed by NCI CTCAEV4.0. Status: First patient enrollment on 12/19/2017. On 11/28/2018, our 6th patient completed the SOR lead-in phase and began combination treatment with SOR and PEM. As of Sept 12, 2019, thirteen pts have enrolled, and 9 pts have received combination treatment. Support: Merck. Clinical trial information: NCT03211416. Research Sponsor: Merck.
A phase III study of futibatinib (TAS-120) versus gemcetabine-cisplatin (gem-cis) chemotherapy as first-line (1L) treatment for patients (pts) with advanced (adv) cholangiocarcinoma (CCA) harboring fibroblast growth factor receptor 2 (FGFR2) gene rearrangements (FEONIX-CCA3). First Author: Mitesh J. Borad, Mayo Clinic Cancer Center, Scottsdale, AZ

**Background:** Pts with adv CCA have poor survival outcomes, and chemotherapy offers limited survival benefit (5-year survival rates: 5-10%; median overall survival [OS], 8-12 months). FGFR2 gene rearrangements are known to be early drivers of oncogenesis in ~15% of pts with intrahepatic (i) CCA. Futibatinib, an oral, highly selective, irreversible FGFR-k inhibitor has shown antitumor activity against a broad spectrum of FGFR-deregulated tumors in preclinical studies. In a previous study, futibatinib demonstrated clinical activity and tolerability in heavily pretreated pts with adv CCA harboring FGFR2 gene rearrangements. This phase 3 trial (FEONIX-CCA3) is designed to evaluate futibatinib vs gem-cis as 1L therapy for pts with adv iCCA harboring FGFR2 rearrangements. Methods: FEONIX-CCA3 is a multicenter, open-label, randomization phase 3 study that will be conducted in pts with metastatic or unresectable iCCA harboring FGFR2 rearrangements. The combination arm will be randomized to receive 20 mg futibatinib once daily until disease progression or other discontinuation criteria are met. The primary endpoint is progression-free survival (PFS) for the combination arm is 7.3 months. Clinical trial information: NCT04000737. Research Sponsor: NuCana.

**TPS601**

Trials in Progress Poster Session (Board #P14), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

A phase II randomized placebo-controlled study investigating the combination of yiv-906 and sorafenib (SORA) in HBV (+) patients (Pts) with advanced hepatozelllcular carcinoma (HCC). First Author: James J. Harding, Memorial Sloan Kettering Cancer Center, New York, NY

**Background:** First-line systemic treatment options for advanced HCC pts are limited to the multi-targeted tyrosine kinase inhibitors, SORA and lenvatinib. Both agents improve outcomes for pts with advanced disease, but are associated with increased rate of grade 3-4 adverse events. Preclinical data indicate YIV-906 increases inflammation in the tumor microenvironment by MI macrophages activation/proliferation resulting in HCC tumor rejection in vivo and reduces SORA associated toxicity. Clinical experience with YIV-906 plus SORA suggests safety and potential clinical benefit to HCC pts with chronic HBV infection. Methods: This is a proof-of-concept, international, multicenter, double-blind, placebo-controlled, randomized phase 2 study designed to compare the efficacy of YIV-906 and SORA to SORA alone in advanced HCC pts (NCT04000737). Key eligibility criteria include age ≥18 years, HBV-associated HCC, ≥1 measurable untreated lesion, Child-Pugh A liver function, and no prior systemic therapy. An estimated 125 pts will be randomized 2:1 to receive the investigational (YIV-906 plus SORA) or control (placebo plus SORA) arm until disease progression or unacceptable toxicity. Pts will be stratified by prior surgical excision (resectable vs non-), geographically and locally adv vs metastatic disease. The primary endpoint is progression-free survival (PFS). Secondary endpoints include objective response rate and disease control rate based on (IRC, OS, PFS or investigator assessment). The anticipated start date is in April, 2020. Research Sponsor: Yivica Inc.
Presentation by: Kjell E. Oberg, Uppsala University Hospital, Sweden

Title: A meta-analysis of the accuracy of a neuroendocrine tumor mRNA biomarker (NETest) in the blood

Background: There is no accurate blood biomarker of neuroendocrine tumor (NET) disease. The inability to effectively assess disease in real-time has hindered management. The advance of genomic medicine and the development of molecular biomarkers has provided a strategy - liquid biopsy - to facilitate management. We reviewed the role of a blood mRNA-based NET biomarker, the NETest, as an in vitro diagnostic (IVD) to assess clinical utility.

Methods: A systematic review of the literature using PRISMA guidelines was undertaken. The methodological quality was evaluated using the QUADAS-2 tool. We identified 10 original scientific papers, which met inclusion criteria. These were assessed by qualitative analysis, and thereafter meta-analysis. We identified 10 original scientific papers, which met inclusion criteria. These were assessed by qualitative analysis, and thereafter meta-analysis.

Results: The ten studies included moderate to high methodological quality. They evaluated NETest usage both as a diagnostic and as a monitoring tool. Meta-analysis identified the diagnostic accuracy of the NETest to be 94.9-96% with a median DOR of 400, +LR of 164 and -LR of 0.05. The NETest was 85.5-86% accurate in differentiating stable from progressive disease. As a marker of natural history, the accuracy was 90-94%. As an interventional/ response biomarker, the accuracy was 94-97%. The pooled AUC for the NETest was 0.954 ± 0.005, with a z-score of 175.06 (p < 0.001).

Conclusions: The NETest is an accurate biomarker suitable for clinical use in NET disease management. The meta-analysis supports the utility of the NETest as an IVD to establish a diagnosis and monitor therapeutic efficacy. The use of a multianalyte genomic test as a biomarker provides information relevant to NET management consistent with observations regarding the utility of liquid biopsy in other oncological disciplines. Research Sponsor: None.

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Presentation by: Suleyman Yasin Goksu, The University of Texas Southwestern Medical Center, Dallas, TX

Title: Trends of survival based on race and ethnicity in gastrointestinal tract neuroendocrine tumor.

Background: There is paucity of data about racial/ethnic disparities in gastrointestinal tract neuroendocrine tumors (GiNET). We aimed to study the race/ethnic differences in disease characteristics and survival in GiNET.

Methods: We gathered the SEER database for data on 2004-2015, and compare it with the biomarker CgA. Methods: Cohorts: GEP-NET (253), BP-NET (49), colon cancer (37), lung cancers (80), benign lung disease (59) and controls (86). GEP-NETS: 645 (65%) had image-detectable disease or were resection-margin (R1) positive. Grading included GI (106), GI (49) and GI (9). BP-NETs, 208 of 49 (57%) had evidence of disease. Grading was GI [14], GI [14]. Disease status (stable [SD] or progressive [PD]) determined by RECIST 1. Blood sampling: NETest (n = 565) and NETest/CgA matched samples (135). NETest (PCR) (>100 score) with positive >20, progressive >40, CgA (ELISA). All samples deidentified, and measurement/analyses blinded. Statistics: Mann-Whitney U-test, McNemar’s test and AUROC. Results: GEPNET: NETest was significantly higher (34.4 ± 1, p < 0.0001) in NET disease versus no NET disease (41.1 ± 1, p < 0.0001), non-NET disease (18.4 ± 0.0004) or controls (7.0 ± 0.5, p < 0.0001). Diagnostic sensitivity was 89%, and specificity 94%. NETest levels were not related to grade (GI: 32 ± 2 vs. GI: 38 ± 3, p = 0.09). NETest levels were significantly higher (30.6 ± 13 vs. NET disease (24.1 ± 1, p < 0.0049). Diagnostic sensitivity 100%. Levels were elevated vs controls (p < 0.0001) and non-NET disease (20 ± 2, p = 0.0001). NETest levels were not related to grade (TC 30 ± 2 vs. AC 30 ± 2, p = NS). Levels were elevated in PD (55 ± 5.5 vs. SD 33.6 ± 2, p = 0.0005). AUCs for detecting disease ranged between 0.89 (GEPNET) (p = 0.003) and 0.8 (matched-GEP-NET) (p = 0.0009). Matched-GEP-NET (135) was significantly more accurate for detecting NETs (99%) than CgA (53%, McNemar’s test Chi² = 87, p = 0.0001), sensitivity (99%) and specificity (96%) were better than CgA (37% and 96% respectively). Conclusions: The NETest is an accurate diagnostic test for both GEP- and BP-NET. It defines clinical status (stable or progressive disease). NETest is significantly more accurate than CgA. The multianalyte genomic blood assessment of NET disease provided clinical information of utility in management. Research Sponsor: None.
A real-world observational study of somatostatin analogue use and costs in Canada, First Author: Winson Y. Cheung, Department of Oncology, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

Background: Somatostatin analogue (SSA) use is indicated in acromegaly and neuroendocrine tumours for symptomatic relief and tumour control. Two long-acting SSA (lorazepetide and octreotide) are currently available, but comparative real-world data on their use are limited. This study evaluated SSA use and costs in Canada. Methods: Claims data from the IQVIA Private Drug Plan (PDP), Ontario Drug Benefit (ODB) program and Régie de l’assurance-maladie du Québec (RAMQ) were compiled. Injection burden, rescue medication use and costs were compared (using unpaired t-test or Wilcoxon test) over a 12-month period from first SSA prescription. Patients (pts) were eligible if the first prescription was dispensed Sept 2015-Jun 2018. Results: 908 pts were included: lanreotide 120 mg, N=375; octreotide long-acting release (LAR) 30 mg, N=533. Lanreotide treatment was associated with a lower weighted average injection burden for 12 months when compared to octreotide (12.54 vs 13.44 injections/pt, respectively; p<0.0001). Pts receiving lanreotide also had lower mean use of rescue medications than those treated with octreotide (0.01 vs 0.05 claims/pt/year), although this difference was greatest during the first month of treatment (mean difference: 0.19; p=0.0001), after which differences in rescue medication use were only significant (p<0.05) at Months 5 and 6. Mean total annual costs (rescue medication + LAR) were lower for lanreotide than octreotide ($27,829.35/pt (N=373) vs $31,255.49/pt (N=530), respectively, p<0.0001). Conclusions: In the absence of clinical trials directly comparing the SSAs, factors driving treatment selection are unclear. Findings from our real-world observational study suggest treatment with lanreotide to be less burdensome and costly than octreotide and may inform treatment decisions with pts. Reference. Ipsen Biopharmaceuticals. Somatuline Autogel Product Monograph. 2018. Available at: http://www.ask.novartispharma.com/download.htm?res=somatostatin_scrip_ e.pdf&resTitleId=789. Research Sponsor: Ipsen Pharma.

609 Poster Session (Board #F12), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Neuroendocrine and carcinoid tumors of the gastrointestinal tract: Epidemiology and outcomes from the National Cancer Database. First Author: Johannes Uhlig, Section of Interventional Radiology, Yale School of Medicine, New Haven, CT

Background: While carcinoid and neuroendocrine tumors (NET) can manifest anywhere throughout the human body, over 2/3 of all independent tumors are gastrointestinal (GI). Methods: The 2019 version of the National Cancer Database was searched for adult patients with carcinoid or neuroendocrine tumors of the GI tract. Tumor incidence, patient demographics, treatment and cancer variables of GI carcinoid/NETs were compared to other GI cancers. Cox proportional hazards models were used to evaluate overall survival (OS). Results: A total of 101,744 patients were included. Carcinoid/NET incidence varied with primary location, with highest proportion in the small intestine (55.7% of all small intestinal cancers). Compared to other histologies, carcinoid/NETs were more commonly found in younger patients (median age 60 vs 68 years, p<0.001) and African Americans (18% vs 12%, p<0.001). Median carcinoid/NET diameter 15 mm vs 40 mm for other cancers (p<0.001). Carcinoid/NETs were diagnosed at lower stages than other histologies (AJCC stage 3/4, 30% vs. 47%, p<0.001), with most metastases in the liver (8.9%). Stage 1/2 carcinoid/NETs were most often treated by surgical ressection with or without concurrent chemotherapy (65%; 22%), whereas stage 3/4 patients received chemotherapy alone or in combination with surgical resection more commonly (39%; 28%). After multivariable adjustment, primary cancer site emerged as an independent prognosticator: longest OS was observed in patients with carcinoid/NET of the small intestines (vs. colorectal frame HR = 0.40, 95% CI: 0.37-0.44, p<0.001). Comparable results were evident in patients with carcinoid/NETs or other metastases (colorectal frame HR = 0.20, 95% CI: 0.17-0.24, p<0.001). Other independent OS prognosticators were patient age, gender, race and comorbidities, as well as tumor size, stage and treatment. Conclusions: Compared to other GI-associated tumors, carcinoid/NETs are more common in younger patients, African Americans, diagnosed with a smaller diameter at low stage. Carcinoid/NETs of the small intestines are associated with improved overall survival compared to other primary disease sites. Research Sponsor: None.

610 Poster Session (Board #F13), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Time from first symptoms to diagnosis in GEP-NET patients: Results from a large German tertiary referral center. First Author: Esra Koca, Goethe University Frankfurt, University Hospital, Department of Gastroenterology, Hepatology and Endocrinology, Frankfurt Am Main, Germany

Background: Patients with neuroendocrine tumors (NET) often go through a long phase between onset of symptoms and initial diagnosis. Methods: Retrospective analysis of 486 patients with GEP-NET (488 tumors) at tertiary referral center from 1984-2020; inclusion criteria: Patients was ≥ 18 years, diagnosis of GEP-NET; de-identified data set (data analysis). Results: 486 patients with GEP-NET were included: colon NET 27/488 (5.5%), other digestive organs 11/488 (2.3%), esophagus 1/488 (0.2%), stomach 1/488 (0.2%), rectum 27/488 (5.5%), small intestine 11/488 (2.3%), pancreas 32/488 (6.6%), liver 33/488 (6.8%), other 357/488 (73.1%). Mann-Whitney U test was used to compare groups. Conclusion: Patients with neuroendocrine tumors often go through a long phase between onset of symptoms and initial diagnosis. Further investigation is needed to clarify the role for surgery. Methods: Utilizing the National Cancer Database, we identified patients with pancreatic neuroendocrine tumors. Tumors were stratified based on size (≤1cm, 1-2cm and >2 cm). Mann-Whitney U and Kruskal-Wallis tests were used to compare continuous variables and Pearson’s Chi-square test was used to compare categorical variables. Unadjusted survival analyses were performed using the Kaplan-Meier method. Multivariate analysis (MVA) was performed to identify predictors of survival. All statistical tests were two-sided and p<0.05 was considered significant. Results: We identified 17,921 patients. (<1cm, 1214, 1-2cm, 4325, and >2cm, 12,382) with a median age of 61.8 (18-90). Males more often presented with tumors >2cm, 56% vs 44%, p<0.001. Tumors >2cm were more likely to be poorly differentiated (PD), p<0.001, have node positive disease, p<0.001 and less likely to undergo R0 resection, p<0.001. Tumors <1cm and well differentiated (WD) the median and overall 5-year survival in the O group was not reached (NR) (77%) vs 142.6 months (87%) in the surgery groups, p<0.04; in the 1-2 cm WD group 95.7 months and 60% vs NR and 94%, p<0.001. Similarly in the PD tumors <1cm the median and overall survival was 32.9 months and 24% in the O vs NR and 81%, p<0.001; in the 2-3 cm group 14.8 months and 19% vs NR and 73%, p<0.001. There were no differences in survival in patients undergoing PR or E, p=0.09. MVA revealed age, grade, Charlson Deyo score, tumor size, tumor location, and surgery (PR or E) were all independent predictors of survival. Conclusions: While observation is currently an acceptable option for the management of small <1cm WD PNET, we found an improvement in survival in the surgery group. Benefits from the surgical approach, enucleation and pancreatic resection did not differ in overall survival. Surgery for PNET should be considered as the first line treatment of these patients. Research Sponsor: None.

Evaluation of the current treatment strategies for pancreatic neuroendocrine tumors. First Author: Kenneth Lee Meredith, Florida State University College of Medicine/Sarasota Memorial Hospital, Sarasota, FL

Background: The management of pancreatic neuroendocrine tumors (PNET) varies between observation (O), pancreatic resection (PR) and enucleation (E). Currently, size, grade and location are used to determine which treatment strategy may be employed. Our aim is to evaluate the evidence to clarify the role for surgery. Methods: Utilizing the National Cancer Database we identified patients with pancreatic neuroendocrine tumors. Tumors were stratified based on size (<1cm, 1-2cm and >2 cm). Mann-Whitney U and Kruskal-Wallis tests were used to compare continuous variables and Pearson’s Chi-square test was used to compare categorical variables. Unadjusted survival analyses were performed using the Kaplan-Meier method. Multivariate analysis (MVA) was performed to identify predictors of survival. All statistical tests were two-sided and p<0.05 was considered significant. Results: We identified 17,921 patients. (<1cm, 1214, 1-2cm, 4325, and >2cm, 12,382) with a median age of 61.8 (18-90). Males more often presented with tumors >2cm, 56% vs 44%, p<0.001. Tumors >2cm were more likely to be poorly differentiated (PD), p<0.001, have node positive disease, p<0.001 and less likely to undergo R0 resection, p<0.001. Tumors <1cm and well differentiated (WD) the median and overall 5-year survival in the O group was not reached (NR) (77%) vs 142.6 months (87%) in the surgery groups, p<0.04; in the 1-2 cm WD group 95.7 months and 60% vs NR and 94%, p<0.001. Similarly in the PD tumors <1cm the median and overall survival was 32.9 months and 24% in the O vs NR and 81%, p<0.001; in the 2-3 cm group 14.8 months and 19% vs NR and 73%, p<0.001. There were no differences in survival in patients undergoing PR or E, p=0.09. MVA revealed age, grade, Charlson Deyo score, tumor size, tumor location, and surgery (PR or E) were all independent predictors of survival. Conclusions: While observation is currently an acceptable option for the management of small <1cm WD PNET, we found an improvement in survival in the surgery group. Benefits from the surgical approach, enucleation and pancreatic resection did not differ in overall survival. Surgery for PNET should be considered as the first line treatment of these patients. Research Sponsor: None.

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Implications of neuroendocrine tumor and diabetes mellitus on patient outcomes and care: A matched case control study. First Author: Nina J. Karlin, MayoClinic Arizona Division Hematology Oncology, Phoenix, AZ

Background: The aim of this study was to examine the impact of diabetes mellitus (DM) on survival in neuroendocrine tumor and the impact of neuroendocrine tumor on glycemic control in DM. Methods: Patients with newly diagnosed neuroendocrine tumor with and without DM were matched 1:1 according to age, gender, and year of cancer diagnosis (2005-2017). The file was linked to the electronic medical record to obtain information on DM and neuroendocrine tumor therapies and laboratory results. There were 59 matched pairs (total 118 patients) included in the analysis. We compared characteristics between cases and controls and assessed survival with the Kaplan-Meier method and Cox proportional hazards model. Mixed models compared hemoglobin A1c and glucose levels over time. Results: Median age of patients at diagnosis was 67 (40-86); 41% had stage IV disease. Women constituted 49% of the study population; 22% had pancreatic neuroendocrine tumor and 45% had another GI primary neuroendocrine tumor. No differences in race/ethnicity, marital status, alcohol or tobacco use were detected between cancer patients with and without DM. Mean BMI was significantly different between DM and non-DM patients (31.0 [7.90] versus 26.4 [5.27]); p = 0.011. Among those with DM, mean HbA1c during the year following cancer diagnosis was 7.3%. Mean glucose was significantly different between DM (159.1 [43.5]) versus non-DM pts 117 [31.5]; (p < 0.001). Median follow-up time was 32.8 (2.4-165.4) months in alive patients. Three year survival was estimated at 72% (95% CI: 60-86%) for DM patients versus 80% (95% CI: 70-92%) in non-DM patients by Kaplan Meier method (p = 0.82 log rank test). Hazard ratio (stratification for matched pairs) = 1.33 (95% CI: 0.56 - 3.16; p = 0.51). Conclusions: DM did not adversely impact survival in patients with neuroendocrine tumor. Neuroendocrine tumor and its treatment did not affect glycemic control. This should be reassuring to oncologists and endocrinologists who treat patients with neuroendocrine tumors and diabetes. Research Sponsor: None.

The antidiarrheal efficacy of a proprietary amino acid mixture (enterade) in neuroendocrine tumor patient. Diarrhea in these patients could be due to excessive serotonin production, secondary to post-operative short gut syndrome, steatorrhea from somatostatin analogs, bile acid co-conjugation, and/or bacterial overgrowth. In this study we summarize our single center experience with enterade. Methods: Medical records of all the NET patients treated with enterade for symptomatic diarrhea were retrospectively reviewed after appropriate IRB approval. Patients were treated at Markey cancer center between May 2017-June 2019. Results: Total 98 patients were offered enterade. Enterade was instructed to be taken as one 8 Oz bottle BID for 4 weeks. Only 14.7% lived in zip codes where > 20% did not graduate high school (no HSD). The majority were treated at community comprehensive cancer centers (43.8%) or academic/research centers (35.2%). Overall, 3358 (24.5%) presented with metastasis at diagnosis. The 5-year OS for the entire cohort was 78.5%. The 5-year survival was worse in patients with lower median income (73.8% [ < $38,000] vs 81.5% [ > $63,000]; p < 0.0001), lower education (74.9% [ > 20% no HSD]) vs 80.7% [ < 7% no HSD]; p < 0.0001), those not living in proximity to a metro area (73.8% [not metro adjacent]) vs 78.7% [metro/adjacent]; p = 0.0004) and those treated at a community cancer center (73.6% [community] vs. 80.1% [academic], p < 0.0001). Factors predictive of worse OS were lower income, lower education, treatment at a community cancer center and not living in proximity to a metro area. Patient demographic and socioeconomic factors play an important role in OS for patients with mNETs and access to care must be considered in this subpopulation of cancer patients. Research Sponsor: None.

Phase I dose-escalation trial of trifluoridinotipiracil (TAS-102) and temozolomide in the treatment of advanced neuroendocrine tumors. First Author: Nataliya Volodymyrivna Uboha, University of Wisconsin, Carbone Cancer Center, Madison, WI

Background: Systemic chemotherapy plays a role in treating neuroendocrine tumors. Trifluoridinotipiracil (FTD/TPI), known as TAS-102, is an antineoplastic agent that is non-cross resistant with fluorouracil and capecitabine and that has a different toxicity profile. We are presenting results from a phase I portion of the study evaluating safety of FTD/TPI in combination with TMZ in patients with neuroendocrine tumors. Methods: Phase 1 portion to the study utilized a "3+3" design to determine maximum tolerated doses (MTD) of FTD/TPI and TMZ when administered in combination. Patients with advanced NETs of any grade were eligible for participation. FTD/TPI was taken twice a day on days 1-5 and TMZ was taken daily on days 8-12 of a 28 day cycle. 3 dose levels (Lv) were evaluated. FTD/TPI was started at a goal dose of 35 mg/m2 twice daily. Three doses of TMZ were studied: 100, 150 and 200 mg/m2. Growth factor support was required during DLT evaluation period for all patients starting with the fourth subject on study. Results: Sixteen evaluable subjects (6 females, median age 64) enrolled in the phase 1 portion of the study (4 on Lv1, 6 on Lv2, 4 on Lv3). Lv3 had high grade tumors, R1/6 had non-GI or unknown primary. No DLTs were observed on Lv1. One DLT was observed on Lv2 (grade 3 fatigue and inability to resume treatment) and 1 DLT on Lv3 (grade 4 thrombocytopenia). Overall the treatment was well tolerated. 7 subjects had grade ≥ 3 AEs at least possibly related to treatment, with neutropenia and lymphopenia being the most common. 4 subjects required dose reductions. 7 subjects remain on active treatment. 4 subjects discontinued treatment due to AEs and 1 due to clinical disease progression. Efficacy data is being collected and will be presented at the meeting. Two patients had established MTD of FTD/TPI (35mg/m2 twice daily) and TMZ (200 mg/m2). This regimen is well tolerated. Enrollment into expansion cohort for patients with advanced Grade ≥2 pancreatic NETs is ongoing (NCT02943733). Clinical trial information: NCT02943733. Research Sponsor: Taiho IncUniversity of Wisconsin Carbone Cancer Center.
Outcomes after high-dose radiation in management of neuroendocrine neoplasms. First Author: Katherine Chen, University of California San Francisco Medical Center, San Francisco, CA

Background: In this study, we analyze outcomes after the use of high-dose radiation therapy (RT) in management of neuroendocrine neoplasms (NE Ts) at a high-volume center. Methods: We performed a retrospective review of patients who received high-dose RT (defined as biologically effective dose (BED) >40) for their NENs. Patients with small cell lung cancer and Merkel cell carcinoma were excluded, given their unique treatment paradigms. Results: 114 patients completed a radiation course with BED >40 for their NEN (median BED 70, range 44-180). Most tumors were gastrointestinal in origin (n = 20); additional primary sites included lung (n = 11), head and neck (n = 10), cervix (n = 6), other (n = 9) and unknown (n = 5). 56% (n = 34) had well-differentiated (WD) neuroendocrine tumors, and 44% (n = 27) had poorly-differentiated (PD) neuroendocrine carcinomas. Disease stage at the time of RT was localized/locally advanced (LLA, n = 27), or metastatic/recurrent (MR, n = 34). The intent of RT was definitive (n = 18), postoperative (n = 10), for oligoprogression (n = 18), or purely palliative (n = 15). 48 patients had follow-up imaging at a median follow-up of 20 months after radiation. Outcomes were grouped by differentiation and stage, with median time to progression (mTTP) in months (Table). 8% of patients had local progression, while 44% developed new metastases, including 38% of WD-LLA, 47% of PD-LLA, 37% of WD-MR, and 67% of PD-MR disease with progressively shorter median time to progression (26, 10, 8, and 3 months, respectively). Conclusions: These data suggest that focal, high-dose radiation has a role in the management of NE Ts. Local failure is rare in patients with WD-LLA and PD-LLA disease. The predominant pattern of failure is development of new metastases, which appear to occur sooner and more frequently in patients with PD and MR disease. Research Sponsor: None.

<table>
<thead>
<tr>
<th>No evidence of active disease</th>
<th>Local progression at RT site</th>
<th>New metastases</th>
<th>Progression of existing metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>WD-LLA (n = 8)</td>
<td>5 (62%)</td>
<td>0 (0%)</td>
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<td>PD-LLA (n = 15)</td>
<td>8 (53%)</td>
<td>1 (7%)</td>
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<td>PD-MR (n = 20)</td>
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<td>2 (66%)</td>
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<td>Total (n = 48)</td>
<td>22 (46%)</td>
<td>4 (8%)</td>
<td>9 (19%)</td>
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</table>

Exploring telotristat ethyl's antiproliferative effects in patients with carcinoid syndrome (TELEACE): A real-world observational study. First Author: Michael Morse, Duke University Medical Center, Durham, NC

Background: Serotonin may have proliferative effects on neuroendocrine carcinoid syndrome (TELEACE): A real-world observational study. Methods: We performed a retrospective analysis of patients with SSAs for metastatic/unresectable G3 NETs, querying data from 1992 - present. Inclusion criteria were: centrally reviewed pathology confirming well-differentiated morphology, G3 based on WHO classification, SSA monotherapy, and radiological data available to assess response. Patients who had prior lines of treatment were included as long they subsequently were treated with single-agent SSA. Poorly-differentiated tumors were excluded. The primary endpoint was PFS. Best overall response was determined by radiographic response, stabilization, or progression of tumor size. Results: Ninety patient records were reviewed, with 14 meeting inclusion criteria (diagnosed 2014 - 2018). Median Ki-67 proliferative index was 25%. Two patients (14%) had a partial response to SSA therapy, five (36%) had stable disease, and seven (50%) had progressive disease. The estimated median PFS was 4.4 months (95% CI 2.9 - 24). Of the 7 patients with stable disease or partial response, the median time to progression was 8.7 months. Three patients had stable disease for greater than 9 months (24, 29 and 42 months, respectively). Overall survival was not estimable. There was no association of Ki-67 index with PFS based on a proportional hazards model adjusting for age. This is the first report on the efficacy of SSAs for G3 NE Ts. Although half of the patients in our series had at least stable disease, the PFS was modest at only 4.4 months. Their favorable side-effect profile compared to cytotoxic chemotherapy, SSAs may present an attractive option to be further explored in a prospective fashion. We are presently updating this data by reassessing response using RECIST criteria. Research Sponsor: None.

A phase II trial of atezolizumab and bevacizumab in patients with advanced, progressive neuroendocrine tumors (NETs). First Author: Daniel M. Halperin, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Neuroendocrine tumors (NETs) are relatively rare and heterogeneous tumors arising throughout the aerodigestive tract, which are incurable and life-limiting when metastatic. Prior studies of checkpoint inhibitors in NET patients have yielded minimal evidence of efficacy. Historically, effective therapies for advanced, progressive NE T NET yield response rates less than 10% and progression-free survival (PFS) durations of approximately 11 months, as compared to approximately 4.5 months with placebo. Methods: We undertook a phase II basket study of atezolizumab in combination with bevacizumab in patients with rare cancers, and present here the data from the pancreatic NET (pNET) cohort and extrapancreatic NET (epNET) cohort, each of which included 20 patients with grade 1-2 NET that was progressive under any prior therapy. Patients received 1200mg of atezolizumab and 15mg/kg of bevacizumab IV q 21 days. The primary endpoint was confirmed objective response by RECIST 1.1. Results: The confirmed objective response rate with this combination was 20% (95% CI 6-44%) in the pNET cohort and 15% (95% CI 3-38%) in the epNET cohort. The median PFS in the pNET cohort is 19.6 months (95% CI 10.6-90.6), while it was 14.9 months (95% CI 6.1-9R.6) in the epNET cohort, 1-year PFS was 75% and 52%, respectively. The combination was well-tolerated in this patient population, with the most common related treatment-emergent adverse events being hypertension (47.5%), proteinuria (37.5%), and fatigue (35%). The most common related grade 3/4 adverse events were hypertension (20%) and proteinuria (7.5%). Conclusions: The combination of atezolizumab and bevacizumab demonstrated moderate clinical activity in patients with advanced NETs. As pre-treatment and on-treatment biopsies were obtained for all patients, correlations with immune infiltration, mutations, and transcriptome alterations should provide additional insight into the mechanisms of response and resistance. Clinical trial information: NCT03074513. Research Sponsor: Genentech/Roche.

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The benefits of upfront primary tumor resection for metastatic small bowel neuroendocrine tumors: A population-based analysis. First Author: Sean Bennett, University of Toronto, Toronto, ON, Canada

Background: Early resection of the primary tumor in metastatic small bowel neuroendocrine (SB-NET) remains controversial. Conflicting data exist regarding its clinical and survival benefits. We compared the long-term outcomes of upfront small bowel resection (USBR) and non-operative management (NOM) for metastatic SB-NETs to improve patient outcomes. Research Sponsor: CIHR Project GrantOther Foundation.

Methods: A population-based analysis of patients with SB-NET metastatic at diagnosis between 2001-2017 was conducted by linking administrative datasets. USBR was defined as resection within 6 months of diagnosis. Primary outcomes were subsequently unplanned acute care admissions and small bowel related surgery. Secondary outcome was overall survival (OS). USBR and NOM patients were matched 2:1 using a propensity-score including age, sex, year of diagnosis, socioeconomic status, institution academic status, and functional status. We used time-to-event analyses with cumulative incidence functions and univariate Andersen-Gill regression for primary outcomes, and Kaplan-Meier methods and univariate Cox regression for OS. E-value methods assessed the potential for residual confounding. Results: Of 1000 patients identified, 785 (78.5%) had USBR. The matched cohort included 348 patients with USBR and 174 with NOM. Matched groups were well balanced with standardized mean differences <10% for matched variables. Patients with USBR had lower 3-year risk of subsequent admissions (72.6% vs 86.4%, p < 0.001) than those with NOM, with hazard ratio (HR) 0.72 (95%CI 0.57-0.91). USBR was associated with lower risk of subsequent small bowel related surgery (15.4% vs 40.3%, p < 0.001), with HR 0.41 (95%CI 0.30-0.56). OS was superior for USBR patients compared to NOM (HR 0.55, 95% CI 0.44-0.69). E-values indicate it was unlikely that the observed risk estimates could be explained by an unmeasured confounder. Sensitivity analysis excluding emergent resections to define USBR did not alter the results. Conclusions: USBR for metastatic SB-NETs was associated with clinical benefits over NOM, in terms of decreased subsequent admissions and interventions, and improved survival. USBR should be considered for metastatic SB-NETs to improve patient outcomes. Research Sponsor: CIHR Project GrantOther Foundation.

Treatment outcomes of patients with G3 neuroendocrine neoplasms. First Author: Henning Jann, Charité – Universitätsmedizin Berlin, Berlin, Germany

Background: Extra-pulmonary neuroendocrine carcinomas (NEC) and neuroendocrine tumors (NET) G3 are aggressive neoplasia that are associated with a limited prognosis. Data on this entity is scarce and optimal treatments are only poorly defined. Methods: 105 patients (94; 43.8% and 5; 9; 56.2%) with histologically confirmed NEC and neuroendocrine tumors (NET) G3 were included into this study. Clinical and pathological characteristics at diagnosis, therapies, outcomes and follow-up were collected and analyzed. Results: Primary tumour site NEC was pancreas (n = 83), neuroendocrine tumour G3 (NET G3; n = 12) or mixed neuroendocrine non-neuroendocrine neoplasms G3 (MiNEN G3; n = 10) were included into this study. Clinical and pathological characteristics at diagnosis, therapies, outcomes and follow-up were collected and analyzed. Conclusions: G3 NEC had significantly worse outcome compared to NEC G2. Survival rates between NEC G3 and G2 were statistically different (mOS, median, 15.5 vs 27.9 months). Median survival for NEC G3 was significantly lower than for NEC G2 (p = .001). Median survival for NEC G3 was significantly lower than for NEC G2 (p = .001). Median overall survival (mOS) was 19.2 (±1.6) months and was significantly higher in NET G3 (38 vs. 16.8 months in NEC; p = .012). First-line therapy in most patients was cisplatin or carboplatin in combination with etoposide (n = 64; 61.0%), followed by FOLFOX (n = 29; 27.6%). Twelve Patients (11.4%) received other chemotherapy. Best overall response to first-line chemotherapy was CR (5.7%), PR (52.4%) SD (17.1%) and PD (2%). In patients with Ki-67 < 55% (n = 40) no significant difference was observed between chemotherapy arms. Conclusions: Primary tumour site NEC was pancreas (n = 83), neuroendocrine tumour G3 (NET G3; n = 12) or mixed neuroendocrine non-neuroendocrine neoplasms G3 (MiNEN G3; n = 10) were included into this study. The only curative treatment is surgery, which in many cases is not an option due to metastatic disease at diagnosis. The NETTER-1 study showed high efficacy and low toxicity of peptide receptor radionuclide therapy (PRRT) in midgut NETs. Here, we present our initial experience with PRRT in the NETTER-1 trial. Methods: Fifty-five patients (27 males and 25 females, 37 – 81 y, mean = SD: 61.8 ± 10.6 years) with documented progressive disease (PD) were enrolled in the study. In the interim OS analysis, 6 deaths occurred. In contrast to the NETTER-1 trial, PRRT in our patient cohort was performed later in the course of treatment (median lines of therapy before PRRT: 4 ± 1.3). Conclusions: Our preliminary data show overall good results of PRRT in patients with NET. Results: 22/52 (42%) patients completed all 4 cycles of PRRT. 18/52 (34%) patients are currently being treated. 12/52 (23%) patients had to discontinue treatment. Hematotoxicity was the only side effect which can be related to PRRT. The 6-month and 9-month PFS rate was 82.4% and 66.8% respectively vs. 89% and 84% in the NETTER-1 trial. The ORR was 36% vs. 18% in the NETTER-1 trial. In the interim OS analysis, 6 deaths occurred. In contrast to the NETTER-1 trial, PRRT in our patient cohort was performed later in the course of treatment (median lines of therapy before PRRT: 4 ± 1.3). Conclusions: Our preliminary data show overall good results of PRRT in patients with NETs. However, compared to the NETTER-1 trial, PRRT is shorter which is most likely due to the extensive pretreatment, but ORR was higher. Research Sponsor: None. Interim evaluation of response to therapy.

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Conclusions: We identified two copy number changes that can serve as predictive biomarkers in G3 NENs, as they confer an increased risk of death by as high as 10x to the carriers. Further, G3 NENs are characterized by a distinct transcriptomic similarity across all NENs regardless of their site of origin.

Methods: Comprehensive genomic sequencing of high-grade neuroendocrine neoplasms (G3 NENs). Between August 2017 and July 2019 a total of 107 patients were eligible NEN patients on an institutional, IRB approved protocol, who had NGS as standard of care and were treated in the past 24 months were included. Tumors were categorized by location and histologic grade. We explored the actual and theoretical eligibility for tumor agnostic treatment. Globally 102 clinical trials included patients with NEN and specific mutations. NGS detected one (1%) case of MSI high and one (1) TRK fusion.

Results: Between August 2017 and July 2019 a total of 107 patients were eligible. Globally 102 clinical trials included patients with NEN and specific mutations. NGS detected one (1%) case of MSI high and one (1) TRK fusion.

Conclusions: NGS can point to clinical trial eligibility and guide genetic counseling and should probably be a standard approach in the evaluation of new metastatic NEN patients. Research Sponsor: None.
Background: Neuroendocrine neoplasms (NENs) are heterogeneous tumors which originate from various organs and are of variable aggressiveness based on grade and morphology. Current biomarkers for NENs lack specificity, especially for high-grade NENs (small and large cell neuroendocrine carcinomas). HpG80, progastrin, is a novel biomarker which is easily synthesized by gastric antrum G cells, and then processed into gastrin by multiple enzymatic processes. In pathological conditions, the GAST gene, which encodes HpG80, was shown to be over-expressed in human solid tumors from various primary sites. HpG80 is upregulated and released from the tumor cells and becomes detectable in the blood. This study is the first to explore HpG80 in NENs. Methods: HpG80 was quantified in the plasma from 31 NEN patients using DxPG80 technology (ECS-Progastrin, Switzerland). Progastrin concentrations in 18-70 YO (n = 557) and 18-25 YO (n = 137) healthy blood donors were compared to 31 stage IV NENs patients. The study was IRB approved. Results: Mean age of study cohort at the time of blood collection was 60.9 years. 21 patients had grade 1 and 2 well differentiated NET. 10 patients had high grade NEN (Small cell, large cell and poorly differentiated NEC). High grade sub cohort also included two well differentiated grade 3 NET patients. Mean HpG80 in NENs was 14.17 pm as compared to 2.04 pm and 0.99 pm in 18-70 and 18-25 YO control groups (p < 0.0001), respectively. Subgroup analysis of NENs revealed mean HpG80 of 24.61 pm in high-grade NENs (n = 10) vs 10.88 pm in G1/G2 NETs (n = 21). Conclusions: This first-ever study of plasma HpG80 in NENs suggests HpG80 may be a diagnostic and prognostic blood-based biomarker in both low and high-grade NENs and further study is warranted. A prospective trial is ongoing in high-grade NEN to evaluate role in monitoring of disease (NCT03958045) and further studies in low-grade NETs are underway. This research was supported by Cancer Center Support Grant (CCSG) from the National Cancer Institute (P30 CA177558) and ECS Progastrin. Research Sponsor: ECS-Progastrin, Switzerland.

Poster Session (Board #GI1), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Causes of death following neuroendocrine tumors diagnosis: A United States population-based analysis. First Author: Anas M. Saad, Cleveland Clinic Foundation, Cleveland, OH

Background: Neuroendocrine tumors (NET) are heterogeneous in terms of prognosis based on location, grade, and stage. In this study we report causes of deaths (COD) in patients with NET. Methods: We used the Surveillance, Epidemiology, and End Results (SEER) Program to collect data of patients diagnosed between 2000 and 2016 and report COD following NET diagnosis. Results: We reviewed 94,399 NET cases of which 38,692 died during the follow-up period. The highest number of deaths (5,721) occurred within less than a year of diagnosis. In the first year of diagnosis, 73% (73,000) patients died from NETs followed by other cancers (11.2%) and cardiac diseases (CD) (4.6%). As time passed, NET deaths decreased to be responsible for 24.3% of deaths after > 10 years of diagnosis, while other cancers (14%) and CD (19.7%) became more common. When dividing NET cases by grade, NETs were responsible for 42.8%, 63.4%, and 81.2% of deaths in G1, G2, and G3, respectively, while other cancers were responsible for 16.2%, 11.8%, and 7.2% of deaths, respectively and CDs were responsible for 12.3%, 7.2%, and 3.2% of deaths, respectively. For G1 localized NET, non-NET cancers (22.2%) was the most common COD followed by NET (19.7%) and CD (16.8%). For G2 localized NET, NET was COD in 31.1% of cases followed by non-NET cancers (22.4%) and CD (13.8%). In metastatic disease, NET was the most common COD regardless of grade. Conclusions: In G1 and G2 localized NET, deaths were mostly secondary to non-NET causes. Therefore, counseling patients regarding surveillance with cancer-screening and focusing on prevention from non-cancer deaths is important. On the other hand, NET is responsible for most deaths in metastatic NET regardless of grade. Further advances in systemic therapies are needed to improve the outcomes of advanced disease. Research Sponsor: None.

Poster Session (Board #GI2), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Blood neuroendocrine gene transcripts (NETest) as a diagnostic of pancreatic neuroendocrine tumors and to identify the efficacy of surgical resection. First Author: Stefano Partelli, Ospedale San Raffaele, Milan, Italy

Background: Surgery is the only treatment for cure of pancreatic neuroendocrine tumors (PNET). There are no effective biomarkers to assess completeness of resection and predict recurrence. The aims of this study were to evaluate the performance of net ests in PNET patients and to compare NETest with CgA in very early postoperative period. Methods: We retrospectively investigated consecutive patients with NETest and CgA analyzed pre and postoperatively (n = 20). The NETest was an accurate diagnostic of PNETs. Blood for NETest and CgA were collected preop and on postop day 30 (P30). Transcript measurement: real-time quantitative reverse transcription PCR and multisample algorithmic analysis (NETest) (normal 0-20, > 20 stable and > 40 progressive disease; CgA: (ELISA) (normal < 109ng/ml)). Analysis: Student’s t test, Mann-Whitney U test and Fisher’s exact test. Data: mean ± SEM. Results: Surgical resections (n = 30) were: 26 R0, 2 R1, 2 R2. In vitro diagnostic: Preop NETest positive in all 30 (NETest: 38±4) (1005) whereas CgA levels positive (220±66ng/ml) in 9 (30%), p < 0.0001. Surgery R0: (n = 26): NETest significantly decreased from pre-op of 45±3 to 21±4 (p < 0.001) at P30. Post-operatively 13 (50%) exhibited an elevated score. One patient (Ki67 18%; extensive nodal involvement) had a score of 80, consistent with residual progressive disease. The remaining 12 had NETest levels of 27 at P30 D0. CgA was elevated in 8 (31%) with no decrease at P30 (d44ng/ml vs. 109±22ng/ml), R1/R2 (n = 4): NETest scores unchanged (42±17 vs 46±16) at P30, CgA levels unchanged (378±332 vs. 753±634ng/ml). Conclusions: The NETest is an accurate in vitro diagnostic biomarker for PNET (100%). After R0 resection NETest decreases indicate the blood test is concordant with tumor removal. Elevated post-resection scores are consistent with residual disease and with reported recurrence rates after pancreatic surgery. CgA exhibited no clinical utility. Last implication for pancreatic surgery, the NETest provides an early indication of high risk recurrence patients who can be stratified for further therapy. Clinical trial information: NCT03012789. Research Sponsor: None.
TPS634  
Trials in Progress Poster Session (Board #P17), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

A phase II study of enterahe in neuroendocrine tumor (NET) patients with quality-of-life limiting bowel movement frequency. First Author: Satya Das, Vanderbilt University Medical Center, Nashville, TN

Background: BM frequency in NET pts is a major cause of morbidity. Though typically associated with serotonin excess in pts with carcinoid syndrome (CS), it can also occur in pts without CS due to etiologies such as small bowel syndrome, biliary obstruction, steatorrhea from somatostatin analogs (SSAs) and complications from chemotherapy/immunotherapy/biologics. Enterahe is an oral rehydration solution comprised of 5 amino acids, which has demonstrated pre-clinical and clinical potential to improve small intestinal intestinal barrier function and limit BM frequency in patients with quality-of-life limiting BM frequency (QoL-LBM). A total of 100 pts who were on SSAs and had not reached QoL-LBM on SSAs were randomized into two groups: SSAs alone vs. SSAs + Enterahe. The study was conducted between 10/2017 and 3/2018. Analysis is ongoing.

Methods: We conducted a phase II parallel cohort study in CS and non-CS NET pts (NCT 0473017). To be eligible, pts must be experiencing an average of ≥ 4 daily BM while on standard-of-care (SOC) therapies (SSAs, antidiarrheals). Pts will be categorized into CS or non-CS cohorts based upon biochemical evaluation which includes plasma 5-HIAA/24-hour urine 5-HIAA, VIP or gastrin levels. Eligible pts will undergo observation during weeks 1–4 (baseline period). During weeks 5–8, pts will consume Enterahe twice per day (Enterahe period) while during weeks 9–12, pts will stop Enterahe and resume observation. Daily stool diaries for each pt will be assessed to compute differences in mean bowel movement number between baseline and Enterahe periods.

