# 2019 Gastrointestinal Cancers Symposium

## Guide to Abstracts

<table>
<thead>
<tr>
<th>Cancers of the Esophagus and Stomach</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancers of the Pancreas, Small Bowel, and Hepatobiliary Tract</td>
<td>46</td>
</tr>
<tr>
<td>Cancers of the Colon, Rectum, and Anus</td>
<td>119</td>
</tr>
</tbody>
</table>

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Pembrolizumab versus chemotherapy as second-line therapy for advanced esophageal cancer: Phase III KEYNOTE-181 study. First Author: Takashi Kojima, Department of Gastroenterology and Gastrointestinal Oncology, National Cancer Center Hospital East, Kawasaki, Japan

Background: Patients with advanced esophageal cancer after first-line chemoradiotherapy (chemoradiotherapy) have a poor prognosis and limited treatment options. We present results of the phase 3 KEYNOTE-181 study of pembrolizumab vs investigator’s choice chemo as second-line therapy for patients (pts) with advanced/metastatic squamous cell carcinoma (SCC) and adenocarcinoma of the esophagus or Siewert type II or III adenocarcinoma of the esophagogastric junction (EGJ) (NCT02564263).

Methods: Eligible pts were randomized 1:1 to pembrolizumab 200 mg Q3W for up to 2 years or investigator’s choice chemo of paclitaxel, docetaxel, or irinotecan. Randomization was stratified by histology (SCC vs adenocarcinoma) and region (Asia vs rest of world). Primary end points were OS in the SCC, PD-L1 combined positive score (CPS) ≥10, and ITT populations. Results: 628 pts were randomized including 401 with SCC, and 222 with CPS ≥10. As of October 15, 2018, the median follow-up was 7.1 mo (pembrolizumab) vs 6.9 mo (chemo). Pembrolizumab was superior to chemo for OS in CPS ≥10 (N=222; median 9.3 vs 6.7 mo; HR 0.69; 95% CI 0.52-0.93; 15, 2018, the median follow-up was 7.1 mo (pembrolizumab) vs 6.9 mo (chemo). Pembrolizumab revealed a significantly improved OS compared with chemo as second-line therapy for advanced esophageal cancer with PD-L1 CPS ≥10, with a more favorable safety profile. These data support pembrolizumab as a new second-line standard of care for esophageal cancer with PD-L1 CPS ≥10. Pembrolizumab as chemo as first-line therapy for advanced esophageal cancer is ongoing (NCT03189719). Clinical trial information: NCT02564263.

Oral Abstract Session, Thu, 2:15 PM-3:45 PM and Poster Session (Board #D12), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Efficacy and safety of trifluridine/tipiracil (FTD/TPI) in patients (pts) with metastatic gastric cancer (mGC) with or without prior gastrectomy: Results from a phase III study (TAGS). First Author: David H. Ison, Memorial Sloan Kettering Cancer Center, New York, NY

Background: The phase 3 study TAGS demonstrated that the novel oral therapy FTD/TPI for mGC presents an effective and manageable safety profile for pts with heavily pretreated mGC. In an earlier single-arm Japanese phase 2 trial in mGC, no differences were found in the pharmacokinetics of either FTD/TPI or in pts with or without prior gastrectomy. We evaluated the efficacy and safety of FTD/TPI in pts with or without prior gastrectomy within the TAGS study.

Methods: In this global phase 3 study of adult pts with mGC who had received ≥2 prior regimens of chemotherapy, pts were randomized 2:1 to receive FTD/TPI (35 mg/m2 BID on days 1-5 and 8-12 of each 28-day cycle) or placebo, plus best supportive care. We performed a preplanned analysis of efficacy and safety endpoints in pt subgroups with or without prior gastrectomy. Results: Of 507 randomized pts, 221 (44%) had a prior gastrectomy (FTD/TPI, 147/337; placebo, 74/70). Baseline pt characteristics were balanced across pt subgroups. FTD/TPI prolonged survival versus placebo regardless of gastrectomy (table). The frequency of neutropenia/leukopenia appeared to be higher among FTD/TPI-treated pts with vs without gastrectomy, but this did not result in more treatment discontinuations (table). Conclusions: In the TAGS study, subgroup analysis demonstrated that FTD/TPI is an effective treatment option with manageable safety profile for pts with or without prior gastrectomy.

Cancer of the Esophagus and Stomach

Pembrolizumab in patients (pts) with metastatic gastric cancer (mGC) with or without prior gastrectomy: Results from a phase III study (TAGS). First Author: Hirohito Ohmori, Minori, Ehime, Japan

Background: Here, we report the results of the phase 3 study TAGS showing that pembrolizumab in pts with mGC who had prior gastrectomy or not (n=507) is a feasible and effective treatment option. The TAGS study included pts with mGC with or without prior gastrectomy.