Endpoints: The primary endpoint of the study is reduction in BM frequency in individual pts between baseline and Enterahe periods. Based on parameters utilized in a prior study, we will assume that the mean daily reduction in bowel movements from baseline is equal to 1.5 (standard deviation of change = ±1.5) representing a large effect size = 1.0. A sample of 12 pts in each cohort will provide nearly 90% power to detect this effect size based on a one-sample t-test (α = 0.05). An additional 3 pts will be added to each cohort to account for potential dropouts. Key secondary study endpoints include differences in pt-reported QOL outcomes (FACT-D), pt weight, intravenous fluid requirements, use of SOC antidiarrheals, and differences between baseline and Enterahe periods. Accrual for the study will be ensuing shortly. Clinical trial information: NCT04073017, Research Sponsor: Entracin Health.

TPS635  
Trials in Progress Poster Session (Board #P18), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

A phase II trial of pembrolizumab in combination with cisplatin or carboplatin and etoposide in chemotherapy naive patients with metastatic or resectable high-grade gastroenteropancreatocarcin or lung neuroendocrine carcinoma. First Author: Robert A. Ramirez, Louisiana State University Health Sciences Center, New Orleans, LA

Background: Combination chemotherapy (CTX) is the mainstay of treatment for patients with advanced high-grade gastroenteropancreatic neuroendocrine carcinoma (GEPNECs) and large cell neuroendocrine carcinomas (LCNECs) of the lung. Pembrolizumab (PDM) is a humanized antibody to the programmed cell death receptor (PD-1), which blocks the interaction with its cognate ligands, PD-L1 and PD-L2. PEM blocks the protective mechanism of cancer cells and allows the immune system to destroy them. Combination CTX and immunotherapy has shown efficacy in other malignancies including small cell lung cancer. The purpose of this study is to test the efficacy, safety, and tolerability of combination CTX with PEM in patients with high-grade GEPNEC or LCNEC of the lung who are CTX naive. Methods: This is an open label, phase II, single institution, multi-site trial using PEM in combination with either cisplatin or carboplatin and etoposide in patients with high grade GEPNEC or LCNEC of the lung who are CTX naive. Patients with a histologic diagnosis of a GEPNEC with a Ki-67 of 55% or higher or a LCNEC of the lung will be eligible. Patients must be metastatic or resectable; chemotherapy naive; have at least one measurable lesion per RECIST 1.1, have an ECOG performance score of 0-1; and have a predicted life expectancy > 3 months. Approximately 36 GEPNEC and 6 LCNEC of the lung patients will be enrolled. Patients will receive PEM 200mg IV in combination with cisplatin 80 mg/m2 or carboplatin AUC 6 on day 1 and etoposide 100mg/m2 on days 1-3 of a 21-day cycle. Tumor response will be assessed by CT scan every 6 weeks using RECIST 1.1. Those patients who have responsive or stable disease after 4 cycles of platinum-based CTX will move to maintenance PEM every 3 weeks for up to 2 years. The primary endpoint will be progression free survival. Results: This study is open to enrollment. Clinical trial information: NCT03901378, Research Sponsor: Merck.
Phase II study of nanoliposomal irinotecan (nal-IRI) with 5-fluorouracil (5-FU)/folinic acid (FA) in refractory advanced high-grade neuroendocrine cancer (HG-NEC) of gastroenteropancreatic (GEP) or unknown origin.

**First Author:** Medhavi Gupta, Roswell Park Cancer Institute, Dept. of Medicine, Buffalo, NY

**Background:** The incidence of GEP HG-NEC is increasing and the prognosis is poor. Etoposide-platinum (EP) combination is considered the standard (std) therapy (Rx), but survival is less than 1 year. There is an unmet need for an optimal 2nd line Rx in these patients (pts). Nal-IRI has shown efficacy in small cell lung cancer (pathologically similar to HG-NEC) and in 2nd line pancreatic adenocarcinoma. In a retrospective study, HG-NEC pts with progression on 1st line EP when treated with 2nd line FOLFIRI (FA+5-FU+ IRI) had a good response and a tolerable safety profile (Hentic et al, 2012). Based on this data and the fact that no std 2nd line Rx option exists in HG-NEC, we are evaluating the efficacy of nal-IRI+ 5-FU/FA in a prospective single-arm multicenter study.

**Methods:** Advanced GEP or unknown origin HG-NEC pts with progressive disease/intolerance to 1st line Rx with EP or temozolomide/capecitabine; ECOG PS 0-2 would receive nal-IRI 70 mg/m2, FA 400 mg/m2 followed by 5-FU 2400 mg/m2 on D1 & 15 of 28-days cycle. Rx to continue till disease progression or unacceptable toxicity. Tumor assessment by CT/MRI per RECIST 1.1 q6 wks. Primary end point is to measure ORR (CR+PR). Secondary endpoints include PFS, TTP, OS, safety and QOL changes. Assuming a historic ORR of 15% with std Rx, 37 pts (upto 41 pts considering non-evaluable pts) are required to show an ORR of 30% at a power of 80% at 1-sided significance of $\alpha = 0.1$. In stage 1, $n_1=18$ pts will be enrolled. If 3 or more responses are seen, an additional $n_2=19$ pts to be enrolled. If 8 or more responses are observed of the $n = 37$ evaluable pts, the Rx would be considered promising for further study. Genomic mutational profiling to be conducted on pre-study tumor samples and correlated with circulating tumor DNA (CT DNA). CT DNA level, assessed serially, will be correlated with Rx response and disease recurrence. We plan to accrue over 3 years at 3 sites. As of August 2019, 1-patient has been enrolled. The trial is funded by Ipsen Pharmaceuticals and the North American Neuroendocrine Tumor Society through the Clinical Investigator Scholarship. Clinical trial information: NCT03736720. Research Sponsor: Ipsen Pharmaceuticals Other Foundation.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Randomized Phase III Study of FOLFOX Alone and with Pegilodecakin as Second-line Therapy in Patients with Metastatic Pancreatic Cancer (SEQUOIA). First Author: J. Randolph Hecht, David Geffen School of Medicine at UCLA, Santa Monica, Los Angeles, CA

Background: Effective therapies are limited for advanced metastatic pancreatic ductal adenocarcinoma (PDAC) patients (pts) who have progressed after 1st line gemcitabine-based chemotherapy (Gem). FOLFOX has clinical activity in Gem-refractory PDAC pts. A phase 1 trial demonstrated promising activity with pegilodecakin (PEG; pegylated IL-10) and FOLFOX in Gem-refractory PDAC pts, providing rationale for the phase 3 trial (SEQUOIA; NCT02923921). Herein, we report PFS, ORR per RECIST 1.1, and safety. Assuming OS HR of 0.74, the study was powered to 85% at 2-sided α = 0.05 with ~566 pts to detect superiority of PEG + FOLFOX. Results: As of Sept 9, 2019, 567 pts were randomized to PEG + FOLFOX (283) or FOLFOX (284). The majority (94.7%) had 1st line Gem-refractory disease. The mOS was 14.9 months for PEG + FOLFOX and 10.1 months for FOLFOX (6.3 months vs HR = 0.981, 95% CI [0.808, 1.190], p = 0.8144). ORR was 4.6% on the PEG+FOLFOX arm and 5.6% on the FOLFOX arm. Grade 3 adverse events were 5% higher on the PEG+FOLFOX arm than on FOLFOX arm (25.2% vs. 36.6%, anemia (16.2% vs. 4.0%), neutropenia (29.5% vs. 22.7%), and fatigue (17.6% vs. 10.8%). Conclusions: The addition of PEG to FOLFOX did not improve efficacy (OS, PFS, ORR) in advanced PDAC pts who have progressed after 1st line Gem-containing therapy. Safety findings were consistent with previous data observed per chemotherapy; toxicity was manageable and tolerable. Clinical trial information: NCT02923921. Research Sponsor: Eli Lilly and Company.

Randomized, multicenter, phase II trial of gemcitabine (G), cisplatin (P) and pegilodecakin (PEG) as monotherapy (0.8mg/d if < 80 kg and 0.8mg/d if ≥ 80 kg) after 1st line Gem. FOLFOX has clinical benefit in Gem-refractory PDAC patients (pts) who have progressed after 1st line gemcitabine-based chemotherapy (Gem). FOLFOX has clinical activity in Gem-refractory PDAC pts. A phase 1 trial demonstrated promising activity with pegilodecakin (PEG; pegylated IL-10) and FOLFOX in Gem-refractory PDAC pts, providing rationale for the phase 3 trial (SEQUOIA; NCT02923921). Herein, we report PFS, ORR per RECIST 1.1, and safety. Assuming OS HR of 0.74, the study was powered to 85% at 2-sided α = 0.05 with ~566 pts to detect superiority of PEG + FOLFOX. Results: As of Sept 9, 2019, 567 pts were randomized to PEG + FOLFOX (283) or FOLFOX (284). The majority (94.7%) had 1st line Gem-refractory disease. The mOS was 14.9 months for PEG + FOLFOX and 10.1 months for FOLFOX (6.3 months vs HR = 0.981, 95% CI [0.808, 1.190], p = 0.8144). ORR was 4.6% on the PEG+FOLFOX arm and 5.6% on the FOLFOX arm. Grade 3 adverse events were 5% higher on the PEG+FOLFOX arm than on FOLFOX arm (25.2% vs. 36.6%, anemia (16.2% vs. 4.0%), neutropenia (29.5% vs. 22.7%), and fatigue (17.6% vs. 10.8%). Conclusions: The addition of PEG to FOLFOX did not improve efficacy (OS, PFS, ORR) in advanced PDAC pts who have progressed after 1st line Gem-containing therapy. Safety findings were consistent with previous data observed per chemotherapy; toxicity was manageable and tolerable. Clinical trial information: NCT02923921. Research Sponsor: Eli Lilly and Company.

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Determine when endoscopic ultrasound (EUS) changes management for patients with pancreatic cystic neoplasms. First Author: Hasrit Sidhu, University of British Columbia Faculty of Medicine, Vancouver, BC, Canada

Background: Pancreatic cystic neoplasms (PCNs) are being incidentally detected at an increased rate due to the widespread use of CT and MRI. CT and MRI cannot always differentiate between malignant and benign PCNs. EUS is an emerging tool that provides higher quality descriptions of pancreatic cysts and can be used to differentiate between benign and malignant features. Considering that EUS is a resource-dependent tool, we hope to identify the PCN cases in which EUS changes management. Methods: We conducted a retrospective case-control chart review evaluating patients who were diagnosed with pancreatic cysts and underwent EUS for analysis between January 1, 2010 and December 31, 2017. We determined whether EUS correctly identified high-risk features (HRFs) relative to CT/MRI and whether EUS upstaged or downstaged the CT/MRI diagnosis to change overall patient management. Results: EUS was found to have a high specificity (95%) for all high-risk features identified in the AGA and FG guidelines and a low sensitivity (< 70%) for all high-risk features except cyst size > 3 cm (82.3%) and mural nodule < 5 mm (100%). EUS was found to change management in 29.4% of cases (18.2% upstaged, 11.2% downstaged). EUS screening led to a total of three adenocarcinoma diagnoses, in which two were reported to be invasive. Conclusions: The high specificity of EUS supports its use in the differentiation of high-risk PCNs identified on cross-sectional imaging. Its low sensitivity indicates that the reliance on operator experience may be a substantial limitation resulting in inconclusive diagnoses. In conclusion, considering that EUS is a resource-dependent tool, we hope to identify the PCN cases in which EUS changes management. Its low sensitivity shows the importance of improving operator experience, though caution is required because the PPV is still low. Research Sponsor: None.

Weight loss as an untapped early detection marker in pancreatic cancer. First Author: Jonathan J. Hue, University Hospitals Cleveland Medical Center, Cleveland, OH

Background: Pancreatic cancer has the worst survival of common cancers and there are no reliable early detection tests. While prior reports link unintentional weight loss (>5% decrease from baseline) to pancreatic cancer, there is currently no study documenting the frequency of this presenting sign using raw patient weight data. Methods: Patients at our institution with a pancreatic neoplasm (n=288) were queried using ICD-9 code 157.9 and ICD-10 code C25.9. Retrospective review identified 95 patients with pancreatic ductal adenocarcinoma and two or more prediagnosis weights (>7 days apart). Date of diagnosis was defined by the date of positive biopsy or encounter with surgical or medical oncology. Standard statistical analysis was performed. Results: Among the 95 patients, there was a slight preponderance of female (65.3%) and Caucasian (54.7%) patients. The median age at diagnosis was 71 (range: 41-90) and the median BMI was 25.6 kg/m² (range: 15.4-49.5). 9.5% presented with clinical stage I disease, 27.3% with stage II, 9.5% with stage III, and 53.7% with stage IV. Within 1 year of diagnosis (range: 9-365 days), median weight loss was 7.1% of body weight (range: 0.2-34.5%). In this period, 71.6% of patients lost greater than 5% body weight and 32.6% lost over 10% (Table). In the 6 months before diagnosis (range: 9-180 days), median weight loss was 6.4% (range: 0.2-24.2%). A subgroup analysis of early (I, II) and late stage (III, IV) patients showed that those with late stage at presentation lost significantly more prediagnosis weight compared to the early stage patients (median 8.2% vs 5.6%, p<0.02) in a median of 175 days. Prior to diagnosis of late stage patients, 80.0% lost over 5% body weight and 38.3% lost over 10%. Conclusions: Diagnosis of pancreatic cancer is preceded by weight loss in the majority of cases, even at an early stage. Monitoring unintentional weight loss in otherwise asymptomatic patients may be an inexpensive and practical way to detect pancreatic cancer. Research Sponsor: University Hospitals Ventures.

Evaluation of ICD codes and phecodes for the identification of pancreatic cancer in a large genomic database. First Author: Chelsea Anne Isom, Vanderbilt University Medical Center, Nashville, TN

Background: Large genomic databases linked to electronic health records promise to shed light on molecular mechanisms underlying rare diseases, such as pancreatic cancer. However, accurately identifying patients with the desired phenotype can be challenging. This is particularly the case for pancreatic tumors since ICD codes do not distinguish between pancreatic adenocarcinoma (PDAC) and pancreatic neuroendocrine tumors (pNET). Previous studies have shown that ICD codes aggregated by phenotype, known as “phecodes”, have a higher accuracy in identifying specific phenotypes than ICD codes themselves; however, their performance in identifying cancers of the pancreas has not been studied. Methods: From a large deidentified genomic database, two queries were performed to identify all adults with pancreatic cancer for a GWAS study, one using ICD-9/10 codes and the other using phecodes. The medical records for all patients identified from both queries were then reviewed to confirm the presence and histologic type of pancreatic cancer. Results: Of the 99,985 genotyped adults in the database, ICD-9/10 codes identified 1,247 patients with pancreatic cancer, compared with only 422 patients identified by the phecode query. All patients in the phecode cohort were also found in the ICD cohort. Of the 1,247 patients in the ICD cohort, 760 were confirmed to have pancreatic cancer on review of the health records (594 with PDAC, 166 with pNET) whereas in the phecode cohort, only 251 were confirmed to have pancreatic cancer (159 with PDAC, 92 pNET). The positive predictive value (PPV) for PDAC in the ICD query was 47%, compared with 38% for the phecode cohort. The ICD and phecode cohorts had similarly low numbers of pre-malignant cystic tumors (5% in each cohort) and other peripancreatic tumors (3%). Conclusions: In this large genomic database, the use of ICD-9/10 codes for pancreatic cancer was able to identify nearly three times as many patients with pancreatic cancer and had a higher PPV compared to using phecodes. Therefore, ICD codes, rather than phecodes, should be used to identify patients with pancreatic cancer for subsequent genotyping analysis, though caution is required because the PPV is still low. Research Sponsor: None.

Pathological examination of CT findings of tumor infiltration to the peripancreatic plexus in pancreatic cancer. First Author: Takashi Miyamoto, Division of Hepato-Biliary-Pancreatic Surgery, Shizuoka Cancer Center, Nagazumi, Japan

Background: The radiographic diagnosis of tumor infiltration into the peripancreatic plexus in pancreatic cancer is important because it is related to the classification, however, it is difficult to distinguish the abnormal shadow along the artery caused by inflammation or cancer infiltration. The aim of this study is to investigate CT values of the abnormal shadow along artery could distinguish between inflammation and tumor invasion. Methods: Study 1: Of 26 patients who underwent DP-CAR between 2009 and 2018, we analyzed 19 patients who had dynamic CT and obtained sagittal slice taken 120 seconds after injection with less than 2.5 mm slice thickness. At first, we measured CT values at upper and lower point of CeA and CHA each sagittal slice using CT. Next, we evaluated tumor invasion at the upper and lower plexus of CeA and CHA in each section of the pathologic specimen, and evaluated the relationship between the tumor invasion and the CT value. Study 2: Using these 19 patients and 40 patients who underwent DP for PDAC between 2010 and 2014, we analyzed the relation between CT value and long-term states. Results: Study 1: CT value was totally measured at the 606 points using 19 patients who underwent DP-CAR. At the 490 points, we did not observe cancer infiltration and fibrosis. At the 70 points, we observed fibrosis without cancer cells. At the 46 points, we observed cancer infiltration. CT value was significantly higher in the tumor infiltration group than that in the without cancer infiltration and fibrosis group (P < 0.05). Study 2: The best cut-off of CT value of the presence of cancer infiltration was 44.9 HU using ROC curve (AUC = 0.861). The median survival time of patients who had the points of CT value > 44.9 HU around arteries was significantly shorter than that of patients who did not have the points of CT value > 44.9 HU (2.7 vs. 4.55 years, p = 0.03). Conclusions: The CT value around the arteries was significantly higher in the patients of pathological tumor infiltration than that in the points of fibrosis without cancer cells. The best cut-off of CT value of wedge infiltration around arteries is 44.9 HU, and the presence of the point of CT value > 44.9 HU around arteries was associated with poor survival. Research Sponsor: None.
Detection of circulating tumor DNA in pancreatic cancer. 

**First Author:** Daniel King, Stanford University, Palo Alto, CA

**Background:** Pancreatic cancer remains a leading cause of cancer-related death. Improved detection of early relapse or early failure of chemotherapy also has the potential to further improve outcomes. Exploring circulating tumor DNA (ctDNA) in this setting is an area of active investigation.

**Methods:** We previously developed an approach, CAPP-Seq, combining high-depth sequencing with several strategies of error-suppression to identify minute amounts of circulating tumor DNA. We then trained and validated a new classifier panel for pancreatic cancer from 640 tumors from three data sources (TCGA, ICGC, UTSW), targeting 265 kb of the genome. We enrolled two cohorts of patients with pancreatic cancers at Stanford Cancer Center: (1) patients with localized tumors undergoing resection with curative intent, and (2) patients with unresectable or metastatic disease under systemic therapy.

**Results:** As of August 2019, we recruited 131 patients with at least one blood collection, with 63% having resectable disease and 27% having advanced disease; 59 patients had 2 or more blood collections. Stage distribution included 34% stage I, 33% stage II, 18% III, 16% IV disease. Approximately 15% had normal CA19-9 levels. Deep sequencing (4,000X unique depth) of an initial set of resected pancreatic tumors and matched germline specimens identified 16 non-synonymous coding mutations per case (median=3, n=14), with the most frequently mutated genes including KRAS (79%), TP53 (50%), SMAD4 (29%). Among newly diagnosed treatment-naïve patients with resectable adenocarcinoma (n=9), we detected ctDNA in 4 patients (44%) prior to surgery including with AFs ranging from 0.21% - 0.88%. Subsequent sequencing will compare patients with and without neoadjuvant therapy prior to resection, selection of unresectable patients across a larger range of tumor burden and across multiple timepoints, and integration of large-scale copy number variant detection using low-pass whole-genome sequencing.

**Conclusions:** Circulating tumor DNA monitoring with CAPP-Seq shows promise for improved detection of PDAC. Two key applications include early detection of minimal residual disease after resection and early assessment of response to chemotherapy. Research Sponsor: Stanford Cancer Institute.

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Efficacy of chemotherapy for patients with unresectable or recurrent pancreatic adenosquamous carcinoma: A multicenter retrospective analysis.

**First Author:** Yukio Yoshida, Okinawa Chubu Hospital, Uruma, Okinawa, Japan

**Background:** Pancreatic adenosquamous carcinoma (PAC) is a rare variant of pancreatic ductal adenocarcinoma (PDAC). Although unresectable or recurrent PAC is usually treated by systemic chemotherapy, there are few reports which show the efficacy of chemotherapy. The aim of this study was to evaluate the efficacy of chemotherapy for patients (pts) with unresectable or recurrent PAC. **Methods:** We collected data retrospectively from 24 Japanese institutions. The selection criteria were as follows: (1) histologically or cytologically proven PAC (non-surgical specimens were eligible if squamous cell carcinoma (SCC) was detected), (2) unresectable or recurrent disease treated with 1st line chemotherapy between April 2001 and December 2017. **Results:** This study included 138 pts with median age of 66 years (range: 36-85). The majority of pts were diagnosed with biopsy and only 5% were detected by fine needle aspiration. About 60% of pts were diagnosed with biopsy and only SCC was detected. Characteristics were as follows: median age 61, 93 (69%) males, 19 (14%) with metastasis, 15 (11%) with jaundice, 34 (25%) with ascites, 42 (30%) with pleural effusion. **Conclusions:** As of August 2019, we recruited 131 patients with at least one blood collection, with 63% having resectable disease and 27% having advanced disease; 59 patients had 2 or more blood collections. Stage distribution included 34% stage I, 33% stage II, 18% III, 16% IV disease. Approximately 15% had normal CA19-9 levels. Deep sequencing (4,000X unique depth) of an initial set of resected pancreatic tumors and matched germline specimens identified 16 non-synonymous coding mutations per case (median=3, n=14), with the most frequently mutated genes including KRAS (79%), TP53 (50%), SMAD4 (29%). Among newly diagnosed treatment-naïve patients with resectable adenocarcinoma (n=9), we detected ctDNA in 4 patients (44%) prior to surgery including with AFs ranging from 0.21% - 0.88%. Subsequent sequencing will compare patients with and without neoadjuvant therapy prior to resection, selection of unresectable patients across a larger range of tumor burden and across multiple timepoints, and integration of large-scale copy number variant detection using low-pass whole-genome sequencing. Circulating tumor DNA monitoring with CAPP-Seq shows promise for improved detection of PDAC. Two key applications include early detection of minimal residual disease after resection and early assessment of response to chemotherapy. Research Sponsor: Stanford Cancer Institute.

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Impact of biliary metal and plastic stents on preoperative staging for pancreatic cancer. 

**First Author:** Nasrine Hachem, Fox Chase Cancer Center, Philadelphia, PA

**Background:** Multiple studies have shown the superiority of biliary metal compared with plastic stents for pre-operative (preop) biliary drainage in pancreatic cancer (PDAC). Despite the importance of preop cross-sectional imaging, particularly in the era of neoadjuvant treatment, there is no data on the impact of such stents on the quality of preop cross-sectional imaging. We hypothesize that biliary metal stents negatively impact the accuracy of preop cross-sectional imaging in pancreatic cancer, with unknown impact for the adequacy of surgical candidacy. **Methods:** Data of all patients undergoing pancreatic resection for PDAC between 1/1/2012 and 1/1/2018 was retrospectively abstracted. Clinical staging based on preop cross-sectional imaging following biliary stent placement (within 2 months prior surgical resection) was compared with the surgical pathology (staging gold standard). Accuracy of clinical and surgical pathology staging was compared. Logistic regression was performed to control for biliary stent type, neoadjuvant treatment and patient baseline characteristics including BMI and type of imaging.

**Results:** 312 patients underwent pancreatic resections. 118 patients required preop biliary drainage in setting of PDAC, including 92 ERCPs of which 83 were successful (46 plastic and 37 metal stents). 76 patients underwent neoadjuvant chemoradiation therapy. Surgical pathology revealed following stages: 0 n = 4, 1A n = 5, 1B n = 8, 2A n = 20, 2B n = 24, 3 n = 1, 4 n = 14, 96% underwent preop CT and 4% MRI pancreas protocol imaging. Exact correlation between clinical and surgical pathology was in only 48% of cases (57% plastic, 46% metal stent), with 28% of cases all overstaging, 4% clinical understaging, 16% clinical under staging and 4% unable to stage due to artefacts. More importantly, 8% patients were incorrectly staged to be surgical candidates (14% plastic, 6% metal). Controlling for stent type, neoadjuvant treatment and BMI did not impact preop cross-sectional imaging accuracy. **Conclusions:** Despite their impact on preop cross-imaging biliary metal stents did not negatively impact the accuracy and patient selection for surgical candidacy compared with biliary plastic stents in PDAC. Research Sponsor: None.
Prognostic factors associated with short-term survival (STS) in advanced pancreatic cancer (APC): A multicenter analysis from the CHORD consortium.

First Author: Sakshi Mehta, Juravinski Cancer Centre, Hamilton, ON, Canada

Background: The survival of patients (pts) with APC (locally advanced/metastatic) is significantly shorter; however, in some pts, it remains extremely short. Previous studies have evaluated the clinical, pathologic and treatment characteristics associated with STS in APC. Methods: Pts with APC (between 2011-2017) were included in the analysis. Descriptive analyses were conducted for demographic, tumor and treatment characteristics between pts who survived < 90 days using Wilcoxon rank-sum test and Chi-square test for continuous and categorical variables respectively. Multivariable logistic regression was performed to identify association between pts’ characteristics and STS. Results: A total of 580 pts were included in the analysis: median age 68, 53% male, 92% metastatic and 53% ECOG 0/1. STS < 90 days occurred in 152 pts (26.2%), with 65.1% not receiving any chemotherapy. Median overall survival for STS was 49 days vs. 276 days for non-STs. At least 1 cycle of chemotherapy was administered to 358 pts; mean duration of first-line chemotherapy for pts with STS < 90 was 15.0 (SD 2.5) cycles (N=53), compared to 7.6 (SD 1.1) cycles (N=305) for pts surviving > 90 days. Prognostic factors associated with STS < 90 days were neutrophil/lymphocyte ratio, LDH, metastatic disease, ECOG and not receiving chemotherapy (Table). Other clinical factors (BMI, smoking history, diabetes) and laboratory values (platelet, baseline CA19-9, estimated GFR) were not prognostic.

Conclusions: In a multicenter database of Canadian academic centers, < 1/3 of pts received at least 1 cycle of chemotherapy. Prognostic factors associated with STS include routine laboratory values, not receiving chemotherapy, ECOG and the presence of metastatic disease. Further evaluation of factors related to not receiving chemotherapy, and why chemotherapy is discontinued could improve the outcomes of pts with STS. Research Sponsor: None.

No. of factors n median OS HR 95% CI p

<table>
<thead>
<tr>
<th>Variable</th>
<th>&lt;90 days vs 90 days OS (95% CI)</th>
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<tr>
<td>Metastatic disease</td>
<td>10.97 (2.36-51)*</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Not receiving chemotherapy</td>
<td>41.2 (2.16-75)*</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Multivariable logistic regression</td>
<td>Cox model (HR; 0.42, 95% CI; 0.31-0.57, p = 0.001)</td>
<td></td>
</tr>
</tbody>
</table>

**Table:** Prognostic factors associated with short-term survival (STS) in advanced pancreatic cancer (APC)
Real-world eligibility of advanced pancreatic (APC) patients for maintenance olaparib. 

Poster Session (Board #H4), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Background: The POLO trial demonstrated an improvement in progression-free survival (PFS) for patients with platinum-based first-line therapy. This study aims to identify the proportion of real-world APC patients eligible for olaparib, and to determine the PFS and overall survival (OS) after DC16. Methods: APC patients treated with first-line FXX in Alberta were identified (2011-2018). We conducted an analysis of baseline characteristics to identify factors associated with DC16. Results: We identified 165 APC patients treated with FXX with unknown BRCA 1/2 status, of which 56% were males and median age at diagnosis was 59 years (interquartile range 38-75 years). Of these, 72 (44%) had DC16. Normal LDH and ALP, and albumin more than 35 g/L were associated with a higher likelihood of having DC16 (table). The PFS of patients with DC16 was significantly higher than those with DC<16 weeks (9.3 v 2.5 months, p<0.02, 95% CI 1.05-3.32, P<0.001). In patients who had DC16, median PFS and OS from that point were 5.6 months and 17.9 months, respectively. Conclusions: Less than half of real-world patients treated with first-line FXX would be eligible for olaparib by the criteria of DC16 with FXX. Median PFS after DC16 is 5.6 months with FXX in patients with unknown BRCA 1/2 status. This provides a baseline for future trials evaluating maintenance strategies. Patients with APC and high disease burden (higher ALP and LDH) and low albumin are less likely to have DC16. Research Sponsor: None.

Poster Session (Board #H8), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Gemcitabine and nab-paclitaxel in older adults with metastatic pancreatic cancer: Are two doses per cycle enough? First Author: Arthur Winer, NYU Langone Medical Center, New York, NY

Background: The dosing of Gemcitabine and Nab-Paclitaxel (GA), a frontline therapeutic standard of care for metastatic pancreatic cancer, namely FOLFIROX (FFX) and gemcitabine + nab-paclitaxel (GNP) after demonstrating a statistically significant and relevant increase of overall survival. However, there are some important uncertainties regarding how many patients are candidate to each of these new regimens (FFX or GNP). Metastatic patients were included. Med age 63 y (38-83 y), 99% adenocarcinoma. 40% located in the head of pancreas. ECOG 87% 0-1, 89% had liver metastasis. In the 1st line 49.6% were treated with FXX and 50.4% with GNP. 53% of the pts received a 2nd line (82% after FXX 75% after GNP). The median OS was 12 months with no statistically significant differences between both regimens (12.7m for FXX vs 10.2 m for GNP). Elevated Ca 19.9 levels and Neutrophil-Lymphocyte ratio (NLR) increased the risk of death. Patients who received both regimens in first/second line had a median OS longer than 15 months whereas the sequence, 32 patients (27%) were older than 70 yrs, 13 (41%) were treated with FXX and 19 (59%) with GNP. The median OS for patients older than 70 was 9.5m versus 12.3m for patients younger than 70. Conclusions: In our setting the use of FXX and GNP for treating metastatic pancreatic cancer is quite similar. Superiority could not be demonstrated for any of the schemes in first-line. Overall survival was determined by basal Ca 19.9 and NLR. Patients receiving both regimens (FFX or GNP) in first/second line whichever the sequence, exhibited the best survival rates. In our series elderly patients had poor survival rates. Research Sponsor: None.

Safety and efficacy of chemotherapy in older adults with locally advanced and metastatic pancreatic ductal adenocarcinoma (PDAC). First Author: Lorena Ostios, Beth Israel Deaconess Medical Center, Hematology/Oncology Division, Boston, MA

Background: PDAC is often diagnosed in patients (pts) ≥75yrs. However, older adults represent a small proportion of subjects in prospective trials, and there is little reported on the safety and efficacy of chemotherapy in this population. Methods: Records were reviewed on all pts ≥75yrs treated with chemotherapy for locally advanced and metastatic PDAC at a single institution from April 2010 - March 2018. Response rate (RR), progression free survival (PFS), overall survival (OS) and toxicities were compared among the different regimens, and among pts < or ≥80yrs. Survival was estimated with the Kaplan-Meier method and compared by log-rank test. Univariate analyses were performed by Fisher’s exact test and multivariate analyses by a Cox-regression model to identify factors associated with PFS and OS in this population. Results: 67 pts were treated, median age 68yrs (range 75-90); stage III (34, 50%) and IV (33, 49%). Chemotherapy regimens included gemcitabine alone (39), gemcitabine/nab-paclitaxel (17), gemcitabine/vinorelbine (1), FOLFIBOX (1) and FOLFIRINOX (2). 59 (88%) pts required dose adjustments due to toxicity; no differences by age or regimen. RR, PFS, and OS did not differ by age or regimen (Table), although sample size was small. Age ≥80yrs was associated with reduced PFS (p 0.03). On univariate analyses liver metastases and performance status (PS)-1 were associated with reduced OS; PS-1 was associated with reduced OS on multivariate analysis. Conclusions: Among pts with locally advanced and metastatic PDAC ≥75yrs, there were no differences in RR, PFS or OS by chemotherapy regimen. PS was the only variable associated with reduced OS. Older adults with ≥75yrs should be considered to benefit from chemotherapy for non-resectable PDAC. Research Sponsor: None.

Clinical outcomes of FOLFIRINOX and gemcitabine-nab-paclitaxel for metastatic pancreatic cancer in the real-world setting. First Author: Fabio Franco, Hospital Universitario Puerta de Hierro-Majadahonda, Madrid, Spain

Background: Randomized clinical trials have established new chemotherapeutic standards of care for metastatic pancreatic cancer, namely FOLFIRINOX (FFX) and gemcitabine + nab-paclitaxel (GNP) after demonstrating a statistically significant and relevant increase of overall survival. However, there are some important uncertainties regarding how many patients are candidate to each of these new regimens (FFX or GNP). Non-metastatic patients were excluded. An exploratory analysis was performed in the elderly population. Results: From Jan 2012 to Dec 2017, a total of 119 pts (M/F 58/42 %) were treated. Med age 63 y (38-83 y), 99% adenocarcinoma. 40% located in the head of pancreas. ECOG 87% 0-1, 89% had liver metastasis. In the 1st line 49.6% were treated with FXX and 50.4% with GNP. 53% of the pts could receive a 2nd line (82% after FXX 75% after GNP). The median OS was 12 months with no statistically significant differences between both regimens (12.7m for FXX vs 10.2 m for GNP). Elevated Ca 19.9 levels and Neutrophil-Lymphocyte ratio (NLR) increased the risk of death. Patients who received both regimens in first/second line had a median OS longer than 15 months whereas the sequence, 32 patients (27%) were older than 70 yrs, 13 (41%) were treated with FXX and 19 (59%) with GNP. The median OS for patients older than 70 was 9.5m versus 12.3m for patients younger than 70. Conclusions: In our setting the use of FXX and GNP for treating metastatic pancreatic cancer is quite similar. Superiority could not be demonstrated for any of the schemes in first-line. Overall survival was determined by basal Ca 19.9 and NLR. Patients receiving both regimens (FFX or GNP) in first/second line whichever the sequence, exhibited the best survival rates. In our series elderly patients had poor survival rates. Research Sponsor: None.
Survival outcomes based on sequence of therapy using FOLFIRINOX and nab-paclitaxel + gemcitabine in metastatic pancreatic ductal adenocarcinoma.

First Author: Kelsey Baron, Division of Internal Medicine, Interventional Medical Center, Murray, UT

Background: Optimal sequence of therapy for patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) is unknown. FOLFIRINOX (FFX) and Gemcitabine + Nab-paclitaxel (AG) are standard first line (1L) therapies. They have never been prospectively compared. Therefore, we retrospectively compared the overall survival (OS) of patients treated with 1L AG and second-line (2L) FFX compared to those treated with 1L FFX and 2L AG.

Methods: Patients with mPDAC treated with 1L FFX followed by 2L AG, or vice versa were identified using the Flatiron Health EHR-derived nationwide database. To avoid immortal time bias, patients who received no 2L were included. OS from the initiation of 1L was compared with Kaplan Meier curves and log rank analysis. A Cox model, stratified by deciles of propensity score (PS), was used to estimate the effect of treatment on OS with adjustment for differences between the groups. Results: 3,042 patients were identified. 2,001 patients received 1L AG. Among these patients, 1,446 received 2L FFX, and 555 received no 2L. 1,041 patients received 1L FFX. Among these patients, 496 received 2L AG, and 549 received no 2L. Median OS and 1-year OS for those treated with 1L AG followed by 2L FFX or no therapy was 6.1 months (95% CI: 5.6 – 6.5) and 25% (95% CI: 0.23 – 0.26). Median OS and 1-year OS for patients treated with 1L FFX followed by AG or no therapy was 8.7 months (95% CI: 7.9 – 9.2) and 36% (95% CI: 0.33 – 0.39). The propensity stratified hazard ratio between these two groups was 0.76 (95% CI: 0.69 – 0.83), favoring 1L FFX. Median OS for patients treated with 1L FFX and 2L AG versus 1L AG and 2L FFX was not significantly different (12.0 vs. 12.5 m; HR: 1.04; 95% CI: 0.90 – 1.20).

Conclusions: In analyses of real-world data, 1L FFX was associated with increased OS in propensity analysis. For patients who received both FXX and AG, median OS was similar, regardless of the sequence.

Research Sponsor: None.

Efficacy of second-line chemotherapy after standard combination chemotherapy in patients with metastatic pancreatic cancer: The results from the NAPOLÉON study.

First Author: Masaru Fukahori, Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine, Kurume, Japan

Background: Gemcitabine plus nab-paclitaxel (GnP) and FOLFIRINOX (FFX) have been established as standard first-line combination chemotherapy (CTx) for patients with metastatic pancreatic cancer (MPC). However, the efficacy of second-line CTx and the significance of combination CTx in clinical practice are unclear. We therefore investigated the efficacy of second-line CTx in patients with MPC.

Methods: Data were collected from CTX-naive MPC patients treated with first-line combination CTx at 14 hospitals in the Kyushu area of Japan from December 2013 to June 2018. The median overall survival (mOS) from second-line treatment was compared between patients who received second-line CTx (CT group) and those who received best supportive care (BSC group). Furthermore, in the CT group, the mOS was compared between the patients who received mono-CTx and those who received mono-mCTx. To control potential bias in the selection of second-line treatment, we also conducted a propensity score-adjusted analysis.

Results: A total of 255 patients received GnP or FFX as first-line CTx. Of these, there were 156 (61%) in the CT group and 77 (30%) in the BSC group. The number of patients who received FXX/GnP as first-line CTx was 79 (51%)/77 (49%) in the CT group and 15 (20%)/62 (80%) in the BSC group, respectively (P < 0.01). The mOS in the CT group was significantly longer than that in the BSC group (5.2 vs. 2.7 months; hazard ratio [HR] 0.42; 95% confidence interval [CI] 0.30–0.57; P < 0.01). In the CT group, 69 (57%) patients received combination CTx, and 67 (43%) received mono-CTx. There was no significant difference in the mOS between the combination CTx and mono-CTx patients (5.5 vs. 4.4 months; HR 0.88; 95% CI 0.62–1.26; P = 0.88) and 5.6 vs. 4.4 months; adjusted HR 0.85; 95% CI 0.56–1.30; P = 0.47).

Conclusions: Among patients with MPC receiving second-line treatment, the CT group had a significantly longer mOS than the BSC group, but combination CTx showed no improvement in the survival duration compared with mono-CTx. None.
Comparison of clinicopathological characteristics and prognosis of borderline resectable pancreatic cancer according to the location of the primary tumor.

First Author: Tsuyoshi Takeda, Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan

Background: Little is known about the clinicopathological and prognostic differences between borderline resectable (BR) pancreatic head (PH) and pancreatic body/tail (Pbt) cancer. Therefore, we conducted this study to compare the clinicopathological features and prognosis of BR pancreatic cancer (PC) according to the location of the primary tumor.

Methods: We retrospectively investigated consecutive patients with BR PC who initiated neoadjuvant chemotherapy (NAC) between March 2015 and April 2019. We compared clinicopathological characteristics and prognosis between PH and Pbt cancer. Furthermore, multivariate survival analysis was performed using cox proportional hazard model.

Results: A total of 104 patients with BR PC (median age 68, male 49%) were included in this study. The location of the tumor was PH 72 and Pbt 32, respectively. The initial regimen of NAC was nab-paclitaxel/gemcitabine in 102 and gemcitabine in 2, respectively. The median cycle of NAC was 4. Median age, sex, primary tumor size, performance status, neutrophil to lymphocyte ratio, and serum level of carbohydrate antigen 19-9 at the time of the initiation of NAC were not significantly different between PH and Pbt cancer, while the modified Glasgow prognostic score (mGPS) was lower in Pbt cancer (mGPS = 0; 78% vs. 94%, p = 0.05). RO/R1 resection rate (81% vs. 69%, p = 0.03) and median survival time (528 days vs. NA, p = 0.13) were also not different between PH and Pbt cancer. Multivariate survival analysis revealed that RO/R1 resection (HR, 0.11; p < 0.01) and PH (HR, 2.29; p = 0.03) were independent prognostic factors for survival in patients with BR PC. Out of the PH group, 9/24 (38%) patients had a higher rate of mGPS score of 0 compared to Pbt cancer. Furthermore, RO/R1 resection (HR, 0.11) and PH (HR, 2.29) were independent prognostic factors for survival in patients with BR PC. None.

Conclusions: Although R0/R1 resection rate was similar between PH and Pbt cancer, Pbt cancer had a higher rate of mGPS score of 0 compared to PH cancer. Furthermore, RO/R1 resection (HR, 0.11) and PH (HR, 2.29) were independent prognostic factors for survival in patients with BR PC. None.

663 Poster Session (Board #H16), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

A real-world evidence analysis of periampullary cancers in an academic hospital in Chile. First Author: Luis Villanueva, Hospital Clinico Universidad de Chile, Santiago, Chile

Background: Periampullary cancers can originate in the pancreas, duodenum, bile duct or structures of the ampullary complex. The treatment of choice in early stages of periampullary cancer is pancreaticoduodenectomy. The management post-surgery can depend on the histology pattern, and the overall survival can vary in different subgroups.

Methods: A retrospective cohort study. We examined patients (pts) with invasive periampullary cancer undergoing pancreaticoduodenectomy at the Hospital Clinico Universidad de Chile between 2002 to 2018. We analyzed epidemiological, clinical, surgical, and histological data. OS and the hazard ratio (HR) were established by GraphPad Prism 8.0.

Results: Thirty-seven cases were registered. Twenty-two (59%) pts were men. The mean age was 62.5 (43-93 years). The histological subtypes were: 15 pts (40.5%) intestinal group (IN), 20 pts (54%) pancreatobiliary group (PB), 1 pt (2.7%) mixed and 1 pt (2.7%) signet ring cell type. A full concordance between histology and immunohistochemistry (CK20, CK7, CDX2, MUC1 and MUC2) patterns was 66% of the PB group, and 0% of the IN group. The stage IB was most frequent in all of the group (36.4%). The most frequent stages were IB (66.6%) in the IN type and IIIA (46%) in the PB type. The level of Ca19-9 was higher the PB group than IN group (629.7 ± 415 U/ml, respectively). Seven pts received postoperative adjuvant treatment such as FOLFIRI, capecitabine, and gemcitabine. The median OS was 133.5 months (mo) in the intestinal group and 32.6 mo in PB group (P = 0.02). The HR was 0.38 (95% CI of ratio 0.33 to 1.084). The 5-year OS was 75.2% and 45.7% in the IN and PB group, respectively.

Conclusions: Periampullary cancer remains very challenging because it is a rare malignancy and present diverse histological pattern. These factors influence the OS and OS of the disease. Our results showed clinically and statistically relevant differences in the staging, levels of Ca19-9, and OS of the IN and PB subtypes. Our patients received few post-operative therapies such as chemotherapy; this factor could influence the OS in the high-risk group. According to our data, a personalized treatment by histological type should consider in this disease.

Research Sponsor: None.

664 Poster Session (Board #H17), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Comparing survival outcomes for neoadjuvant therapy versus adjuvant therapy in the management of stage 1 pancreatic adenocarcinoma: A National Cancer Database study. First Author: Samit Kumar Datta, Aurora Health Care, Milwaukee, WI

Background: We are in the midst of a paradigm shift in the treatment of stage 1 pancreatic ductal adenocarcinoma (PDAC) from surgery first followed by adjuvant Neoadjuvant therapy (NAT) to first followed by surgery and this is reflected in the current NCCN guidelines as well. Despite these two modalities are limited. AIM: To compare long term survival between Surgery + AT and NAT + Surgery in a large National Cancer Database for stage 1 PDAC.

Methods: We identified patients with the NCDB with surgically resected AJCC clinical stage 1, 1A, and 1B PDAC between 2004-2016. Patients were stratified into two groups to assess outcomes: AT and NAT. Patients with incomplete survival and sequence of therapy were excluded. Baseline demographic data, 90-Day Mortality, Median survival, and Hazard ratios (HR) for survival was evaluated.

Results: 9070 pts with Clinical stage 1A, 1B PDAC between 2004-2016 were identified. Of these 7453 pts had surgery followed by AT; and 1564 pts had NAT followed by surgery. There was a statistically significant difference in age (66.0 ± 9.9 years for AT vs. 64.7 ± 9.78 years for NAT, p = 0.007) but no difference in Charlson Comorbidity Scoring (p = 0.618) or sex (p = 0.073). 90-Day Mortality was 0.35% in the AT group compared to 0.83% in the NAT group (p = 0.001). Median survival was 28.5 (95% CI 26.5-29.9) months in the NAT group compared to 25.4 (95% CI 24.7-26.1) months in the AT group. With AT as the reference group for survival, there was a HR of 0.904 (95% CI 0.845-0.968, p = 0.003) for NAT.

Conclusions: In this retrospective cohort of patients, NAT was associated with increased overall survival. However, NAT was associated with an increased 90-day mortality. A randomized controlled trial is necessary to further support the superiority of NAT in the management of stage 1 PDAC. None.

665 Poster Session (Board #H18), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Impact of dose reductions on clinical outcomes among patients (pts) with metastatic pancreatic cancer (mPC) treated with liposomal irinotecan (nal-IRI) in oncology clinics in the United States. First Author: Paul Cockrum, Ipsen Biopharmaceuticals, Cambridge, MA

Background: The recommended starting dose for nal-IRI is 70mg/m2 (free base, equivalent to 80 mg/m2 salt-based dosing). This study evaluates the impact of nal-IRI dose reductions on clinical outcomes.

Methods: Using the nationwide Flatiron Health electronic health record-derived database, identified data were extracted and analyzed for adult mPC pts treated with nal-IRI Jan 2014-Jan 2019 and who initiated treatment at approximately the RD. 257 mPC pts treated with nal-IRI (median age: 68y, IQR: 61 – 73) were identified initiating therapy at approximately the RD. 26.5% (N = 68) of pts experienced a DR during treatment. Mean 6-week CD was 175.8 mg/m2 (SD: 77.9) among pts with no DR. For pts with DR, mean CD was 191.8 mg/m2 (53.2). Median DoT was 6.1 wks (IQR: 2.1 – 15.3). Pts that experienced a DR had a longer median DoT: 15.1 (7.1 – 23.0) vs. 4.3 wks (2.1 – 12.1) for pts with no DR. Overall Median OS (mo) was 4.2 months (95% CI: 3.7 – 5.4). mOS for DR pts was 7.2 mos (95% CI: 5.5 – 9.7) and 3.7 mos (3.0 – 4.3) for pts who did not experience a DR.

Conclusions: This real-world analysis suggests that reducing the dose of subsequent administrations of nal-IRI during treatment is associated with pts remaining on therapy longer, experiencing a larger CD, and a longer OS. Additional real-world prospective studies are necessary to characterize the impact of nal-IRI dosing on clinical outcomes. Ipsen Biopharmaceuticals.
Changes in glucose tolerance after pancreatectomy in patients with pancreatic ductal adenocarcinoma. First Author: Sachio Shirakawa, Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Kobe University Graduate School of Medicine, Kobe, Japan

Background: Diabetes mellitus (DM) is reported to be related to pancreatic ductal adenocarcinoma (PDAC). Long-standing DM is a risk factor for PDAC, meanwhile, quite a few patients with PDAC develop DM as a paraneoplastic disorder and some papers reported that DM affected prognosis for PDAC. In this study, we investigated pre- and post-operative glucose tolerance in patients with pancreatectomy for PDAC or other methods. Methods: This single-center prospective study included 69 patients with pancreatectomy (40 pancreaticoduodenectomy (PD) and 29 distal pancreatectomy (DP)) who received 75-g oral glucose tolerance test (OGTT) and glucagon test pre- and one month postoperatively. Plasma glucose, insulin, and C-peptide (CPR) at 0-, 30-, 60-, and 120-min during OGTT and 0- and 6-min during glucagon test were obtained. Results: The data and statistical analysis were analyzed. Results: The age was 62 (29%) PDAC patients: 12 (30%) in PD group and 8 (28%) in DP group. Nine patients with PDAC (45%) and seven patients (18%) without PDAC demonstrated DM type in preoperative OGTT. After pancreatectomy, 11 patients (55%) with PDAC and seven patients (15%) without PDAC experienced improvement in OGTT (P=0.0005). Greater improvement in homeostasis model assessment insulin resistance that were obtained by OGTT and used to measure insulin resistance, was noted after surgery in PDAC patients compared with non-PDAC patients (P=0.14 vs 0.5 in PD group, P=0.07; 0.8 vs 0.06 in DP group). Delta CPRs obtained by glucagon test were significantly decreased postoperatively (3.0 to 1.1 ng/mL, P=0.0001 in PD group; 3.3 to 1.8 ng/mL, P<0.0001 in DP group). In survival analysis, fasting plasma glucose >110 mg/dL (HR 3.9, 95%CI 1.5-10, P=0.005) and the average of plasma insulin >25 μU/mL during OGTT (HR 0.36, 95%CI 0.14-0.93, P=0.035) were significant prognostic factor for PDAC. Conclusions: Pancreatectomy impaired insulin secretion and improve insulin resistance especially in PDAC patients. About 90% patients demonstrated the improvement of glucose tolerance after surgery. Of note, glucose tolerance differed between PDAC and other disease, and affect the survival outcome for PDAC patients. Research Sponsor: None.

Impact of prior irinotecan exposure on outcomes of metastatic pancreatic cancer (mPC) patients. First Author: Eileen Mary O'Reilly, Memorial Sloan Kettering Cancer Center, New York, NY

Background: Published data suggests prior exposure to irinotecan infers a lower likelihood of benefit to liposomal irinotecan. This analysis seeks to expand understanding of patterns of care among patients with metastatic pancreatic cancer (mPC) and how prior irinotecan therapy impacts outcomes in mPC. Methods: Using the Flatiron Health EHR-derived database, data were extracted and analyzed for treated mPC patients (pts) between Jan 1, 2014 and Jun 30, 2019. Therapies of interest included: gemcitabine/neb-paclitaxel (GnP), FOLFIRINOX (FFX), and liposomal irinotecan/5FU/LV (nal-IRI). The reference date for each treatment group was the date of treatment initiation. Prior irinotecan was defined as any irinotecan given in a prior regimen in mPC diagnosis. Cox proportional hazard (PH) methods were used to calculate mortality hazard ratios (HRs). HRs were adjusted to account for demographics and relevant covariates. Pts with prior exposure to irinotecan were used as the reference population for the Cox PH model (an HR = 1 represents worse survival for exposed pts relative to the unexposed). Results: N=1,978 were included in this analysis. The median age at treatment initiation, and the proportion of pts previously treated with irinotecan are reported in table. Crude mortality was: GnP pts, HR 0.93 [95% CI: 0.77 - 1.13], adjusted HR, 0.94, 0.76 - 1.15]; nal-IRI pts, HR 0.81 [0.64 - 1.02, adjusted HR: 0.89, 0.67 - 1.19]; HR for FOLFIRI was 0.55 [0.38 - 0.78, adjusted HR: 0.51, 0.33 - 0.79]. HRs are not reported for FFX and FOLFIRI due to the small numbers with prior irinotecan exposure. Conclusions: In mPC, prior irinotecan treatment may not preclude benefit from subsequent treatment with nal-IRI or GnP as can be seen from the adjusted and unadjusted HRs. These findings are hypothesis-generating and need to be considered in the context of wide CIs, retrospective nature and the limitations of such data. Further research is required to understand the treatment gaps for pts with mPC. Research Sponsor: Ipsen Biopharmaceuticals.

A multicenter clinical randomized phase II study of investigating duration of adjuvant chemotherapy with S-1 (six versus 12 months) for patients with resected pancreatic cancer: PACS-1 study. First Author: Youichi Yamashita, Department of Gastroenterological Surgery, Kumamoto University, Kumamoto, Japan

Background: Although adjuvant chemotherapy with S-1 has improved overall survival and progression-free survival (PFS) in patients with resected pancreatic cancer, the duration of adjuvant chemotherapy with S-1 has not established yet. Methods: We did a randomized, multicenter, phase 2 trial undertaken at 15 hospitals in Japan. Patients who were Eastern Cooperative Oncology Group performance states of 0 or 1 and aged 20 years or older were eligible. Patients with resected pancreatic cancer were randomly allocated to S-1 for 6 months or 12 months. The primary endpoint was overall survival rate. Secondary endpoints included PFS and safety. Results: The population consisted of 82 patients in the S-1 for 6 months group and 82 patients in the S-1 for 12 months group. The 2-year overall survival rate was 71.4% in the S-1 for 6 months group and 65.4% in the S-1 for 12 months, and the median overall survival was 31.0 months in the S-1 for 6 months group and 26.3 months in the S-1 for 12 months group. The Hazard ratio (HR) was 1.23, 95%CI 0.76-1.99, p=0.371. The PFS at 2 years was 56.8% in the S-1 for 6 months group, and 51.2% in the S-1 for 12 months. The HR for recurrence of S-1 for 6 months, compared with S-1 for 12 months, was 1.23 (95%CI 0.76-1.99, p=0.392). Twenty-nine (35.3%) patients in the S-1 for 6 months group and 46 (56.6%) in the S-1 for 12 months group discontinued treatment before completion. In regard to patients completed treatment, the S-1 for 12 months group showed tendency to favorable prognosis on PFS compared with the S-1 for 6 months group (log-rank test; p=0.175). Conclusions: In patients with resected pancreatic cancer, adjuvant chemotherapy with S-1 for 6 months is not superior to that for 6 months in terms of median overall survival and PFS. For patients who can tolerate adjuvant chemotherapy with S-1 for 6 months well, continuing treatment for up to 12 months may improve the prognosis. Research Sponsor: None.
FOLFIRINOX (FFX) in first-line (IL), 2295 pts with IL gemcitabine plus nab-paclitaxel (gem-nab), 218 pts with second-line (2L) FOLFOX, 56 pts with 2L FOLFIRI, and 178 pts with 2L liposomal irinotecan (nal-IRI) based therapy. Observed rates of anemia and neutropenia are shown in the table below. Lymphopenia rates were similar across regimens and ICs were not statistically significant. ICs for pts with any grade anemia were $3864, $3818, $3536, $3978, and $2963 for FFX, gem-nab, FOLFOX, FOLFIRI, and nal-IRI treated pts, respectively. Pts for any grade neutropenia were $2382 for FFX, $2440 for gem-nab, $2688 for FOLFOX, $3551 for FOLFIRI and $2307 for nal-IRI. Conclusions: Any grade anemia ICs ranged from $2963 ($3154, $4400) for nal-IRI to $3978 ($2241, $5817) (FOLFIRI), and any grade neutropenia ICs ranged from $2307 ($703, $4313) (nal-IRI) to $3551 ($2172, $6039) (FOLFIRI). Pts treated with nal-IRI had similar any grade AE rates but lower ICs, which suggests lower severity of AEs. These results are consistent with Flatiron Health’s lower rates of grades 3+ neutropenia and anemia. Research Sponsor: Ipsen Biopharmaceutical Inc.

First Author: Emily Walzer, Temple University Hospital, Philadelphia, PA

Background: PC affects 57,000 people in the U.S. annually with poor long-term outcomes. NAT for advanced pancreatic cancer (APC) is a matter of debate often influenced by access to drugs. This analysis was conducted to compare outcomes based on 1LTx selection and ST in APC.

Methods: We assessed patients (pts) with APC who received either FFX or GN during 2010-2019 at three Canadian institutions. As well as the ST used. The main objective was to assess survival. Kaplan method and log-rank test were used for survival curves. Results: This retrospective study included 231 pts; ILTtx included 143 pts on FFX and 88 pts on GN. PFS was 16.2 months (95%CI, 12.0-19.6) vs 16.6 (95%CI, 13.2-19.8) months with GN (p=0.24). Kaplan-Meier curves were used for categorical data and Kaplan-Meier curves for survival when comparing those who had upfront surgery versus surgery following NAT. Results: 352 pts with localized disease at diagnosis were included in our analysis with a median age of 65 y (range 38-89) and 45% females. NAT was used in 225 (64%) pts while 109 pts (31%) had upfront surgery and 18 pts (5%) received no treatment. Adjuvant therapy was given to 77% of pts after upfront surgery and 48% of pts after surgery following NAT. NAT regimen consisted of chemotherapy (CTx) and radiation for 48%, CTx alone for 8% and radiotherapy alone for 44% of pts. Of those receiving CTx, 24% received tripe agent while 51% and 25% received dual and single agent therapy. PT factors (age, CCI, gender, BMI, smoking status, race) did not differ between those receiving upfront surgery and surgery following NAT but upfront surgery was associated with a lower stage at diagnosis (p < 0.0001). Surgical resection after NAT occurred in 79 pts (35%) with median overall survival of 26.3m vs 19.7m (p = 0.06) in those who had upfront surgery. Survival rates at year 1, 3 and 5 years were 94%, 34%, and 38% for pts with and without surgery vs 90%, 48%, and 28% for those with and without surgery (p = 0.006). Conclusions: Use of NAT is prevalent, yet only 35% of pts make it to surgical resection. Survival was improved for pts who did not receive surgery following NAT. Long-term survival following NAT was not statistically significant. Additional research is warranted to define the optimal NAT approach for pts with borderline resectable PC. Research Sponsor: None.

First drug selection versus sequential treatment in advanced pancreatic cancer: Does it really matter? Multi-institutional Canadian perspective. First Author: Ivan Barrera, Jewish General Hospital, McGill University, Montreal, QC, Canada

Background: FOLFIRINOX (FFX) and Gemcitabine with nab-Paclitaxel (GN) are both proven to be superior to Gemcitabine (G) in the first line treatment (1LTx) for advanced pancreatic cancer (APC). Yet, the optimal 1LTx selection or sequential Tx (ST) has not been fully established. Therefore, the best choice for ILTtx is a matter of debate often influenced by access to drugs. This analysis was conducted to compare outcomes based on ILTtx and ST in APC.

Methods: We assessed patients (pts) with APC who received either FFX or GN during 2010-2019 at three Canadian institutions. As well as the ST used. The main objective was to assess survival. Kaplan method and log-rank test were used for survival curves. Results: This retrospective study included 231 pts; ILTtx included 143 pts on FFX and 88 pts on GN. PFS were similar in both regimens. The median PFS of FFX was 5.5 months (95%CI: 5.0-6.7) vs 6.2 (95%CI, 5.8-6.7) months with GN (p=0.08). Kaplan-Meier curves were used for categorical data and Kaplan-Meier curves for survival when comparing those who had upfront surgery versus surgery following NAT. Results: 352 pts with localized disease at diagnosis were included in our analysis with a median age of 65 y (range 38-89) and 45% females. NAT was used in 225 (64%) pts while 109 pts (31%) had upfront surgery and 18 pts (5%) received no treatment. Adjuvant therapy was given to 77% of pts after upfront surgery and 48% of pts after surgery following NAT. NAT regimen consisted of chemotherapy (CTx) and radiation for 48%, CTx alone for 8% and radiotherapy alone for 44% of pts. Of those receiving CTx, 24% received tripe agent while 51% and 25% received dual and single agent therapy. PT factors (age, CCI, gender, BMI, smoking status, race) did not differ between those receiving upfront surgery and surgery following NAT but upfront surgery was associated with a lower stage at diagnosis (p < 0.0001). Surgical resection after NAT occurred in 79 pts (35%) with median overall survival of 26.3m vs 19.7m (p = 0.06) in those who had upfront surgery. Survival rates at year 1, 3 and 5 years were 94%, 34%, and 38% for pts with and without surgery vs 90%, 48%, and 28% for those with and without surgery (p = 0.006). Conclusions: Use of NAT is prevalent, yet only 35% of pts make it to surgical resection. Survival was improved for pts who did not receive surgery following NAT. Long-term survival following NAT was not statistically significant. Additional research is warranted to define the optimal NAT approach for pts with borderline resectable PC. Research Sponsor: None.
Distinct clinical characteristics of young-onset pancreatic cancer patients. First Author: Suleyman Yasin Goksu, The University of Texas Southwestern Medical Center, Dallas, TX

Background: Young-onset pancreatic adenocarcinoma (YOPC) is uncommon but there are limited studies for these patients. We used a population based registry to compare the characteristics and outcomes of young-onset vs. older patients with pancreatic adenocarcinoma. Methods: We selected the patients with pancreatic adenocarcinoma from the SEER registry diagnosed between 2004 and 2015. Cases with age of diagnosis less than 50 were termed young-onset pancreatic cancer. Stage 4 patients were excluded. We compared baseline characteristics of YOPC vs. older using Chi-square. Kaplan Meier and multivariable Cox regression were used for survival analysis of these patients. Results: Of 28,904 patients, 1,415 (4.9%) had YOPC while 27,489 (95.1%) were older. YOPC were more likely to have stage 3 compared to older patients with PC (31.6% vs. 25.3%). YOPC had a higher rate of surgery than older patients (40% vs. 29.1%, p < 0.001), were more likely to be male, black and of Hispanic ethnicity. The primary tumor location was not different between the two groups. Overall survival (OS) was higher in YOPC versus older patients (12 vs. 8 months, p < 0.001). The analysis of multivariable Cox regression confirmed that there is a significant association between survival and YOPC group after adjusting for stage, grade, gender, ethnicity, surgery and race (HR 1.23, 95% CI: 1.13-1.33, p < 0.001). Conclusions: Patients with non-metastatic YOPC represent a group of patients with distinct clinical characteristics. YOPC have a higher rate of surgery and better overall survival compared to older patients. Research Sponsor: None.

Clinicopathological features of pancreatic cancer-related diabetes. First Author: Michael Lee, BC Cancer, Vancouver, BC, Canada

Background: Epidemiological studies suggest pancreatic ductal adenocarcinoma (PDAC) may be strongly interrelated with diabetes. However, little is known about the clinicopathological features of pancreatic cancer related diabetes. Methods: A retrospective chart review was undertaken of all patients with advanced PDAC treated with at least one cycle of palliative chemotherapy at BC Cancer, Vancouver between Jan 2012-Dec 2015. Diagnosis of diabetes was determined by consultation documentation and/or fasting glucose >7mmol/L or HbA1c >48mmol/L. Peripancreatic diabetes is defined as diabetes diagnosis < 3 years prior to PDAC diagnosis. Results: 578 patients were identified with median age 66 (49-81), 54.6% male, 39.5% non-smoker and 63.5% ECOG 0/1. 27.3% confirmed diabetics, of which 75.8% (197/259) have peripancreatic diabetes. At initial diagnosis, 11.2% were deemed upfront resectable, 44.0% borderline/locally advanced, and 55.1% metastatic. Median overall survival (OS) for the cohort based on stage of disease at initial diagnosis for borderline, locally advanced and metastatic was 22 months (16.1-27.6), 12 months (10.1-13.9) and 6 months (5.0-7.0) respectively. There was no association with diabetes status and OS noted (p = 0.58). Statistical differences were noted in BMI (24.1 v 26.1, p = 0.003), and proportion of Charlson comorbidity index (CCI) of 2 (2.2 v 88.3%, p < 0.01) between non-diabetic and diabetic patients respectively. Statistical difference between peripancreatic diabetes compared to long-term diabetes were noted in resectable status (18.6 v 7.6%, p = 0.048), weight loss >2kg (78.6 v 60.5%, p = 0.035), hypertension (25.9 v 59.8%, p = 0.002) and dyslipidemia (85.5 v 42.7%, p = 0.024). Conclusions: The majority of patients diagnosed with advanced PDAC with diabetes appeared to develop diabetes within 3 years prior to diagnosis. Further studies to assess the potential role of pancreatic cancer screening investigations in newly diagnosed diabetes are warranted. Research Sponsor: Research Sponsor: None.
Implementation of systematic genetic counseling (GC) and multigene germline testing (MGT) for pancreatic cancer (PC) patients (pts). First Author: Matthew B. Yurgelun, Dana-Farber Cancer Institute, Boston, MA

Background: GC identifies cancer susceptibility gene variants in 4-10% of unselected PC pts. Such data have prompted national guidelines to recommend GC of all PC of all pts, but the benefits and barriers to implementing systematic testing are unknown. This study’s aim was to study the implementation of universal GC for all PC pts seen in an academic oncology practice. Methods: In 12/2016, all Dana-Farber Cancer Institute (DFCI) gastrointestinal oncology PC pts were referred for GC for PC and MGT. In 10/2018, workflows were changed such that PC pts were automatically scheduled for GC consultation on the same day as their initial oncologic evaluation (unless patients opted out), rather than relying on provider referral. Clinical and germline data were collected on a consecutive cohort of PC pts undergoing GC and MGT from 3/1/2017-3/31/2019. Two additional months (4/1-5/31/2019) were collected for clinical quality assessment purposes.

Results: 2019-5/31/2019) were collected for clinical quality assessment purposes.

Methods used by somatic labs, re-fit published baselines. With a 365-day lead-time, NN obtained a BIDMC-DD test AUC of 0.61 (CI 0.52 - 0.70) (Baecker et al, 2019). Conclusions: Models based on data-driven feature selection out-perform models that use predefined sets of known clinical correlates and can help in early prediction of PDAC development. Research Sponsor: None.
**PANCREATIC CANCER**

682 Poster Session (Board #J13), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

**Extent of lymph node resection and effect on pancreatic cancer overall survival. First Author: Brian Cox, Cedars Sinai Medical Center, Los Angeles, CA**

**Background:** Lymph node (LN) metastases affect overall survival (OS) in pancreatic cancer (PC). However, a LN sampling threshold does not exist. We examined the rate of nodal sampling on overall survival (OS).

**Methods:** Patients with Stage III-IV PC (n = 214) were identified from the National Cancer Database (NCDB). After adjusting for age, gender, grade, stage, and Charlson-Deyo score, multiple binomial logistic regression analyses assessed the impact of the LN ratio (LNR) on OS. LNR was defined as the number of positive LNs over the number of LN examined. Regression analyses, a Cox-Regression, and a Kaplan-Meier survival curve assessed how many LN should be sampled.

**Results:** A total of 13,673 patients, median age 69 years (55-90), were included. Most were Caucasian (86.6%) males with Charlson-Deyo scores 1 (90.3%) and moderately to poorly differentiated PC (90.1%). Median number of LN examined was 15 (1-75) with a median of 1 positive LN (0-35). As expected, increased number of positive LNs was associated with reduced OS, p < 0.001. After data normalization, an increasing LNR was associated with a 12-fold likelihood of death (OR: 11.9, p < 0.001) (CI 6.0, 23.7). Subsequent regression models established evaluation of 16 LNs as the greatest predictor of OS. A regression model evaluating < or = 16 lymph nodes was performed to ascertain the effects of age, gender, ethnicity, grade, stage, and LN examined on OS. The logistic regression model correctly classified 74.5% of cases with a specificity of 99.6% (p < 0.001). Examination of < 16 LN, Caucasian race, grade, stage, and higher Charlson-Deyo scores were significantly associated with decreased OS. If > 16 LNs were examined, patients had a 15-fold likelihood of better OS, p < 0.001 (C14,1.6). An adjusted Cox Regression showed increased HR of 1.2, p < 0.001 (C1.12, 1.1). An incomplete Kaplan Meier survival curve predicted > 16 LN examined are associated with an increase in OS of 2.8 months [log-rank: 32.0, p < 0.001].

**Conclusions:** Patients undergoing curative intent resection for PC should have adequate nodal sampling. Stratification of patients by LNR may provide useful information of OS. Examination of > 16 LNs impacts OS in patients with Stage III-IV PC. Research Sponsor: None.

683 Poster Session (Board #J4), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

**Goals of care designations in advanced pancreatic cancer patients undergoing palliative chemotherapy. First Author: Matthew Anaka, University of Alberta, Edmonton, AB, Canada**

**Background:** Discussion of goals of care (GoC) is a key part of quality care for patients with palliative cancer. Numerous studies have shown that documentation of GoC in this population is low. In 2014, Alberta Health Services launched a health-system wide initiative to provide patients with physical copies of their GoC designation intended to be available at all health-system interfaces. Here we describe rates of GoC documentation in the period surrounding this initiative. **Methods:** This is a retrospective cohort analysis of 240 patients with locally advanced or metastatic pancreatic cancer treated with palliative chemotherapy from 2012-2015 in Alberta, Canada. Data were obtained from outpatient electronic medical record documentation and the provincial cancer registry. **Results:** 63.8% (153/240) of patients had a documented GoC discussion, with 60.4% (145/240) receiving a specific GoC designation. 59.6% (143/240) of patients were referred to palliative care, with 19.9% (64/334) by radiation oncologists, 27.2% (91/334) were by palliative care physicians, and 19.2% (64/334) by other inpatient physicians during hospital admissions. At least 9.6% (32/334) referenced discussions that occurred prior to initial consultation with an oncology physician. **Conclusions:** The majority of pancreatic cancer patients undergoing palliative chemotherapy had a documented GoC designation during the study period. Providing patients with physical copies of their GoC designation may therefore represent a simple but effective means of increasing GoC documentation in the outpatient oncology setting. Research Sponsor: None.

684 Poster Session (Board #J15), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

**Risk factors for severe neutropenia among pancreatic cancer patients receiving nab-paclitaxel and gemcitabine combination therapy. First Author: Kazuyoshi Kawakami, Department of Pharmacy, Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan**

**Background:** Albumin-bound paclitaxel (nab-paclitaxel) and gemcitabine combination therapy (GnP therapy) significantly extends overall survival in patients with metastatic pancreatic cancer, compared to conventional gemcitabine monotherapy. However, severe neutropenia (Grade ≥ 3) occurred in 67.6% of patients in the Japanese phase II/III trials of GnP therapy, and is often a limiting factor. The purpose of this study was to identify the risk factors for severe neutropenia in pancreatic patients receiving GnP therapy in clinical settings.

**Methods:** A retrospective study of 222 consecutive patients with pancreatic cancer who received GnP therapy at the Cancer Institute Hospital from December 2014 to December 2016 was conducted. Univariate and multivariate analyses were used to compare blood test values and patients’ characteristics between patients with no neutropenia or Grade 1/2 (non-serious) neutropenia and those with Grade ≥ 3 (severe) neutropenia.

**Results:** There were 19 patients (8.6%) with severe neutropenia in patients receiving GnP therapy. However, severe neutropenia (Grade ≥ 3) occurred in 21% of patients (53.2%) and 15 patients (6.8%), respectively. Multivariable logistic regression analysis indicated that ANC (absolute neutrophil count) < 3.0 x 10^9/l [OR: 4.806, 95% CI 2.416-9.558, p = 0.000] (T-Bil > 1.6 mg/dl [OR: 2.607, 95% CI 1.040-3.708, p = 0.037]) and CRP > 0.13 mg/dl (OR: 2.3% (10/334) were by medical oncologists, 2.3% (10/334) were by radiation oncologists, 27.2% (91/334) were by palliative care physicians, and 19.2% (64/334) by other inpatient physicians during hospital admissions. At least 9.6% (32/334) referenced discussions that occurred prior to initial consultation with an oncology physician. **Conclusions:** The majority of pancreatic cancer patients undergoing palliative chemotherapy had a documented GoC designation during the study period. Providing patients with physical copies of their GoC designation may therefore represent a simple but effective means of increasing GoC documentation in the outpatient oncology setting. Research Sponsor: None.

685 Poster Session (Board #J16), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

**The role of neoadjuvant chemotherapy in elderly patients with borderline or locally advanced pancreatic cancer: Is it safe and feasible? First Author: Atsushi Oba, Department of Surgery, University of Colorado School of Medicine, Aurora, CO**

**Background:** For borderline resectable (BRPC) or locally advanced pancreatic cancer (LAPC), neoadjuvant (NAT) FOLFIRINOX or gemcitabine plus nab-paclitaxel (GnP) are standard treatment options and these regimens have shown a survival advantage over single-agent gemcitabine. However, the role of these modern therapeutic regimens in elderly patients is debatable. In this analysis, we evaluated the outcomes of neoadjuvant treatment (NAT) with combination chemotherapy in elderly patients. **Methods:** 230 consecutive patients who underwent neoadjuvant treatment for BRPC/LAPC discussed and planned for NAT at the University of Colorado Cancer Center from January 2011 to March 2019 were reviewed. 214 patients who received FOLFIRINOX (n = 143) or GnP (n = 71) were eligible for analysis. We divided all patients into three groups (< 70, 70-74, ≥75 years) and compared the short- and long-term outcomes. **Results:** Of 214 patients, patients < 70 (n = 147) received FOLFIRINOX more frequently than the other groups (p < 0.001); FOLFIRINOX: 115 cases, GnP: 32 cases, 70-74 years (n = 33): FOLFIRINOX: 15 cases, GnP: 18 cases, and ≥75 years (n = 34): FOLFIRINOX: 13 cases, GnP: 21 cases. Resection rates were not statistically different between three groups (< 70: 62%, 70-74: 70%, ≥75: 56%, p = 0.504). There was a slight trend towards worse survival in the two older groups (Median Survival Time (MST): < 70: 23.2 mo., 70-74: 19.5 mo., ≥75: 17.6 mo., p = 0.075) The FOLFIRINOX group was superior to GnP group in all three groups (MST: < 70: 25.6 vs 18.2 mo., p = 0.017; 70-74: 33.2 vs 16.1 mo., p = 0.029; ≥75: not reached vs 16.1 mo., p = 0.155). There were no toxic deaths or 30 day mortality after pancreatectomy in the study population. **Conclusions:** Neoadjuvant combination chemotherapy regimens were safe and feasible for elderly patients. Neoadjuvant therapy with FOLFIRINOX was associated with a survival advantage vs GnP and is an option for fit and elderly patients ≥75 years. Research Sponsor: None.
686 Poster Session (Board #J17), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Adverse events (AEs) with maintenance olaparib in patients with a germ-line BRCA mutation (qBRCAm) and metastatic pancreatic cancer (mPAC): Phase III POLO trial. First Author: Michèle Reni, IRCCS Ospedale, San Raffaele Scientific Institute, Milan, Italy

Background: In POLO (NCT01284195), maintenance olaparib was well tolerated and led to statistically significant progression-free survival benefit vs placebo in patients with a qBRCAm and mPAC whose disease had not progressed on first-line platinum-based chemotherapy (HR 0.53; 95% CI 0.35-0.82) (Golan et al. NEJM 2019). We analyzed common AEs and their management in POLO. Methods: Patients were randomized (3:2) to maintenance olaparib (tablets; 300 mg bid) or placebo until disease progression or unacceptable toxicity. AEs were graded using CTCAE v4.0. Results: Of 154 randomized patients, 151 were treated (olaparib, n=99; placebo, n=60) and included in safety analyses. Median treatment duration was 6.0 months (m) for olaparib and 3.7 m for placebo. Management of fatigue/asthenia, nausea, anemia and vomiting included supportive treatment and/or dose modification; few patients discontinued treatment due to AEs (Table). Of patients with anemia, 14 olaparib recipients experienced a blood transfusion while on study treatment; one olaparib recipient received a blood transfusion while on treatment; one olaparib recipient received a blood transfusion while on study treatment. Management of nausea included supportive treatment and/or dose modification; 21 placebo recipients received supportive treatment. Management of vomiting included supportive treatment; 6 placebo recipients received supportive treatment. Conclusions: The AE profile of maintenance olaparib in patients with a qBRCAm and mPAC was consistent with that seen in other tumor types. Common AEs of fatigue/asthenia, anemia, nausea, and vomiting occurred early, were manageable and led to few treatment discontinuations. Clinical trial information: NCT01284195. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, N.J., USA.

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*p=0.03, †p=0.16

688 Poster Session (Board #J19), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Perioperative complication rates following neoadjuvant therapy in pancreatic adenocarcinoma. First Author: Christopher R. Deig, Oregon Health & Science University, Portland, OR

Background: Whether upfront resection or total neoadjuvant therapy is superior for the treatment of potentially resectable pancreatic adenocarcinoma (PDAC) remains controversial. The impact of neoadjuvant treatment on major perioperative complication rates for patients (pts) undergoing resection for PDAC is commonly debated. We hypothesized that rates would be comparable among patients receiving neoadjuvant chemoradiation (neo-CRT), neoadjuvant chemotherapy alone (neo-CHT), or upfront surgery. Methods: This is a retrospective study of 208 pts with PDAC who underwent resection within a multidisciplinary pancreato-biliary program at an academic tertiary referral center between 2011-2018. Data were abstracted from the medical record, an institutional cancer registry and NSQIP databases. Outcomes were assessed using the chi-square test for categorical variables and the Student’s t-test for continuous variables. Results: Of 208 pts identified: 33 locally advanced, borderline or upfront resectable pts underwent neo-CRT, 35 borderline or resectable pts underwent neo-CHT, and 140 resectable pts did not undergo neoadjuvant therapy. There were no statistically significant differences in major perioperative complication rates between groups. Overall rates were 36.4%, 34.3%, and 26.4% for pts who underwent neo-CRT, neo-CHT alone, or upfront resection, respectively (p = 0.38). No significant differences were observed in complication rates (35.3% vs. 26.4%; p = 0.19) or median hospital length of stay (28 days vs. 20 days; p = 0.87) in pts who received any neoadjuvant therapy versus upfront resection. There were two perioperative deaths in the neo-CRT group (6.1%), zero in the neo-CHT group, and four in the upfront resection group (2.9%); p = 0.22. Conclusions: There were no significant differences in major perioperative complication rates, hospital length of stay, or post-operative mortality in pts who underwent neoadjuvant therapy (neo-CRT or neo-CHT alone) versus upfront surgery. Notably, neo-CHT had comparable perioperative complication rates to neo-CHT alone, which suggests neoadjuvant radiation therapy may not pose additional surgical risk. Research Sponsor: None.

687 Poster Session (Board #J18), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Outcomes of advanced gastrointestinal (GI) cancer patients in relationship to opioid use: An individual patient data pooled analysis from eight clinical trials. First Author: Omar M Abdel-Rahman Abdelsalam, Cross Cancer Institute, Edmonton, AB, Canada

Background: The current study aims at assessing the patterns of opioid use, and evaluating the impact of opioid use on survival outcomes among patients with advanced GI cancers who were included in eight clinical trials. Methods: De-identified datasets of eight clinical trials evaluating first-line systemic treatment for advanced GI cancers (NCT0124786; NCT00844649; NCT00290966; NCT00678535; NCT00699374; NCT00272053; NCT00305188; NCT00334176) were accessed from the Project Data Sphere platform. These trials evaluated patients with pancreatic, gastric, hepatocellular and colorectal carcinoma. Multivariable logistic regression analysis was used to evaluate factors predicting the use of opioids. Kaplan-Meier survival estimates were used to compare survival outcomes in each disease entity among patients who did or did not receive opioid treatment. Multivariable Cox regression analysis was used to assess the impact of opioid use on survival outcomes in each disease entity. Results: A total of 3441 participants were included in the current analysis. The following factors predicted a higher probability of opioid use within logistic regression analysis: younger age (p = 0.004), non-white race (p = 0.001), higher ECOG score (p < 0.001) and pancreatic primary site (p < 0.001). Use of opioids was consistently associated with worse overall survival in patients who received opioids (HR = 1.245; 95% CI: 1.063-1.459; p = 0.007), gastric cancer (HR = 1.725; 95% CI: 1.403-2.122; p < 0.001), hepatocellular carcinoma (HR = 1.841; 95% CI: 1.480-2.290; p < 0.001) and colorectal cancer (HR = 1.651; 95% CI: 1.380-1.975; p < 0.001). Conclusions: Opioid use is consistently associated with worse overall survival among patients with different GI cancers. Further studies are needed to evaluate the underlying mechanisms of this observation. Research Sponsor: None.

689 Poster Session (Board #J20), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Efficacy and safety of second-line nab-paclitaxel plus gemcitabine (nab-P+GEM) after progression on first-line FOLFIRINOX in advanced pancreatic ductal adenocarcinoma (PDAC): Multicenter retrospective analysis. First Author: Changhoon Yoo, Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

Background: FOLFIRINOX is one of standard first-line regimes for patients (pts) with advanced PDAC. However, there is no globally established second-line regimen after failure of FOLFIRINOX. Although gemcitabine-based regimens are recommended by multiple guidelines and widely used in daily practice, further analysis is needed to reveal the magnitude of clinical benefit with these regimens. Nab-P+GEM is another standard second-line regimen for PDAC, but there are no reliable data as second-line therapy for PDAC. Therefore, we aimed to analyze the results of nab-P+GEM after progression on FOLFIRINOX in pts with advanced PDAC. Methods: Between Feb 2016 and Feb 2019, a total of 103 pts with histologically documented PDAC who received nab-P+GEM after progression on first-line FOLFIRINOX were identified among 5 referral cancer centers in South Korea. Results: Median age was 60 years and 50 pts (49%) were male. All but one pts had ECOG performance status of 0 at the time of nab-P+GEM. At the time of nab-P+GEM, 25 (24%) and 73 (76%) pts had locally advanced and metastatic disease, respectively. Median overall survival (OS) and progression-free survival (PFS) with nab-P+GEM was 9.8 months (95% CI: 8.9-10.6) and 4.6 months (95% CI: 3.7-5.5), respectively. Among pts with measurable disease (n = 95), partial response and stable disease were achieved in 8 (8%) and 56 (54%), respectively. Median OS from the start of first-line FOLFIRINOX was 20.9 months (95% CI: 15.2-26.6). Most common adverse event of all grade was anemia (7%), followed by neuropathy (60%), fatigue (52%), thrombocytopenia (45%), and peripheral neuropathy (30%). Most common grade 3-4 adverse events were neutropenia (36%), anemia (9%), and peripheral neuropathy (8%). Conclusions: In medically fit pts with advanced PDAC who failed on first-line FOLFIRINOX, nab-P+GEM was effective and well tolerated as second-line therapy. Research Sponsor: Celgene.
Tumor downsizing following neoadjuvant therapy for borderline-resectable pancreatic adenocarcinoma. First Author: Joseph Arturo Reza, AdvendHealth Orlando General Surgery Residency, Orlando, FL

Background: Downstaging of pancreatic adenocarcinoma in patients presenting with nonmetastatic, unresectable disease has proven to be associated with improved clinical outcomes. Efforts at rescuing these patients from surgical candidates are commonly attempted with a combination of systemic and radiation strategies. In this study, we aimed to determine tumor downsizing in patients that underwent neoadjuvant systemic therapy followed by a curative-intended surgical resection. Methods: A retrospective review of consecutive patients that underwent surgical resection for pancreatic adenocarcinoma following a course of neoadjuvant therapy was performed. Basic demographics, endoscopic ultrasound (EUS) findings, chemotherapy regimens and duration, rates of radiotherapy, type of surgical procedure and pathologic results were recorded. Tumor response to neoadjuvant therapy was established by correlating EUS-to pathologic tumor dimensions. Analysis of the data was done using Mann-Whitney U test, Pearson correlation and Chi-square when indicated. Results: A total of 97 patients were analyzed; 40 underwent neoadjuvant chemotherapy (13 patients also received concurrent radiation therapy). In those 57 patients that were resected upfront, EUS tended to underestimate tumor sizes significantly compared to pathologic dimensions, with an average difference between dimensions of 0.66 cm (p = 0.0004). Within the group treated with neoadjuvant chemotherapy, 90% of patients had downsizing at an average of 8% of tumor size. There were no differences in rates of tumor downsizing between FOLFIRINOX or Gemcitabine/Nab-paclitaxel treated patients in addition, there were no correlations in margin status (R0) based on chemotherapy used, with both regimens achieving a similar rate of R0 resections (mean 61%). The type of chemotherapy regimen used did not affect the ratio of positive lymph nodes harvested. Conclusions: In patients that present with borderline resectable pancreatic adenocarcinoma, a course of neoadjuvant therapy results in tumor downsizing in a significant number allowing for margin negative resections. These results were seen regardless of the chemotherapy regimens utilized. Research Sponsor: None.

Phase Ib study of gemcitabine, nab-paclitaxel, and ficlatuzumab in patients with advanced pancreatic cancer. First Author: Kimberly Perez, Dana-Farber Cancer Institute, Boston, MA

Background: Paired-related homeodomain transcription factor 1 (Prrxl) isomorphs are involved in pancreatic development, pancreatic, and carcinogenesis. Hepatocyte growth factor (HGF) is a transcriptional target of Prrxl. Ficlatuzumab is a recombinant humanized HGF antibody, that inhibits HGF/c-Met binding and HGF-induced c-Met phosphorylation. In preclinical pancreatic ductal adenocarcinoma (PDAC) models, inhibition of Prrxl-HGF signaling using ficlatuzumab and gemcitabine reduced primary tumor volume and c-MET pathway activity. Methods: Sixty-nine patients with untreated metastatic PDAC enrolled in a phase Ib (N = 6 pts) and ficlatuzumab at 20mg/kg with GA was advanced to the phase 1b (N = 24 pts) and ficlatuzumab combined with nab-paclitaxel and Gemcitabine evaluated. Results: 24 pts (sex, 12M:12F; median age, 69 years [range, 51-82 years]) were enrolled. No dose-limiting toxicities were identified in the phase Ib (N = 6 pts) and ficlatuzumab at 20mg/kg with GA was advanced to the expansion phase (N = 18 pts). By RECISTv1.1 in the full study population, 7 (29%) pts had partial response, 15 (63%) had stable disease, and 2 (8%) could not be evaluated. Median progression-free survival was 8 months (range, 3-16 months), 4 pts are still on study treatment. The primary toxicities attributed to ficlatuzumab included hypoalbuminemia (grade 3, 21%), any grade, 91% and edema (grade 3, 8%; any grade, 91%). Nine (38%) of the 24 pts discontinued study treatment due to these toxicities prior to disease progression. Conclusions: The combination of ficlatuzumab with gemcitabine and nab-paclitaxel is associated with durable treatment responses but also significant hypoalbuminemia and edema that may impair treatment tolerability. Serial blood samples were collected for monitoring HGF measurements, and mandatory pretreatment surgical test sections were collected from these patients to become a hypoxia biomarker and an edema biomarker. A phase 2 trial is currently enrolling. Research Sponsor: AVEO Oncology.
Multicenter retrospective observational study of pancreatic cancer with positive peritoneal lavage cytology intended for surgical resection. **First Author:** Akiko Todaka, Division of Gastrointestinal Oncology, Shizuoka Cancer Center, Shizuoka, Japan

**Background:** Although macroscopically curative resection has been performed for pancreatic cancer with positive peritoneal lavage cytology (CYI), the prognosis is poor in most reports. In 2013, the JASPAC01 trial showed that S-1 was superior to Gemcitabine (GEM) as adjuvant chemotherapy for resected pancreatic cancer, and S-1 was also administered to the patients with CYI who had undergone macroscopically curative resection. **Methods:** This is a multicenter retrospective observational study that collected data of the patients with pancreatic adenocarcinoma who were diagnosed with CYI between 2007 and 2015 and had no other noncurable factors. **Results:** One hundred twenty-seven patients were enrolled from 14 institutions, and 3 were excluded due to liver metastasis or non-adenocarcinoma. The median age was 67 years old and almost patients had PS 0 or 1. Of the 124 patients, 114 underwent macroscopically curative resection and the median overall survival (OS) and recurrence-free survival (RFS) were 16.7 and 7.2 months. Of the resected patients, 80 (73%) had no early recurrence and started PS. After surgery, juvant chemotherapy. Adjuvant chemotherapy regimens were S-1 in 43 patients (54%), GEM in 31 (39%) and others in 6 (7%). The median OS was 21.0 months with S-1 and 19.2 months with GEM (HR: 0.73, 95%CI: 0.44-1.22, P = 0.23), whereas the median RFS was 10.2 and 7.1 months (HR: 0.58, 95%CI: 0.36-0.95, P = 0.03), respectively. **Conclusions:** After the JASPAC01, most patients with pancreatic cancer with CYI received macroscopically curative resection and treated with S-1 as adjuvant therapy, however the efficacy is not sufficient. We should consider appropriate treatment strategies for patients with pancreatic cancer with CYI intended for surgical resection. **Research Sponsor:** Shizuoka Cancer Center Medical Fund.

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Phase II study of preoperative chemotherapy with nab-paclitaxel and gemcitabine followed by chemoradiation for borderline resectable or node-positive pancreatic ductal adenocarcinoma. **First Author:** Emerson Yu-sheng Chen, Oregon Health & Science University, Portland, OR

**Background:** Pre-operative therapy for resectable pancreatic ductal ade- nocarcinoma (PDAC) may eliminate micro-metastatic disease early and help achieve negative surgical margins. The present study is based on the hypothesis that gemcitabine/nab-paclitaxel chemotherapy followed by chemoradiation with fluoropyrimidine is a feasible and efficacious pre-operative treatment for borderline resectable or node-positive PDAC. **Methods:** This is a single-arm phase II trial to evaluate pre-operative treatment with 2 cycles of gemcitabine 1000 mg/m² and nab-paclitaxel 125 mg/m² on days 1, 8, 15 over 28 fractions with concurrent 5-fluorouracil or capecitabine prior to surgical resection. Patients were eligible if they met borderline resectable criteria or a PS ≤ 1. After CT, they were eligible to receive up to 4 additional cycles of gemcitabine/nab-paclitaxel. The primary endpoint was the R0 resection rate. Secondary endpoints included response to pre-operative therapy, overall toxicities, relapse-free survival, and overall survival. **Results:** Nineteen of 24 screened patients have been enrolled. Median age was 68, 10 (53%) were female, and 4 (21%) were non-Caucasian. Eleven (78%) had head of pancreas cancers, 13 (68%) exhibited both arterial and venous involvement, and 12 (63%) had positive clinical nodes. All 19 patients received 2 months of gemcitabine/nab-paclitaxel, of which 17 patients continued to chemo-radiation (1 developed metastatic disease and I moved out of state). In the interval between chemo-radiation and surgery, 3 developed metastatic disease, 1 became unresectable, I withdrew from study, and 1 was deemed too frail for surgery. Nine have undergone successful pancreatic resection, and 2 are pending resection. **Conclusions:** Pre-operative gemcitabine/nab-paclitaxel followed by chemo-radiation with fluoropyrimidine is feasible in patients with borderline resectable PDAC and represents another strategy to FOLFIRINOX-based therapy. A planned interim analysis is ongoing. Clinical trial information: NCT02427841. Celgene, Other Foundation.