Methods: A phase III, randomized, double-blind, placebo-controlled study to evaluate pembrolizumab versus chemotherapy as second-line therapy for patients (pts) with metastatic gastric or gastroesophageal junction adenocarcinoma (GAMMA-1). Aims: To determine the efficacy and safety of pembrolizumab in pts with mGC (pts with or without prior gastrectomy) who do not achieve complete response (CR) after a regimen of chemotherapy. The primary end points were progression-free survival (PFS) and OS at the interim analysis. Results: A total of 507 pts were randomized (221 pts with prior gastrectomy and 286 pts without prior gastrectomy). PFS, PFS2 (time to second progression), and OS were significantly better in the pembrolizumab arm compared with the control arm (p<0.001, log-rank test). Pembrolizumab was also associated with a lower rate of grade 3-4 adverse events compared with chemotherapy (12% vs 35%). The most common grade 3-4 adverse events were fatigue, diarrhea, nausea, vomiting, and neutropenia. Conclusion: Pembrolizumab is an effective second-line treatment for pts with mGC who have received prior gastrectomy or not. Visit gicasym.org to search for the full list of abstract authors and their disclosure information.

Safety and efficacy of durvalumab following trilobalim therapy for locally advanced esophageal and GEJ adenocarcinoma: Early efficacy results from Big Ten Cancer Research Consortium study. First Author: Hiva Mamdani, Indiana University, Indianapolis, IN

Background: The standard of care for locally advanced esophageal adenocarcinoma (LA-EAC) is concurrent chemoradiation (CRT) followed by esophagectomy. Approximately 30% of patients (pts) achieve complete pathologic response (pCR). Post-CRT, relapse is the most common event in pts who achieve a pCR. There is an unmet need for effective and safe treatment for pts with advanced esophageal and GEJ adenocarcinoma (LA-EAC). The TAGS study showed that the addition of pembrolizumab to mFOLFOX6 for pts with mGC is associated with increased OS and manageable toxicity. Durvalumab is a monoclonal antibody that inhibits programmed cell death ligand-1 (PD-L1) and is approved for the treatment of advanced non-small cell lung cancer (NSCLC). The TAGS study demonstrated that pembrolizumab added to mFOLFOX6 improves OS, ORR, and OS rate in pts with advanced esophageal and GEJ adenocarcinoma. This phase 3 study evaluated the efficacy and safety of durvalumab following trilobalim therapy for pts with locally advanced esophageal and GEJ adenocarcinoma. This study included pts with locally advanced esophageal and GEJ adenocarcinoma (LA-EAC) who had undergone CRT and were not suitable for surgery. Primary objective was 1-yr DFS. Secondary objectives were recurrence-free survival, OS, and safety.

Methods: Methods: This was a phase III, randomized, double-blind, placebo-controlled study to evaluate durvalumab (200 mg) vs placebo as consolidation therapy in pts (pts with locally advanced esophageal and GEJ adenocarcinoma (LA-EAC) who had undergone CRT and were unsuitable for surgery."

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6 Rapid Abstract Session, Thu, 1:00 PM-1:45 PM and Poster Session (Board #D16), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
FOLFOX versus POF (paclitaxel plus FOLFOX) versus IP PAC (intraperitoneal paclitaxel plus FOLFOX) as a first-line treatment in advanced gastric cancer (AGC): A multicenter, randomized phase II trial, FNF-004 trial. First Author: Ranibha Lin, Fujian Cancer Hospital, Fujian Medical University Cancer Hospital, Fuzhou, China

Background: Double regimens are commonly accepted for AGC in East Asia. However, triple regimens are recommended in west countries. POF regimen (reported in 2007, 2008, 2009, 2010 ASCO) appeared to be of good efficacy and was well tolerated in patients with AGC. Intraperitoneal paclitaxel showed high local concentration in abdominal cavity and low systemic toxicity. The aims of this study were to find out if the POF and IP PAC was more effective with manageable side effects than FOLFOX in AGC (reported in 2017 ASCO-GI for feasibility analysis). Methods: The patients with AGC were randomized to three groups. The POF consisted of a 3-hour infusion of paclitaxel 135 mg/m², followed by FOLFOX omitted S-Fu bolus. The IP PAC consisted of paclitaxel 80 mg/m² intraperitoneally plus FOLFOX. Every 14 days repeated for all three regimens. Up to 9 cycles of treatment were administered, followed by S-1 until disease progression. The primary endpoint was PFS. Results: Between Nov 2015 and May 2018, 189 pts (30 POF, 29 IP-PAC, 30 FOLFOX) were randomly allocated. PFS, OS and RR were seen in the table below. POF was better in PFS and RR than FOLFOX, although no statistically significant difference in RR, IP PAC was trend to be better in PFS than FOLFOX, but not in RR, OS was unremarkable. The most common adverse events of grade 3 or 4 were neutropenia and neuropathy, but no significant difference among three groups. Conclusions: Both POF and IP PAC improved survival compared to FOLFOX. Only POF, not IP PAC, improved response rate compared to FOLFOX. Clinical trial information: NCT02845908.