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Phase II clinical trial of novel agent PBI-05204 in patients with metastatic pancreatic adenocarcinoma (mPDA). **First Author:** Marc Thomas Roth, Vanderbilt-Ingram Cancer Center, Nashville, TN

**Background:** Treatment options novel agents are needed to improve disease outcomes. PBI-05204 (Phoenix Biotechnology, Inc., San Antonio, TX) is a modified supercritical carbon dioxide extract of Nerium oleander leaves. Oleandrin, the extract’s major cytotoxic component, has demonstrated anti-tumor activity in various tumor cell lines. In a human PDA orthotopic model, this preparation reduced tumor burden as monotherapy. Pharmacodynamic studies suggest PBI-05204’s mechanism of action is through inhibition of the PI3k/Akt/mTOR pathway. **Methods:** A phase II single-arm, open-label study to determine the efficacy of PBI-05204 in patients (pts) with mPDA refractory to standard therapy was conducted. The primary endpoint was overall survival (OS) with the hypothesis that 50% of pts would be alive at 4.5 months. Secondary objectives included safety, progression-free survival (PFS), and overall response rate. Pts received oral PBI-05204 daily until progressive disease (PD), unacceptable toxicity, or pt withdrawal. Radiographic response was assessed every two cycles. **Results:** Forty-one pts were enrolled; two never received treatment and one was found to have a neuroendocrine tumor after pathological re-evaluation, leaving 38 pts for analysis. Median age at time of enrollment was 65.0 years. The median time from initial diagnosis to treatment was 16.9 months. The primary reason for withdrawal was PD (45.2%). Ten pts were alive at 4.5 months (26.3%) with a mPFS of 56 days (corresponding to first restaging). One objective response (2.6%) was ob- served for 162 days. Grade 3 treatment-emergent adverse events occurred in 63.2% of pts with the most common attributed to drug (all grades) being fatigue (36.8%), vomiting (23.7%), nausea (18.4%), decreased appetite (18.4%), and diarrhea (15.8%). **Conclusions:** PBI-05204 did not meet its primary endpoint for OS in this study. Recent preclinical data indicate an important role for PBI-05204 against globostatin-related pathways combined with chemotherapy, such as temozolomide, and radiotherapy. A ran- domized Phase II trial is currently being designed. Clinical trial information: NCT03239717. Research Sponsor: Phoenix Biotechnology, Inc., San Antonio, TX.

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A pilot clinical trial of p53/p16-independent epigenetic therapy for pancreatic ductal adenocarcinoma (PDA). First Author: Davendra Sohal, University of Cincinnati, Cincinnati, OH

Background: PDA treatment is limited to cytotoxic drugs. A key factor limiting their efficacy is TP53 mutations, omnipresent in PDA, which counteract apoptosis-mediated cell kill. We evaluated a novel epigenetic approach using decitabine (Dec) to inhibit DNA methyltransferase 1 (DNMT1) and effect cancer cell cycle exit by epithelial-differentiation, combined with tetrahydrodronide (THU) to inhibit cytidine deaminase (CDA) and thereby permit oral bioavailability and solid-tissue distribution of Dec. Methods: Open-label single-arm, IRB-approved clinical trial at Cleveland Clinic and University Hospitals for patients with metastatic PDA that had progressed on prior chemotherapy. ECOG PS of 0-2. Treatment was oral, weight-based, with Dec 10-20 mg, and THU 500-1000 mg daily, 5 days/week. Primary endpoint was DNMT1 protein levels at 16-week vs baseline biopsies. Results: From Apr to Aug 2017, we enrolled 13 patients. Median age was 65 (range 44-74) years; 7 (54%) males; 11 (85%) Caucasians. Median time from diagnosis was 13 (3.9-53.5) months, with a median of 2 (1-3) prior lines of therapy. Baseline ECOG PS was 0/1 in 12 (92%) patients. All patients started study drugs; median time on treatment was 35 (4-63) days, and on study 72 (25-105) days. The most frequent adverse events attributable to the study drugs were anemia (n=5), and anorexia, dehydration, nausea, fatigue, febrile neutropenia and decreased lymphocyte count, in 3 patients each; no deaths. Eight (62%) patients underwent evaluation scans at 8 weeks, showing stable disease in 1 patient and progression in 7. Common reasons for coming off of study drugs were progression (n=6), physician discretion (n=1), and adverse events (n=2). Overall, 6 patients died; median survival was 3.1 months, and patients did not reach the 16-week biopsy. Shifts in blood counts, a sensitive indicator of Dec systemic activity, were unexpectedly mild, and plasma CDA enzyme activity was increased versus count, in 3 patients each; no deaths. Eight (62%) patients underwent evaluation scans at 8 weeks, showing stable disease in 1 patient and progression in 7. Common reasons for coming off of study drugs were progression (n=6), physician discretion (n=1), and adverse events (n=2). Overall, 6 patients died; median survival was 3.1 months, and patients did not reach the 16-week biopsy. Shifts in blood counts, a sensitive indicator of Dec systemic activity, were unexpectedly mild, and plasma CDA enzyme activity was increased versus other cancer and normal controls. Conclusions: This first-of-its-kind study demonstrated feasibility and safety of the novel oral epigenetic therapy. Systemically elevated CDA in these patients requires higher doses of THU; a likely candidate for future evaluation.

Multicenter phase I/II study of intravenous gemcitabine + nab-paclitaxel combined with intraperitoneal paclitaxel for pancreatic ductal adenocarcinoma patients with peritoneal metastasis. First Author: Suguru Yamada, Nagoya University Graduate School of Medicine, Gastroenterological Surgery, Nagoya, Japan

Background: Pancreatic ductal adenocarcinoma (PDAC) patients with peritoneal metastasis (peritoneal deposits and/or positive peritoneal cytology) have an extremely poor prognosis, and an effective treatment strategy remains elusive. Methods: The aim of this study was to determine the recommended dose (RD) for a combination of intravenous (IV) gemcitabine, intravenous nab-paclitaxel, and intraperitoneal (IP) paclitaxel in chemotherapy-naive PDAC patients with peritoneal metastasis and to evaluate the clinical efficacy and safety. Gemcitabine and nab-paclitaxel was administered IV combined with paclitaxel IP on days 1, 8, and 15, followed by 1 week of rest. The frequency of dose-limiting toxicity was evaluated and the RD was determined. The primary endpoint of the phase II part was 1-year overall survival (OS) rate. The secondary endpoints were antitumor effect, symptom relief effect, safety and OS. Results: In the phase I part, RD for IV gemcitabine, IV nab-paclitaxel and IP paclitaxel were determined as 800 mg/m², 75 mg/m², and 20 mg/m², respectively. A total of 46 patients were enrolled in the phase II part and drugs were delivered at the RD. All patients had positive intraperitoneal cytology and 29 patients (63.0%) had the peritoneal dissemination. The median treatment period was 6.0 (0-22.6) months. The response rate and disease control rate were 45.7% and 95.7%, respectively. Ascs disappeared in 40.0% and cytology turned negative in 67.4%. Median CA19-9 decrease ratio was 84.4 (6-9.9%) %. The median survival time was 12.8 (3.1-32.7) months, and the 1-year survival rate was 52.2%. Finally, conversion surgery was performed in 8 (17.4%) patients and those who received conversion surgery survived significantly longer than those who did not (not reached vs. 117.7 months, P = 0.0070). Grade 3/4 hematologic toxicities occurred in 76.0% and nonhematologic adverse events in 15.0%, of which 6.5% were bowel obstructions. Conclusions: This regimen has shown promising clinical activity with acceptable tolerability in chemotherapy-naive PDAC patients with peritoneal metastasis. Clinical trial information: NCT02847000. Research Sponsor: Case Comprehensive Cancer Center.
704 Poster Session (Board #K15), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Phase III, international, randomized trial of adjuvant nab-paclitaxel plus gemcitabine (nab-P + G) versus gemcitabine (G) for resected pancreatic cancer (APACT): Recurrence patterns. First Author: Vaibhav Sahai, University of Michigan, Ann Arbor, MI

Background: APACT did not meet the primary endpoint of independently assessed disease-free survival (DFS) with nab-P + G vs G; overall survival showed a nominal improvement. Here, we report recurrence patterns by resection status. Methods: A total of 866 treatment-naïve patients (pts) with histologically confirmed pancreatic cancer, R0(R1) resection, CA19-9 < 300 U/mL, and ECOG PS ≤ 1 were randomized to receive weekly nab-P + G or G on days 1, 8, and 15. Stratification: resection (R0/R1); lymph node status (LN−/LN+); geographic region. Disease recurrence was per investigator review of CT/MRI scans. Results: Of 571 (66%) pts with investigator-assessed DFS events (median follow up, 35.4 mo), 543 had radiographic progression with 764 recurrent lesions (> 20 events: liver, 271; unspecified abdominal organ, 52; lung, 130; surgical bed, 70; mesenteric nodes, 54). Most pts (73%) had only abdominal, 6% had only distant, and 10% had only local recurrence (Table). Although more pts with R1 vs R0 status had recurrence (72% vs 60%), patterns were generally similar, and local recurrence was similarly low. Conclusions: Most recurrences in APACT were distant and in abdomen (liver). Recurrence patterns were generally similar in pts with R0 and R1 status, with low rates of local recurrence. These data may help make more informed pt management decisions. Additional data on patterns by baseline characteristics will be presented. Clinical trial information: NCT01964430. Research Sponsor: Celgene Corporation.

705 Poster Session (Board #K16), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Attenuated regimen of biweekly gemcitabine/nab-paclitaxel in patients aged > 65 years with advanced pancreatic cancer (APC). First Author: Hasan Rehman, Northwell Health Cancer Institute, Lake Success, NY

Background: Treatment with gemcitabine/nab-paclitaxel confers a survival benefit over gemcitabine monotherapy in APC. However, such treatment can be associated with significant toxicities especially in older patients. We present practical disadvantages related to a weekly schedule along with financial cost. We retrospectively analyzed patients > 65 years of age with APC who received a modified biweekly regimen of gemcitabine/nab-paclitaxel to evaluate efficacy and toxicity. Methods: Patients aged > 65 years with chemo-naïve APC and ECOG PS ≤ 2 were studied. Patients were treated with a modified regimen of gemcitabine 1000 mg/m² and nab-paclitaxel 125 mg/m² every 2 weeks on days 1 and 15 of a 28-day cycle. Patients were evaluated for progression-free survival (PFS) and overall survival (OS) with analyses performed using Kaplan-Meier method. Adverse events were recorded on the day of chemotherapy. CA19-9 was measured every cycle and restaging scans were performed every two cycles. Results: Seventy-three patients (median age: 73; range: 66 - 93) were treated with biweekly gemcitabine/nab-paclitaxel as first-line treatment. The median OS and PFS were 9.1 months and 4.8 months respectively. 66% of patients received growth factor support based on ASCO guidelines and no patients developed neutropenic fever. The incidence of grade 3 or higher toxicity was 2%, 7%, 3%, and 5% respectively. Dose reductions of gemcitabine and nab-paclitaxel were required in 10% and 4% patients respectively. Conclusions: In patients > 65 years of age with APC, a modified regimen of biweekly gemcitabine/nab-paclitaxel was tolerable and had longer PFS when compared with historical control from the MAPCT study. This regimen allowed for less dose reductions, reduced healthcare costs from additional appointments, travel-related cost, as well as favorable side effect profile while maintaining responders. This regimen might be the most suitable for elderly patients with APC and carries a higher OS rate of 60% in the first-line setting. Further studies are warranted to identify the reasons why not all patients with resectable pancreatic cancer undergo resection. Further studies are needed to identify why resectable patients are not proceeding to resection and which specific NAT approaches benefit patients the most. Research Sponsor: None.

706 Poster Session (Board #K17), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Single institutional analysis of resectable pancreatic cancer. First Author: Jeff Wisanen, Mayo Clinic, Rochester, MN

Background: In recent years, there has been a shift towards neo-adjuvant treatment (NAT) of non-metastatic pancreatic cancer in the hopes of improving negative margin rate, lymph node negativity, recurrence and survival. Even patients deemed resectable based on NCCN criteria are receiving NAT but data for these patients remains limited. This current study evaluated the outcomes of patients diagnosed with resectable pancreatic adenocarcinoma. Methods: Patients were retrospectively identified through the Mayo Clinic, Rochester SPORE pancreatic cancer registry as well as the search of the electronic medical record via Advanced Cohort Explorer from May 2011 to 2016. Baseline demographics, tumor characteristics, treatments rendered, and outcomes were collected. Variables were analyzed for association with recurrence from time of surgery and survival from time of diagnosis using Kaplan-Meier curves and Cox proportional hazards regression. Results: A total of 520 patients with resectable pancreatic adenocarcinoma were identified. 72 patients received upfront chemotherapy with 44 (61.9%) proceeding to surgical resection. 62 patients received upfront chemotherapy followed by radiation with 33 (52.6%) proceeding to surgical resection. 12 patients received upfront radiation alone with 7 (58.3%) proceeding to surgical resection. 374 patients did not receive any NAT with 293 (78.3%) proceeding to surgical resection. In total, 377 (72.5%) went to resection. Median time to recurrence from surgery was 27.7 months vs. 21.7 months for NAT and upfront resection, respectively (HR 0.87, 95% CI 0.60-1.27, p = 0.48). Median overall survival from diagnosis for those receiving NAT was 40.6 months vs. 24.7 months for those receiving upfront resection (HR 0.62, 95% CI 0.41-0.92, p = 0.02). Conclusions: This study shows an approximate 16 month improvement in overall survival of patients receiving upfront NAT for resectable pancreatic adenocarcinoma. This might be due to a better selection of patients. It also highlights that not all patients with resectable cancer receive resection. Further studies are needed to identify which resectable patients are not proceeding to resection and which specific NAT approaches benefit patients the most. Research Sponsor: None.

707 Poster Session (Board #K18), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

The development of therapeutic cancer vaccine for pancreatic cancer. First Author: Hirotoki Yamaue, Second Department of Surgery, Wokayama Medical University, School of Medicine, Wakayama, Japan

Background: A previous phase II/III trial using a single cancer peptide vaccine derivation from vascular endothelial growth factor receptor (VEGFR)2 for patients with advanced pancreatic cancer did not demonstrate the overall survival (OS) benefit (Yamaue et al. Cancer Sci 2015). For the next trial, we conducted a multicenter phase II study using multipeptide cocktail vaccine named OCV-C01 derived from a novel higher immunogenic antigen KIF20A, VEGFR1 and VEGFR2 combined with gemcitabine in postoperative adjuvant setting. Methods: 41 patients with advanced pancreatic cancer were enrolled. The primary endpoint was disease-free survival (DFS) of 6 months and secondary endpoints included OS, safety and immunological analyses on peptide-specific cytotoxic T lymphocyte (CTL) activity and KIF20A expression in resected pancreatic cancer. Results: The median DFS was 15.8 months (95% confidence interval CI, 11.0-20.6), and the DFS rate at 18 months was 34.6% (95% CI, 18.3-51.6). The median OS was not reached and the OS rate at 18 months was 69.0% (95% CI, 48.8-82.5). The administration of OCV-C01 was well tolerated. In the per protocol set, there were significant differences in DFS between patients with and without KIF20A-specific CTL responses (p = 0.027), and between patients with and without KIF20A expression in resected pancreatic cancer tissues (p = 0.014). In addition, all four patients who underwent R0 resection with KIF20A expression had no recurrence of pancreatic cancer with KIF20A-specific CTL responses. Conclusions: OCV-C01 combined with gemcitabine was tolerable with a favorable median DFS of 15.8 months. In cancer vaccine treatment, positive expression of targeted antigen is essential to improve the therapeutic setting was more suitable than advanced state of cancer. Clinical trial information: UMIN000007991. Research Sponsor: Health and Labour Sciences Research Grants of the Ministry of Health Labour and Welfare in Japan.
**Poster Session (Board #K19), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

**Efficacy of SBP-101, in combination with gemcitabine and nab-paclitaxel, in first-line treatment of metastatic pancreatic ductal adenocarcinoma.**

**First Author: Dusan Kolarsek, University of Adelaide, Adelaide, SA, Australia**

**Background:** SBP-101, a polyamine metabolic inhibitor, inhibited growth in 6 human pancreatic ductal adenocarcinoma (PDA) cell lines and 3 murine xenograft tumor models of human PDA. SBP-101 monotherapy in heavily pre-treated PDA patients (>2 prior regimens, N=4) showed a median survival of 5.9 months at the optimal dose level. Purpose: To assess the safety, tolerability, PK, and efficacy of SBP-101 in combination with gemcitabine (G) and nab-paclitaxel (A) in patients with previously untreated metastatic PDA.

**Methods:** In a modified 3+3 dose escalation scheme, subcutaneous injections of SBP-101 were dosed at 0.2, 0.4 or 0.6 mg/kg/day 1-5 of each 28-day cycle. G and A were dosed intravenously on Days 1 and 8 of each cycle. Efficacy was assessed by CA19-9 levels, objective response as assessed by RECIST criteria, progression-free survival (PFS) and overall survival (OS). Results: Twenty-five patients were enrolled in 3 cohorts (N=4, 2; N=7, 3; N=4) and received up to 6 cycles of treatment (7 subjects are ongoing in cohorts 2 and 3). The most common adverse events related to SBP-101 are fatigue (N=4), nausea (N=2) and injection site pain (N=2). There is no evidence of SBP-101-related bone marrow suppression or peripheral neuropathy. One patient in cohort 2 developed grade 3 reversible liver enzyme elevation. PK parameter in cohort 1 were below the limits of detection at most time points, but plasma Cmax and AUCt were measurable in cohorts 2 and 3. In those cohorts, CA19-9 levels decreased 76-95% in 7 of 8 evaluable subjects (1 additional subject TBD) with 5 patients achieving partial responses (4 ongoing) and 1 achieving stable disease. Median PFS and OS have not yet been reached. Conclusions: Preliminary results suggest SBP-101 is well tolerated when administered with G and A. Signals of efficacy support continued development of SBP-101 in combination first-line treatment for PDA. Clinical trial information: NCT0342799. Research Sponsor: Sun BioPharma, Inc.

**Poster Session (Board #K22), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

**Modified FOLFIRINOX versus sequential chemotherapy ((FOLFIRI/FOLFOLFOX) as second-line treatment for advanced pancreatic adenocarcinoma: A real-world analysis.**

**First Author: Shun Tazuka, Kanagawa Cancer Center, Yokohama, Japan**

**Background:** Therapy options for second-line treatment of advanced pancreatic adenocarcinoma (PDAC) are limited and preferred regimens have not been established. This study compared the efficacy and safety of modified FOLFIRINOX (mFFX) and sequential chemotherapy (FOLFIRI/FOLFOLFOX) as second-line treatment for advanced PDAC. **Methods:** This was a retrospective single-center analysis of all patients who received mFFX or sequential chemotherapy at the KPCC. Post HOC analyses of O, PD studies (PARP inhibition – PBMCs; cytokeratin 18 + serum; H2AX foci – hair follicles), and exploratory predictive marker studies (tumor – NGS; RNA exome sequencing) are ongoing. Clinical trial information: JIRCTIN0361929. Research Sponsor: Cancer Research UK. Pharmaceutical/Biotech Company.

**Poster Session (Board #K20), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

**A phase I study of olaparib in combination with capcitabine-based chemoradiation (CRT) in patients (pts) with locally advanced pancreatic cancer (LAPC).**

**First Author: T.J. Jeff Evans, University of Glasgow, Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom**

**Background:** Olaparib is a potent inhibitor of PARP-1, which has a critical role in signalling DNA single strand breaks (SSB) as part of base excision repair pathway, and may have radio-sensitizing effects due to impaired resolution of radiation induced SSB. We hypothesize that O may potentiate the effects of X-CRT in pts with LAPC. **Methods:** Eligible pts with LAPC, ECOG ≤ 1, tumor diameter <6 cm, with stable or progressive disease (SD) or response (RR) to current induction chemotherapy, were treated with 1 of 4 escalating doses of O given bid starting on day -3, and then in combination with X (830 mg/m2 bid) and radiotherapy (50.4 G in 28 fractions) in all administering Mon-Fri. **Results:** Toxicities (DLT) were determined on clinical and lab toxicity assessments (NCI-CTCAE v4.03) performed weekly from the start of O until completion of O plus X-CRT (i.e. 6 weeks). Dose escalation continued with a rolling-six design until the Maximum Tolerated Dose (MTD) was reached. Blood samples for PK analyses of O and PD measurement (inhibition of PARP activity) were collected 3 times: on day 1 of each treatment week 1 + X-CRT. Results: 18 pts, (9 m, 9 f, 1, ECOG 0/1 (n=6/2)), age range 49-81 (median=70) years, with histologic (14) or cytologic (4) proven LAPC, had received induction chemotherapy with gemcitabine (GEM) (n=2), GEM + X (12), or FOLFIRINOX (3) with partial response (n=4) or stable disease (n=14). Pts received 2-12 cycles of O and X-CRT up to 6 cycles of treatment (7 subjects are ongoing in cohorts 2 and 3). The patients have been enrolled in 3 cohorts (1: N=4, 2: N=7, 3: N=4) and received 150 mg/m2 of O X-CRT. DLTs were observed in 2 pts (both at 200mgm2 bid): 1 pt with grade 3 nausea (on optimal anti-emetics) and grade 3 fatigue, 1 pt with grade 3 anemia. 6 pts were subsequently recruited at 150mg/m2 bid with no DLTs. No DLTs (n=1) response (1 pt each at 150mg/m2 bid) and 1 pt (at 100 and 150 mgd bid) had progressive disease; the remaining 14 pts had SD. **Conclusions:** The recommended dose (RP2) of O is 150mg/m2 bid when given in combination with X + CRT in LAPC. Recruitment of up to 12 pts with borderline operable LAPC at the RP2 is ongoing. Post HOC analyses of O, PD studies (PARP inhibition – PBMCs; cytokeratin 18 - serum; H2AX foci – hair follicles), and exploratory predictive marker studies (tumor - NGS; RNA exome sequencing) are ongoing. Clinical trial information: JIRCTIN0361929. Research Sponsor: Cancer Research UK. Pharmaceutical/Biotech Company.

**Poster Session (Board #K20), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

**Pancreatic ductal adenocarcinoma (PDAC), BRCA: Detailed analysis and outcomes of cohort from Memorial Sloan Kettering Cancer Center (MSK).**

**First Author: Parisa Momtaz, Memorial Sloan Kettering Cancer Center, New York, NY**

**Background:** Given encouraging responses of platinum agents and poly-ADP-ribose polymerase inhibitors (PARPi) in BRCA mutated (mut) PDAC, we sought to identify patients (pts) with a personal history of BRCA1/2 mutation. **Methods:** Institutional database at MSK with IRB approval was queried for pts with PDAC. **Results:** n= 526 (274 men, 252 women) median age of 64 (range 20-91) at diagnosis. n = 78 (26%) had a BRCA1/2 mutation (n = 21 BRCA1, n = 57 BRCA2). n = 54 (43%) had a family history of BRCA1/2-related malignancies (35pts) with a personal history of other BRCA-associated malignancies. n = 66 (52%) AJCC stage IV, of these 43pts (65%) received platinum-based therapy with a partial response (PR) in 39pts (81%), median duration 7 months (range 0.5-39m). n = 40 (32%) received ≥ 4 lines of therapy (range 1-6 lines); n = 44 (35%) received PARPi and 11% (n = 34) received immunotherapy. Median OS for the entire cohort 32.1m (95% CI 23.9, 42.6). Median OS for stage II (9.9m (95% CI 8.3, 11.7)), stage III (43m (95% CI 33.9, 53.2)) and stage IV (91m (95% CI 1.16, 12.8)). We did not observe a statistically significant difference in OS between BRCA vs non BRCA pts. **Conclusions:** BRCA mut PDAC constitutes a small but likely distinct biologic subgroup. Improved outcomes were notable relative to historical data, possibly due to the integration of platinum and PARPi therapy and possibly due to contribution from disease biology. Research Sponsor: None.
The role of immunotherapy on the survival of pancreatic cancer patients.

First Author: Saber Ali Amin, University of Nebraska Medical Center, Omaha, NE

Background: Immunotherapy has revolutionized the treatment landscape of many malignancies, but its therapeutic role in pancreatic cancer (PC) remains unclear. The objective of this study is to investigate the impact of immunotherapy on the overall survival of PC patients who had undergone surgery for their primary lesions in the pancreas using the National Cancer Database (NCDB). Methods: Patients with pancreatic adenocarcinoma were identified from NCDB. Cox proportional hazard models were employed to assess the impact of immunotherapy on survival after being stratified by surgery and adjusted for age of diagnosis, race, sex, place of living, income, education, treatment facility type, insurance status, year of diagnosis, and treatment types such as chemotherapy and radiation therapy. Results: Of 252,280 patients who were analyzed, 214,632 (85.08%) had definitive surgery, and 37,638 (14.92%) did not get definitive surgery of the pancreas. In the surgery group, 351 (0.93%) received immunotherapy and 213,804 (99.61%) did not. In the no surgery group, 6 patients received atezo + BL-8040 versus control in MORPHEUS-pancreatic ductal adenocarcinoma (M-PDAC) and MORPHEUS-gastric cancer (M-GC).

The role of para-aortic lymph node sampling in pancreatic cancer surgery.

First Author: Yusuke Kazami, Department of Digestive and HBP Surgery, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan

Background: In the management of pancreatic cancer, para-aortic lymph node (PALN) metastasis is regarded as distant metastasis, and systemic treatment is recommended. However, imaging study is not perfect to detect all PALN metastasis by definition. Although recent evidence has been controversial. We hypothesized that sampling of PALNs on exploration could allow us to avoid pancreatic resection for patients who would not benefit. In this study, we evaluated the incidence and the effect on the long-term outcomes for patients with potentially resectable pancreatic cancer. Methods: Three hundred and ninety-two patients who had PALNs sampled upon potentially resectable pancreatic cancer from 2005 through 2014 were included in the study. All patients were appropriately staged preoperatively with CT/MRI and those with suspected PALN metastasis were not considered as candidates for resection. The patients whose resections were aborted because of liver metastasis or peritoneal dissemination discovered on exploration, or those who died within 30 days after the operation were not included. Evaluated outcomes were incidence of PALN metastasis and their recurrence-free and overall survivals (RFS, OS). Results: The patients’ median age was 74 years, and 58.6% was man. 67.8% had tumors at pancreatic head. Preoperative chemotherapy was given only on 16 patients (3.2%). Among 392 patients with PALNs sampled, 53 (13.5%) patients had metastasis. Resection was completed on 40 patients and resection was aborted on the rest. Among patients who underwent pancreatic resection, median RFS and OS were 10 and 12 months for patients with PALN metastasis, compared to 17 and 26 months for those without PALN metastasis (p < 0.0009 for RFS and p < 0.001 for OS). The 5-year OS rates for patients with without PALN metastasis were 5.9% and 25% (p < 0.001). Among 53 patients with PALN metastasis, OS were not different between the patients who underwent resection and those who did not. In median 17 months, 5 patients died without resection, 0 patients died with recurrence.

Visits gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
A phase I/II study combining a TMZ-CD40L/-4/1BBL-armed oncolytic adenovirus and nab-paclitaxel/gemcitabine chemotherapy in advanced pancreatic cancer: An interim report. First Author: Benjamin Leon Musher, Baylor College of Medicine, Houston, TX

Background: Pancreatic ductal adenocarcinoma (PDAC) has been highly resistant to immunotherapeutics to date. LOAd703, an oncolytic adenovirus with transgenes encoding TMZ-CD40L and -4/1BBL, has been shown to lyse tumor cells selectively, induce anti-tumor cytotoxic T-cell responses, reduce myeloid-derived suppressor cell (MDSC) infiltration, and induce tumor regression in preclinical studies. Methods: In this phase I/I trial, patients with unresectable or metastatic PDAC are treated with LOAd703 intratumoral injections and standard nab-paclitaxel/gemcitabine (nab-P/G) chemotherapy. Starting on cycle 1 day 15 of nab-P/G, LOAd703 is injected with image guidance into the primary pancreatic tumor or a metastasis every 2 weeks for 6 injections. In the event of sustained tumor control, subjects are eligible to receive 6 more injections. Three dose levels of LOAd703 are being investigated using a BOIN dose escalation design. Primary endpoints are safety and feasibility. Secondary endpoints include response rate and overall survival. Results: To date, 13 subjects are evaluable for safety and feasibility. Three patients were treated at dose 1 (5x10^10 VP), 4 subjects at dose 2 (1x10^11 VP), and 6 subjects at dose 3 (5x10^11 VP). The most common adverse events (AEs) attributed to LOAd703 have been fever, chills, nausea, and increased transaminases. AEs have been transient and grade 1-2, with the exception of a grade 3 transaminase elevation in 1 subject receiving dose 3 (the only dose-limiting toxicity observed thus far). During protocol treatment, circulating MDSCs decreased in 8/13 subjects while effector memory T-cells increased in 6/10 subjects. At the lowest dose level, best response was stable disease, and 6/10 patients had partial responses. Clinical trial information: NCT0270596, LOKON pharma, Other Foundation.

Neoadjuvant gemcitabine and nab-paclitaxel followed by concurrent capcitabine/radiation in borderline resectable (BR) pancreatic cancer: A single-institution experience. First Author: Niraj K. Gupta, St. Vincent Cancer Care, Carmel, IN

Background: Neo-adjuvant therapy is becoming a preferred approach in the management of BR pancreatic cancer patients. There is no consensus on an ideal treatment regiment. We report our experience with a combination of nab-Paclitaxel/Gemcitabine followed by concurrent Capcitabine and radiation treatments in BR pancreatic cancer patients. Methods: A prospectively maintained database of patients with BR pancreatic cancer undergoing neoadjuvant treatments at our cancer center between 1/2010-11/2017 was reviewed. All treatments were given with image guidance (IGRT) and radiation dose was 60 Gy in 30 fractions (2 Gy/fraction). Within this series, 29 patients with unresectable PDAC were identified. Pts received nab-P (125mg/m^2) on day 1 + S-1 (100mg/m^2) once daily for 3 weeks of 4 cycles. Results: Median age was 59 yrs (42-76), 19 Males and 13 females. At least 2 cycles of Gem/nab-paclitaxel, none of the pts had progressive disease. Thirty patients (93%) were able to complete all 4 cycles of Gem/nab-paclitaxel. Twenty nine (90%) received capcitabine and radiation treatments. Imaging to assess response was done 4 weeks after completing radiation and the results were: 2 CR, 11 PR, 14 SD, 2 PD. Surgery was performed 6-8 weeks after completing radiation. Twenty six (88%) underwent planned resection, 2 had PD, 3 declined surgery and 1 had significant decline in PS. Twenty two out of Twenty six patients undergoing surgery had a RO resection (80%). Grade-III/IV toxicities with the neo-adjuvant treatments were seen in 41% and 7% of the pts, respectively. No thirty day post-op mortality, pancreatic leak or re-operations were observed. The median PFS among all patients was 11.7 months, 2 yr OS 49% and median OS was 27.6 months, compared to 23.4 months, 65% and median OS not reached, in patients who underwent surgical resection. Conclusions: Nab-Paclitaxel and Gemcitabine followed by concurrent capcitabine/radiation in BRPC patients is a feasible treatment strategy with acceptable toxicity-profile for patients with BR pancreatic cancer. Research Sponsor: None.

Efficacy and safety of nab-paclitaxel plus S-i(nab-P/S-i) versus nab-paclitaxel plus gemcitabine (nab-P/Gem) for first-line chemotherapy in advanced pancreatic ductal adenocarcinoma (apDAC): A randomized study. First Author: Yuan Zong, Department of Gastrointestinal Oncology, National Cancer Institute of Carcinogenesis and Translational Research (Ministry of Education(China), Peking University Cancer Hospital and Institute, Beijing, China

Background: Nab-P/Gem significantly improved survival compared with gem in patients (pts) with metastatic PDAC, but the ORR was limited to 23% with increased myelosuppression. Two phase II trials demonstrated high ORR of 60.0% (p=1) with nab-P/S-1 and showed less hematologic toxicity use for nab-P/S-1. A randomized (1:1) phase II trial was conducted. Eligibility required treatment-naive pts with unresectable PDAC. Pts received nab-P-125mg/m^2 on day 1 + S-1 80-120mg orally per day on day 1-7 every 2 weeks or nab-P-125mg/m^2 + Gem 100mg/m^2 on days 1,8 every 3 weeks. With an increase of ORR from 25% to 50%, 100 pts were required for 90% power at a two-sided significance level of 0.05. We enrolled 40 pts for a pilot study. Primary endpoints were ORR and 6-month PFS rate. Secondary endpoints were ORR of primary lesion, DCR, PFS, OS and safety. Results: 40 pts were enrolled between 06/2018 and 06/2019, including locally advanced (27.5%) and metastatic (72.5%) PDACs. 42.5% were male and the median age was 61 (range, 36-75) yrs. Median duration of treatment was 2.3 months in nab-P/S-1 (n = 20) and 2.7 months in nab-P/Gem (n = 20). In the intention-to-treat (ITT) population, the ORR and DCR were 35.0% vs 25.0% (P = 0.49) and 70.0% vs 70.0%, respectively. The ORR of primary lesion was 30.0% vs 25.0% (P = 0.72). In the evaluable pts (nab-P/S-1 n = 18, nab-P/Gem n = 18), the ORR and DCR of primary lesion were 38.9% vs 27.8%, 77.8% vs 77.8% and 35.3% vs 29.4%, respectively. With the median follow-up of 5.0 (range, 3.0-14.4) months, the median PFS and 6-month PFS rate was 6.3 vs 5.7 months and 56.1% vs 36.2%(P = 0.61) for nab-P/S-1 and nab-P/Gem, respectively. The median OS have not reached. Grade III/IV toxicities occurred in 30.0% nab-P/S-1 and 30.0% nab-P/Gem; leukopenia/neutropenia (35.0% vs 25.0%), febrile neutropenia (0 vs 5.0%), rash (0 vs 5.0%) and diarrhea (10.0% vs 0). Conclusions: Compared with nab-P/Gem, nab-P/S-1 had higher ORR, ORR of primary lesion and longer PFS without significant difference. Nab-P/S-1 developed a trend towards lower hematologic toxicity. Follow up for the randomized trial is ongoing. Clinical trial information: 0363630B. Research Sponsor: None.

Efficacy of preoperative FOLFIRINOX in potentially curable pancreatic cancer. First Author: Hamed Javan, McGill University, Montréal, QC, Canada

Background: Although Folfirinox (FFX) prolonged survival in metastatic and adjuvant setting, the role of preoperative FFX is still controversial. Our aim is to evaluate how surgery after neoadjuvant FFX with or without radiotherapy (RT) affects the clinical outcome in these patients. Methods: This is a single institution, phase 2 prospective study. Based on resectability criteria (NCCN-V.1.2017), patients prospectively were divided into 3 groups of resectable, borderline resectable (BR), locally advanced (LA). Patients received 6 cycles of preoperative FFX. Patients with adequate response, underwent resection. Continuation of chemotheraphy or radiation was given to the patients who were deemed unresectable after 6 cycles. Primary objective is time to progression (TTP), and secondary objectives are safety, R0/R1 resection rate, response rate (RR) and overall survival (OS). Results: 20 consecutive patients with pancreatic adenocarcinoma enrolled. The frequency of each group was 4, 8, 8 patients, respectively. Median age was 64 years old (range, 49-78). 45% of patients had primary tumor in head or uncinate process, 25% of cases presented with normal CA 19-9 value, 85% (17/20) of patients completed the preoperative treatment. Folfirinox was given within median of 11.5 weeks (range, 8-17) and median of 6 cycles (range, 1-17). Median relative dose intensity (ROI) was 85.89%. Grade III-IV (G3+4) adverse event (CTCAE 4.03) observed in 47.4% (9/19), RR (RECIST) was 86% (19/22). Best response was partial response (PR) in stable disease (9/20), with ROI of 103.6% and 66.7% (12/18). Resection rate was 64.3% (9/14, 1 case scheduled for resection). NO and negative lymph node (LN) achieved in 87.50% (7/8) and 62.50% (5/8) of patients. Complete pathological response (pCR) was seen in one patient (12.5% (1/8)). Patient’s safety and tolerability was good and OS will be reported during the meeting. Conclusions: Preoperative FFX was associated with high clinical and pathological response rate translating in high resection rate in majority of BRPC and LAPC, and appears to be a safe treatment strategy. Patients were treated higher FFX dose intensity than it was reported in adjuvant setting. However, these results need to be assessed in a randomized trial. Clinical trial information: NCT03167112. Research Sponsor: None.
Efficacy and safety of mFOLFIRINOX in patients with borderline resectable and locally advanced unresectable pancreatic cancer: Intention-to-treat population analysis. First Author: Inhwan Hwang, Asan Medical Center, University of Ulsan, Seoul, South Korea

Background: Borderline resectable pancreatic cancer (BRPC) and locally advanced unresectable pancreatic cancer (LAUPC) are heterogeneous disease entities with various prognosis. Based on the phase III PRODIGE trial, mFOLFIRINOX has been widely used for the management of patients with BRPC and LAUPC. Considering the lack of large phase 3 trial of mFOLFIRINOX for BRPC and LAUPC, real-life evidence of mFOLFIRINOX is needed.

Methods: In this retrospective analysis, 199 patients who received at least one dose of (m)FOLFIRINOX between February 2013 and January 2017 were included. Endpoints of this study were objective response rates (ORR), surgical resection rate, progression-free survival (PFS) and overall survival (OS).

Results: Median age was 60 years (20-82), 33% were male. Pancreas head (n=112, 56.3%) was the most common primary tumor site, followed by body (n=42, 21.1%) and multifocal (n=34, 17.1%). By an independent radiology review, patients were classified to BRPC (n=75, 37.7%) and LAUPC (n=114, 62.3%). With median 40.3 months (95% CI, 36.7-43.8) of follow-up duration in surviving patients, ORR was 26.6% (n=53), median PFS and OS were 10.6 months (95% CI, 9.5-11.7) and 17.1 months (95% CI, 13.2-20.9), respectively. There was no difference in PFS and OS between BRPC and LAUPC (median PFS 11.1 months, 95% CI, 8.8-12.1 vs. 10.7 months 95% CI, 8.4-11.8, p=0.47); (median OS, 18.4 months [95% CI, 16.1-20.8] vs. 17.1 months [95% CI, 13.2-20.9], p=0.50). Curative-intent surgery (RO and RI) was done in 63 patients (33.2%, 49 for RO and 14 for RI) after treatment with (m)FOLFIRINOX. Resection rates were 58.2% in BRPC patients and 19.4% in LAUPC patients (p<0.001). In patients who underwent curative-intent surgery, median disease-free survival since surgery was 10.4 months (95% CI, 8.3-12.5 ) and there was no difference according to the baseline disease extent (BRPC vs. LAUPC): 10.0 months (95% CI, 7.5-12.5) vs. 12.0 months (95% CI, 3.7-20.3, p=0.37). Conclusions: (m)FOLFIRINOX is effective therapy for BRPC and LAUPC patients. Significant proportion of patients could receive curative-intent surgery. Research Sponsor: None.

The impact of pancreatic cancer resection in the era of effective systemic treatment. First Author: Yaacov Richard Lawrence, Sheba Medical Center, Ramat Gan, Israel

Background: Surgical resection is the only curative modality in pancreatic cancer, yet the vast majority of patients undergoing surgery succumb of their disease. No randomized studies have been performed to assess the survival impact of surgery in pancreatic cancer. The aim of this study was to assess whether the era of effective systemic treatments, the survival advantage of surgical resection would be lessened.

Methods: A meta-analysis of published phase III clinical trials in pancreatic cancer in both the post resection adjuvant setting and the locally advanced unresectable setting was performed. Data was stratified by tumor resection. The survival advantage of surgical resection would be lessened. Surgical resection is the only curative modality in pancreatic cancer.

Poster Session (Board #L11), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Comparison of cost of care for Medicare FFS patients with pancreatic cancer by chemotherapy regimen. First Author: Jared Hirsch, Milliman, Inc., New York, NY

Background: To analyze total cost of care for patients with pancreatic cancer by FDA-Approved/NCCN Category 1 regimen. Methods: Cancer episodes were identified using a methodology similar to the Medicare Oncology Care Model (OCM) in the 2014-2016 100% Medicare Limited Data Set (LDS) claims files. Index dates were established for chemotherapy claims that did not occur within 6 months of another chemotherapy claim for all Medicare fee-for-service beneficiaries. Cancer episodes were defined as the 6-month period following an index date. Each episode was assigned a cancer type based on the plurality of cancer ICD 9/10 diagnosis codes that occurred on chemotherapy claims in the episode. Episode costs were calculated from claim paid amounts, and DME and other Part B spending was estimated using episodes created in the 5% Medicare LDS files using the same methodology. We analyzed total episode costs for three FDA-Approved/NCCN Category 1 pancreatic cancer regimens: gemcitabine plus nab-paclitaxel (gem-nab), FOLFIRINOX (FFX), and liposomal irinotecan (nal-IRI).

Results: We identified 110,618 cancer episodes in 2016, of which 4,018 were for pancreatic cancer (average age at index: 71.3 years). Pancreatic cancer patients in these episodes were treated with gem-nab (45% of episodes), FFX (14%), and nal-IRI (44%). The main cost drivers across all regimens were Part B drugs and inpatient services. Episode costs were $41,749, $42,086, and $45,851 for patients receiving gem-nab, FFX, and nal-IRI, respectively. Part B chemotherapy costs were $13,065 (gem-nab), $3,095 (FFX), and $18,472 (nal-IRI; all p<0.001). Other Part B costs were $7,343 (gem-nab), $17,013 (FFX), and $10,479 (nal-IRI); and inpatient service costs were $9,044 (gem-nab), $9,069 (FFX), and $5,108 (nal-IRI). Conclusions: Total episode costs for pancreatic cancer care were similar among three FDA-Approved/NCCN Category 1 regimens, but the components of the cost differed. Episodes with gem-nab had the largest Part B chemotherapy costs and the lowest inpatient service costs. Episodes with FFX and gem-nab had similar inpatient service costs, which were higher than episodes with nal-IRI. Episodes with FFX had the highest other Part B drug costs. Research Sponsor: Ipsen Biopharmaceuticals Inc.
Randomized phase II trial of chemoradiotherapy with S-1 versus combination chemotherapy with gemcitabine and S-1 as neoadjuvant treatment for resectable pancreatic cancer (JASPAC 04). First Author: Hiromika Toyama, Division of Hepato-Biliary-Pancreatic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan

Background: Although neoadjuvant treatment (NAT) has been widely employed for resectable pancreatic ductal adenocarcinoma (PDAC), it is still unclear what kind of regimen is recommended. The aim of the study is to investigate which chemoradiotherapy (CRT) with S-1 or combination chemotherapy with gemcitabine (GEM) and S-1 is more promising as NAT for resectable PDAC. Methods: Patients with resectable PDAC were enrolled and randomly assigned into either CRT group or chemotherapy group. In the CRT group, a total radiation dose of 50.4 Gy in 28 fractions was administered and S-1, at a dose of 30, 40 or 50 mg according to the body surface area, was orally provided twice a day on the same day of irradiation. In the chemotherapy group, GEM was intravenously administered at a dose of 1000 mg/m² on day 1 and 8 and S-1 was orally provided at a dose of 30, 40 or 50 mg according to the body surface area twice daily on day 1 to 14 followed by one week rest. Patients in the chemotherapeutic group received two cycles of this regimen. Surgery was performed between 15 and 56 days after the last day of NAT. The primary endpoint was 2-year progression-free survival (PFS) rate. With 50 patients in each group, the study had 80% power assuming a threshold 2-year PFS rate of 25% and an expected 2-year PFS rate of 40% at 0.05 one-sided alpha. The trial was registered with the UMIN Clinical Trial Rегистraion as UMIN000014894. Results: From April 2014 and April 2017, 103 patients were enrolled from 11 institutions in Japan. One was excluded because of ineligibility; therefore 50 patients in CRT group and 51 patients in chemotherapy group constituted the intention-to-treat analysis. The 2-year PFS rate was 45% (90% CI, 33-60%) in the CRT group and 55% (43-65%) in the chemotherapy group (p = 0.52). The hazard ratio for chemotherapy to CRT was 0.78 (0.46:1.31). The median survival time was 37.7 (95% CI, 30.3-NE) in the CRT group and NE (29.9-NE) in the chemotherapy group (p = 0.30). There was no treatment-related death in both groups. Conclusions: Combination chemotherapy with GEM and S-1 may be more promising compared with CRT with S-1 as NAT for resectable PDAC. Clinical trial information: UMIN000014894. Research Sponsor: Pharma-Valley Shizuoka Industrial Foundation.

A prospective trial of elemental enteral feeding in patients with pancreatic cancer cachexia (PANCAX-1). First Author: Andrew Eugene Hendler, Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA

Background: Unintentional weight loss affecting > 85% of pancreatic cancer (PC) patients contributes to low therapeutic tolerance, reduced quality of life, and overall mortality. Optimally, we strive to keep our patients at baseline body weight; however, it is not uncommon for patients to experience weight loss despite enteral feeding. Methods: Pancreatic adenocarcinoma patients with cachexia (> 5% unintentional weight loss within the previous 6 months) were provided a jejunal tube peptide-based diet for 3 months. Primary outcome was weight stability (0.1 kg/BMI unit decrease). Secondary outcomes included changes from baseline in LBM, bone mineral density (BMD), total body fat mass (BFM), handgrip strength, physical activity (Fitbit), and CA19-9 and CRP. Planned interim analysis was performed after 14 patients completed treatment. Results: From 31 consenting patients, 16 were evaluable for the chemotherapy outcome. Patients receiving enteral therapy were 39% male, median age 69 (49 to 85 years), and 74% ECOG I. A summary of change in outcomes at 3 months from baseline is shown in Table. The primary endpoint of weight stability in 10 (62.5%) patients was met, thus completing study. Overall survival was 6.2 months (3.3 9.9 months) for evaluable patients (n=16). Weight stability was statistically associated with LBM (Pearson’s correlation: 0.87, p <0.001), but not survival (HR: 0.94, 95% CI 0.32-2.83, p=0.92). Conclusions: Peptide-based enteral feeding resulted in weight stabilization and improvements in lean body mass and physical function. Further randomized trials assessing nutritional support in advanced patients are warranted. NIH/NCATS Grant # UL1TR000124. Clinical trial information: NCT02400398. Research Sponsor: U.S. National Institutes of Health.

Clinical outcome of initially unresectable pancreatic cancer patients: Conversion surgery after modified FOLFIRINOX or gemcitabine nab-paclitaxel. First Author: Yuta Usuda, Japanese Foundation for Cancer Research, Tokyo, Japan

Background: Although pancreatic cancer (PC) is unfavorable clinicopathology, the prognosis of resectable PC has been improving due to gemcitabine-based neoadjuvant chemotherapy. Meanwhile, the prognosis of unresectable (UR) PC remains poor. In highly selected patients, however, conversion surgery (CS) has been performed with good outcome. Indication criteria of CS remain unestablished because the number of patients who underwent CS was very small in each institution. Methods: From 2014 to 2018, 485 consecutive patients with UR-PC who received modified FOLFIRINOX (mFFX) / Gemcitabine Nab-Paclitaxel (GnP) chemotherapy were reviewed. Among them, patients with disease control for more than 8 months were enrolled and divided into two groups; patients who underwent CS (CS group) and patients who did not undergo CS (non-CS group). We compared clinical characteristics and survival outcomes between groups. Surgical indications were as follows: 1) Decreasing trend in CA19-9, 2) With response for chemotherapy in imager, 3) Disease control more than 8 months, 4) Decision in Cancer board as for metastatic cases. Results: In UR-PC patients, 358 patients had distant metastasis (MPC) and 127 patients had locally advanced (LA) PC. The overall survival (OS), progression free survival (PFS) and conversion rate of LAPC were significantly better than MPC (OS: 21 vs. 13 months, PFS: 12 vs. 7 months, Conversion rate: 16 vs. 5%, p < 0.001). Chemotherapy regimen (mFFX/GnP) had no significant difference in survival outcome. Between CS group (n = 39) with non-CS group (n = 160), age, sex, body mass index, location of lesion, CEA, CA19-9, regimen of chemotherapy and history had no significant differences. The median survival time of CS group was significantly better than that of non-CS group (OS: NA vs. 21 months, p < 0.001; PFS: 24 vs. 14 months, p = 0.01). In CS group, median operative duration was 909 minutes, blood loss was 735 ml, hospital stay was 26 days, and there were no 90-days mortality case. Conclusions: In our retrospective study, CS for UR-PC can be safely performed, and among carefully selected patients, reasonable short and term long outcomes can be obtained without acceptable morbidity rate. Research Sponsor: None.

Outcomes and efficacy of neoadjuvant chemoradiation versus chemotherapy in localized pancreatic cancer. First Author: Asmita Chopra, Department of Surgery, University of Pittsburgh, Pittsburgh, PA

Background: Neoadjuvant therapy is increasingly used for pancreatic cancer (PDA). The comparative efficacy of neoadjuvant chemoradiation (NC) versus chemotherapy (NCRT) remains uncertain. We aimed to compare NC and NCRT outcomes, survival endpoints, and associated costs. Methods: Single-center analysis of PDAs treated with NC or NCRT between 2008-2018. Average treatment effects (ATE) were estimated after matching patients who received palliative chemotherapy, results in improved weight, lean body mass (LBM), and handgrip strength. Methods: Pancreatic adenocarcinoma patients with cachexia (> 5% unintentional weight loss within the previous 6 months) were provided a jejunal tube peptide-based diet for 3 months. Primary outcome was weight stability (0.1 kg/BMI unit decrease). Secondary outcomes included changes from baseline in LBM, bone mineral density (BMD), total body fat mass (BFM), handgrip strength, physical activity (Fitbit), and CA19-9 and CRP. Planned interim analysis was performed after 14 patients completed treatment. Results: From 31 consenting patients, 16 were evaluable for the chemotherapy outcome. Patients receiving enteral therapy were 39% male, median age 69 (49 to 85 years), and 74% ECOG I. A summary of change in outcomes at 3 months from baseline is shown in Table. The primary endpoint of weight stability in 10 (62.5%) patients was met, thus completing study. Overall survival was 6.2 months (3.3 9.9 months) for evaluable patients (n=16). Weight stability was statistically associated with LBM (Pearson’s correlation: 0.87, p <0.001), but not survival (HR: 0.94, 95% CI 0.32-2.83, p=0.92). Conclusions: Peptide-based enteral feeding resulted in weight stabilization and improvements in lean body mass and physical function. Further randomized trials assessing nutritional support in advanced patients are warranted. NIH/NCATS Grant # UL1TR000124. Clinical trial information: NCT02400398. Research Sponsor: U.S. National Institutes of Health.
results: treatments received, response, and survival. Chart review to extract demographic and clinical characteristics including germline and/or somatic mutation testing. We conducted a retrospective study and identified patients with mPDAC treated with nal-IRI and FUFA who had KRAS mutations. DNA-damage repair deficiency (dDDR), a process that is altered in a subset of patients with PDAC, may be more relevant to patients with mPDAC.

Background: Translational research using patient-derived tumor xenograft (PDX) models is progressing rapidly, and is also becoming widespread in pancreatic cancer research. The purpose of this study was to establish the liver transplant PDX model as artificially-created liver metastasis with cryopreserved primary pancreatic ductal adenocarcinoma (PDX). Methods: The primary PDX from 10 patients were cryopreserved and transplanted into NSG mice using liver pocket method. For engraftment and similarity evaluation, H&E staining and immunohistochemical staining such as Ki-67, p53, SMAD4, and MUC1 were performed. Results: Patient-derived xenograft was succeeded in 6 cases (60%), 10 mice (33.3%), Ki-67 index of primary PDX and the interval of cryopreservation were significantly related to successful engraftment, respectively (p = 0.003, p = 0.007). Conclusions: In this study, we succeeded in establishing a liver transplant PDX mouse model as a preclinical platform. The factors such as Ki-67 index and the interval of cryopreservation would affect the successful establishment. Research Sponsor: None.

731 DNA-damage repair deficiency (dDDR) and response to nanoposomal irinotecan (nan-IRI) in metastatic pancreatic ductal adenocarcinoma (mPDAC). First Author: Sameeha Rau, University of Miami Miller School of Medicine, Miami, FL

Background: Chemotherapy is the standard of care for patients with mPDAC but there are no biomarkers to aid in treatment selection. Nal-IRI with 5-fluorouracil/5-FUFA) improves survival over FUFA in the second-line treatment of mPDAC. Nal-IRI is a topoisomerase inhibitor and its action produces DNA damage leading to cell death. We hypothesize that tumors with dDDR, a process that is altered in a subset of patients with PDAC, may be more sensitive to the effects of Nal-IRI. Methods: Utilizing the IRB-approved pancreas cancer databases at the University of Miami and Wake Forest University, we identified patients with mPDAC treated with nal-IRI and FUFA who had germline and/or somatic mutation testing. We conducted a retrospective chart review to extract demographic and clinical characteristics including treatments received, response, and survival. Results: Among 31 patients identified, the median age was 66y and 47% were female. Nine patients had a DDR mutation: 6 germline and 3 somatic. Median progression-free survival (PFS) in patients with any germline or somatic DDR mutation was 3.2m vs 3.9m for those without (log-rank p = 0.7). When restricted to germline DDR mutations only, the median PFS was not reached with germline DDR vs 4m for those without (log-rank p = 0.22). Presence of DDR was associated with a higher clinical benefit rate (CBR = partial response + stable disease); a DDR mutation was present in 36% of patients who showed clinical benefit vs 15% in those without clinical benefit (p = 0.20). Conclusions: DDR mutations appear to define a subset of patients with mPDAC who may be more sensitive to nal-IRI and FUFA. The PFS and CBR were numerically but not statistically superior, especially in patients with germline DDR mutations. Larger data sets and longer follow-up are needed to confirm this trend. Research Sponsor: None.

732 Homologous recombination deficiency (HRD) by BROCA-HR and survival outcomes after surgery for patients (pts) with pancreatic adenocarcinoma (PC): A single institution experience. First Author: Amy E. Chang, University of Michigan, Ann Arbor, MI

Background: 5-7% of PC pts exhibit deleterious germline mutations (MUT) in HR tumor suppressor genes BRCA1 and BRCA2. BROCA-HR is a targeted capture and massively parallel sequencing assay designed to detect tumor mutation classes including gene rearrangements, copy number variations, and gene aberrations within the Fanconi Anemia-BRCA HR, non-homologous end joining (NHEJ) DNA repair, and DNA mismatch repair pathways. BROCA-HR has been successfully used in breast and ovarian cancer pts for overall prognosis and prediction of response to platinum-based therapies. While BROCA1/2 MUT may confer survival advantage for PC pts if treated with platinum-chemotherapy, the survival impact of HRD is less well defined. Methods: We retrospectively identified 100 consecutive pts with resected PC at University of Washington Medical Center between 1999 and 2008. Formalalin-fixed paraffin embedded resected tumors were sequenced using BROCA-HR. HRD was grouped based on the following deleterious genetic mutations: 1) BRCA1, BRCA2; 2) core HRD: BARD1, BRI1, RAD51C, RAD51D, PALB2, CDK12, NBN; 3) non-core HRD: ATM, ATR, ATRX, BAP1, BLM, CHEK2, FANCA/C/D/E/F/G/L, MRE11, RAD50/51/S1B, RIF1, SLX4; 4) HR proficient. Overall survival (OS) was measured from diagnosis until death or last follow-up. Results: 95 pts had histologically confirmed PC, and 81 pts had adequate tumor DNA for analysis. Six pts (7%) had BROCA1/2 MUT (n = 5), or BROCA1 methylation (n = 1), pt 1% had non-BRCA core HRD (PALB2 MUT), 7 pts (9%) had non-core HRD: ERCC2 (2), CHEK2 (2), ATM, RAD51D, and FANCA MUT (1 each). Median OS was: all pts 193 yrs (95% CI 153, 216); BRCA1/2 pts 3.09 yrs (95% CI 0.41, 12.21); all core HRD pts 121 yrs (95% CI 0.41, 12.21); all core and non-core HRD pts 189 yrs (95% CI 0.57, 4.96); HR proficient pts 193 yrs (95% CI 1.51, 215). There were no OS differences between pts with HRD vs those HR proficient. Conclusions: HRD is common (7%) but does not affect OS for pts with resected PC. Prospective OS trials should test neo/adjuvant therapies including platinum chemotheraphy and PARP inhibitors for pts with HRD. Research Sponsor: National Institutes of Health.
733 Poster Session (Board #L22), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM
Loss of Rnf43 to accelerate KRAS-mediated neoplasia in a clinically relevant genetically engineered mouse model of pancreatic adenocarcinoma. First Author: Abdel Nasser Hosein, University of Texas MD Anderson Cancer Center, Houston, TX
Background: The genetic heterogeneity of pancreatic ductal adenocarcinoma (PDAC) demands a personalized molecular-targeted treatment approach. While activating KRAS mutations are a near ubiquitous event in PDAC, 5-10% of cases display deleterious driver mutations in the Wnt-signaling negative regulator, ring finger 43 (RNF43). Despite this characteristic there are no personalized treatment options for this subset of patients. Methods: We have developed a genetically engineered mouse model (GEMM) of PDAC, driven by an activating mutation in Kras and deletion of Rnf43 under control of a pancreas specific promoter (KRC). Mice were followed for 20 weeks and histological changes and weight were compared to a Kras driven PDAC GEMM (KC). Mice underwent serial magnetic resonance imaging (MRI), with and without dynamic contrast enhancement (DCE) imaging, to evaluate cystic tumor morphology and contrast enhancement during tumor progression. Single cell RNA sequencing (scRNAseq) was also performed to assess changes in single cell populations during tumor progression. Lastly, we established ex vivo cultures from KRC and KC tumors and performed bulk RNA-sequencing (RNAseq) and in vitro pharmacology studies. Results: KRC mice displayed a decrease in overall survival and higher incidence of both high grade pre-neoplastic lesions and invasive PDAC compared to KC mice. Single MRI revealed increased cystic morphology of KRC mice during tumor progression with increasing DCE intensity. scRNAseq from KRC tumors from moribund mice displayed two distinct populations of both macrophages and fibroblasts, similar to our previous report of KC. KRC patients had a longer median OS and survival than KC patients. Mice underwent serial MRI to evaluate changes in tumor morphology and contrast enhancement during tumor progression. By comparing images from day 0 and 21, KRC mice displayed increased tumor volume and contrast enhancement. Conclusions: The differential expression of genes was small with a median PFS of 200 days after Rim (n = 1). Stratification by best response (SD, PR, CR, PD) revealed a trend in PFS for KRC vs KC mice. Further investigation is needed to determine if RNF43 deficiency increases tumor progression in PDAC.

734 Poster Session (Board #M1), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM
Tumor infiltration and cytokine biomarkers of prostate stem cell antigen (PSCA)-directed GOCAR-T cells in patients with advanced pancreatic tumors. First Author: Joanne Shaw, Bellicum Pharmaceuticals, Inc., Houston, TX
Background: PSCA is a cell surface protein overexpressed in approximately 60% of pancreatic cancers. BPX-601 is an autologous GOCAR-T cell therapy engineered to express a PSCA-CD3ζ, CAR and the MyD88/CD40 (iMC) co-stimulatory domain activated by rimiducid (Rim), designed to boost CAR-T performance in solid tumors. The safety and activity of BPX-601 activated in a PSCA metastatic pancreatic cancer is being assessed in a Phase 1/2 clinical trial, BP-012 (NCT027444287). Methods: Phase 1 of BP-012 is a 3+3 dose escalation of BPX-601 (1.25-5 x10^9/kg) administered on Day 0 with a single, fixed-dose of Rim (0.4 mg/kg) on Day 7 in subjects with previously treated PSCA metastatic pancreatic cancer. All 5 subjects in cohort 5 received Rim (1.5 x10^9/kg) and Rim, BPX-601 kinetics, PBMC phenotype, and serum cytokines were assayed by qPCR, flow cytometry, and cytokine multiplex, respectively. Baseline and on-treatment biopsies were evaluated by RNAscope in situ hybridization. Results: BPX-601 cells expanded in all subjects and persisted up to 9 months in 2 subjects (median 42 days). Transient reduction in BPX-601 vector copy number and total T cell count concurrent with Rim infusion, supports margination of activated BPX-601 cells. Increased serum cytokines, such as INFγ and GM-CSF, were observed following BPX-601 infusion with further elevation after Rim activation. All subjects with evaluable on-treatment biopsies had infiltration of BPX-601 cells (n = 3) proximal to tumor cells. 5-15 days after Rim, but not in an end of treatment biopsy > 200 days after Rim (n = 1). Stratifaction by best response (SD, PR, CR, PD) revealed a trend in PFS for KRC vs KC mice. Further investigation is needed to determine if RNF43 deficiency increases tumor progression in PDAC.

735 Poster Session (Board #M2), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM
Real-world outcomes in pancreatic adenocarcinoma (PDAC) and persona types with implications for standard of care (SOC) therapy (TX). First Author: Emanuel Petricoin, George Mason University, Fairfax, VA
Background: Molecular profiling (MP) for PDAC has gained increased acceptance and we previously demonstrated that targeting actionable mutations can improve patient (pt) outcomes. However, the correlations of diverse patterns of molecular alterations with outcomes following SOC TX are largely unknown. Methods: We analyzed longitudinal outcomes of 1355 PDAC pts who underwent MP and received SOC TX. “Persona” types were established based on the molecular characteristics of each pt using unsupervised clustering, as well as a supervised review defined by our molecular tumor board, following classifications reported in previous studies. Progression-free survival (PFS) for each type was assessed based on the choice of first-line TX (i.e. FOLFIRINOX [FFX] vs. gemcitabine + nab-paclitaxel [GA]). Statistical comparisons were made against all other types within a specific TX group. Results: The prognostic/predictive value of the persona types for 1st-line TX revealed distinct differences in outcomes (Table). As expected, the DDR deficiency type was associated with a significantly improved PFS for pts treated with FTX but not for GA. In addition, pts in the cell cycle type had a worse PFS compared to other persona types for both FFX and GA. Using this platform, we will further subdivide the persona types into molecular subtypes and associate these with pt outcomes. Conclusions: Our analyses demonstrate that specific molecular persona types exist in PDAC pts and can be linked to TX outcomes. Ultimately, knowing the persona type/subtype early in a pt’s TX course may help personalize TX to improve outcomes. Research Sponsor: The Pancreatic Cancer Action Network, Pharmaceutical/Biotech Company

736 Poster Session (Board #M3), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM
Gene expression profiling of unresectable pancreatic cancer patients treated with gemcitabine, nab-paclitaxel, metformin, and dietary supplements (DS). First Author: Vincent Chung, City of Hope, Duarte, CA
Background: Pancreatic cancer commonly causes weight loss and many patients take supplements to improve nutrition but also for any potential anticancer properties. We conducted a pilot trial evaluating a standardized ds, metformin and dietary supplements in patients with stage 4 PDAC. Methods: We analyzed baseline serum cytokine levels in 18 patients. NanoString Human Immune Profiling and Pan-Cancer Pathways were performed to evaluate changes in gene expression with treatment. Results: The differential expression of genes was small with dietary supplements alone and in combination with chemotherapy. After 2 months of treatment, 17 genes were upregulated while 4 genes were down regulated. At the time of tumor resistance, 33 genes were upregulated while 17 genes were downregulated. We observed downregulation of tumor suppressor gene expression with upregulation in growth factor pathways. Interestingly, SFRY2 mRNA expression was also up regulated which functions as a negative feedback regulator of multiple receptor tyrosine kinases. Conclusions: Increasing number of genes were upregulated with continued treatment. The most common pathway affected was cell cycle and apoptosis. During the initial supplement run in period from D-6 to C1D1, IL-8 mRNA expression was upregulated the most. IL-8 is a neutrophil chemotactic factor secreted by cells involved in the innate immune response as well as pancreatic cancer cells associated with a pro-inflammatory state. Treatment with gemcitabine and nab-paclitaxel decreased the IL-8 mRNA expression. Additional studies with longer course of treatment with supplement alone would be required to explore its impact on differential gene expression. Research Sponsor: Biomedical Research and Longevity Society, Inc.

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Comparison of gemcitabine delivery and tumor response in a pressurized pancreatic retrograde venous infusion versus systemic infusion in an orthotopic murine model. First Author: Diego Vicente, Moores Cancer Center, San Diego, CA

Background: Pancreatic ductal adenocarcinoma (PDAC) is associated with limited response to systemic therapy (ST). Elevated tumor interstitial fluid pressures (IFP) inhibit penetration of ST. Regional Pressure-Enabled Drug Delivery has recently demonstrated improved response for liver tumors in a clinical trial. However, this delivery method has not been evaluated in PDAC. We compared gemcitabine (Gem) by systemic delivery vs. a novel pressurized Pancreatic Retrograde Venous Infusion (PRVI) method in an orthotopic PDAC mouse model. Methods: PDAC murine cell line (KPC4580P) tumors were transplanted onto the pancreatic tail of C57BL/6j mice. Groups of 15 mice were randomly assigned to PRVI Gem, Gem/PRVI saline (Control), or intraperitoneal Gem (Systemic) groups. Five mice from the PRVI and Systemic groups were randomly selected after one hour post infusio to evaluate Gem tumor concentrations by liquid chromatography - tandem mass spectrometry (ng/mg) and the remainder of mice were euthanized after 7 days to evaluate treatment response. Results: Tumor concentrations of Gem were significantly higher following PRVI compared to Systemic (128 ± 19, p < 0.01) at one hour after treatment. Seven days after treatment, PRVI Gem mice demonstrated lower mean tumor volume (mm³) than Systemic Gem and Control mice (274 ± 85 vs. 629, p < 0.01, respectively). Histologic evaluation of tumors demonstrated decreased cellularity in the PRVI Gem mice compared to Systemic and Control mice (35 ± 78 vs. 71%, p = 0.01, respectively). No differences were seen in Ki67% or immune cell infiltrate between groups. Conclusion: PRVI Gem resulted in increased PDAC Gem concentrations and improved treatment responses with decreased tumor burden and cellularity. These findings suggest that pressurized regional chemotherapy infusion overcomes the elevated PDAC IFP and justifies additional translational preclinical studies with other chemotherapeutics (including immunomodulating antibodies) with different physicochemical properties. Research Sponsor: TriSalus Life Sciences, Westminster, CO.

Poster Session (Board #M7), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Translational analysis from SCALOP trial: CCL5 as a prognostic biomarker and a potentially actionable target in locally advanced pancreatic cancer (LAPC). First Author: Sonnath Mukherjee, University of Oxford, Oxford, United Kingdom

Background: SCALOP was a multi-centre phase II RCT where 114 patients with LAPC were received 3 cycles of Gemcitabine and Cabazitaxel (GEMCAP) and those with stable/responding disease (n = 74) were randomised to Gem-RT or Cap-RT. The trial showed superiority of Cap-RT. Baseline blood samples of randomised patients were analysed for 35 circulating biomarkers. In vivo study was undertaken with candidate biomarker (CCL5) to test actionability. Methods: Patients plasma samples were used in multiplexed magnetic Luminex assays. A commercial CCL5 antibody (Implugen, San Diego, CA). Orthoptic KrasG12D;P53flox/flox;Pdx1cre- (KPC) tumors were implanted in B6-mice and treated with Gem, CCR5-inhibitor (Ccrs5) maraviroc (MV), PDI inhibitor (PD1), PDI+MV alone and in combination with MRI guided small animal Radiotherapy (RT). Immunohostotyping was performed by IHC and Aurora Cytek spectral flow cytometry. Results: Baseline biomarker data was available on 63/74 randomised patients. Of the 35 biomarkers tested, only CCL5 was found to be significantly associated with OS with a median OS of 18.5 (95% CI: 11.76-21.32) vs 11.3 (9.86-15.51) months (low vs high), and HR 1.37 (95% CI: 1.04-3.65; p = 0.02). OXCGX assay demonstrated lower mean tumor volume (mm³) than Systemic Gem and Control mice (274 ± 85 vs. 629, p < 0.01, respectively). Histologic evaluation of tumors demonstrated decreased cellularity in the PRVI Gem mice compared to Systemic and Control mice (35 ± 78 vs. 71%, p = 0.01, respectively). No differences were seen in Ki67% or immune cell infiltrate between groups. Conclusion: PRVI Gem resulted in increased PDAC Gem concentrations and improved treatment responses with decreased tumor burden and cellularity. These findings suggest that pressurized regional chemotherapy infusion overcomes the elevated PDAC IFP and justifies additional translational preclinical studies with other chemotherapeutics (including immunomodulating antibodies) with different physicochemical properties. Research Sponsor: TriSalus Life Sciences, Westminster, CO.

Poster Session (Board #M8), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Homologous recombination deficiency (HRD) scoring in pancreatic ductal adenocarcinoma (PDAC) and response to chemotherapy. First Author: Grainne M. O’Kane, Princess Margaret Cancer Centre, Toronto, ON, Canada

Background: Whole genome sequencing (WGS) can reveal patterns of substitution signature bases and structural variation characteristic with tumours deficient in homologous recombination repair. We evaluated the published HRDetect score and a novel HRD hallmark score (HRD-HS) in patients receiving the combination chemotherapy (cCT) on the COMPASS trial for advanced PDAC. Methods: The HRD-HS incorporates 10 genomic characteristics of HRD-PDAC with a score ≥ 4 defining HRD, HRD-HS and an HRDetect score ≥ 0.7 were applied to WGS data and overall survival (OS) and response (ORR) evaluated. Sensitivity and specificity were ascertained. Results: As of 05/19, 205 eligible patients (pts) were enrolled and 186 received cCT including modified FOLFIRINOX (105 pts) and gemcitabine/nab-paclitaxel (n = 76 (41%)). HRD-HS had a sensitivity of 87.5% and specificity of 100% in detecting HRD-PDAC. In contrast, HRDetect (n = 0.7) had sensitivity of 51.9% and specificity of 100%; sensitivity increased to 73.7% when using a cutoff score of ≥ 0.99. 23/186 (12%) pts were classified as HRDetect+ and median OS was 15.3 months (mo) vs 8.7 mo in HRDetect+ pts (HR 0.44, 95% CI 0.27-0.70, p = 0.009). In platinum treated pts, median OS was 18.1mo (HRDetect+) vs 9.3mo (HRDetect-) (HR 0.38 95%CI 0.21-0.69, p = 0.02). HRD-HS predicted the longest median OS for platinum of 21.0mths. ORR in HRDetect+ was not different to HRDetect- pts treated with cCT, however in those receiving platinum the ORR was 50% vs 19% respectively (p < 0.001). Of the false positives by HRDetect, 46% had a non-BRCA1 tandem duplicator phenotype (TDP). The trial group comprised 81% of all patients enrolled. HRD-HS was caused by inactivation of BRCA2/1, PALB2, RAD51C and RAD51C; all TDP patients were pathogenic. Pathogenic ATM and CHEK2 germline variants were present in 3 pts with evidence of a second somatic hit or LOH, none of these identified as HRD by either classifier nor considered a TDP. Conclusion: HRD-HS most correctly identified HRD-PDAC patients than the HRDetect score classifies additional patients sensitive to cCT, especially platinum. The TDP cohort may be responsive to DNA damaging agents warranting further evaluation. Clinical trial information: NCT02750657. Research Sponsor: Ontario Institute Cancer Research, Pancreatic Cancer Canada.

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Clinical significance of MUC4 isoforms in pancreatic cancer patients. First Author: Christopher Thompson, Univ of NE Medical Center, Omaha, NE

Background: Pancreatic adenocarcinoma (PC) is a highly aggressive cancer with a 5-year survival rate around 9% with majority of patients diagnosed at advanced stage. Prior studies describe transcriptomic alterations during tu- morogenesis, of which novel and progressive expression of mucin 4 (MUC 4) is significant. Mucins are large secreted or membrane-tethered glycoproteins that have been shown to be of pathogenic importance in PC. Methods: We ex- plored differential expression and survival outcomes based on mucin ex- pression using TCGA PC patients (n = 151). RNA-Seq reads were realigned to all known mucin splice variant (SV) sequences. Hazard ratios (HR) were calculated for all SVs (n = 123), and SVs with significant HRs were plotted on Kaplan-Maier survival curves comparing expression about the median. The MUC4 SV (MUC4 Δ6) was selected for validation in patient tumor samples (n = 17) due to PC tumor cell-specific expression and in-frame deletion of a single exon. After discovery of significant mucin SVs, we designed a gold- nanoparticle (GNP) assay to specifically detect MUC4 Δ6 in circulation from PC patient plasma. Results: In the absence of significant mucin-based sur- vival differences, we expanded our analysis to include mucin SV transcripts. Through hazard and survival analyses, we identified 3 MUC1 SVs with better survival (SV1 HR = 0.6, p = 0.03; SV2 HR = 0.6, p = 0.05; SV3 HR = 0.6, p = 0.04), and one each of MUC4 (HR = 1.93, p = 0.28) and MUC6 (HR = 1.90, p = 0.27) with worse prognosis. In a validation cohort, we found 10 samples had a high cellularity (HC) gene signature. Expression of MUC4 Δ6 was 4804.7 copies/ 100,000 GAPI copies in the HC population and expressors above the median had a median survival of 197 days compared to 397 days for low expressors. Our novel GNP assay detected MUC4 Δ6 transcripts at minimum concentrations of 100 FM with a synthetic RNA. Uniquely, our assay detects the MUC4 Δ6 SV but not wild-type variant. Conclusions: We were able to de- termine that expression of specific mucin SVs are prognostic in PC patients. We developed technology to detect MUC4 Δ6 transcript in circulation using a novel GNP assay. Future studies will seek to stabilize the nanoparticles and modify them for potential diagnostic purposes in a clinical setting. Research Sponsor: U.S. National Institutes of Health.

Pancreatic cancer intratumoral microbiome and characteristics within paired patient samples. First Author: Sonal Suresh Noticewala, University of Texas MD Anderson Cancer Center, Houston, TX

Background: While most studies evaluating the microbiome in gastrointestinal cancers analyze stool, little is known about the microbiota of the peri- tumoral and intra-tumor environment. Here, we evaluated the intra-tumor and peri-tumoral (duodenum and normal pancreas) microbiome for paired duodenal, normal pancreas and resected tumor specimens from pancreatic cancer patients. The purpose of this study was to describe the similarities and differences within patient microbiota. Methods: Fifteen specimens from 5 patients with pancreatic cancer patients were collected during surgical resection. Genomic bacterial DNA was extracted from these specimens and underwent 165 rRNA sequencing. Alpha (Inverse Simpson) and beta diversity were calcu- lated, and relative abundances of individual bacterial species were com- pared. Sorenson distance was used to evaluate the spread in beta diversity between paired sample types. Results: Of the five patients who underwent resection, the following baseline characteristics were obtained: median age = 65 years (range 55-80 years), 2/5 patients were treated with gemcitabine/ nabxarane, 3/5 patients were treated with oxaliplatin, irinotecan, fluorouracil, and levocorvin (FOLFIRINOX); 4/5 patients received pre-operative radiation. 16s sequencing analysis of the pancreatic tumor showed the dominant genus to be Escherichia/Shigella (10.6%). Bradyrhizobium (10.1%) was dominant in the normal pancreas. Escherichia/Shigella (14.3%) was abundant in the du- odenum. There was a trend towards higher alpha diversity in tumor vs. normal duodenum/ pancreas (p = 0.12). Sorenson distance was statistically different between sample types (p = 0.004), with duodenal samples most consistent (distance = 67.82), and tumor vs. normal pancreas (61.86) and tumor vs. other tumoral tissues of which novel and progressive bacterial species are present. This suggests that the pancreatic tumor microbiome is distinct from the normal pancreas and duodenal microbiome, which indicates tumor specific bacteria should be studied. In future studies, intra-tumoral microbiome may be more relevant to associations with outcomes and treatment response than stool or intestinal microbiome studies. Research Sponsor: None.

Whole genome and transcriptome analysis and the link between insulin receptor aberration and diabetes in PDAC. First Author: Michael Lee, BC Cancer, Vancouver, BC, Canada

Background: Pancreatic ductal adenocarcinoma’s (PDAC) association with diabetes development remains poorly understood. The insulin receptor (INSR) can divert insulin signaling from metabolic to oncogenic pathway activation through alternative splicing of INSR in several cancer types. Methods: 54 treatment naive patients with metastatic PDAC underwent fresh tumour bi- opsy in the BC Cancer Personalized Oncogenecology (POG) and PanGen studies (NCT02155621, NCT02869802) for whole genome (WGA) and transcriptome analysis (RNASeq). Copy status and expression of INSR were correlated with T2DM status, Moiiffit subtypes, and overall survival (OS). The findings were then correlated with 92 resected PDAC from the International Cancer Genome Consortium (ICGC). Results: 13/54 (24%) had confirmed T2DM at enrollment, and had poorer OS compared to non-diabetic PDAC patients, independent of Moiiffit subtype, HR 3.2 (1.5-6.5), p < 0.001. Diabetics were more likely to have hypertension (64 v 11%, p < 0.001), dyslipidemia (57 v 16%, p=0.013), and to be older (61.5 ± 58 years, p=0.004) and smokers (71.4 v 21.6%, p=0.05). WGA revealed significant enrichment of heterozygous INSR copy loss in T2DM (69%) compared to all other patients (24%; p=0.03) and an enrichment of INSR copy loss for metastatic PDAC relative to resected PDAC in ICGC (35 v 18%, p=0.03). Heterozygous INSR copy loss (n = 17/54) was an independent predictor of worse OS (10.8 v 15.1 months, HR 2.29 (1.20-4.36), p=0.012), and it interacted with diabetes status (p=0.023). Moiiffit basal (vs. classical) subtype (n = 17/54, of which 8/17 have INSR copy loss) was also an independent predictor of worse OS (10.8 v 15.1 months, HR 2.29 (1.20-4.36), p=0.012), and it interacted with diabetes status (p=0.023). Moiiffit basal (vs. classical) subtype (n = 17/54, of which 8/17 have INSR copy loss) was also an independent predictor of worse OS (8 v 17 months, HR 2.29 (1.20-4.36), p=0.012). Whilst there was no interaction between INSR status and Moiiffit subtype on OS (p=0.727), INSR expression is lower in basal subtype, p<0.001. Conclusions: Presence of T2DM in our cohort is an independent predictor of worse OS, consistent with published literature. Alteration in the insulin signaling pathway with heterozygous copy loss of INSR was associated with poorer prognosis, diabetes development and overlapped with Moiiffit basal subtype. Research Sponsor: Terry Fox Research Institute, BC Cancer Foundation, Pancreas Centre BC.

Clinical significance of monitoring KRAS in tissue and plasma of pancre- atic cancer patients. First Author: Fumiki Watanabe, Jichi Medical University, Saitama, Japan

Background: KRAS monitoring provides valuable information for early di- agnosis and prediction of treatment outcome in colorectal cancer. KRAS- mutation is observed in only half of colon cancer patients, whereas it is detected in 80-90% of pancreatic cancer patients. Therefore, investigating KRAS DNA in plasma by KRAS monitoring may be even more valuable in pancreatic cancer patients. In this study, we elucidated the clinical significance of KRAS monitoring in pancreatic cancer patients during treatment. Methods: KRAS in tumor tissues was analyzed during surgery samples by Sequenom MassARRAY (MSA) and had poorer OS compared to non-diabetic PDAC patients, independent of Moiiffit subtype, HR 3.2 (1.5-6.5), p < 0.001. Diabetics were more likely to have hypertension (64 v 11%, p < 0.001), dyslipidemia (57 v 16%, p=0.013), and to be older (61.5 ± 58 years, p=0.004) and smokers (71.4 v 21.6%, p=0.05). WGA revealed significant enrichment of heterozygous INSR copy loss in T2DM (69%) compared to all other patients (24%; p=0.03) and an enrichment of INSR copy loss for metastatic PDAC relative to resected PDAC in ICGC (35 v 18%, p=0.03). Heterozygous INSR copy loss (n = 17/54) was an independent predictor of worse OS (10.8 v 15.1 months, HR 2.29 (1.20-4.36), p=0.012), and it interacted with diabetes status (p=0.023). Moiiffit basal (vs. classical) subtype (n = 17/54, of which 8/17 have INSR copy loss) was also an independent predictor of worse OS (8 v 17 months, HR 2.29 (1.20-4.36), p=0.012). Whilst there was no interaction between INSR status and Moiiffit subtype on OS (p=0.727), INSR expression is lower in basal subtype, p<0.001. Conclusions: Presence of T2DM in our cohort is an independent predictor of worse OS, consistent with published literature. Alteration in the insulin signaling pathway with heterozygous copy loss of INSR was associated with poorer prognosis, diabetes development and overlapped with Moiiffit basal subtype. Research Sponsor: Terry Fox Research Institute, BC Cancer Foundation, Pancreas Centre BC.

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CEACAM6 as a candidate biomarker for pelareorep sensitivity in pancreatic adenocarcinoma (PDAC). First Author: Anne M. Noonan, The Ohio State University Comprehensive Cancer Center, Arthur G. James Cancer Hospital, Columbus, OH

Background: Pelareorep is a proprietary formulation of live, replication-competent, naturally-occurring Reovirus Type 3 Dearing strain. A randomized Phase II trial of pelareorep in combination with carboplatin and paclitaxel in first-line treatment of metastatic PDAC (NCT02880588) was performed. Although pelareorep did not improve the primary endpoint of progression-free survival compared to carboplatin and paclitaxel alone, impressive durable responses were seen in the pelareorep arm in some patients (pts). Further, prior studies have noted the immunomodulatory carcinogenic matrix metalloproteinase-1 associated cell adhesion molecule (CEACAM6/CD66c) as a receptor for specific viral subtypes. We thus speculated that altered CEACAM6 levels may be predictive for pelareorep sensitivity. Methods: Pre-treatment tissue biopsies were collected prior enrolment for all 73 pts on study. Evaluative pts with transcriptomic data was available for only 31 pts. RNA was purified from FFPE tissue and gene expression analysis was performed using SensationPlus FFPE Amplification and WT labelling kit and the Human Transcriptome Array 2.0. CEACAM6 protein expression was determined by immunohistochemistry. Differential gene expression and survival analysis were performed using R/Bioconductor. Appropriate corrections for multiplicity were performed. Results: When comparing extraordinary responders in the pelareorep treated arm to those with poor outcomes, low levels of pelareorep mRNA expression were associated with prolonged PFS in pelareorep-treated pts (adjusted p = 0.05). This effect was not seen in non-pelareorep treated pts. The luminal, but not the cytoplasmic immunohistochemistry, score, was highly correlated with mRNA expression levels of CEACAM6, p = 0.001. Modulation of CEACAM6 in vitro and in vivo are underway. Conclusions: CEACAM6 may be a candidate biomarker of sensitivity to pelareorep and, in theory, could improve viral trafficking of this compound in tumor cell. Clinical trial information: NCT02880588. Research Sponsor: U.S. National Institutes of Health, William Hall Fund for Liver and Pancreatic Cancer Research.

CEACAM6 as a candidate biomarker for pelareorep sensitivity in pancreatic adenocarcinoma. First Author: Satoru Furuhashi, Hamamatsu University School of Medicine, Hamamatsu, Japan

Background: Perineural invasion (PNI) is commonly seen in pancreatic ductal adenocarcinoma (PDAC) and worsens the postoperative prognosis. However, the detail mechanisms of PNI in PDAC remains unclear. Tenasin C (TNC), an extracellular matrix glycoprotein, is abundant in cancer stroma and modulates tumor progression. In this study, we hypothesized that TNC could enhance PNI in PDAC. The aim of this study was to investigate the roles of TNC in the tumor-nerve microenvironment of PDAC. Methods: We immunohistochemically examined TNC expression in 78 resected PDAC specimens. TNC staining intensity in perineural sites at the invasive front was classified as low or high, by examined TNC expression in 78 resected PDAC specimens. TNC staining intensity in perineural sites at the invasive front was classified as low or high. The luminal, but not the cytoplasmic immunohistochemistry score, was highly correlated with mRNA expression levels of CEACAM6, p = 0.001. Modulation of CEACAM6 in vitro and in vivo are underway. Conclusions: CEACAM6 may be a candidate biomarker of sensitivity to pelareorep and, in theory, could improve viral trafficking of this compound in tumor cell. Clinical trial information: NCT02880588. Research Sponsor: U.S. National Institutes of Health, William Hall Fund for Liver and Pancreatic Cancer Research.

748 Poster Session (Board #M15), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

The potential of Tenasin C in the tumor-nerve microenvironment to enhance perineural invasion and correlate with locoregional recurrence-related poor prognosis in pancreatic ductal adenocarcinoma. First Author: Satoru Furuhashi, Hamamatsu University School of Medicine, Hamamatsu, Japan

Background: Perineural invasion (PNI) is commonly seen in pancreatic ductal adenocarcinoma (PDAC) and worsens the postoperative prognosis. However, the detail mechanisms of PNI in PDAC remains unclear. Tenasin C (TNC), an extracellular matrix glycoprotein, is abundant in cancer stroma and modulates tumor progression. In this study, we hypothesized that TNC could enhance PNI in PDAC. The aim of this study was to investigate the roles of TNC in the tumor-nerve microenvironment of PDAC. Methods: We immunohistochemically examined TNC expression in 78 resected PDAC specimens. TNC staining intensity in perineural sites at the invasive front was classified as low or high, by comparison with adjacent non-cancerous tissues in the same section. The relevance between TNC expression and clinical pathological features were retrospectively analyzed. Furthermore, interactions between cancer cells and nerves after supplementation with TNC were investigated using in vitro coculture model with a PDAC cell line and neonatal mouse dorsal root ganglion (DRG). Results: High perineural TNC expression at the invasive front, seen in non-pelareorep treated pts. The luminal, but not the cytoplasmic immunohistochemistry score, was highly correlated with mRNA expression levels of CEACAM6, p = 0.001. Modulation of CEACAM6 in vitro and in vivo are underway. Conclusions: CEACAM6 may be a candidate biomarker of sensitivity to pelareorep and, in theory, could improve viral trafficking of this compound in tumor cell. Clinical trial information: NCT02880588. Research Sponsor: U.S. National Institutes of Health, William Hall Fund for Liver and Pancreatic Cancer Research.

749 Poster Session (Board #M16), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Molecular genetic changes in solid pseudopapillary neoplasms (SPN) of the pancreas. First Author: Elisa M. Rodriguez-Matta, University of Puerto Rico School of Medicine, San Juan, PR

Background: Solid Pseudopapillary Neoplasms (SPNs) of the pancreas are rare accounting for 1-2% of all pancreatic tumors. Previous studies had shown that a pathogenic mutation of the CTNNBI gene is present in over 90% of the SPN tumors with very limited information available on the specific molecular changes present in SPN. Here we report the results of next generation genetic testing of a large series of SPN tumors from the Foundation Medicine database. Methods: Foundation Medicine database from 07/2012 to 04/2019 was reviewed. A total of 31 cases of SPN tumors were identified out of 12,892 cases (93%) had a CTNNBI mutation, one had a CDKN2A mutation and the other had no detectable mutations. Most cases had additional mutations aside from the CTNNBI, the most common were TPS3 (3 cases, 9.6%) and LRRP2 (2 cases, 6.4%). Other accompanying mutations were seen just once. Twenty-five percent of these cases had actionable gene mutations, each found in one case including: MSH2, BRCA2, ATM, XRCC3, ATRX, PTEN, ESRT, CDKN2, and PIK3CA.

Conclusions: Next generation genetic testing of SPN tumors involves the clinical benefit since it identifies actionable mutations in 29% of the cases. Research Sponsor: None.
Early progression (progr) in patients (pts) with metastatic pancreatic cancer (mPaC) and a germline BRCA mutation (gBRCAm): Phase III POLO trial of olaparib (O) versus placebo (P). 

First Author: Teresa Macarulla, Vall d’Hebron University Hospital and Vall d’Hebron Institute of Oncology, Barcelona, Spain

Background: In POLO (NCT02184195), maintenance O was associated with significant progr (by blinded independent central review) or death within 4 m of randomization. A stepwise logistic regression model included baseline (BL) factors age, albumin, lactate dehydrogenase (LDH), global health status (GHS) and physical functioning (PhysF) as continuous variables, and discrete variables listed in the Table. Results: 62/154 randomized pts (40%) were defined as early progressors (EP) (Table). Due to missing BL data, the multivariate analysis included 127 pts (56% EPs [44%]). Lower BL PhysF score (continuous) was significantly associated with early progr (P = 0.02); no difference for partial/complete response (PR/CR) vs stable disease (SD).

Conclusions: While small sample size limited analysis power, PhysF score was the only BL factor significantly associated with early progr in pts with a gBRCAm and mPaC in the POLO trial of maintenance O vs P. Clinical trial information: NCT02184195. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp, subsidiary of Merck & Co, Inc, Kenilworth, NJ, USA.