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<tr>
<th></th>
<th>POF (n = 30)</th>
<th>IP PAC (n = 29)</th>
<th>FOLFOX (n = 30)</th>
<th>P value (HR, 95%CI)</th>
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<tbody>
<tr>
<td>PFS (m, 95% CI)</td>
<td>8.04 (5.65-11.42)</td>
<td>7.08 (5.41-9.33)</td>
<td>6.31 (4.93-8.46)</td>
<td>0.467 (0.240-0.907)</td>
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<tr>
<td>OS (m, 95% CI)</td>
<td>14.3 (10.0-19.6)</td>
<td>12.6 (9.1-17.0)</td>
<td>10.6 (7.4-14.3)</td>
<td>0.129 (0.066-0.257)</td>
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<tr>
<td>RR (n, %)</td>
<td>1.0 (1.0)</td>
<td>0.6 (0.4-0.9)</td>
<td>0.4 (0.2-0.8)</td>
<td>0.023 (0.013-0.040)</td>
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7 Rapid Abstract Session, Thu, 1:00 PM-1:45 PM and Poster Session (Board #D17), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
Poster-group controlled trial of esophagectomy versus chemoradiotherapy in patients with clinical stage I esophageal cancer (JCGOS052). First Author: Ken Kato, Division of Gastrointestinal Medical Oncology, National Cancer Center Hospital, Tokyo, Japan

Background: Esophagectomy (E) is the standard of care for stage I esophageal squamous cell carcinoma (ESCC), while chemoradiotherapy (CRT) is a treatment option. A prospective randomized trial including randomized arms to confirm the non-inferiority of CRT to E for stage IA ESCC was conducted. Methods: Patients (pts) with thoracic ESCC, adenocarcinoma, or basaloid cell carcinoma with stage I (T(N)M0), age 20 to 75, performance status 0 to 1, and adequate organ function were eligible. If pts had a preference, they were randomly allocated to E with 2-3-field lymph node dissection (arm A) or CRT (arm B). However, if pts had a preference and refused randomization, they were allocated to pts preference arm, E (arm C) or CRT (arm D). CRT consisted of cisplatin and 5-Fu with radiation at the dose of 60 Gy concurrently. The primary endpoint was overall survival (OS) of arm A and B, secondary endpoint included OS of arm C and D using inverse probability weighting with propensity score. The planned sample size in arm A and B was 54 pts in total with one-sided alpha of 15%, power of 75% and non-inferiority margin of HR as 1.78. The sample size in arm C and D was at least 156 pts in each arm with one-sided alpha of 2.5%, power of 85% and non-inferiority margin of HR as 1.78. Results: Between December 2006 and February 2013, 379 (Arm A: 47, B: 71, C: 209 D: 159) pts were randomized. PFS, OS were not calculated due to small number of randomized arms. Patients characteristics of arm C and D were as follows: median age 62 and 65, male (%): 82.8 and 88.1, PS 0 (%): 99.5 and 98.1. All histologic type was SCC except one basaloid cell carcinoma in arm C. The 3- and 5-year OS were 94.7% and 86.5% in arm C, and 93.1% and 85.5% in arm D (adjusted HR 1.05; 95% CI 0.67-1.64 [>1.78]). Treatment related death were observed in two pts in arm C and none in arm D. Conclusions: Though the accrual of randomized arms was short, CRT showed trend to better survival, but not inferiority of CRT to E in pts preference arms. CRT is considered as a treatment option for stage IA ESCC with organ preservation. Clinical trial information: UMIN0000000551.

B Rapid Abstract Session, Thu, 1:00 PM-1:45 PM and Poster Session (Board #D18), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
Evaluation of efficacy of nivolumab by baseline factors from ATTRACTION-2. First Author: Yoon-Koo Kang, Department of Oncology, Asan Medical Center, Seoul, Korea, Republic of (South)