Pancreatic adenocarcinoma: Clinical associations, treatment, and outcomes. First Author: Mindy L. Hartgers, Mayo Clinic, Rochester, MN

Background: Pancreatic adenocarcinomas (PASC) are rare malignancies, with limited evidence regarding best treatment options. The Mayo Clinic Pancreatic Cancer SPORE Registry was utilized to compare/contrast outcomes for pancreatic cancers with a squamous component to pancreatic ductal adenocarcinoma (PDAC). Methods: Patients were identified from the SPORE Registry (2000-2019), and were reviewed and confirmed by expert pathologists. Demographic and clinical information was ascertainment from medical records and risk factor questionnaires. A case control study of patients with PASC vs PDAC was conducted. PASC patients were also followed for outcome and treatment records were extracted. Results: Of 2584 total patients with pancreatic cancers, 45 cases of PASC and 2438 with PDAC were identified. There were no differences in age (median 69 vs 67 years, p=0.42), sex (male 64.4% vs 56.6%, p = 0.29), BMI (27.41 vs 27.78 kg/m², P=0.50), or ever-smoking (61.0% vs 55.3%, P=0.47), with a borderline association with reported diabetes (17.8 vs 29.9%, p =0.08). Compared to PDAC, PASCs were more likely to involve the body/tail (48.9 vs 33.2%, P = 0.02) and had poorer overall survival, adjusted for age, gender, and stage (median 7.1 vs 12.8m, HR 1.89, P=0.0004). Of 9 PASC pts treated with neoadjuvant intent, 4 were surgically resected, median survival was 7 months. Eleven pts underwent upfront surgery, with variable adjuvant treatments. Median OS post surgery was 18m (range 7-51). Of 14 patients presenting with metastatic disease, median survival was 4.5 m (range 1-22). With regard to systemic chemotherapy, for neoadjuvant or metastatic disease median duration of treatment was 7 months (range 0.5-29). Median adjuvant neoadjuvant or metastatic disease was 18m (range 2-6m) for FOLFIRINOX (N13). Conclusions: The diagnosis of PASC carries an even poorer outcome than pancreatic adenocarcinoma. Tumors are more likely to arise in the distal pancreas, and patients may be less likely to report associated diabetes. Limited antitumor activity was noted with multi-agent chemotherapeutic regimens. Prospective trials will be needed to clarify choice of regimen in the future. Research Sponsor: None.

Prognostic utility of inflammation biomarkers in a PDAC trial involving the human anti-CTGF antibody pamrevlumab. First Author: Mark D. Sternlicht, FibroGen, Inc., San Francisco, CA

Background: Pancreatic ductal adenocarcinomas (PDAC) often exhibit desmoplasia, elevated baseline (BL) factors age, albumin, lactate dehydrogenase (LDH), global health status (GHS) and physical functioning (PhysF) as continuous variables, and discrete variables listed in the Table. Results: 62/154 randomized pts (40%) were defined as early progressors (EP) (Table). Due to missing BL data, the multivariate analysis included 127 pts (56% EPs [44%]). Lower BL PhysF score (continuous) was significantly associated with early progr (P = 0.02); no difference for partial/complete response (PR/CR) vs stable disease (SD).

Conclusions: While small sample size limited analysis power, PhysF score was the only BL factor significantly associated with early progr in pts with a gBRCAm and mPaC in the POLO trial of maintenance O vs P. Clinical trial information: NCT02184195. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp, subsidiary of Merck & Co, Inc, Kenilworth, NJ, USA.

Noninvasive comprehensive genomic profiling from plasma ctDNA in pancreatic cancer patients. First Author: Danielle S. Bitterman, Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA

Background: The use of comprehensive genomic profiling (CGP) is increasing in pancreatic ductal adenocarcinoma (PDAC) as knowledge improves regarding molecular drivers of tumorigenesis and effective targeted therapies emerge. However, adequate tissue sampling is often limited. Plasma-based CGP offers a non-invasive approach to assess biomarkers that may impact treatment decisions. Methods: We retrospectively evaluated genomic and clinical data from 97 PDAC patients with circulating tumor DNA (ctDNA) testing from 9/2016-8/2019 (Guardant Health, Inc.). ctDNA alterations were detected in 82% (40/49), test failure in 14% (7/49), and no alterations detected in 8% (8/49). Of these patients, tissue-based CGP showed that 71% (35/49) of patients had potentially actionable alterations (2 activating BRAF SVNS, 1ERBB2 CNV, 1ERBB2 activating SVN, 1KRAS G12C, and 3 indels in Homologous Replication Deficiency genes). Median turnaround time was 8 days. 51% (49/97) of patients had both plasma-based CGP and tissue-based CGP. Of these patients, tissue-based CGP detected 1 actionable in 82% (40/49), test failure in 14% (7/49), and no alterations detected in 4% (2/49). Conclusions: Plasma-based CGP detected ctDNA alterations in 90% of samples tested and 90% of all samples. Potentially actionable mutations were found in 8% of patients, with prompt processing time allowing for rapid decision making. Research Sponsor: None.
Exceptional responses to ipilimumab/nivolumab (ipi/nivo) in patients (pts) with refractory pancreatic ductal adenocarcinoma (PDAC) and germline BRCA or RAD51 mutations. First Author: Greetel Terrero, Jackson Health System, Miami, FL

Background: Immune checkpoint inhibitors (ICIs)’ have not shown meaningful clinical activity in unselected patients (pts). BRCA-deficient tumors have increased genomic instability, including increased tumor mutation burden (TMB), more tumor-infiltrating immune cells, and enrichment of a T cell-inflamed signature. We hypothesized that pts with mutations in BRCA or other homologous recombination repair genes may be sensitive to ICIs.

Methods: Utilizing the IRB-approved PDAC database at the University of Miami, we identified pts with relapsed/refractory PDAC with pathogenic germline mutations who were treated with combination ICI’s (ipi 1mg/kg and nivo 3mg/kg every 21 days followed by nivo 240mg every 2 weeks).

Results: Five pts were identified (1 BRCA1, 2 BRCA2, 1 RAD51C and 1 RAD51D). Among the 3 evaluable pts, there was one complete response (CR), one partial response (PR) and one had progressive disease (PD). The pt with a CR had BRCA1; he had resection followed by adjuvant gem/cape and had a biopsy-proven recurrence in the lung and retroperitoneum 8y after the end of adjuvant therapy. He received ipi/nivo at recurrence and achieved a CR, ongoing for 17m on nivo maintenance. The patient with a PR had RAD51C; he was diagnosed with mPDAC and received FOLFOXIRINOX for 6m, followed by nabpaclitaxel on a trial for 12m. Upon PD, the disease quickly progressed on Sflu/liposomal irinotecan, gemcitabine/nab-paclitaxel/cisplatin and FOLFOXIRINOX. He then started ipi/nivo with immediate improvement in pain and tumor markers. A radiological PR was seen after 2 doses and is ongoing for 3m with continued clinical and tumor marker improvement. The 3rd evaluable pt had BRCA2 and had PD with an exponential rise in tumor markers accompanied by clinical deterioration. Response data on the final two pts were pending at the time of submission and will be presented at the meeting.

Conclusions: In this biomarker selected cohort, 2 out of 3 evaluable pts with PDAC had impressive responses to ipi/nivo. PDAC has generally been refractory to ICI therapy but this series suggests that this subgroup may be responsive to ICIs. Further evaluation is warranted. Research Sponsor: None.

Patterns of failure after adjuvant stereotactic body radiation therapy in patients with pancreatic cancer with close or positive margins. First Author: Ankur K. Patel, Department of Radiation Oncology, UPMC Hillman Cancer Center, University of Pittsburgh School of Medicine, Pittsburgh, PA

Background: There is no consensus on treatment volumes for stereotactic body radiation therapy (SBRT) in patients with pancreatic cancer (PCa). Herein, we report patterns of failure following adjuvant SBRT for close/positive margins in patients with pancreatic cancer, which may inform appropriate target volume design for SBRT.

Methods: An IRB-approved retrospective review of patients with PCa treated with adjuvant SBRT for close/positive margins from 2009-2018 was conducted. Patterns of failure were assessed by review of imaging and were defined as local (LF), regional (RF), local and regional (LRF), or distant (DF). The Kaplan-Meier method was used to calculate long-term failure rates. In-field failures were defined as failures within defined LF/RF/LRF (planning target volumes). The location of LFs was compared to the RTOG consensus volumes for adjuvant treatment of PCa to determine if conventional radiation volumes would have included the LF. Results: Seventy-six patients were treated with adjuvant SBRT for close (51.3%) or positive (48.7%) margins, with a median follow-up of 17.0 months (interquartile range [IQR] 7.4-28.3 mos.). Adjuvant SBRT was delivered at a median of 2.2 months after surgery (IQR 1.7-3.0 mos.). Most patients (81.6%) received 36 Gy in 3 fractions. The median PTV volume was 17.8 cc (IQR 12.3-25.2 cc). Upon examination of first failure sites, crude rates of isolated LF, isolated RF, isolated LRF, and DF +/- LF or RF were 9.2%, 6.6%, 2.6%, and 56.6% respectively; 2-year rates were 12.4%, 11.5%, 7.0%, and 66.5%, respectively. Thirty-two patients (42.1%) developed a LF at some point during follow-up. Of 28 LFs with available plans and imaging, 21.4% were in-field failures, while the remainder were outside (60.1%) or partially outside (17.9%) the PTV. Most LFs outside the PTV (90.9%) would have been encompassed by the RTOG consensus target volumes for postoperative conventional radiation.

Conclusions: In patients with PCa who received adjuvant SBRT for close/positive margins, the majority of LFs are outside the PTV. Future trials involving SBRT or hypofractionated radiation should consider expansion of treatment volumes if feasible. Research Sponsor: None.

Evaluation of the ratio of plasma fibrinogen to platelet in resectable pancreatic cancer. First Author: Yusuke Arakawa, Tokushima University, Tokushima, Japan

Background: Several prognostic factors were reported in pancreatic cancer such as neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and fibrinogen/platelet ratio (FPR). NLR and PLR are well known to be associated with poor overall survival (OS) and progression-free survival (PFS) in pancreatic cancer patients. FPR was reported as one of the factors that can predict the prognosis of pancreatic cancer. Other ratios such as neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and fibrinogen/platelet ratio (FPR) were assessed in this study.

Methods: Between 2004 and 2019, one hundred and sixty-three patients in our institution with curative resection for pancreatic cancer were enrolled in this retrospective study. The cases of non-curative resection were excluded.

Results: In this study, the FPR was evaluated in patients with resectable pancreatic cancer. The FPR was compared with the plasma fibrinogen and platelet ratios. The FPR was also compared with other ratios such as neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and fibrinogen/platelet ratio (FPR). The FPR was found to be a significant prognostic factor in patients with pancreatic cancer. The FPR was found to be a significant prognostic factor in patients with pancreatic cancer.

Conclusions: The FPR was found to be a significant prognostic factor in patients with pancreatic cancer. The FPR was found to be a significant prognostic factor in patients with pancreatic cancer. The FPR was found to be a significant prognostic factor in patients with pancreatic cancer.
Analysis of panreatobiliary adenocarcinoma (PBC) treatment response and resistance utilizing circulating tumor DNA (ctDNA). First Author: Madhulika Banerjee, University of Arizona College of Medicine, Tucson, AZ

Background: Accurate disease monitoring in PBC is instrumental for optimal therapeutic decision-making. CA 19-9 is the most utilized biomarker, though it has limited sensitivity. Specifically, it can be falsenegative and cannot be used in CA 19-9 non-secretors (n=5). ctDNA is a potentially helpful monitoring aid and surrogate for PBC n-S. Serial ctDNA could identify emerging resistant driver mutations. Our study prospectively examined ctDNA in PBC patients receiving treatment and retrospectively correlated it with clinical response. Methods: We performed genomic testing of ctDNA from metastatic PBC patients’ plasma from 11/2016 to 08/2019. This included 77 patients, of those, 18 had >1ctDNA measurement with 49 correlative data points in total. Demographics, serial CA 19-9 levels and imaging results were collected. ctDNA analysis by parallel sequencing of amplified target genes (74) using Guardant360 was obtained. We correlated imaging and CA 19-9 responses with molecular alterations in patients receiving systemic chemotherapy. Descriptive statistics and logistic regression of the data was performed. Results: Of those included, median age was 66 yo, 50% male, and 92% pancreatic ductal adenocarcinoma. Baseline ctDNA showed 103 mutations including TP53 12.6%, KRAS 9.7%, MET 6.8%, APC, ARID1A and NFI 4.8% each, and others < 3%. 44% of patients were n-S with 75% having both TP53 and KRAS mutations, APC, ARID1A, and NFI were only present in n-S. 91% vs 90% KRAS and 84% vs 78% TP53 of n-S and secretors (S), respectively, had correlation between ctDNA levels and imaging response. S TP53 and KRAS mutations correlated to CA19-9 levels and scans in 76% and 70% responses. New TP53 subclonal variant mutations were the most common resistance mutations for all progresses (75%). A logistic regression model of imaging progression on change in CA19-9 secretion and TP53 or KRAS expression was not statistically significant. Conclusions: Baseline ctDNA level changes (TP53 and KRAS) can potentially act as a biomarker of response in PBC, specifically in n-S. TP53 subclonal mutations were the most common resistant alterations at progression and can be explored as future targets. This is being explored in larger prospective trials. Research Sponsor: None.

Impact of CDKN2A/B status in pancreatic cancer (PC). First Author: Kaitlin Annunzio, Medical College of Wisconsin, Milwaukee, WI

Background: PC is a lethal disease with limited treatment options. We utilized Comprehensive Genomic Profiling (CGP) to identify putative prognostic and/or predictive biomarkers. Methods: We retrospectively reviewed PC patients (pts) at our institution who underwent CGP (n = 103) from 11/2016 to 08/2019. CGP was performed on hybrid-capture, adaptor ligation-based libraries for up to 315 genes plus 47 introns from 19 genes frequently rearranged in cancer. Pt subtypes were described as the first systemic therapy. Median overall survival for patients with LPC, LAPC, and mPC was 30.7, 28.8 and 9.6 months respectively. Thirty-eight (91%) pts with LAPC underwent curative intent surgery compared to 15 (65%) pts with LAPC (p = 0.019). Thirty-five (95%) pts with wild type (WT) CDKN2A and 47 (94%) pts with WT CDKN2B underwent curative intent surgery compared to 13 (65%) at 60 (9%) and 47 (94%) pts with CDKN2A and CDKN2B respectively (n = 0.03 and p < 0.0001 respectively). The response to chemotherapy was statistically significantly higher in pts with WT CDKN2A (53%) and CDKN2B (48%) compared to pts with GAs in CDKN2A (19%) and CDKN2B (12%) (p = 0.03 and p = 0.05, respectively). Conclusions: GAs in CDKN2A/B may have a predictive and possibly a prognostic impact. The clinical validity and biological relevance of these findings need to be further explored in larger studies. Research Sponsor: U.S. National Institutes of Health.
Poster Session (Board #N7), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Analysis of associations of CXCRI3 ligands with immune microenvironment and aggressiveness in murine and human pancreatic ductal adenocarcinoma. First Author: Andrew Cannon, University of Nebraska Medical Center, Omaha, NE

Background: The complex milieu of cytokines within pancreatic ductal adenocarcinoma (PDAC) promotes tumor progression and immune suppression thereby contributing to the dismal prognosis of patients with PDAC. The roles of many cytokines, including CXCRI3 ligands, in PDAC have not been thoroughly investigated. Methods: Bioinformatics analyses of PDAC microarray and TCGA datasets were used to identify cytokines overexpressed in PDAC, their association with patient survival as well as the expression of cognate cytokine receptors. Comparative analysis of cytokine expression in Kras<sup>LSL-G12D</sup>-PDAC, Kras<sup>LSL-G12D</sup>-Pdx1-Cre (KPC) and Kras<sup>LSL-G12D</sup>-Pdx1-Cre (KC) murine PDAC models were used to validate these findings. Pathway and CIBERSORT analyses were employed to determine mechanistic basis of altered survival associated with cytokines of interest. Results: Of the 149 cytokines analyzed, CXCRI3 ligands CXCL9 and CXCL10 were highly and consistently overexpressed in PDAC datasets. Concurrently, CXCL9, CXCL10 and PF4 were overexpressed in the aggressive KPC murine model compared to the indolent KC model. CXCRI3 showed robust expression in PDAC in microarray, TCGA and IHC analyses. Interestingly, high expression of CXCRI3 ligands was associated with shorter overall survival (p = 0.04 for CXCL9, 10 and 11 and p = 0.02 for PF4) while high expression of CXCR3 was associated with increased overall survival (p = 0.03). Pathway analysis of genes correlated with CXCRI3 and/or its ligands showed that CXCRI3 ligands may promote T-cell exhaustion (p < 0.001). Finally, CIBERSORT analysis of TCGA data demonstrated that high CXCR3 expression was associated with increased CD8<sup>+</sup> and naive B-cell signatures and decreased Treg cells signatures. High CXCR3 ligand expression was associated with increased CD8<sup>+</sup> T-cell, and M1 macrophage, and loss of NK-cell signatures (< 0.05).

Conclusions: CXCRI3 ligands are overexpressed in PDAC and are associated with poor survival, likely related to alterations in tumor immune infiltrate activity and may represent targets to augment anti-tumor immunity. Research Sponsor: U.S. National Institutes of Health.

Poster Session (Board #N8), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Serum glycoproteomic-based liquid biopsy for the detection of pancreatic ductal adenocarcinoma. First Author: Pashtoon Murtaza Kasi, Mayo Clinic, Jacksonville, FL

Background: Non-invasive biomarkers with high sensitivity and specificity would be of great value for patients with Pancreatic Ductal Adenocarcinoma (PDAC). This would aid in early detection and serve other purposes that liquid biopsies’ are being explored in. Besides circulating tumor DNA (ctDNA) and methylolation markers, glycosylation markers hold great potential promise. We developed a novel workflow using high-resolution quantification of site-specific protein glycosylation by liquid chromatography and tandem mass spectrometry to evaluate the clinical utility of glycoproteomics signature for patients with PDAC. Methods: Serum samples from newly diagnosed PDAC patients and controls were obtained from a commercial biobank (Indiumed, Hamburg, Germany), and a panel of 504 glycan motifs, representing 73 previously reported proteomic markers, was determined. Age-adjusted general linear regression models were used to evaluate the differential abundance of each marker, and stepwise variable selection was used for model construction. Results: We analyzed 45 PDAC and 136 control samples. PDAC patients (60% male) had a mean age of 67 (±11 years) with 4.4%, 71.1%, 4.4% and 20% at stage 1, 2, 3, 4, respectively. Controls were with benign history after pelvic mass surgery; with a mean age of 61 (±11 years). Twenty-six glycopeptidic markers showed statistically highly significant differential abundance among cases and controls (p<4e-4 each) and were highly reproducible(Pearson’s r > 0.85), which were glycoformes in proteins that have previously been found to be associated with PDAC. Fourteen of these markers displayed >0.8 area under the curve of the receiver operating characteristic (AUC). Multivariable logistic regression modeling with backward selection yielded a classification model with an AUC of 0.94 (95% CI: 0.89-0.99), sensitivity of 91% (95% CI: 75-97%) and specificity of 86% (95% CI: 81-92%). Conclusions: Circulating glycoproteomic biomarkers may be useful in the early detection and clinical management of PDAC patients; offering a new platform to explore and validate. Research Sponsor: InterVenn.

Poster Session (Board #N9), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Genomic associations in metastatic pancreatic cancer (mPC). First Author: Anil Kumar Rengan, Temple University Hospital, Philadelphia, PA

Background: mPC is an aggressive cancer, and molecular profiling provides further insight into pathogenesis and treatment. We sought to illustrate the molecular landscape of mPC in relation to post-metastatic survival and VTE incidence. Methods: With IRB approval, we retrospectively analyzed charts of mPC patients who underwent molecular profiling. Fisher’s exact test (categorical) and Mann-Whitney test (continuous) were used to compare groups. Log-rank test, Cox proportional hazards model and weighted Cox regression were used for survival analysis. Results: Between 2009 and 2018, 98 out of 902 mPC patients (19.5%) underwent molecular testing. Concurrent KRAS and TP53 mutations were found in 62.3% of patients (24.0% KRAS and 0.5% TP53). Concurrent KRAS and TP53 mutations were positively associated with VTE (OR 2.55 and 2.71, respectively; p < 0.05). There was no association between any mutation and metastatic site. Negatively, there was a significant negative association between tobacco use and the development of VTE (OR 0.43 and 0.30, respectively; p < 0.05). Finally, CIBERSORT displayed age-adjusted genotype markers, was determined. Age-adjusted genectic associations were employed to determine mechanistic basis of altered survival associated with cytokines of interest. Results: Of the 149 cytokines analyzed, CXCRI3 ligands CXCL9 and CXCL10 were highly and consistently overexpressed in PDAC datasets. Concurrently, CXCL9, CXCL10 and PF4 were overexpressed in the aggressive KPC murine model compared to the indolent KC model. CXCRI3 showed robust expression in PDAC in microarray, TCGA and IHC analyses. Interestingly, high expression of CXCRI3 ligands was associated with shorter overall survival (p = 0.04 for CXCL9, 10 and 11 and p = 0.02 for PF4) while high expression of CXCR3 was associated with increased overall survival (p = 0.03). Pathway analysis of genes correlated with CXCRI3 and/or its ligands showed that CXCRI3 ligands may promote T-cell exhaustion (p < 0.001). Finally, CIBERSORT analysis of TCGA data demonstrated that high CXCR3 expression was associated with increased CD8<sup>+</sup> and naive B-cell signatures and decreased Treg cells signatures. High CXCR3 ligand expression was associated with increased CD8<sup>+</sup> T-cell, and M1 macrophage, and loss of NK-cell signatures (< 0.05).

Conclusions: CXCRI3 ligands are overexpressed in PDAC and are associated with poor survival, likely related to alterations in tumor immune infiltrate activity and may represent targets to augment anti-tumor immunity. Research Sponsor: U.S. National Institutes of Health.

Poster Session (Board #N10), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

The effect of TGF-β on PD-L1 expression on PDAC TAMs. First Author: Katarzyna Trebska-McGowan, University of Tennessee Health Science Center, Memphis, TN

Background: Pancreatic Ductal Adenocarcinoma (PDAC) has less than a 10% five year survival and will become the second leading cause of US cancer mortality in the next decade. Immunotherapy, such as checkpoint inhibition against increased T-cell death ligand (PD-L1) has not been successful in treatment of PDAC patients. Both tumor associated macrophages (TAMs) and the TGF-β protein are ubiquitous in PDAC tumors. We hypothesize that TGF-β increases the overall number of TAMs and degree of PD-L1 expression of TAMs in PDAC tumors. In this study, we have a mouse pancreatic cancer cell line derived from a genetically engineered mouse model (KPC mice that spontaneously implanted this cell line into the pancreas of immunocompetent C57BL/6 (B6) mice. In groups of 5 each, mice were treated with saline (control) or TGF-β. TAMs expressing PD-L1 in the pancreas and metastatic lesions in the liver. Results: A percent of leukocytes in the tumor, PDAC liver metastases had more TAMs compared to tumors in the pancreas (33 ± 5% vs 10 ± 4%, P = 0.001). Compared to controls, TGF-β treatment significantly increased the percent of PD-L1 expressing TAMs (32 ± 6% vs 12 ± 5%, P = 0.013, see Figure) in the pancreas but no effect was evident on TAM density. In liver metastases, treatment with TGF-β decreased the overall TAM density (P = 0.039) but did not affect the number of PD-L1 positive TAMs. Conclusions: TGF-β plays a pivotal role in the progression of PDAC and demonstrates context dependent activity. Our results suggest that an immunosuppressive effect mediated by PD-L1 expression on TAMs may be initiated by TGF-β. Future investigations should focus on understanding the role of the PDAC-TAM interaction to develop effective immune therapies for PDAC patients. Research Sponsor: SSAT - Society for Surgery of Aimentary Track.
Survival outcomes of pancreatic intraepithelial neoplasm (PanIN) versus intraductal papillary mucinous neoplasm (IPMN) associated pancreatic adenocarcinoma. First Author: Timothy McGinnis, University of Kansas Cancer Center, Westwood, KS

Background: Pancreatic intraepithelial neoplasms (PanINs) and intraductal papillary mucinous neoplasms (IPMNs) are common pancreatic adenocarcinoma precursor lesions. However, data regarding their respective associations with prognosis is lacking. Methods: We retrospectively evaluated 72 resected pancreatic adenocarcinoma cases at the University of Kansas between Aug 1, 2009 and March 2019. Patients were divided into either one of two groups, PanIN or IPMN, based on the results of the surgical path report. We compared baseline characteristics, overall survival, and progression free survival between the two groups, as well as OS and PFS based on local or distant tumor recurrence. Results: 52 patients had PanIN and 20 patients had IPMN. Demographic and baseline characteristics are as follows (PanIN/IPMN): Median age 62.5/69, Gender (male) 63%/65%, ECOG status (0-1) 98%/85%, pancreatic head tumors 87%/70%, pancreatic body tumors 6%/15%, pancreatic tail tumors 7%/15%, Abnormal CA19-9 diagnosis 79%/67%, Comorbidity Index 5/5 respectively. Median PFS was 26.2 months (95% CI: 21.4-31.0) for PanIN and 74.3 months (95% CI: 51.7-132.9) for IPMN (p < 0.004). Median OS was 70.3 months (95% CI: 35.4-105.2) for PanIN and 78.8 months (95% CI: 33.2-124.4) for IPMN (p = 0.03). Within the PanIN group, median OS after recurrence was 73.5 months (95% CI: 68.8-73.4) for local recurrence and 46.7 months (95% CI: 39.2-54.2) for distant recurrence (p = 0.330). Conclusions: Patients who had a IPMN associated pancreatic cancer had better PFS and OS when compared to patients with PanIN associated pancreatic cancer. In patients with PanIN associated cancer that recurred, OS was better with local recurrence compared to distant recurrence but did not meet statistical significance. The results need to be validated in a larger cohort. Research Sponsor: None.

Impact of surveillance among patients with resected pancreatic cancer following adjuvant chemotherapy. First Author: Selina Wong, BC Cancer Agency, Vancouver, BC, Canada

Background: Pancreatic adenocarcinoma carries a poor prognosis and high risk of recurrence even after surgery and adjuvant chemotherapy (AC). Guidelines recommend against routine surveillance imaging due to lack of evidence supporting a survival benefit. With efficacious post-treatment chemotherapy options, it is unclear whether surveillance scans allow for early detection of asymptomatic disease and therefore an opportunity to offer fit patients chemotherapy. We describe the patterns of surveillance in patients followed at a Canadian provincial cancer agency and determine whether routine imaging after AC is associated with receipt of palliative chemotherapy (PC). Methods: A retrospective review was completed to identify patients treated at British Columbia (BC) Cancer centres between January 1, 2010 and December 31, 2016 who had undergone curative intent resection and received at least one cycle of AC. Baseline characteristics, number of scans done after completing AC to recurrence, and PC were collected. Logistic regression analysis was performed. Results: A total of 151 patients followed at BC Cancer were identified. Patients who recurred within 28 days after AC were excluded, leaving 142 patients, of which 115 patients had recurrence. We defined 2 cohorts based on number of scans done between completion of AC and recurrence: those with 0-1 scans were “symptomatic” recurrences (22 patients, median age 68y, 64% female, and 72% node-positive) and those with >1 scan were “surveillance” recurrences (93 patients, median age 64y, 43% female, and 81% node-positive). Patients who underwent surveillance scans were more likely to receive PC at time of recurrence, though statistical significance was not reached (OR 2.31, 95% CI 0.75-6.58, p = 0.17). Conclusions: Despite guidelines, the majority of patients treated in BC underwent surveillance imaging. Within the limits of our sample size, we demonstrated a trend towards increased likelihood of receiving PC in patients who receive surveillance scans following AC. With efficacious PC options available, studies to evaluate whether receipt of PC in asymptomatic recurrences detected on imaging translates into improved survival and/or quality of life are warranted. Research Sponsor: None.

Association of neutrophil, platelet, and lymphocyte ratios with prognosis in metastatic pancreatic cancer. First Author: Jessica Allen, University of Kansas Medical Center, Kansas City, KS

Background: High mortality associated with pancreatic ductal adenocarcinoma (PDAC) warrants research into prognostic factors. We examined the relationship between the daily rate of change of CA19-9 over the first 90 days of treatment (DRC90) and pretreatment levels of neutrophils, lymphocytes, and platelets with overall survival (OS) and progression free survival (PFS) in patients with stage IV PDAC that received chemotherapy. Methods: We retrospectively evaluated 102 locally advanced and metastatic PDAC patients treated at KU Cancer Center between Jan 2011 and Sep 2019. We compared the ratio of pretreatment absolute neutrophil count to pretreatment absolute lymphocyte count (NLR) and the ratio between pretreatment platelet count to pretreatment absolute lymphocyte count (PLR) with OS and PFS. We also compared DRC90 to OS and PFS. Log-rank trend test using the mean of NLR, PLR, and DRC90 as the threshold for two groups within each variable. Results: Baseline demographics are shown in the table. Pts with median NLR (4.6) had significantly lower OS (p = 0.0444) and PFS (p = 0.0483) than Pts below the mean. Pts with PLR ≤ mean (3.9) did not have significantly different OS (p = 0.507) or PFS (p = 0.643) than Pts below the mean. Pts with DRC90 ≤ mean (% -1) did not have significantly different OS (p = 0.342) or PFS (p = 0.313) than Pts below the mean. Conclusions: Pts with NLR ≤ median (4.6) had significantly lower OS and PFS than Pts with NLR below the mean. This implies the possibility of NLR as a prognostic marker in PDAC that could guide treatment approach but needs validation in a larger cohort. Research Sponsor: None.

Clinical outcomes of first-line FOLFIRINOX versus gemcitabine plus nab-paclitaxel in metastatic pancreatic cancer at the Yale Smilow Healthcare System. First Author: Timil Patel, Yale School of Medicine, New Haven, CT

Background: FOLFIRINOX (FFX) and Gemcitabine plus nab-paclitaxel (GN) are established first line (IL) therapies for metastatic pancreatic cancer (MPC) but real-world data on their comparative effectiveness is limited. Methods: All cases of MPC treated with IL FFX or GN at Yale Smilow Healthcare System were manually abstracted from the electronic medical record. Categorical and continuous variables were compared between IL FFX and GN cohorts via the Chi-squared and Wilcoxon rank-sum tests. Median OS was calculated by the Kaplan-Meier method. Results: We identified 363 MPC pts treated with IL FFX or GN; 269 (74%) pts were treated with FFX and 94 (26%) with GN as IL therapy. 204 (56%) pts were treated at the main campus and 159 (44%) at a CCC. Demographic and baseline characteristics (FFX/GN) were as follows: gender (male) 55%/49%; race (white) 82% / 77%; age; < 76 90%/79% (P < 0.001), 332 (99%) of pts received no prior therapy; 21 (6%) had prior surgery plus adjuvant gemcitabine and 10 (3%) had surgery alone. 98% of FFX-treated pts were treated with upfront DR, compared to 78% of GN-treated pts (P = 0.003). 78% and 53% of FFX and GN-treated pts, respectively, had subsequent DR (P = 0.001). Median TTD was 4.8 months with FFX and 3.4 months with GN (P = 0.0029) and the median OS was 11.3 months with FFX versus 7.2 months with GN (P < 0.0001). After 1L, 33% and 61% of FFX- and GN-treated pts, respectively, received no further chemotherapy (P = 0.001). Conclusions: In the largest manually abstracted retrospective analysis to date, MPC pts treated with IL FFX were younger, more likely to receive 2L therapy, and had increased survival compared to pts treated with GN. The OS of pts treated with FFX was similar to the OS reported by Conroy et al despite upfront dose attenuations in 98% of pts. A randomized trial is needed to confirm optimal sequencing of chemotherapy in MPC. Research Sponsor: None.

First Author: Timil Patel, Yale School of Medicine, New Haven, CT

Background: Patients (pts) receiving treatment for metastatic pancreatic cancer (MPC) experience significant symptoms, treatment related side effects and psychosocial burden. The ASCO guidelines recommend early palliative care consultation (PCC) to improve quality of life and survival. However, limited real-world data is available regarding the timing of PCC, hospice enrollment and location of death (LOD) in pts with MPC. Methods: We conducted a retrospective observational analysis of pts treated with chemotherapy for MPC at the Yale Smilow Cancer Hospital and affiliated community cancer centers (CCC) from January 2011 to April 2019. Patient demographics, treatment dates, initial PCC, enrollment of hospice at the time of death and LOD were manually abstracted from the electronic medical record. Univariate and multivariable logistic regression analyses were conducted to predict for PCC and death outside the hospital. Results: Of 363 pts identified with MPC who received chemotherapy, 38% (138) had a PCC. 67% (93) of patients’ initial PCC was in the hospital versus 33% (45) in the outpatient setting. The median time from the start of first-line chemotherapy to the first PCC was 5.2 months (interquartile range [IQR] 1.2–12.9). The median time from the first PCC to death was 1.5 months (IQR 0.5–4.4). At the time of our analysis, 300 pts had died and of those 76% (229) were enrolled on hospice at the time of death while 24% (71) were not. With respect to LOD, 47% (139) of pts died at home with hospice, 31% (94) at an inpatient hospice facility and 22% (67) died in the hospital. Female gender was associated with an increased likelihood of a PCC (HR 1.78, 95% CI 1.07–2.94, P = 0.026). Pts treated at a CCC were less likely to have a PCC (HR 0.21, 95% CI 0.12–0.36, P < 0.001). A PCC was not associated with a higher likelihood of death outside the hospital (HR 1.39, 95% CI 0.75–2.29, P = 0.346). Conclusions: Although most pts with MPC enrolled on hospice, PCC is generally underutilized. In fact, many pts receive PCC near the end of life and in the hospital. Further studies are warranted to determine how best to incorporate early PCC to maximize supportive care for pts with MPC. Research Sponsor: None.

Prognostic significance of familial pancreatic cancer after surgery. First Author: Koji Tetzuka, Division of Hepato-Biliary-Pancreatic Surgery, Shizuoka Cancer Center, Shizuoka, Japan

Background: Familial pancreatic cancer (FPC) is defined as two first-degree relatives with pancreatic cancer. It is known that the risk of developing pancreatic cancer increases in those who have a family history of pancreatic cancer in first-degree relatives. However, the prognostic significance of FPC after surgery is not fully understood. Methods: Patients who underwent pancreatectomy for pancreatic ductal carcinoma between January 2008 and December 2016 were retrospectively reviewed. The prognostic significance of FPC was analyzed in 423 patients. A total of 423 patients underwent pancreatectomy for pancreatic ductal carcinoma. FPC was identified in 32 (7.6%) patients. Recurrence occurred in 72% of all resected cases and in 88% of FPC-resected cases. Multivariate analysis revealed FPC (hazard ratio [HR] 1.60; P = 0.010), microscopic venous invasion (HR 1.64; P = 0.010), p16 negativity (HR 1.39; P = 0.010), and R1 resection (HR 1.65; P = 0.010), and lack of adjuvant chemotherapy (HR 2.27; P < 0.001) as independent predictors for recurrence-free survival (RFS). The univariate analysis revealed that FPC is significantly associated with worse overall survival (OS) (P = 0.018). The multivariate analysis showed that FPC was not an independent predictor of OS. This cohort was divided into 314 patients (FPC: 18 patients, non-FPC: 296 patients) who received adjuvant chemotherapy (AC group) and 109 patients (FPC: 14 patients, non-FPC: 95 patients) received no adjuvant chemotherapy (no AC group). In AC group, FPC is an independent predictor for RFS (HR 3.03; P < 0.001) and OS (HR 2.23; P = 0.018). In no AC group, FPC is not a predictor for RFS and OS. Conclusions: This study may show that FPC has a significant impact on RFS and OS after resection in patients who received adjuvant chemotherapy. Research Sponsor: None.

Prognostic value (PV) of pathologic response (PR) to neoadjuvant chemotherapy (NC) alone in resected pancreatic cancer (PDAC): Initial analysis. First Author: Vincent J. Picozzi, Virginia Mason Hospital and Medical Center, Seattle, WA

Background: As neoadjuvant Rx for resected PDAC often includes chemoradiation, the PV of PR to NC alone is of interest. We began analysis of the impact of NC alone in this setting. Methods: Patients (pts) were identified from the Virginia Mason PancreatoBiliary Cancer Database. Inclusion criteria: 1) Dx 1/2010 – 3/2019; 2) Path dx PDAC stage III-IV; 3) NC (any type) as sole neoadjuvant Rx Rx 4) complete surg path data; 5) longitudinal OS known. Exclusion criteria: 1) neoadjuvant chemoradiation; 2) unknown NC (outside providers only). Histologic response was scored as follows: 1) No response, 2) <15% response, 3) 15–50% response, 4) >50% response. Results: For 534 pts are in Table. Median (med) 1/2 was 33 months (mo). In univariate analysis, all path features examined were statistically significant re med/5 yr OS. In multivariate analysis, risk increased with tumor size (HR 1.9, 95% CI 1.1–3.2) and tumor differentiation (HR 1.8, 95% CI 1.1–3.1) independent of other variables. Conclusions: In univariate analysis, all PR features after NC had med/5 yr OS, especially tumor size and histologic response score. NC type was not significant. 2) In multivariate analysis, risk increased with tumor size and tumor differentiation. 3) This data needs extension to a bigger pt base/correlation with other variables (Ca 99.9, postop Rx, recurrence pattern etc.) for greater utility (now underway). 4) This approach may aid postop Rx decision-making in this setting. Research Sponsor: Virginia Mason PancreatoBiliary Cancer Fund.
Young-onset pancreas cancer (PC) in patients less than or equal to 50 years old at Memorial Sloan Kettering (MSK): Descriptors, genomics, and outcomes. First Author: Anna M. Varghese, Memorial Sloan Kettering Cancer Center, New York, NY

Background: For individuals ≤ 50 years old, cancer incidence is increasing, particularly gastrointestinal and obesity related cancers (Sung, Lancet Public Health 2019). Limited details are known about young onset PC. Herein, we report the epidemiologic, pathologic, and molecular characteristics of PC in patients (pts) ≤ 50 years old. Methods: MSK institutional database was queried for medical and treatment history, genomics, and outcomes in pts ≤ 50 years old diagnosed with PC between January 2008 and July 2018. Neuroendocrine cancers were excluded. Overall survival (OS) from date of PC diagnosis was estimated using Kaplan-Meier methods. Results: N = 450 pts ≤ 50 years old with a diagnosis of PC were identified. Ninety-six percent had adenocarcinoma, and 4% had acinar cell carcinoma/other histologies. Table summaries demographics. Median OS was 16 months in the entire cohort and 11.3 months in stage IV disease. For N = 236 pts diagnosed after 2014, 119 (50%) underwent successful somatic testing with at least one alteration identified, and 21/119 tumors were RAS wild-type with identification of several actionable alterations (NRG1 fusions (n=2), NTRK fusions (n=2), IDH1 R132C (n=1), and microsatellite instability (n=1)). N = 11 pts had germline testing (routine after 2015), and 33/114 (29%) had pathologic germline alterations, including BRCA1/2 (n=18), CHEK2 (n=3), PALB2 (n=3), ATM (n=2), MLH1 (n=1), and MSH2 (n=1). Conclusions: Pathogenic germline alterations are present in a substantial percentage of pts with young onset PC, and actionable somatic alterations are seen frequently in the subgroup of young onset PC RAS wild-type tumors. These observations underpin the need for germline and somatic profiling in PC. Research Sponsor: None.

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Retrospective analysis of institutional outcomes with FOLFIRINOX versus nab-paclitaxel plus gemcitabine in metastatic pancreatic cancer. First Author: Amisha Singh, University of Arizona College of Medicine, Tucson, AZ

Background: With an estimated six percent five-year survival, metastatic pancreatic adenocarcinoma is one of the most lethal cancers in the United States. Previously, treatments with FOLFIRINOX (FFX) or gemcitabine plus nab-paclitaxel (G+A) have demonstrated improved overall survival versus gemcitabine alone. The purpose of this study is to compare institutional outcomes for the two regimens, FFX vs. G+A in metastatic pancreatic cancer. Methods: We conducted a retrospective review of medical records of all metastatic pancreatic cancer patients from 2010 to 2018 who received first line treatment with FFX or G+A at University of Arizona Cancer Center. Results: Thirty-five patients received combination treatment with G+A and 29 patients received FFX. Patient demographics: median age was 66 years in FFX vs 70 years in the G+A group; baseline CA-19-9 was 791 in FFX vs 738 in the G+A group. Median ECOG score was 1 for both groups. Median overall survival was 11.5 months in the FFX group (range 0-39 mos) vs 5 months in the G+A group (range 0-37 mos). Overall survival at 6 months was 75.9% vs 51.4% in FFX vs G+A groups respectively. Median progression-free survival was 6 months with FFX (range 0-25 mos) and 3 months with G+A (range 0-24 mos). Twenty-one of 29 patients in the FFX group pursued second line treatment, compared to 12 of 35 patients in the G+A group. Time to next treatment was 6 months in the FFX group vs 5 months in the G+A group. More progressed patients were noted with FFX, the most common being neurotoxicity and neutropenia, leading to treatment discontinuation due to adverse effects in 31% of patients, compared to 3% of patients in the G+A group. FFX patients required a higher median no. of office visits (35 visits vs 18 visits in the G+A group). Conclusions: FFX showed improved progression-free survival vs G+A; however, this could be due to more patients pursuing second line treatment in the FFX group. Compared to G+A, FFX patients had higher rates of treatment discontinuation due to adverse effects, FFX patients also required more office visits and further analysis is necessary to assess whether this resulted in poorer quality of life and increased total cost of care for patients treated with FFX. Research Sponsor: None.

Does aberrant hepatic arterial anatomy impact the complication rate or survival following resection of pancreatic adenocarcinoma? First Author: Nicketti M Handy, Virginia Mason Medical Center, Seattle, WA

Background: Patients with aberrant hepatic arterial anatomy (AHAA) are susceptible to tumor invasion and/or ligation during resection of the pancreatic head. The purpose of this study is to determine if AHAA negatively impacts perioperative outcomes or survival. Methods: All patients who underwent either pancreaticoduodenectomy or total pancreatectomy for pancreatic ductal adenocarcinoma (PDAC) between 2005 and 2014 at our center were retrospectively reviewed. Univariate logistic regression was used to compare outcomes between patients with conventional hepatic anatomy to those with AHAA. Survival analysis was performed by Kaplan-Meier method with log rank test. Results: During the study period, 330 patients underwent resection for PDAC. 69 (20.9%) with aberrant hepatic arterial anatomy. The presence of AHAA does not significantly increase operative time (p=0.110) or length of stay (p=0.518). The overall frequency of complications (49.3% vs 37.9%, p=0.088) was higher in the AHAA group, but not significantly so. Certain postoperative complications are more common in the AHAA group, namely superficial surgical site infection (18.8% vs. 8.8%, p=0.018) and pancreatic fistula (18.8% vs. 10.0%, p=0.042). However, deep SSIs, need for blood transfusion, respiratory failure, DGE, bleed from GDA/pseudoaneurysm, biliary fistula, chyle leak, PV thrombus, fascial dehiscence, and reoperation are not statistically different between the two groups. There is a trend for reduced overall survival in the AHAA group that is not statistically significant (p=0.10). Conclusions: Aberrant hepatic arterial anatomy is encountered in greater than 20% of pancreatic surgery patients, and its presence may increase the rate of certain postoperative complications such as superficial surgical site infection and pancreatic fistula. Research Sponsor: None.

Retrospective analysis of institutional outcomes with FOLFIRINOX versus nab-paclitaxel plus gemcitabine in metastatic pancreatic cancer. First Author: Stephanie Lelond, CancerCare Manitoba, Winnipeg, MB, Canada

Background: Pancreatic cancer is lethal. Chemotherapy can improve survival by months; however, many patients experience an overwhelming burden of cancer-associated symptoms and poor quality of life (QOL). Early palliative care (EPC) alongside standard oncologic care results in improved QOL and survival in patients with lung cancer. Although international guidelines recommend EPC for patients with advanced pancreatic cancer (PANC), the benefit is not known. Objectives: The primary objective is to test for change in QOL between baseline (BL) and 16 weeks (wk). Secondary objectives are to test for change between BL and 16 wk in (a) symptom control; and (b) depression and anxiety. Methods: This prospective case-crossover study of patients with PANC provides EPC plus standard oncologic care. Primary oncology clinics refer patients to an EPC team led by a palliative care physician and a clinical nurse specialist. BL questionnaires are completed prior to initial EPC assessment, then every 4 wk until wk 16. EPC visits are every 2 wk for the first month, every 4 wk until wk 16, and then as needed. QOL, symptom control, anxiety and depression are measured using the FACT-Hep tool, ESAS-r, HADS and PHQ-9, respectively. A generalized linear model will test for statistically significant change in scores between BL and 16 wk; chemotherapy (yes/no) is included as a confounding covariate; model fit will be assessed. A sample size of 20 patients provides 80% power after controlling for covariate effects. 40 patients will be enrolled to account for missing data. To date, 28 patients have enrolled and 17 have completed the intervention. Significance: The benefit of EPC for patients with PANC is not known, however, EPC is increasingly recognized internationally by patients and stakeholders as a critical intervention which may improve both QOL and satisfaction with care. The Canadian Partnership Against Cancer’s report on the patient experience states “the best possible patient experience means all people with cancer have equitable access to high quality person-centered palliative care”. This study offers access to EPC and provides an environment in which the benefit of an integrated approach is evaluated. Research Sponsor: CancerCare Manitoba Foundation, Pharmaceutical/Biotech Company.
Demoralization and depression in pancreatic cancer patients. First Author: Jar-Yee Liu, Cedars-Sinal Medical Center, Los Angeles, CA

Background: Demoralization is a maladaptive coping response to stressful situations characterized by thoughts of hopelessness, helplessness, and loss of meaning and purpose. Psychometrically, it is measured using the Demoralization-Scale II (DS-II), a validated questionnaire that yields a patient-reported quantification (scale 0-32) of demoralization. Previous studies involving patients with progressive disease have uncovered a strong positive correlation between demoralization and depression, respectively measured by DS-II scale and Patient Health Questionnaire (PHQ-9) surveys. Here, we aim to characterize demoralization and its relationship to depression in pancreatic cancer patients, a unique patient population in terms of its poor prognosis. We hypothesize that demoralization is highly prevalent in the pancreatic cancer patient population and strongly correlated with depression. Methods: Eligible patients with an active pancreatic cancer diagnosis, after consenting to an IRB approved protocol, will be administered the DS-II and PHQ-9 surveys to yield psychometric measurements for analysis. The primary objective of this project is to determine the association between demoralization (DS-II) and depression (PHQ-9) in pancreatic cancer patients. Secondary objectives include associations between demoralization and ethnicity, sexual orientation, suicidal ideation, education, cancer stage, and disease progression. Data will be analyzed via simple linear regression. An ANOVA will also be conducted using DS-II groups as the categorical variable and PHQ-9 scores as the continuous variable, and vice versa. This is a multi-institutional study to be conducted at Cedars-Sinai Medical Center, New York University, University of Washington, UC San Francisco, and Lewis Katz Schools of Medicine. Research Sponsor: None.

A phase I study of nanoliposomal irinotecan and 5-fluorouracil/leucovorin in combination with interleukin-1α-antagonist for advanced pancreatic cancer patients with cachexia (OnFX). First Author: Katelyn Mae Atkins, Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinal Medical Center, Los Angeles, CA

Background: Patients with pancreatic cancer have the highest rate of weight loss among all advanced cancers. Of which, the majority develop cachexia, characterized by progressive and involuntary loss of weight and skeletal muscle mass. In preclinical studies, interleukin-1α (IL-1α) antagonism has been found to neutralize tumor angiogenesis and onco-inflammation. Early studies in patients with cachexia have screened and 21 enrolled. Clinical trial information: NCT03207724. Sponsor: None.

Improving cascade genetic testing for families with inherited pancreatic cancer (PDAC) risk: The GENetic Education, Risk Assessment and TESting (GENERATE) study. First Author: Matthew B. Yurgelun, Dana-Farber Cancer Institute, Boston, MA

Background: 4-10% of PDAC patients harbor pathogenic germline variants in cancer susceptibility genes, including APC, ATM, BRCA1, BRCA2, CDKN2A, EPCAM, MLH1, MSH2, MSH6, PALB2, PMS2, STK11, and TP53. For families with such pathogenic variants, the greatest potential impact of germline testing is to identify relatives with the same variant (cascade testing), thereby providing the opportunity for early detection and intervention of PDAC and other associated cancers. Numerous factors limit cascade testing in real-world practice, including family dynamics, widespread geographic distribution of relatives, access to genetic services, and misconceptions about the importance of germline testing, such that the preventive benefits of cascade testing are often not fully realized. The primary aim of this study is to analyze two alternative strategies for cascade testing in families with inherited PDAC risk. Methods: 1000 individuals with a confirmed pathogenic germline variant in any of the above genes in a 1st/2nd degree relative and a 1st/2nd degree relative with PDAC will be remotely enrolled through the study website (www.GE-NERATEstudy.org) and randomized between two methods of cascade testing (individuals with prior genetic testing will be ineligible): Arm 1 will undergo pre-test genetic education with a pre-recorded video and live interactive session with a genetic counselor via a web-based telemedicine platform (Doxy.me), followed by germline testing through Color Genomics; Arm 2 will undergo germline testing through Color Genomics without dedicated pre-test genetic education. Color Genomics will disclose results to study personnel and directly to participants in both arms. All participants will have the option of pursuing additional telephone-based genetic counseling through Color Genomics. The primary outcome will be uptake of cascade testing. Secondary outcomes will include self-reported genetic knowledge, cancer worry, distress, decisional preparativeness, familial communication, and screening uptake, which will be measured via longitudinal surveys. Enrollment is underway nationwide as of May, 2019. Clinical trial information: NCT03762590. Research Sponsor: Stand Up To Cancer-Lustgarten Foundation Pancreatic Cancer Interception Translational Cancer Research Grant (Grant Number: SU2C-AACR-DT25-17).

Aparationib in combination with S-1 for the second-line treatment of advanced pancreatic cancer (APC). First Author: Junjie Hang, Changzhou No.2 People's Hospital, Changzhou, China

Background: The prognosis for patients with advanced pancreatic cancer (APC) is extremely dismal. First-line treatment for APC is gemcitabine/S-FU-based chemotherapy with no standard second-line treatment. Anti-angiogenic therapy combined with chemotherapy has shown its effects in improving the outcomes in a variety of cancers. Aparationib is an oral tyrosine kinase inhibitor that selectively targets VEGFR2. Some preclinical studies and several case reports showed the anti-tumor effect of aparationib in pancreatic cancer, but there is no evidence from clinical trial to confirm it. This study aims to evaluate the efficacy and safety of aparationib in combination with S-1 as the second-line therapy for patients with APC. Methods: In this open-label, single-arm, randomized phase II study, we will recruit 30 patients with pathologically proven advanced pancreatic cancer after the failure of first-line chemotherapy. All patients are aged 18-70 years with ECOG PS 0-2 and will receive aparationib at an initial dose of 500mg/m² on a continuous basis, and oral S-1(60mg/d for BSA < 125m², 80mg/d for 125 < BSA < 15m², and 100mg for BSA > 15m², orally) twice a day on days 14 of a 21-day cycle. Primary endpoint is PFS. Secondary endpoints include OS, duration of response, ORR and DCR. The safety of aparationib + S-1 will be evaluated by CTCAE v4.0. Translational research will be performed in blood (before and on-treatment); cytokine profile to explore predictive and prognostic biomarkers. Clinical trial information: NCT03662035. Research Sponsor: CSCO-Henri Bill Backlund Foundation for Cancer Research.
A pilot study of intratumoral SD-101 (toll-like receptor 9 agonist), nivolumab, and radiotherapy for treatment of chemotherapy-refractory metastatic pancreatic adenocarcinoma. First Author: Justin Chen, University of California Davis Comprehensive Cancer Center, Sacramento, CA

Background: Pancreatic adenocarcinoma is an aggressive disease projected to be the second leading cause of cancer-related death. A majority of patients have advanced disease on diagnosis. Combination chemotherapy is first-line for advanced disease but limited by toxicity and median survival under 1 year. SD-101 is a toll-like receptor 9 agonist that is injected intratumorally to increase immunogenicity in the tumor microenvironment. Localized radiation can further enhance this via antigen release and potential abscopal effects. Immunotherapy has revolutionized care for various solid organ malignancies but not yet for pancreatic cancer. Therefore, the combination of SD-101, localized radiation, and checkpoint inhibitor is a promising therapeutic strategy for metastatic pancreatic adenocarcinoma. Methods: Six patients with chemotherapy-refractory, liver-metastatic pancreatic adenocarcinoma will be evaluated for combination SD-101, radiation, and nivolumab. SD-101 is injected intra-tumorally into a liver metastasis on days 1, 8, 15, 29 with optional dosing days 43 and 57. Localized radiation (6–10 Gy per fraction) to the lesion involved will be given on days 1, 3, 5, 8, and 10. Nivolumab will be given at 240 mg every 2 weeks starting day 2 until progression or unacceptable toxicity. Blood samples will be collected at baseline and at regular intervals while on treatment. Biopsies will be obtained at baseline and on day 29. Primary objectives are to evaluate safety and tolerability, defined so if ≤5 patients reach day 29 without experiencing grade ≥3 treatment-related toxicity. Secondary objectives include preliminary efficacy as defined by disease control rate, duration of response, progression-free survival, and overall survival. Exploratory objectives include objective response rate and biomarker correlates (T-cell clonality, tumor mutational burden, tumor infiltrative immune cell subsets, and immune-related gene expression profile). Blood and biopsy specimens will be analyzed using flow cytometry, qRT-PCR, 16S sequencing, and immunohistochemistry on biopsy specimens.

Clinical trial information: NCT04050085. Research Sponsor: Private, individual donor. Drug-only support from Bristol-Myers Squibb and Dynavax.

Vitamin D receptor agonist paricalcitol plus gemcitabine and nab-paclitaxel in patients with metastatic pancreatic cancer. First Author: Kimberly Perez, Dana-Farber Cancer Institute, Boston, MA

Background: Patients(pts) with metastatic pancreatic cancer (PC) have a median survival of less than one year even with use of multiligand chemotherapy programs. Pancreatic tumors are composed of multiple cell types and an extracellular matrix (ECM) that may directly impede chemotherapy delivery. Cancer-associated fibroblasts (CAFs) in the tumor microenvironment secrete pro-inflammatory factors and components of the extracellular matrix. In PC laboratory models, engagement of the vitamin D receptor (VDR) by VDR agonists shifts CAFs toward a more quiescent phenotype with reduced tumor growth and improved chemotherapy penetration (Sherman, Cell, 2014). Paricalcitol is a synthetic VDR agonist used in patients with secondary hyperparathyroidism due to chronic kidney disease. A prior pilot study evaluated IV paricalcitol with gemcitabine (G) and nab-paclitaxel (A) before surgical resection in patients with resectable PC (NCT02030860). Methods: Pts with previously untreated metastatic PC will be enrolled in a 2-stage study consisting of a safety run-in and a randomized phase 2 study (NCT03520790). In the run-in stage, 36 pts will be randomized 1:1:1 to G (1000 mg/m2) and A (125 mg/m2) given 3 weeks on and 1 week off vs (a) paricalcitol 25 mcg IV thrice weekly, (b) paricalcitol 60 mcg oral daily, or (c) placebo oral daily. Grade 3/4 hypercalcemia or genitourinary stones will be considered dose limiting. Tumor response will be assessed using RECIST v1.1. Secondary endpoints include safety, response rates, and progression-free survival. Trial funding provided by SU2C, CRUK, Lustgarten Foundation, and AACR. Clinical trial information: NCT03520790. Research Sponsor: SU2C, Lustgarten Foundation, and AACR.

Trials in Progress Poster Session (Board #03), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Trials in Progress Poster Session (Board #04), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

First Author: Kim Perez, University of California Davis Comprehensive Cancer Center, Sacramento, CA

Background: Patients(pts) with metastatic pancreatic cancer are currently limited. Eryaspase, asparaginase (ASNase) en-capsulated in red blood cells (RBCs) is an investigational product under development. Following infusion, asparagine and glutamine are actively transported into RBCs where they are hydrolyzed by the encapsulated enzyme. ASNase has recently been reported to improve overall survival (OS) and progression-free survival (PFS). The safety profile of eryaspase was ac-ceptable. The results of this Phase 2b study provided a rationale for initiating this confirmatory Phase 3 pivotal trial (TRYBeCa-1). Methods: TRYBeCa-1 is a randomized, open-label Phase 3 trial (N = 500) of eryaspase combined with chemotherapy in patients with adenocarcinoma of the pancreas who have failed only one prior line of systemic anti-cancer therapy for advanced pancreatic cancer and have measurable disease. Patients are randomized in a 1:1 ratio to receive gemcitabine/Abraxane or intronotan-based therapy (FOLFIRI (FOLinic acid Fluorouracil-Irinotecan)). Intronotan will be given on days 1, 8, 15, 29 with optional 2nd dose injection on day 5/fluorouracil/leucovorin) with or without eryaspase, administered as IV infusion on Day 1 and Day 15 of each 4-week cycle. Key eligibility criteria include performance status 0 or 1, stage IV disease; documented evidence of disease progression; and adequate hematologic, hepatic, and renal function. The primary endpoint is OS. Key secondary endpoints include PFS and objective response rate, safety, quality of life, pharmacokinetics, and pharmacodynamics, and biomarker researcher. A hazard ratio in OS of 0.725 is being targeted which represents a conservative estimate based on the Phase 2b data. Being highly clinically relevant. An IDMC will be established to review safety at regular intervals and review efficacy data at the planned interim and final analyses. Clinical trial information: NCT03665441. Research Sponsor: Erytech.

Trials in Progress Poster Session (Board #06), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

First Author: Garcia Chioriean, University of Washington and Fred Hutchinson Cancer Research Center, Seattle, WA

Background: PDA is characterized by invasiveness and therapeutic re-sistance in part due to a desmoplastic stroma and an immunosuppressive microenvironment (Provenzano PP, Hingorani S. Br J Cancer 2013). PD1/PD-L1 inhibitors have no single durable response in PDA, except for pembrolizumab in mPDA pts refractory to 1st line therapy with median overall survival (OS) of 6 months. We hypothesize that stroma remodeling with PEGPH20 sensitizes PDA to immune therapy, and stroma and immunologic biomarkers will identify pts most likely to benefit. In this trial we will evaluate the efficacy, safety, and translational biomarkers of PEGPH20 plus pembrolizumab in patients (pts) with hyaluronan (HA)-high refractory metastatic ductal adenocarcinoma (mPDA). First Author: E. Gabriela Chioriean, University of Washington and Fred Hutchinson Cancer Research Center, Seattle, WA

Methods: Eligible pts have ECOG PS 0–1, ≥2 prior therapies for PDA, life expectancy ≥12 wks, able/willing to have tumor biopsies at baseline and after 6 wks of treatment. PEGPH20 dosing is 3 μg/kg IV QW and pembrolizumab 200 mg iv Q3W (2-4 hrs after PEGPH20 on wk 1) in 3-wk cycles. All pts receive prophylactic low molecular weight heparin. Primary endpoint: progression-free survival (PFS). Secondary endpoints: safety, OS, response rates. Translational endpoints: flow cytometry of peripheral and intratumoral immune cells, T-cell receptor sequencing, immune transcriptome, immune subsets IHC, circulating cytokines, serum plasma and tumor HA levels. For the primary endpoint of PFS, with a sample size of 31 evaluable pts, a one-sided α-level of 0.05, assuming 12 mos of accrual and 6 mos of follow-up, this study has 80% power to detect a difference between the null hypothesis median PFS of 3 mos vs. the alternate hypothesis of a median PFS of 6 mos. Since the IDMC was activated in May 2019 and is open to accrual; 6 pts were enrolled as of 24 Sept 2019. Clinical trial information: NCT03634332. Research Sponsor: Merck, Halozyme.
**TPS786** Trials in Progress Poster Session (Board #07), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

**Stereotactic MR-guided on-table adaptive radiation therapy (SMART) for locally advanced pancreatic cancer.** First Author: Parag Parkh, Henry Ford Cancer Institute, Detroit, MI

**Background:** Standard dose radiation therapy has been unsuccessful in inoperable pancreatic cancer; with a negative study (LAP07) for conventional chemotherapy and dropping of the stereotactic body radiation therapy arm in Alliance A205501. Recently, reports of using high dose ablative radiation therapy has been associated with increased survival in retrospective studies. Moreover, technological advances with MR-guided radiation therapy offer improved targeting and the ability to change the radiation delivery on a daily fashion; allowing ablative radiation doses over one week. However, it is not clear whether this can be done safely on a multistitutional basis. **Methods:** We are conducting the largest prospective study of ablative radiation therapy in pancreatic cancer. The study is a single arm, multi-institutional phase II, industry sponsored study to investigate the safety and efficacy of Stereotactic, MR-guided, on-Table-Adaptive Radiation Therapy (SMART). Eligibility criteria include locally advanced and borderline resectable pancreatic cancer patients with ECOG PS of 0 or 1; who have non-metastatic disease after a minimum of 3 months of any systemic therapy; including investigational agents. Patients will receive MR-guided radiation therapy to a dose of 50 Gy / 5 fractions; with maximum tumor coverage delivered each fraction that allows keeping the gastrointestinal organs at risk to a dose of 33 Gy or less. Primary endpoint is grade 3 of higher gastrointestinal toxicity at 90 days. Secondary endpoints are overall survival at 2 years, distant progression free survival at 6 months, and changes in patient related quality of life at 3 and 12 months. Target sample size was calculated to show at a significance level 0.05, a reduction of the toxicity rate to 8% or lower by using SMART compared with 15.8%, the toxicity rate of conventionally delivered chemoradiation at a power level 0.8. Given an expected 15% drop-out, the enrollment goal is 132 patients. Descriptive statistics will be used for secondary objectives. The study opened in January, 2019 and is currently opened at 4 centers; with other US and international sites pending. Sponsored by Viewray, Inc. Clinical trial information: NCT03626644. Research Sponsor: Viewray, Inc.

**TPS788** Trials in Progress Poster Session (Board #09), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

**A phase I study to evaluate the safety and tolerability of AB680 combination therapy in participants with gastrointestinal malignancies.** First Author: Johanna C. Bendel, Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN

**Background:** Metastatic pancreatic ductal adenocarcinoma (mPDAC) expresses very high levels of CD73 among tumor types, and CD73 expression level is a known poor prognostic factor in PDAC. Adenosine, a product of AMP breakdown by CD73, is highly immunosuppressive against effector T & NK cells in the tumor microenvironment. AB680 is the first clinical-stage small-molecule CD73 inhibitor, which is highly potent, pharmacodynamically active, and safe in healthy volunteer dose escalation studies. Targeting the adenosine pathway in combination with standard of care regimens may have a more profound effect on activating and inducing sustained anti-tumor immunoLOGY. **Methods:** This is a Phase 1/ib, open-label, dose-escalation, and dose-expansion study to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and clinical activity of AB680 in combination with AB122 (anti-PD-1 antibody) and standard chemotherapy (nab-paclitaxel [NP] and gemcitabine [Gem]) in participants with first line (1L) mPDAC. In the dose-escalation, Phi portion, increasing dose levels of AB680 are administered every 2 weeks (Q2W) in combination with AB122 (240 mg Q2W) and NP/Gem (Gem 1000 mg/m² + NP 125 mg/m² IV on Days 1, 8) and IS of each 28-day cycle. Up to 30 participants may be evaluated in Phi dose-escalation. In the dose-expansion, Phi portion, AB680 will be administered at the recommended dose for expansion in combination with AB122 and NP/Gem in up to 40 participants. Adverse events will be graded according to NCI CTCAE 5.0 and antitumor activity assessed using RECIST v1.1. **Conclusions:** This Ph1/ib study is the first to target the adenosine axis using a highly potent small-molecule inhibitor of CD73, AB680, in L mPDAC in combination with standard of care chemotherapy (NP/Gem) and a PD-1 antibody (AB122). Future results will be shared in upcoming scientific conferences. Clinical trial information: NCT04046762. Research Sponsor: Arcus Biosciences, Inc.

**TPS789** Trials in Progress Poster Session (Board #010), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

**Tyme-88-Panc Part 2: A randomized phase II/III of SM-88 with MPS as third-line in metastatic PDAC.** First Author: Shubham Pant, University of Texas MD Anderson Cancer Center, Houston, TX

**Background:** Patients with metastatic pancreatic cancer who have progressed on two prior lines of therapy have a poor prognosis with an overall survival in the range of 2-2.5 months. (Manax, et al. J Clin Oncol 37, 2019 suppl 4; abstr 226) There is currently no standard of care for these patients, but several studies have demonstrated improved outcomes. SM-88 (DL-α-methyltyrosine; racemetyrosine [USAN]) is a proprietary dysfunctional tyrosine derivative and is the backbone of SM-88 used with MPS (Methoxsalen 10mg, Phenyoitn 50mg and 260mg of dexamethasone daily), all administered orally. Tyme-88 monotherapy has been well tolerated, with improvement in survival in select patients with heavily pretreated PDAC who achieved stable disease on therapy (HR 0.8, p = 0.02). Circulating tumor cells (CTCs) were prognostic and decreased on therapy with SM-88 potentially identifying a subgroup of PDAC that may be most likely to benefit from therapy (Noel et al. Annal Oncol V30, Suppl 4, 2019). Preliminary radiomic analysis of the largest metastases at baseline suggested the same benefits including a correlation with baseline CTCs, changes in CTCs on therapy and OS (Oceam et al, Annal Oncol, V30, Suppl 5, 2019). Here, we describe a randomized, open-label, phase 2/3 trial evaluating the efficacy of SM-88 + MPS vs physician choice of treatment as third line therapy for patients with metastatic PDAC. **Methods:** This is a multi-center Phase 3 study of patients ≥18 years with metastatic PDAC that progressed after 2 lines of chemotherapy (gemcitabine [gem] and S-fluorouracil [S-FU] based) with an ECOC <2. Randomization will be 1:1 with 250 patients being stratified by site, ECOG, and choice of chemotherapy. SM-88 will be administered at a dose of 450mg twice daily (900 mg/day). Primary end point is Overall Survival (OS). Secondary end points include progression free survival, response rate, duration of response, pharmacokinetics, safety and CTCs. Clinical trial information: NCT03532756. Research Sponsor: Tyme Inc.

**TPS790** Trials in Progress Poster Session (Board #011), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

**A phase II, open-label pilot study evaluating the safety and activity of Nab-IRI in combination with S-FU and oxaliplatin in preoperative treatment of pancreatic adenocarcinoma (NEO-Nal-IRI Study) (NCT03483038).** First Author: Hiral D. Parekh, University of Florida Health Cancer Center, Gainesville, FL

**Background:** Neoadjuvant treatment for borderline resectable pancreatic cancer (PCa) is increasing in acceptability, but a standard regimen has yet to be established. Multiple studies have demonstrated feasibility and effectiveness of the FOLFIRINOX (S-fluorouracil, leucovorin, oxaliplatin and irinotecan) regimen in the perioperative setting. However, FOLFIRINOX often requires dose modifications, delays and growth factor support due to excessive toxicity which can complicate care delivery when given neoadjuvantly. A phase I study of nab-IRI (IRINOC) in the setting of resectable pancreatic cancer demonstrated safe and effective neoadjuvant delivery. **Methods:** In this phase 2, open-label, multicenter single-arm study focuses on patients (pts) with borderline resectable PCa without metastatic disease. Other key eligibility criteria include age ≥18 years, resectability confirmed by multidi GI tumor board, adequate cardiac, renal, hepatic function and ECOG performance status of 0 to 1. Pts receive FOLFIRINOX regimen and to demonstrate safe and effective neoadjuvant delivery. **Regimen components given every 14 days.**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose</th>
<th>Route/Duration</th>
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<tbody>
<tr>
<td>Nab-IRI</td>
<td>50 mg/m²</td>
<td>IV over 90 minutes</td>
</tr>
<tr>
<td>Oxaliplatin</td>
<td>60 mg/m²</td>
<td>IV over 120 minutes</td>
</tr>
<tr>
<td>Leucovorin</td>
<td>400 mg/m²</td>
<td>IV over 120 minutes</td>
</tr>
<tr>
<td>S-fluorouracil infusion</td>
<td>2400 mg/m²</td>
<td>IV continuous infusion for 46 hours</td>
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TPS791 Trials in Progress Poster Session (Board #012), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

A phase II trial of pharmacological ascorbate, gemcitabine, and nab-paclitaxel for metastatic pancreatic cancer. First Author: Pashtoon Murtaza Kasi, Mayo Clinic, Jacksonville, FL

Background: FOLFIRINOX or gemcitabine/nab-paclitaxel are both frontline chemotherapy options for patients with metastatic pancreas cancer. For most who cannot tolerate the triplet, the latter doublet is the preferred option. Through previous work by our group, pharmacologic ascorbate is known to synergize with gemcitabine; preliminary in vitro data from our group suggests a similar synergistic response with paclitaxel. Though ascorbate has been used in cancer therapy, few robust trials have investigated intravenous delivery of ascorbate to deliver plasma concentrations that are cytotoxic to tumor cells. Our prior studies have demonstrated ascorbate induces oxidative stress and cytotoxicity in pancreatic cancer cells; this cytotoxicity appears to be greater in tumor vs. normal cells. We hypothesize that production of hydrogen peroxide mediates the increased susceptibility of pancreatic cancer cells to ascorbate-induced metabolic oxidative stress, resulting in improved treatment outcomes, which has led to the development of the clinical trial (NCT02905578). Methods: All participants receive gemcitabine (1000 mg/m2 weekly) and nab-paclitaxel (125 mg/m2) on cycle days 1, 8, and 15 of a 28-day cycle. Participants are randomized to ± pharmacologic ascorbate (75-gram infusion 3x weekly) in addition to chemotherapy. Study therapy continues until tumor progression. The primary objective is to determine overall survival in patients when treated with combination gemcitabine, nab-Paclitaxel and high-dose ascorbic acid compared to gemcitabine and nab-paclitaxel in patients with non-resectable pancreatic cancer. Secondary objectives include determining objective response rate as well as progression free survival using RECIST 1.1 criteria employing a blinded reviewer for RECIST measurements. The study opened to accrual in 2018 with a goal of enrolling 65 participants. Oversight: Study is conducted under IND 105715 (J. Cullen, sponsor). The University of Iowa Biomedical IRB (IRB-01) serves as the IRB of record. Clinical trial information: NCT02905578. Research Sponsor: U.S. National Institutes of Health.

TPS792 Trials in Progress Poster Session (Board #013), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

PANOVA-3: A phase III study of tumor treating fields with nab-paclitaxel and gemcitabine for front-line treatment of locally advanced pancreatic adenocarcinoma (LAPC). First Author: Vincent J. Picozzi, Virginia Mason Hospital and Medical Center, Seattle, WA

Background: Tumor Treating Fields (TTFields) are a non-invasive, regional antimitotic treatment modality, which has been approved for the treatment of glioblastoma. TTFields at specific frequency (ISO-200 kHz) are delivered via transducer arrays placed on the skin in proximity to the tumor site. TTFields predominantly act by disrupting the formation of the mitotic spindle during metaphase. TTFields were effective in multiple preclinical models of pancreatic cancer. The Phase 2 PANOVA study, the first trial testing TTFields in pancreatic cancer patients, demonstrated the safety and preliminary efficacy of TTFields when combined with nab-paclitaxel and gemcitabine in both metastatic and LAPC. The Phase 3 PANOVA-3 trial (NCT03377491) is designed to test the efficacy and safety of adding TTFields to nab-paclitaxel and gemcitabine combination in LAPC. Methods: Patients (N = 556) with resectable or locally advanced PDAC will be enrolled in this prospective, randomized trial. Patients should have an ECOG score of 0-2 and no prior progression or treatment. Patients will be stratified based on their performance status and geographical region, and will be randomized 1:1:1 to TTFields plus nab-paclitaxel and gemcitabine or to nab-paclitaxel and gemcitabine alone. Chemotherapy will be administered at standard dose of nab-paclitaxel (125 mg/m2) and gemcitabine (1000 mg/m2 once weekly). TTFields (ISO 100 kHz) will be delivered at least 18 hours/day until local disease progression per RECIST Criteria V1.1. Follow up will be performed q8w, including a CT scan of the chest and abdomen. Following local disease progression, patients will be allowed monthly for survival. Overall survival will be the primary endpoint and progression-free survival, objective response rate, rate of resectability, quality of life and toxicity will all be secondary endpoints. Sample size was calculated using a log-rank test comparing time to event in patients treated with TTFields plus chemotherapy with control patients on chemotherapy alone. PANOVA-3 is designed to detect a hazard ratio 0.75 in overall survival. Type I error is set to 0.05 (two-sided) and power to 80%. Clinical trial information: NCT03377491. Research Sponsor: Novocure.

TPS793 Trials in Progress Poster Session (Board #014), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

A pilot study of liposomal irinotecan plus 5-FU/LV combined with paricalcitol in patients with advanced pancreatic cancer progressed on gemcitabine-based therapy. First Author: Patrick Grierson, Washington University in St. Louis, St. Louis, MO

Background: Pancreatic ductal adenocarcinoma (PDAC) is predicted to be the second leading cause of cancer-related death by 2030, and is characterized by resistance to chemo- and radiotherapy and a highly fibrotic tumor microenvironment. Front-line therapies for advanced PDAC include FOLFIRINOX and gemcitabine/nab-paclitaxel with median overall survival ranging from 8.5 to 11 months. After progression on gemcitabine-containing therapy, 5-FU/LV/irinotecan is a standard second-line option, however outcomes are still poor. Retrospective studies demonstrate superior survival of advanced PDAC in patients with high serum levels of 25(OH) vitamin D. Notably, the PDAC tumor microenvironment is enriched in cancer-associated fibroblasts that favorably respond to vitamin D, prolonging survival in combination with chemotherapy in mouse models. Furthermore, vitamin D suppresses catabolism of irinotecan in gastrointestinal cancer cells, potentiating its efficacy. Therefore, we are conducting an investigator-initiated study of SFU/LV/liposomal irinotecan with paricalcitol as second-line therapy in advanced PDAC. Methods: This is a pilot study of SFU/LV/liposomal irinotecan combined with paricalcitol in patients with advanced PDAC progressed on gemcitabine-based therapy. All patients receive liposomal irinotecan, LV, 5-FU and paricalcitol. Liposomal irinotecan is given at 70 mg/m2 IV over 90 minutes, and 5-FU at 2400 mg/m2 continuous IV infusion over 46 hours, on Day 1 of each 14-day cycle. Paricalcitol IV infusion will precede the above, given according to assigned cohort (75 mcg weekly or 7 mcg/kg weekly). The primary objective of this study is to determine the tolerability of different dose levels of paricalcitol added to the combination regimen of 5-FU/LV/liposomal irinotecan in patients with advanced PDAC. Secondary objectives are measures of efficacy (ORR, PFS, OS, CA19-9 biochemical response rate). Clinical trial information: NCT03883899. Research Sponsor: IPSEN.
Pattern of recurrence after curative resection of stage I-II duodenal adenocarcinoma.

First Author: Andrea Colina, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Duodenal adenocarcinoma (DA) is a rare cancer with limited data regarding the pattern of disease recurrence following resection. Methods: A retrospective review of 115 patients with Stage II-III disease from 3/1994 to 6/2018, at a single high-volume cancer center was conducted. Only patients (pts) who underwent a potentially curative surgical resection (RO/R1 margins) and had a postoperative follow-up radiographic evaluation were included. Periampullary adenocarcinomas were excluded. Clinicopathologic features and patterns of recurrence were compared across cohorts.

Results: Of 76 patients who met inclusion criteria, 7 (9%) were stage I, 25 (33%) stage II, and 44 (57%) stage III. Histologic grade was moderate in 58% and poor in 38%. Median age was 63 years (range, 29-84); 38% were female and RO resection was 97%. Neoadjuvant therapy was given to 14% and adjuvant therapy to 61%. Radiation therapy (XRT) as either adjuvant/neoadjuvant therapy was used in 27%. Median follow-up was 44 (6-293) months. Median time to recurrence was 11mo, with 8% of recurrences occurring within 2 years. Median time to local recurrence (LR) vs. distant recurrence (DR) was 11mo vs. 12mo, respectively, p = 0.42. Stage impacted recurrence rate: 0% in stage I vs. 50% stage 2 vs. 71% stage 3 (p = 0.002). Median time to recurrence was 11mo for stage II and 11mo for stage III (p = 0.04). In total, 4 (5%) pts had LR only, 8 (10%) had LR concurrent with DR, and 32 (42%) had DR only. Recurrence distribution was similar across stage II (LR 8%, LR+DR 5%, DR 77%) and stage III (LR 10%, LR+DR 19%, DR 71%). LR was similar in patients that received XRT (DR = 8%) compared to those who did not (9%). Most common sites of DR were peritoneal (38%), liver (33%), distant lymph nodes (28%), and lung (10%). Conclusions: The recurrence pattern for resected DA is predominantly distant metastatic disease with the majority of recurrences occurring within the first two years. Future therapies should focus on improved systemic therapy, and surveillance should be most intensive in the first two years. Research Sponsor: None.

Is adjuvant chemotherapy beneficial for stage II-III goblet cell tumors of the appendix?

First Author: Katerina Mary Zarka, Winship Cancer Institute of Emory University, Atlanta, GA

Background: Goblet cell tumors (GCT) of the appendix are very rare tumors constituting 2.5%-5.6% of all appendiceal neoplasms. Role of adjuvant chemotherapy (AC) is not established for GCT. This study aims to evaluate the impact of AC in patients that received GCT (10%) compared to those who did not (9%). Most common sites of DR were peritoneal (38%), liver (33%), distant lymph nodes (28%), and lung (10%). Conclusions: The recurrence pattern for resected DA is predominantly distant metastatic disease with the majority of recurrences occurring within the first two years. Future therapies should focus on improved systemic therapy, and surveillance should be most intensive in the first two years. Research Sponsor: None.

Impact of high-risk features for stage II adenocarcinoma of the appendix.

First Author: Mehmet Akce, Winship Cancer Institute, Atlanta, GA

Background: Clinicopathologic high-risk features are frequently utilized in adjuvant chemotherapy (AC) decisions in stage II colorectal cancer and their utility in stage II appendiceal adenocarcinoma (AA) is less established. The aim of this study is to determine the impact of high-risk features on clinical outcomes and whether high-risk features are predictive of AC benefit in stage II AA. Methods: Patients with pathological stage II AA between 2010 and 2015 were identified from the National Cancer Database (NCDB) using ICD-O-3 morphology and topography codes: B140, B480 and C18.1. High risk stage II AA was defined as having at least one of the following clinicopathologic features: T4 tumor, < 12 lymph nodes examined, poorly differentiated histology, positive margins, or lymphovascular invasion. Patients with none of these features were defined as low-risk. Results: A total of 1,040 patients were identified. 51.0% males, 84.5% Caucasian; median age 61 (range, 19-90). 46.4% were determined to have high-risk stage II AA. High-risk status was associated with worse OS compared to low-risk (HR 1.55; 95% CI 1.03-1.79; p = 0.028). High-risk stage II AA patients had significantly worse 5-year OS compared to low-risk patients (67.1% vs. 74.5%, p = 0.0013). AC was administered in 34.4% (n = 166) of high-risk patients and in 36.5% (n = 203) of low-risk patients. Among high-risk patients, AC was not associated with better OS in univariate (HR 0.86; 95% CI 0.59-1.26; p = 0.722) and multivariable analyses (HR 1.35; 95% CI 0.90-2.04; p = 0.324) compared to no AC. Similarly, among low-risk patients, AC was not associated with better OS in univariate (HR 0.92; 95% CI 0.60-1.39; p = 0.813) and multivariable analyses (HR 0.95; 95% CI 0.61-1.51; p = 0.334) compared to no AC. For high-risk patients, 5-year OS was 68.3% in patients that received AC vs. 66.5% in patients that did not (p = 0.722). For low-risk patients, 5-year OS was 74.0% in patients that received AC vs. 76.3% in patients that did not (p = 0.813). Conclusions: High-risk stage II AA patients had significantly worse 5-year OS compared to low-risk patients. AC did not improve survival regardless of high risk features in stage II AA. Research Sponsor: None.

Pilot study to test safety and efficacy ofavelumab in small bowel adenocarcinoma (SBA).

First Author: Dana Backlund Cardin, Vanderbilt-Ingram Cancer Center, Nashville, TN

Background: SBA is rare and often grouped with, and treated like, large intestinal adenocarcinomas. However, SBA has a very different microenvironment and could respond differently to the same therapies, potentially lowering efficacy. This is due to the unique genetic makeup of patients with pathological stage II and III GCT who underwent surgical resection between 2006 and 2015 were identified from the National Cancer Database (NCDB) using ICD-O-3 morphology and topography codes: B243/3, B243/5 and C181. Patients treated with chemotherapy and/or radiation therapy were excluded. Univariate and multivariable analyses were conducted, and Kaplan-Meier Curves were used to compare overall survival (OS) based on treatment received with Log-rank test. Results: A total of 1,046 patients were identified. 53.7% males and 89.0% Caucasian; median age 56 (range, 20-90) years. Distribution across pathological stages II-III was 83.6% (N = 874) and 16.4% (N = 172) consecutively. 8.3% (N = 73) of stage II and 50.6% (N = 87) of stage III patients received AC. In the total cohort, AC was not associated with better OS compared to no AC in univariate analysis (HR 1.84; 95% CI 1.22-2.67; p = 0.001) or multivariable analysis (HR 0.94; 95% CI 0.57-1.52; p = 0.790). For stage II patients, AC was not associated with better OS in univariate (HR 1.24; 95% CI 0.60-2.57; p = 0.562) or multivariable analyses (HR 1.67; 95% CI 0.76-3.64; p = 0.199). Similarly, in stage III patients, AC was not associated with better OS in univariate (HR 0.78; 95% CI 0.48-1.29; p = 0.340) or multivariable analyses (HR 0.55; 95% CI 0.28-1.04; p = 0.067). In the entire cohort 5-year OS for patients that received AC was 83.9% (80.3%, 86.6%) versus 70.7% (60.9%, 78.5%) (p = 0.001) with no AC. For stage II patients, 5-year OS was 77.3% with AC vs. 87.7% with no AC (p = 0.562). For stage III patients, 5-year OS was 64.8% with AC vs. 54.4% with no AC (p = 0.340). Conclusions: AC was not associated with improved 5-year OS in patients with pathological stage II and III GCT compared to no AC. Research Sponsor: None.
Diagnostic performance of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) for the evaluation of hypermetabolic lymphadenopathy mediastinum lower, posterior, and middle, detected by PET-CT with 18F-FDG (PET) (APOGEE Study). First Author: Dominique Bechade, Bergonié Institute, Bordeaux, France

**Background:** In the context of a new cancer or relapse, the high sensitivity (95%) of PET-CT with 18F-FDG can lead to the demonstration of hypermetabolic mediastinal adenopathies. Its lower specificity (Sp) (89%) can require histological examination. We report the results of a prospective, single-center study evaluating the diagnostic performance of EUS-FNA in this indication. **Methods:** Prospective single-center study featuring patients in whom PET had revealed hypermetabolic mediastinal lymphadenopathy requiring diagnostic certainty. All EUS-FNA were performed with a 19-gauge needle (EchoTip, Cook Endoscopy). Main objective: To evaluate the diagnostic performance in terms of Se and Sp of EUS-FNA in the characterization of hypermetabolic mediastinal adenopathies in PET in the context of a new cancer or relapse. Secondary objectives: To evaluate the negative predictive value (NPV) of the EUS-FNA and to evaluate the percentage of surgical diagnostic procedures avoided. The standard technique was a thoracoabdominal CT scan at 6 months and at 12 months. **Results:** 52 patients were eligible and available for the primary endpoint. The most common primary cancers were mammary (17.3%) and bronchial (13.5%). The lymph nodes were analyzed as malignant in 44.2% of cases, benign in 50% of cases and atypical or suspicious in 3.8% of cases. The malignant lymph nodes were metastatic for breast cancer in 21.7% of cases, bronchial cancer in 17.4% of cases, colorectal cancer in 17.4% of cases and prostate cancer in 13% of cases. The Se and the EUS-FNA are 92% (95% CI: 0.74-0.99) and the Sp 100%. NPV was 87% (95% CI: 0.59-0.98). A diagnostic surgical procedure was necessary in 2% of the cases. PET and EUS-FNA often allowed the modification of the therapeutic strategy. **Conclusions:** When a confirmed diagnosis is required, this study confirms the minimality of procedure of EUS-FNA but insufficiently robust to avoid a surgical diagnostic technique. The combination of PET and EUS-FNA may alter the therapeutic strategy that would have been considered after PET alone. Clinical trial information: NCT01892501. Research Sponsor: None.


**Background:** CMS announced plans to pilot an alternative payment model (APM) utilizing a fixed payment per ICD-10 code for 17 malignancies. CMS released payment data used to calculate the base payments. The purpose of this study was to analyze radiotherapy use in patients with gastrointestinal malignancies to obtain baseline utilization and payment prior to the APM start. **Methods:** The CMS database, CY2015-2017, contained payment, anatomic site and limited patient data on 517,988 patients, 48,032 of which were released payment data used to calculate the base payments. The purpose of the study was to evaluate the use of radiotherapy in patients with gastrointestinal malignancies to obtain baseline utilization and payment prior to the APM start. **Results:** Anatomic site breakdown was 4940 A, 16,099 CR, 6,970 P, 14,750 Gastric and 9,739 Esophageal. Cancer in 17.4% of cases and prostate cancer in 13% of cases. The Se and the EUS-FNA are 92% (95% CI: 0.74-0.99) and the Sp 100%. NPV was 87% (95% CI: 0.59-0.98). A diagnostic surgical procedure was necessary in 2% of the cases. PET and EUS-FNA often allowed the modification of the therapeutic strategy. **Conclusions:** When a confirmed diagnosis is required, this study confirms the minimality of procedure of EUS-FNA but insufficiently robust to avoid a surgical diagnostic technique. The combination of PET and EUS-FNA may alter the therapeutic strategy that would have been considered after PET alone. Clinical trial information: NCT01892501. Research Sponsor: None.
Declining use of red blood cell transfusions for gastrointestinal cancer surgery: A population-based analysis. First Author: Jesse Zuckerman, Division of General Surgery, Department of Surgery, University of Toronto, Toronto, ON, Canada

Background: Perioperative anemia is common in gastrointestinal (GI) cancer surgery patients and is often managed with red blood cell transfusions (RCT), which carries risks for inferior oncologic outcomes. Despite level-1 evidence for restrictive transfusion strategies, RCT use is often not consistent with guidelines leading to a high rate of unnecessary transfusions. Understanding of RCT use at the population-level is necessary to develop system-level efforts to minimize perioperative RCT for cancer. We sought to evaluate the secular trends of transfusion in a large North American population.

Methods: We conducted a population-based retrospective cohort study of patients undergoing GI cancer resection between 2007-2018 using linked administrative health datasets in Ontario, Canada. Primary outcome was administration of any RCT during the hospitalization. Temporal RCT trends were analyzed with Cochrane-Armitage tests for trend. Modified Poisson regression assessed trends while controlling for potential confounders.

Results: Of 79,764 patients undergoing GI cancer resection, median age was 69 (IQR: 60-78) years old and 55.5% were male. The most frequent cancer site was colorectal cancer (n = 63,243), followed by esophago-gastric (n = 7,307), hepatopancreato-biliary (n = 6,560), and small bowel (n = 2,704). 30% of patients received RCT. The proportion of patients who received transfusion declined from 26.5% in 2007 to 18.9% in 2018 (p < 0.001). This trend remained consistent when stratified by sex, age, cancer type, operative approach, procedure setting, and institution teaching status. After adjusting for patient and institutional factors, the time period was associated with receipt of RCT with a relative risk of 0.94 (95% CI 0.91-0.96) for 2014-15 and 0.75 (95% CI 0.73-0.78) for 2015-2018 compared to the period of 2007-10.

Conclusions: Over the 11-year study period, we observed a decrease in RCT for GI cancer resection. These findings may reflect the dissemination of clinical guidelines and implementation of patient blood management programs. An evaluation of institutional variation and the relationship with outcomes is warranted to identify opportunities for further improvement. Research Sponsor: Canadian Institute of Health Research, Other Foundation.

The alarming rise in gastric and colorectal cancers in young adult patients: Analysis of large databases. First Author: Amir Ali Khan, City of Hope Comprehensive Cancer Center, Duarte, CA

Background: The alarming rise in the incidence of gastric (GC) and colorectal (CRC) adenocarcinomas in young adults (YA) over the past three decades is not well understood. How YA populations differ from older patients with the same cancer, derived significant benefit in achieving sustained partial response and overall survival (OS), new biomarkers containing 50% of pts at our institution from 2012 and 2018 that received non-FDA approved TT. The clinical characteristics and temporal patterns of non-FDA approved TT use were evaluated. Transfusion-Free Survival (TFS) was defined as the time of initiation of non-FDA approved TT until the last follow-up or death due to any cause. Results: Of 1000 pts, 652 had tumors harboring AMs, however, only 38 pts met study criteria of receiving non-FDA approved TT with sufficient follow up time. Median age was 57.7 years and 92% of pts received at least one prior line of therapy. Majority of the pts (58%) had gastrointestinal tumors. PD-1, microsatellite instability, and tumor mutational burden constituted 50% of pts and 45% of pts received TT with immunotherapy, 14/38 pts had ORR2, 12 (ORR2) and 12 (ORR3) months (mos) was estimated using standard methods for proportions. Kaplan-Meier method was used to estimate PFS and OS. Results: Of 1000 pts, 652 had tumors harboring AMs, however, only 38 pts met study criteria of receiving non-FDA approved TT with sufficient follow up time. Median age was 57.7 years and 92% of pts received at least one prior line of therapy. Majority of the pts (58%) had gastrointestinal tumors. PD-L1, microsatellite instability, and tumor mutational burden constituted 50% of pts and 45% of pts received TT with immunotherapy, 14/38 pts had ORR2, 12 pts had ORR2, and 6/7 pts had ORR3. PFS was estimated to be 2.73 mos (95% CI: 2.33 to 5.39) and OS was 9.93 mos (95% CI: 4.47 to 33.68). Conclusions: The majority of pts had progression within 3 mos of initiating TT indicating a PM approach with non-FDA approved TT may not be an effective strategy. However, a minority of pts (4 with colorectal and 1 with pancreatic cancer), derived significant benefit in achieving sustained partial response and one pt with complete response at 3 years. Although genomic profiling of tumors by a step in the disease progression, direction, we believe this a better and more cost-effective strategies to identify pts who will truly benefit from a PM approach. More PM trials are needed to establish the standard of care to guide real-world practice. Research Sponsor: None.
**807** Poster Session (Board #J11), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

**Family history (FH) of gastrointestinal (GI) cancer and behavioral risks: Analysis of an Internet-based risk assessment tool.** First Author: Ryan M. O’Reeke, Perelman School of Medicine, Philadelphia, PA

**Background:** Certain behaviors are known modifiable risk factors for development of GI cancers. The relationship between family history (FH) of GI cancers and patient’s behaviors is not well understood. The purpose of this study was to assess the association of FH of GI cancer and the uptake of risk assessment counseling. **Methods:** The OncoLink “Reduce My Risk” tool is a publicly available online survey created in 2009 to provide customized information regarding cancer risk. Details of this survey have been reported; research is IRB-approved. Differences between those with v. without FH of GI cancers were analyzed using chi-square test. **Results:** 28,001 surveys were submitted. Median age was 26y (IQR = 18-101), 60% female, 87% lived in North America, 76% White/Non-Hispanic, 64% reported FH of cancer. Individuals with FH of CRC reported eating less red meat (33% v. 34%, p = 0.007) and processed grains (55% v. 59%, p < 0.001), or charred meats (14% v. 19%, p < 0.001), but were equally likely to be vegetarian (9% v. 10%, p = 0.059). Those with FH of esophageal cancer were more likely to have GERD (16% v. 9%), smoke < 1 pack per day (7% v. 4%) and drink alcohol (63% v. 55%) (p < 0.001 for all). Those with FH of gastric cancer were more likely to have H. Pylori or gastric ulcers (5% v. 3%, p < 0.001), but no difference in the consumption of smoked/salted foods (27% v. 25%, p = 0.20). Those with FH of HCC reported no differences in alcohol consumption (56% v. 55%, p = 0.41) or hepatitis B virus (HBV) vaccination (62% v. 62%, p = 0.66). Those with FH of an anal cancer were more likely to have recent anal intercourse (26% v. 16%, p < 0.001) but showed no differences in human papillomavirus (HPV) vaccination (22% v. 22%, p = 0.91). Those with FH of HCC (95% v. 83%, p = 0.035), gastric (16% v. 13%, p = 0.001), esophageal (7% v. 13%, p < 0.001), and anal (21% v. 13%, p < 0.001) cancers were more likely to be smokers; those with a FH of CRC were less likely (11% v. 13%, p = 0.006), and those with FH of pancreatic (12% v. 13%, p = 0.71) or cholangiocarcinoma and melanoma (28% v. 23%, p = 0.35) showed no difference. **Conclusions:** Many individuals with a FH of GI cancers engage in behavioral and other modifiable risk factors that increase risk for GI and other cancers. Future work should explore utility of targeted intervention and screening. Research Sponsor: None.

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**808** Poster Session (Board #J12), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

**Cirulating ensembles of tumor-associated cells in gastrointestinal cancers.** First Author: Dadasheb Akolkar, Datar Cancer Genetics Limited, Nashik, India

**Background:** CEA and CA19-9 are non-specific markers for Gastrointestinal (GI) cancers. Molecular analysis of fecal blood is of limited utility in colorectal cancers. A non-invasive pan-GI cancer blood-based test with high specificity and sensitivity is an unmet medical need. Considering that unprovoked thromboembolism is a significant risk in multiple cancers, we hypothesized that circulating thrombotic emboli in peripheral blood could comprise cancer cells and could serve as a reliable biomarker for detection of GI cancers. **Methods:** We obtained 15ml of blood from 7481 individuals, including 181 cases of Esophageal cancer, 125 cases of Gastric cancer, 448 cases of colorectal cancer and from 6127 asymptomatic individuals with age related elevated risk who underwent evaluation of serum CA19-9 and AFP. Peripheral blood mononuclear cells (PBMC) were isolated by centrifugation and further processes for negative enrichment and harvesting of circulating tumor cell clusters which were characterized by immunostaining. Cirulating Ensembles of Tumor Associated Cells (C-ETACs) were defined as clusters of 3 or more cells which were positive for EpCAM and CK, irrespective of CD45 status. **Results:** C-ETACs were detected in 86.7% of esophageal cancers, 94.4% of gastric cancers and 91.3% of colorectal cancers respectively irrespective of extent (stage / metastatic status) of disease and prior treatments. Overall sensitivity among 754 cancer patients was 90.7%. Among the asymptomatic individuals, C-ETACs were detected in 31 / 366 (8.5%) individuals with elevated CEA and 10 / 152 (6.2%) individuals with elevated CA19-9. C-ETACs were detected in HCC (0.65 v. 0.35), gastric (16% v. 13%), esophageal (7% v. 13%) and anal (21% v. 13%) cancers. **Conclusions:** C-ETACs were ubiquitously detected in cancers of Oesophagus, Stomach and Colorectum regardless of stage and treatment status, and pose significant latent risk of thromboembolic metastasis/recurrence. The relative undetectability of C-ETACs in the asymptomatic cohort indicates causative connection with malignancies and are suitable for screening for these cancers. Research Sponsor: Datar Cancer Genetics Limited.

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**809** Poster Session (Board #J13), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

**Female representation in clinical trials leading to FDA cancer drug approvals for gastrointestinal (GI) cancers between 2008 to 2018.** First Author: Shehara Ramyalini Mendis, BC Cancer, Vancouver, BC, Canada

**Background:** Proportionate representation of women in health research is an area for improvement. This study aims to assess the representation of women in gastrointestinal (GI) cancer clinical trials leading to FDA cancer drug approvals over the past 10 years. **Methods:** FDA cancer drug approvals between 2008-2018 were identified and trial reports supporting approvals sourced. The ratio of female to male (F:M) enrollment was compared with F:M cancer incidence in the U.S., and U.S. cancer prevalence and mortality. **Results:** F:M trial enrollment compared to cumulative U.S. incidence at those tumor sites (0.89 v. 0.86; Odds Ratio for female enrollment (OR) 1.05, 95% Confidence Interval (CI) 1.03-1.06, P<0.0001). At 2014-2018 trials that led to drug approvals in GI cancers there was lower F:M trial enrollment compared to cumulative U.S. incidence at those tumor sites (0.95 v. 0.97, OR 0.99, 95% CI 0.97-1.01, P<0.0001). There was no difference in male enrollment between approvals in this period was similar to overall F:M cancer incidence in the U.S. (0.89 v. 0.86; Odds Ratio for female enrollment (OR) 1.05, 95% Confidence Interval (CI) 1.03-1.06, P<0.0001). In trials that led to drug approvals in GI cancers there was lower F:M trial enrollment compared to cumulative U.S. incidence at those tumor sites (0.55 v. 0.79, OR 0.71, 95% CI 0.68-0.74, P<0.0001). **Conclusions:** Although disparity in female enrollment may be improving across combined FDA cancer drug approval trials, underrepresentation of females has persisted in GI cancer trials when compared to F:M cancer incidence, prevalence and mortality in the U.S. More work is required to determine the drivers of this disparity, in order to mitigate it. Research Sponsor: None.

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**810** Poster Session (Board #J14), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

**The cost of chemotherapy administration: A systematic review and meta-analysis.** First Author: Gursharan Kaur Sohi, Sunnybrook Research Institute, Toronto, ON, Canada

**Background:** Cancer treatment is a significant driver of healthcare costs worldwide, however, the economic impact of treating patients with anti-neoplastic agents is poorly elucidated. Hence, we conducted a systematic review and meta-analysis to estimate the direct costs associated with administering intravenous chemotherapy in an outpatient setting. **Methods:** We systematically searched four databases from 2010 to present and extracted hourly administration costs and the respective components of each estimate. Separate analyses were conducted of Canadian and United States (US) studies, respectively, to address a priori hypotheses regarding heterogeneity amongst administration cost estimates. The Drummond checklist was used to assess risk-of-bias. Data were summarized using medians with interquartile ranges and five outliers were identified; costs were presented in 2019 USD. **Results:** A total of 44 studies were analyzed, including subanalyses of 19 US and seven Canadian studies. 26/44 studies were of moderate or high quality. When components of administration cost were evaluated, physician costs were reported most frequently (24 studies), followed by lab tests (13) and overhead costs (9). The median cost estimate when outliers were excluded was $142/hour (IQR = $103-166). Sensitivity analyses determined the median administration cost in the US was $149/hour (IQR = $118-158), and was $128/hour (IQR = $103-166). There is currently a paucity of literature addressing the costs of chemotherapy administration, and existing studies utilize a patchwork of reporting methodologies which renders direct comparison challenging. Our results demonstrate that the cost of administering chemotherapy is approximately $125-150/hour, globally. This value is dependent upon the region of analysis, inclusiveness of cost subcomponents and sensitivity is an unmet medical need.
Emergency department use at the end of life in elderly patients with gastrointestinal malignancies and mental health comorbidities. First Author: Mehr Khashay, Stanford University School of Medicine, Stanford, CA

Background: Aggressive care at the end-of-life can contradict patients’ wishes, negatively impact patient quality of life, and contribute to overall health care expenditures. Patients with mental disorders (MD) often experience disparities in medical care and have poorer clinical outcomes. We investigated the impact of mental disorders on emergency department (ED) use at the end of life among elderly patients with gastrointestinal (GI) malignancies.

Methods: We conducted a retrospective cohort study using the SEER-Medicare database. We identified patients aged 66 years and older with GI malignancies (colorectal, pancreatic, gastric, hepatic, biliary, esophageal, small bowel, and anal cancer) diagnosed between 2004 and 2013 who had recorded death. We assessed the association between MD (depression, bipolar disorder, psychotic disorder, anxiety, dementia, and substance abuse) and ED use within 30 days of death using logistic regression models.

Results: Of the 160,367 decedents included, 54,461 (34.1%) had at least one MD diagnosis between one year prior to cancer diagnosis and death. Those with MD were more likely to use the ED more than once in the last 30 days of life (14.7% vs. 12.4%, p < 0.01). ED use was highest among decedents with anxiety disorder (15.8%) and substance abuse (16.3%). Among decedents with mental disorders, risk factors associated with ED use at end of life include being male (adjusted odds ratio [aOR] 1.16, 95% confidence interval [CI] 1.10 – 1.22), younger (aOR 1.14, 95% CI 1.10 – 1.23), and black (aOR 1.33, 95% CI 1.23 – 1.45), living in a lower income zip code (1.22, 95% CI 1.13 – 1.30), and having a higher Charlson comorbidity score (aOR 1.71, 95% CI 1.56 – 1.87). ED use was also associated with pancreatic (aOR 1.16, 95% CI 1.08 – 1.25), hepatic (aOR 1.21, 95% CI 1.11 – 1.33), biliary (aOR 1.16, 95% CI 1.13 – 1.30) and esophageal (aOR 1.16, 95% CI 1.04 – 1.29) cancer compared to colorectal cancer. Conclusions: MD is associated with increased ED use at the end of life among elderly patients with GI cancer. Palliative and supportive care including mental health services early in the disease course may improve quality of end-of-life care in this vulnerable population.

Survivorship care engagement with American Indian and Alaska Native survivors of gastrointestinal (GI) cancers. First Author: Christine E. Hill-Kayser, Hospital of the University of Pennsylvania, Philadelphia, PA

Background: American Indian and Alaska Native (AI/AN) survivors are at significant risk for GI cancers, and also represent an underserved medical population. Gastrointestinal cancers represent the third most commonly diagnosed cancers in the AI/AN population, and are a leading cause of death. Survivorship resources tailored for the AI/AN population are sparse and patterns of survivorship care poorly understood.

Methods: The OncoLife survivorship care plan has been through the OncoLink website since 2007. The free and publicly available tool asks survivors and/or their caregivers questions about their experience with GI cancer. Based on responses, the tool generates a personalized report for the patient and their oncologist, including diagnosis, demographics, and treatments, and provides customized guidelines for future care. All research is IRB approved.

Results: Over the past 12 years, the OncoLife tool has been utilized by >85,000 persons, with survivors of GI cancer representing 10-12% of users each year. Most users are women (75%) and Caucasian (80%). American Indian and Alaska Native survivors represent <1% of users since the launch of the tool. Of 519 AI/AN users, median age was 54 years, and 76% identified as female. Of plans created for AI/AN survivors, 13% were for survivors of GI cancers, with the most common GI diagnosis being colorectal cancer (74%), followed by pancreas (11%) and anal (6%). Most plans (73%) were created by HCP, with the remainder by survivors themselves; 20% of AI/AN users completing plans requested information on smoking cessation as part of their care plan.

Conclusions: American Indian and Alaska Native survivors represent a very small minority of survivors utilizing this free Internet-based tool, with most plans for this population being created by healthcare providers and not by survivors themselves. Future efforts should be directed at supporting this underserved population with survivorship care plans, particularly given high risk of morbidity and mortality related to GI cancers. Research Sponsor: Livestrong Foundation.
A retrospective analysis of factors affecting palliative care consult in patients undergoing cytoreductive surgery and HIPEC. First Author: Laila Babar, The Esophageal and Lung Institute, Allegheny Health Network, Pittsburgh, PA

Background: The National Cancer Institute defines palliative care as care given to improve the quality of life (QOL) for patients with life threatening, irreversible disease. The role of palliative care (PC) within oncology is ever evolving and as more studies are being conducted, its role in the improvement of QOL for patients is being widely recognized. Patients undergoing cytoreductive surgery (CRS) are at a high risk for morbidity and mortality and often have severe post-operative symptoms that can worsen their QOL. Here we studied the factors affecting PC consult in order to better overcome them.

Methods: We queried our Electronic Medical Record Epic for a list of patients who underwent cytoreductive surgery with HIPEC or HITEC in the hospital from April 2016-April 2019. Data was manually extracted and patients who didn’t meet our criteria were excluded. Patients were divided on the basis of palliative care consults and differences between the groups were analyzed. Odds ratios/OR with p-value 0.05 and confidence interval (CI) 95% were calculated. Results: We identified 55 patients of whom 34 met our inclusion criteria, 11 male and 23 female with an average age of 56.3 years at the time of diagnosis. 8 patients (23%) had PC; more than 1 comorbidity and age ≥ 50 was associated with a higher likelihood of PC (OR:0.11; CI:0.05-0.26; p=0.02) and (OR: 0.05; CI: 0.0007-0.30; P= 0.006) respectively. Gender, insurance type and marital status did not correlate with PC. Mean age (58.1 vs 55.7) showed a trend towards higher rates of PC in older population.

Conclusions: Approximately one quarter of patients undergoing CRS with HIPEC had a concurrent PC consult. Though this is better than the national average of 11-16%, it continues to be a very small number. PC is not only an end of life service, in fact studies have shown early consultations lead to higher patient satisfaction, improved QOL and better communication. Efforts must be made to engage patients early in the course of treatment and recognize it as an integral part of cancer care. Research Sponsor: None.

815 Poster Session (Board #J9), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

816 Poster Session (Board #J20), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

Comparison of treatment plans feasible through AI enabled multidisciplinary online tumor board solution versus NCCN-based clinical decision support system (CDSS). First Author: Bhawna Sirohi, National Cancer Grid, Mumbai, India

Background: Multidisciplinary tumor boards at Academic Medical Centers (AMC) maximize cancer outcomes. Guidelines based CDSS are alternatives to determine care pathways. Since 2015, 300 AMC cancer experts in USA and India use an AI enabled online tumor board solution, “NAVYA”, to scale low cost access to multidisciplinary expertise, on 7-2 minutes of expert time per decision (ASCO 2017). Methods: Patients who used NAVYA between 5/1/15-8/31/19 were analyzed. Actionable treatment plans generated by NAVYA were compared to NCCN. Actionable treatment plans include chemotherapy protocols (doses, frequencies), radiation protocols (sites, fractions), etc. In actionable specialty level decisions (CT-RT vs. surgery) lack specificity.

Results: 1302 patients (4638 treatment decisions) were analyzed: 6% (794) male, 80% age between 45 to 75, mostly with Colon, Pancreas, Gallbladder, Rectum, or Stomach cancer; 49.7% non-metastatic. Cohort was comparable in terms of race, insurance, first line protocol used, and median OS. NAVYA recommended a patient-specific treatment plan that was not part of NCCN. Second, in 3.2% (148/4638), NAVYA recommended treatment plans for clinical scenarios not covered by NCCN, (for eg, 3rd line therapies). Third, in 74.5% (3452/4638), NAVYA used patient specific criteria including resource constraints and patient preference to choose a treatment plan among the multiple pathways provided by NCCN and added actionable treatment details.

Conclusions: Guideline based CDSS is insufficient to make the vast majority of actionable treatment decisions. Scaling rapid access to multidisciplinary experts is critical. Leapfrogging existing guidelines based CDSS, NAVYA online tumor board makes actionable expert treatment plans possible at a large scale. Research Sponsor: None.

817 Poster Session (Board #K1), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

First analysis of same day pegfilgrastim use with concurrent capectabine-based regimens in pts with GI malignancies. First Author: Nausheen Hakim, Northwell Health Cancer Institute, Lake Success, NY

Background: Pegfilgrastim is administered 24 hrs after chemotherapy to reduce risks of myelosupression. This requires an additional clinic visit, which can be difficult for some patients (pts) due to work and transportation issues. Therefore, administering pegfilgrastim to reduce myelotoxicity. Capecitabine is converted to active effect of opioid therapy. Laxatives are usually used as a first-line treatment for OIC. Treatment options for OIC are switching to other opioids associated with non-oral routes. Naldemedine is an orally active peripherally acting μ-receptor antagonists that was approved in Japan from 2017 for management of cancer-related OIC. The aim of this study is to investigate the relationship between Naldemedine administration and the maximum dose of oral Oxycodone which is the most frequently used oral opioids at our hospital. Methods: During June 2017 and December 2018, a total of 217 patients with cancer-related pain received Oxycodone at our institution. The first group of the patients concurrently received Naldemedine 0.2 mg daily (group A, n = 101), and the second group didn’t receive it (group B, n = 116) for cancer-related OIC reduction. We compared the maximum Oxycodone dose between two groups by medical record retrospectively.

Results: The median age of group A was 69 y.o. (range 20-87 y.o.), and the median age of group B was 67 y.o. (range 27-88y.o.). There was no significant difference in common patient background between group A and B. The median dose of maximum Oxycodone dose of group A was 40 mg/day (range 10-480 mg/day), and that of group B was 20 mg/day (range 10-320 mg/day). There was a significant difference in the median dose of maximum Oxycodone between group A and B (Mann-Whitney U test, P < 0.0001). In Group A, the administration was started in 31 patient Naldemedine and Oxycodone at the same time. As for 70 remaining patients, the administration was started when they had constipation after oxycodone was administered. In those patients, the median days was 19 days from the Oxycodone administration starting date to the Naldemedine administration starting date. Conclusions: Naldemedine administration in patients with cancer-related OIC may increase the maximum dose of oral Oxycodone. Research Sponsor: None.

818 Poster Session (Board #K2), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM

The relationship between naldemedine administration and the maximum dose of oral opioids. First Author: Shinya Kajiiura, Toyama University Hospital, Toyama-Shi, Japan

Background: Opioid-induced constipation (OIC) is the most common side effect of opioid therapy. Laxatives are usually used as a first-line treatment for OIC. Treatment options for OIC are switching to other opioids associated with non-oral routes. Naldemedine is an orally active peripherally acting μ-receptor antagonists that was approved in Japan from 2017 for management of cancer-related OIC. The aim of this study is to investigate the relationship between Naldemedine administration and the maximum dose of oral Oxycodone which is the most frequently used oral opioids at our hospital. Methods: During June 2017 and December 2018, a total of 217 patients with cancer-related pain received Oxycodone at our institution. The first group of the patients concurrently received Naldemedine 0.2 mg daily (group A, n = 101), and the second group didn’t receive it (group B, n = 116) for cancer-related OIC reduction. We compared the maximum Oxycodone dose between two groups by medical record retrospectively.

Results: The median age of group A was 69 y.o. (range 20-87 y.o.), and the median age of group B was 67 y.o. (range 27-88y.o.). There was no significant difference in common patient background between group A and B. The median dose of maximum Oxycodone dose of group A was 40 mg/day (range 10-480 mg/day), and that of group B was 20 mg/day (range 10-320 mg/day). There was a significant difference in the median dose of maximum Oxycodone between group A and B (Mann-Whitney U test, P < 0.0001). In Group A, the administration was started in 31 patient Naldemedine and Oxycodone at the same time. As for 70 remaining patients, the administration was started when they had constipation after oxycodone was administered. In those patients, the median days was 19 days from the Oxycodone administration starting date to the Naldemedine administration starting date. Conclusions: Naldemedine administration in patients with cancer-related OIC may increase the maximum dose of oral Oxycodone. Research Sponsor: None.
Risk factors for cancer-associated thrombosis in advanced cancer patients with chemotherapy or palliative treatment (retrospective study).

First Author: Koki Uehara, Department of Medical Oncology Sasebo Kyosai Hospital, Sasebo, Japan

Background: Cancer-associated thrombosis (CAT) represents the second-leading cause of death in cancer patients. Initial symptoms of venous thromboembolism (VTE) occurs in about 20% of hospitalized cancer patients. CAT is important for safety cancer treatment. However, the risk factors for CAT in Japanese cancer patients have not been well studied. Methods: We retrospectively examined cases that had received chemotherapy or palliative treatment from April 2017 to February 2018 in our hospital using medical records. Results: Fifty-five cases with 37-94 years (23 males and 32 females) were examined. Primary sites of cancers were as below; pancreatic: n = 14 (25%), colorectal: n = 12 (22%), gastric: n = 7 (13%), breast: n = 4 (7%), lung: n = 3 (5%), esophageal: n = 3 (5%), head and neck: n = 3 (5%), and others: n = 9 (16%). Forty-two patients (76%) were treated with chemotherapy, and 12 (22%) of them were diagnosed with CAT at the beginning or during the course of chemotherapy (CAT group). The sites of CAT were as follows; lower extremity type venous thrombosis: n = 10, cerebral infarction: n = 3, pulmonary artery thromboembolism: n = 1, portal vein thrombosis: n = 1, subclavian vein thrombosis: n = 1, and others: n = 2. In 12 patients with CAT, primary sites of cancers were as below; pancreatic: n = 6 (45%), gastric cancer: n = 3 (23%), colorectal, esophageal and ovarian cancer: n = 1 (9%), and 8 patients (60%) received anticoagulant therapy, including 7 patients treated with DOACs. Conclusions: Our analysis showed that patients with confirmed cancer-associated thrombosis were at high risk of CAT. CAT group had more severe symptoms that required prompt medical attention.

Feasibility of endoscopic resection in gastric gastrointestinal stromal tumor. First Author: Yuri Kim, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

Background: Endoscopic resection (ER) can be applied for small SETs of stomach. GISTs can be diagnosed pathologically after resection. Initially we used ESD. Submucosal tunneling endoscopic resection (STER) was introduced for overcoming limitations of ESD. However, STER was very difficult to apply for gastric lesions. We developed new ER method, clip-assisted surgical endoscopy (CASE, Jung’s method). In this study, we evaluate the feasibility of ER for GISTs and compared 3 ER methods. Methods: Medical records of 53 patients who diagnosed GISTs after ER for SETs from 2009 to 2019 were reviewed retrospectively. Average age was 60.0 ± 10.6 years. ESD, STER and CASE were performed for 23, 5, and 25 patients, respectively. Clinical characteristics, procedure times, and outcomes of each endoscopic technique were analyzed. Results: Average pathological size of GIST was 2.1 cm, 94.3% proved to be very low risk of malignant potential. Location of SETs were different; ESD applied mainly for body lesions, STER tried for fundus lesions, CASE also mainly for fundus and high body lesions. Overall RO and RI resection rate was 62% and 35.8%. There are 34 patients who had complications after the procedure (21 micro-perforation, 12 macro-perforation, 1 bleeding), but perforation would be a part of ER procedure for SETs. In ESD, some macroperforations was a reason for surgical conversion. Four patients (2 ESD, 1 STER, 1 CASE) underwent surgical conversion during ER. STER had the longest procedure time (50.3, 95.2 and 40.7 min, P = 0.018). After development of CASE procedure, we can reduce procedure time and on-site surgical conversion. RO resection rate was highest in CASE. No RI resected patients were recurrent so far. Conclusions: ER seems to be safe and effective therapeutic options for removing small gastric GISTs. Using CASE (Jung’s method), ER would be more comfortable especially in the fundus lesions. Research Sponsor: None.
823 Poster Session (Board #K7), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM
Regorafenib as second-line therapy for imatinib-resistant gastrointestinal stromal tumor (GIST). First Author: Tsuyoshi Takahashi, Department of Gastroenterological Surgery, Osaka University, Graduate School of Medicine, Suita City, Osaka, Japan

Background: Imatinib is a standard first line treatment for advanced gastrointestinal stromal tumor (GIST); however, eventually almost all the GISTS become resistant to imatinib. Secondary mutation in KIT is the most relevant cause of imatinib-resistant, as high as 70% of cases. Sunitinib is standard of care for imatinib-resistant GIST with median progression-free survival (PFS) of 24.6 weeks; however, in a preclinical study sunitinib is not active for approximately half of secondary mutations. Regorafenib is active for some secondary mutations resistant to sunitinib in the preclinical study. Therefore, we conducted a phase II study evaluating regorafenib for imatinib-resistant GIST. Methods: Patients with imatinib-resistant advanced GIST were enrolled. Key eligibility criteria were ECOG PS of 0-1 and adequate organ function. Prior exposure of sunitinib was not allowed. The primary endpoint was PFS rate at 24 weeks. cDNA for KIT was evaluated prior to regorafenib administration. Results: A total of 38 patients were enrolled as planned. Median age was 64.5 (39 - 80). Twenty-five patients were male. Primary site was stomach in 17, small intestine in 16. Median PFS was 36.3 weeks and PFS rate at 24 weeks was 47.4% (primary endpoint was not met). Best overall response was PR for 6 (16 %), SD for 25 (63.2 %) and PD for 5 (13 %) patients. Grade 3 or more adverse events (AE) were observed in 25 (66.7 %) patients, Common grade 3 or more AE were hand-foot-skin reaction (n = 9), hypertension (n = 4), hepatotoxicity (n = 4). cDNA was evaluated in 32 patients and among them secondary mutations were observed in 15 patients (47%). PFS was shorter (15.6 weeks) in patients with exon 13 mutation than that in patients without second mutation (49.3 weeks, not statistically significant). Conclusions: Regorafenib demonstrated favorable activity in patients with imatinib-resistant GIST as second line therapy with acceptable toxicity. Secondary mutation in KIT might be a predictor of the efficacy of regorafenib. Clinical Trial information: UMIN00000679.
Research Sponsor: Bayer.

824 Poster Session (Board #K8), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM
Efficacy and safety of larotrectinib in patients with TRK fusion gastrointestinal cancer. First Author: Jordan Berlin, Vanderbilt-Ingram Cancer Center, Nashville, TN

Background: Tropomyosin receptor kinase (TRK) fusions arise from rearrangements of the neurotropic tyrosine kinase receptor kinase (NTRK) 1, 2, or 3 genes and an unrelated gene, creating constitutively active oncogenic drivers that have been detected in a range of adult and pediatric malignancies, but are generally rare in patients with gastrointestinal (GI) cancer. Larotrectinib is a selective TRK inhibitor approved for the treatment of adult and pediatric patients with TRK fusion cancer. Here, we report efficacy and safety data for patients with TRK fusion GI tumors. Methods: Patients with a TRK fusion GI cancer treated with larotrectinib in a phase II clinical trial, NAVIGATE (NCT02576431), were included in this analysis. Larotrectinib was administered at 100 mg twice daily, until disease progression, unacceptable toxicity, death, or withdrawal. Response was assessed by the investigator using RECIST v1.1. Results: As of February 19, 2019, 14 patients with TRK fusion GI cancer (median age 68 y, range 32-84 y) were enrolled. GI tumor types were colon (8), cholangiocarcinoma (2), pancreas (2), appendix (1), and hepatic (1). Fusions involved NTRK1 (n = 12) and NTRK3 (n = 2). Nine patients had ≥ 2 prior lines of therapy. The best response on last prior therapy was 1 partial response (PR). Overall best responses on larotrectinib were: colon cancer, 4 patients had a PR and 4 had stable disease (SD); pancreatic cancer, 1 patient had a PR and 1 had SD; cholangiocarcinoma, 1 patient had a PR and 1 had progressive disease; appendix cancer, 1 patient had SD; response in 1 patient with hepatic cancer was not determined. Median time to response was 1.8 months (range 1.7-2.1). In patients ongoing treatment, the median progression free survival was 5.3 months (95% CI 2.2 - 9.0). Median overall survival was 33.4 months (95% CI 28.2-36.5). Larotrectinib was well tolerated, with most adverse events being grade 1 or 2. Conclusions: Although the sample size is limited, there is evidence of clinical activity with larotrectinib in TRK fusion GI cancer, with a manageable safety profile. TRK fusion GI cancer may represent an under-diagnosed subset of patients with viable treatment options. Clinical trial information: NCT02576431.
Research Sponsor: Bayer AG and Loxo Oncology, Inc, a wholly owned subsidiary of Eli Lilly and Company.

825 Poster Session (Board #K9), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM
Stereotactic radiotherapy in oligometastatic (OM) gastrointestinal (GI) tumors: A single institution retrospective analysis. First Author: Renata Reis Figueiredo, Hospital Sirio-Libanês, Brasília, Brazil

Background: Metastatic GI cancers are mainly treated with systemic treatment (ST), in selected patients (pts), surgery is considered depending on pts characteristics and institutional preferences. Stereotactic Radiotherapy (SRT) is a well described treatment option that may provide good local control and maximize ST results for oligometastatic pts. Methods: This is a single center retrospective study. Data were collected from sequential pts with GI tumors who underwent SRT for OM-GI cancers from May 2014 to July 2019. Information was collected on pts characteristics, primary site, clinical staging at diagnosis, sites undergoing SRT, whether there was progression after the first SRT, time between the first SRT and progression and the last follow-up date. Results: 381 pts underwent SRT in our center, of these, 75 pts had OM-GI tumors and underwent 120 courses of SRT. 50.7% were women, the median age at diagnosis was 60 years and the median follow-up was 36 months. 76% had colorectal cancer (CRC) being 26% from the right, 26% from the left colon and 30% were from the rectum, in 18% of the patients we could not determine sidedness. 35% already had metastatic disease at diagnosis. The lung was the site with largest number of lesions treated with SRT (50), followed by central nervous system (CNS) (42), bones (32), liver (29) and lymph nodes (16). After a median follow up of 15.3 months, 11% of patients were progression-free and only 24% had progressed on treated lesions. The median progression free survival following SRT was 4.5 months (0.6-45.8 range) for distant metastasis and was not achieved for treated sites. Conclusions: This retrospective study adds to the previous body of evidence supporting the use of SRT to improve GI cancer management. Detailed information on pts characteristics, pathology, toxicity and previous treatments will be presented.
Research Sponsor: None.

826 Poster Session (Board #K10), Thu, 12:00 PM-1:30 PM and 4:45 PM-5:45 PM
Clinical activity of avapritinib in ≥ fourth-line (4L+) and PDGFRα Exon 18 gastrointestinal stromal tumors (GIST). First Author: Michael C. Heinrich, OHSU Knight Cancer Institute, Portland, OR

Background: Targeting oncogenic KIT and PDGFRα mutations revolutionized treatment of patients (pts) with advanced GIST; however, nearly all pts succumb to resistant disease. Avapritinib is a potent and selective kinase inhibitor with [KIT]PDGFA selectivity against KIT to > 1000-fold compared to PDGFRα, PDGFRα DB427 and other primary or secondary resistance mutations. Results from the phase 1 NAVIGATOR (NCT02508532) study of avapritinib in pts with advanced GIST are presented. Methods: Adult pts with unreactectable PDGFRα mutant or PDGFRα gene fusion driven GIST treated with larotrectinib in a phase II clinical trial, NAVIGATE (NCT02508532) were analyzed. Efficacy and safety of avapritinib in 4L+ and PDGFRα Exon 18 (Ex 18) mutations treated at the MTD (400 mg)/RP2D (300 mg) were assessed. Results: As of 16 Nov 2018, 237 pts (172 KIT, 62 PDGFRα Ex 18 (56 DB427, 6 non-DB427), 2 PDGFRα N659K, 1 missing) were enrolled including 111 in the 4L+ population (primarily KIT, median 4 prior TKI) and 43 in the Ex 18 population (median 1 prior TKI). The 4L+ ORR was 22% (11 CR, 23 PR (1 pending)), and 52 SD with mDOR of 10.2 months (95% CI: 7.2-NE). The Ex 18 ORR was 86% (3 CR, 34 PR (1 pending)) and 5 SD; mDOR was not reached (95% CI: 11.3-NE). Most AE were grade 1-2, most commonly nausea (63%), fatigue (58%), anemia (49%), periorbital edema (42%), diarrhea (40%), vomiting (40%), decreased appetite (38%), increased lacrimation (33%), peripheral edema (33%) and memory impairment (most common cognitive AE, 29%). 10% of pts discontinued due to a related AE. Grade 3-4 related AE ≥ 2% were anemia, fatigue, hypophosphatemia, hypothyroidism, neutropenia and diarrhea. Conclusions: Avapritinib has important clinical activity in pts with advanced GIST who have no effective therapies. The ORR and DOR of avapritinib in 4L+ exceeds that of approved 2nd and 3rd line therapies and shows impressive activity in DB427 and other Ex 18 mutant PDGFRα GIST. Results suggest avapritinib has the potential to change the treatment paradigm of pts with advanced GIST. Clinical trial information: NCT02508532.
Research Sponsor: Blueprint Medicines Corporation.
Glycogen synthase kinase-3 beta (GSK-3β) blockade with 9-ING-41 in gastrointestinal cancers: The 1801 phase II/III study. First Author: Howard Safran, Brown University, Lifespan Cancer Institute, Providence, RI

Background: 9-ING-41 is a selective GSK-3β inhibitor with significant pre-clinical antitumor activity in a broad spectrum of malignancies as a single agent, and in combination with cytotoxic agents. GSK-3β is a serine/threonine kinase whose overexpression is associated with advanced stage, aggressive tumor growth, and chemoresistance. We report the preliminary results of patients (pts) with gastrointestinal (GI) malignancies.

Methods: Phase Ib/2 study evaluating safety and efficacy of 9-ING-41 as monotherapy and combination therapy in pts with refractory cancers. 9-ING-41 is administered intravenously twice-weekly as a single agent (21-day-cycle) or combined with chemotherapeutic agents, including gemcitabine (GEM), nab-paclitaxel + GEM, carboplatin, or paclitaxel. Study parts 1 and 2 evaluate the safety, describe dose-limiting toxicities (DLTs), determine the maximum tolerated dose and the recommended phase 2 study dose (RP2D) for 9-ING-41 as monotherapy (Part 1) and as combination therapy (Part 2). Part 3 (Simon 2-Stage Phase 2) assess clinical benefit in pts treated with 9-ING-41-based combinations at the RP2D established in Part 2. Response is assessed by RECIST 1.1 criteria in the evaluable lesions.

Results: To date, the study accrued 63 pts. Five dose levels (1, 2, 3, 5, 7 mg/kg) have been completed without DLTs. Part 2 of the study evaluating 9-ING-41-based chemotherapy combinations is ongoing. Five of nine pts with pancreas cancer (PCa) enrolled had stable disease (SD) as the best response; 2 of 9 pts had a 40-45% decline of CA 19-9. One pt completed 6 cycles with 9-ING-41, two pts completed 4 cycles with 9-ING-41/GEM. Two active pts receiving 9-ING-41/GEM achieved SD after 1 and 3 cycles. Three of four pts with adenocarcinoma of the appendix enrolled had SD as the best response; two pts in active treatment are receiving cycles 5 and 6. One out of 13 pts with colo-rectal cancer had SD, 9-ING-41-attributable AE to date are reversible grade 1 transient visual changes (color perception).

Conclusions: 9-ING-41 is well-tolerated with encouraging SD among heavily pretreated pts with carcinoma of the pancreas and appendix. Clinical trial information: NCT03678883. Research Sponsor: Actuate Therapeutics Inc.
Conclusions: of patients. Incidental GISTs were identified during the following surgery: resected at our community cancer center in 15 years were discovered in- 0.65cm and 0.30cm, respectively. Mitotic rate was [44 5 mitosis/50 HPF in 96%]. Based on the FAB classification, colorectal (CRC), gastrointestinal stromal tumors (GIST), and biliary cancers. We are collecting ctDNA, TMs (CEA and CA19-9), and PROs (FACT-G for QOL, [higher scores indicate better QOL]; ESA-s, PRO-CTCAE, and PS) for symptoms; and PHQ-4 (consists of GAS-2 and PHQ-2 for anxiety and depression); higher ESA-s, PRO-CTCAE, and PHQ-4 scores reflect greater symptom burden) at baseline and 4 weeks. ctDNA is benchmarked against somatic tissue alterations, and serially assessed by digital droplet PCR. We correlated median percent change from baseline to 4 weeks for ctDNA, TMs, and PROs with treatment response (clinical benefit [CB], progressive disease [PD]). Results: From April to Au- gust 2019, we have enrolled 38/45 (84.4%) eligible pts (median age = 64 years; 36.8% female). Among these 38 pts, tumor types are PDAC (36.8%), CRC (31.6%), GE (29.9%), and biliary (26.8%). 18/38 pts were evaluable for ctDNA. Change in ctDNA was +42.5% in pts with CB (n = 10) and -19.5% in pts with PD (n = 8; p = 0.025). No correlation was observed between CEA and treatment response (p = 0.367). Change in CA19-9 was -1.5% for pts with CB and +47% for pts with PD (p = 0.019). Changes in PRO-CTCAE (p = 0.345), GAD-2 (p = 0.697), and ESA-s scores (p = 0.764) did not differ between pts with CB and PD. However, changes in PHQ-2 (CB -0% v. PD +22.5%; p < 0.001), PHQ-4 (CB -8.5% v. PD +5%; p = 0.015), and FACT-G (CB +30% v. PD +5%; p = 0.049) were significant. Conclusions: Preliminary analysis suggests that ctDNA and PROs demonstrate promising utility for early prediction of treatment response, with favorable performance relative to standard TMs. Further analyses of larger pt numbers in this ongoing study may clarify the use and integration of these measures to better predict pt outcomes. Research Sponsor: Cancer Center Funds.

Characteristics of gastrointestinal stromal tumors incidentally discov- ered during abdominal surgery. First Author: Meera Joseph Garg, Christiana Care Health Systems, Newark, DE

Background: Gastrointestinal Stromal Tumors (GISTs) are rare sarcomas with 5000 new cases each year. Despite their low incidence, surgeons should be familiar with this pathology since GISTs can be encountered incidentally during surgery (Aparna Raj Parikh, Massachusetts General Hospital, Boston, MA). A retrospective series was conducted by querying pathology and operative reports from a community cancer center between 2005 and 2019 for all GIST diagnoses. Patients identified to have incidental GISTs discovered intraoperatively while undergoing surgery for another indication were the focus of this study. Patient and tumor charac- teristics were evaluated. Results: A total of 195 patients had a diagnosis of a resected GIST during our study period. Of these 195, 48 patients were in- cidentally discovered to have a GIST excised during another index operation. The average age of these patients was 62 years old, 27 were female and 21 male. The primary location of these incidental GISTS in descending frequency was stomach (62.5%, n = 30), small bowel (31.3%, n = 15), colon (42.4%, n = 2) and esophagus (21%, n = 1). The average GIST size for the cohort was 1.7cm, with stomach, small bowel, colon and esophagus measured at 1.8cm, 1.7cm, 0.65cm and 0.30cm, respectively. Mitotic rate was < 5 mitosis/50 HPF in 96% of patients. Incidental GISTs were identified during the following surgery: colon (n = 14), bariatric (n = 13), non-bariatric gastric (n = 10), hernia (n = 4), pancreatic (n = 3), esophageal (n = 2) and other (n = 2). Most incidental GISTS were discovered during elective surgery (83.3%, n = 39) compared to emergency surgery (16.8%, n = 9), and for benign disease (n = 33) compared to malignant (n = 15). Conclusions: Approximately one quarter of all GISTS resected at our community cancer center in 15 years were discovered in- cidentally, and during a wide variety of abdominal surgeries for both benign and malignant disease. Almost all these GISTS were < 2cm, benign, and should be cured with the incidental resection. Abdominal surgeons should be aware of uncertain or atypical GISTs, and should not be apprehensive about resecting since they have indolent characteristics. Larger lesions should trigger expert surgical oncology consultation. Research Sponsor: U.S. National Institutes of Health.
Understanding the expanding armamentarium for GIST: Engaged learning outcomes. First Author: Michelle Arielle Worst, Medscape LLC, New York, NY

Background: Gastrointestinal stromal tumors (GIST) are rare soft-tissue sarcomas that harbor specific genomic alterations, making GIST an ideal model for targeted therapy. Common oncogenic drivers include mutations in the KIT and PDGFR tyrosine kinase. Due to varying resistance patterns to existing TKIs, clinicians are challenged to stay current with new data and how best to integrate new agents into treatment paradigms. The objective of this study was to assess the changes in oncologists’ and gastroenterologists’ knowledge, confidence, and confidence in their participation in education regarding optimal GIST treatment. Methods: The educational activity consisted of a 30-minute online, 2-faculty video discussion with synchronized slides. Educational effect was assessed with a repeated pairs pre-/post-assessment study with a 3-item, multiple choice, knowledge/competence questionnaire and one confidence assessment question. For all questions, each participant served as his/her own control. Pre- and post-assessment scores were compared to determine the relative changes in the proportion of correct responses. A chi-square test assessed statistical significance at the P < 0.05 level. The activity launched 25th June 2019; data were collected until 19th August 2019. Results: Overall significant improvements were seen after education for oncologists (N=52, P < 0.001) and gastroenterologists (N=127, P < 0.01). The relative improvement was 79% for oncologists and 44% for gastroenterologists (pre-/post-assessment average correct response rates were 24%/43% and 23%/33%, respectively). Following the activity, 44% of oncologists and 37% of gastroenterologists were more confident in their ability to select appropriate therapy for patients with metastatic GIST. Conclusions: Participation in an online, 30-minute video discussion CME intervention resulted in statistically significant improvements in knowledge, competence, and confidence of oncologists and gastroenterologists, that may lead to improvements in clinical care. As new data and agents emerge, new educational activities are necessary to reinforce knowledge, close persistent gaps, and increase oncologists’ confidence in this clinical setting. Research Sponsor: Blueprint Medicine.

Phase II study of nivolumab and relatlimab in advanced mismatch repair deficient (dMMR) cancers resistant to prior PD-(L)1 Inhibition. First Author: Katherine M. Bever, The Sidney Kimmel Comprehensive Cancer Center and Bloomberg-Kimmel Institute for Cancer Immunotherapy at Johns Hopkins, Baltimore, MD

Background: Cancers deficient in DNA mismatch repair (dMMR) are highly immunogenic tumors exhibiting high rates of response to immune checkpoint inhibitors targeting the programmed cell death-1 (PD-1)/PD-1 ligand (PD-L1) interaction. These tumors are characterized by high levels of microsatellite instability (MSI-H) and an exceptionally high tumor mutation burden, thought to underlie responsiveness to immunotherapy, with higher predicted immunogenicity of mutation-associated neoantigens. However, primary and acquired resistance are observed and diversity in responses is not fully explained by variations in mutation burden. Other immune checkpoints may be acting in parallel with PD-1/PD-L1, in particular, lymphocyte activation gene 3 (LAG3) metabolism, and mutation activated T cells may play a role in resistance to PD-(L)1 inhibitors (PD-(L)1); therefore, we hypothesized that the addition of LAG3 inhibitor (relatlimab) to the PD-1 nivolumab may overcome resistance in these tumors. Methods: Patients with advanced dMMR/MSI-H cancer who have progressive disease (by RECIST 1.1) during or within 6 months of PD-(L)1 containing therapy, and after at least 12 weeks of therapy, and meet other eligibility will be enrolled. All patients will receive nivolumab 480mg + relatlimab 160mg every 4 weeks until intolerance or progression, or up to a maximum of 2 years. The primary endpoint is objective response rate. Key secondary endpoints include safety, progression free and overall survival, and other response endpoints as measured by RECIST 1.1 and iRECIST criteria. Exploratory objectives will include analysis of the tumor microenvironment on biopsies obtained at baseline and on-treatment, analysis of T cell populations in the tumor and in the periphery and functional characterization of mutation-associated neoantigen-specific T cells. Studies of the microbiome will be conducted on stool and oral wash samples. Enrollment of 21 patients is planned. Clinical trial information: NCT03607890. Research Sponsor: Bristol-Myers Squibb.
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