Background: Nivolumab (Nivo) has shown superior efficacy with manageable safety for G/GEJ cancer refractory to, or intolerant of, standard chemotheraphy in phase 3 study (ATTRACTION-2). Subgroup analysis of OS according to baseline characteristics and disease factors showed Nivolumab provided benefit in all subgroups. However, about half of patients had early disease progression even after administration of Nivo. Here, we explored factors of patients who had early progression after administration of Nivo. Methods: A statistical random forest method, a type of machine learning method, was used to explore clinical factors that could contribute to early progression after Nivo. In this analysis, the outcome variable was 56-day PD rate and covariates were patients’ clinical background factors. Factors were explored by comparing Nivo and placebo arms in all subgroups, constructed with 1) every single factor, 2) every pair of factors coming from the covariates. Results: In a single factor extraction, hyponatremia was identified as the most highly contributing factor to early progression. Of 330 patients in the Nivo arm, 59 patients showed hyponatremia at the baseline. Importantly, in a pair factor extraction, the patient population with hyponatremia and any of high NLR (N = 31, 9.4%, cut off: second tertile), high neutrophil (N = 28, 8.5%, cut off: second tertile), PS1 (N = 50, 15.2%) or no prior use of ramucirumab (N = 55, 16.7%), were found as risk factors of early progression in Nivo. PFS-KM curves were almost overlapped between Nivo and placebo arms in these patients with any pair of these risk factors. Conclusions: Our exploratory analysis suggested that a patient population with both ‘poor general condition’ represented by hyponatremia and PS1, and ‘inflammatory conditions’ represented by high NLR and/or high neutrophil count, would be potential risk factors associated with early progression. This needs further validation with other potential biomarkers in tumor tissue and additional studies. Additional analysis with biomarkers such as PD-L1 will be presented at the meeting. Clinical trial information: NCT02267343.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
The difference of the gut microbiota of gastric cancer in relation to Helicobacter pylori positivity and negativity. First Author: Mijn Seol, Research & Development Center for Bobankhealing Inc., Seongnam-Si, Korea, Republic of (South)

Background: Helicobacter pylori (HP) is a major risk factor for gastric cancer, however, only 2% of HP+ people develop adenocarcinoma. In this study, we have compared the intestinal microbiota composition related to HP status among gastric cancer patient using 16sRNA gene-based metagenomic sequencing analysis and culture-based method. Methods: Stool samples were collected from 18 gastric cancer patients. 16sRNA genes were sequenced on the Illumina MiSeq platform and further analyzed to evaluate the gut bacterial community. The bacteria strains of fecal sample were isolated in aerobic and anaerobic condition. Results: Metagenomics analysis of fecal sample showed four major phyla: Firmicutes, Bacteroidetes, Proteobacteria and Actinobacteria were dominant. Firmicutes were the most dominant phylum. Within this phylum, the relative abundance of Clostridiales including Ruminococcus was higher in the HP(-) group, whereas Lactobacillales including streptococcus was higher in HP(+) group. In addition the relative abundance of Bacteroidetes in HP(-) group and Actinobacteria (especially, genus Bifidobacterium) in HP(+) group was observed highly. In the bacterial culture-based approach, bacteria strains belonged to Clostridiales such as Clostridium perfringens, Ruminococcus feacis, Blautia sp., Capprococcus come were isolated in HP(-) sample. In HP(+) sample, Klebsiella, Bacteroides, Bifidobacterium were isolated. Bacillus species, Escherichia/Shigella was enriched regardless of HP status. Streptococcus was not cultivated in HP(+) group, but isolated in HP(-) group in anaerobic condition.

Methods: Tislelizumab, a humanized IgG4 mAb with high affinity and specificity for PD-1, was specifically engineered to minimize FcγR binding on macrophages, thus abrogating antibody-dependent phagocytosis, a potential mechanism of T-cell clearance and resistance to anti-PD-1 therapy. This phase 2 study (NCT03469597) evaluated safety, tolerability, and antitumor activity of first-line tislelizumab plus chemotherapy in Chinese pts with advanced GC/GEJ or esophageal cancer; data from the GC/GEJ cohort are presented here. Methods: Adult pts with histologically or cytologically confirmed HER2 negative GC/GEJ were treated with tislelizumab (200 mg IV Q2W) + oxaliplatin (130 mg/m² IV Q3W) for up to 6 cycles + capecitabine (1000 mg/m² BID, Days 1-14 Q3W). AEs were assessed per CTCAE v4.03; tumor responses were assessed every 9 wks. Results: As of 13 June 2018, 15 GC/GEJ pts (median age, 59 yrs; M/F, 14:1) were enrolled; median treatment duration was 111 days (range 12-251). AEs in ≥2 pts considered related to chemotherapy and/or tislelizumab are detailed in the Table. No fatal AEs occurred. Three pts discontinued treatment due to ascites or decreased neutrophils, AST, or total bilirubin. With a median follow-up of 181 days, 46.7% (n = 7) had confirmed PR; 20% (n = 3) had SD, 13.3% (n = 2) with non-target disease only at baseline had non-CR/non-PD, 6.7% (n = 1) had PD, and 13.3% (n = 2) did not have evaluable disease. ORR and DCR were 46.7% (n = 7/15) and 80% (n = 12/15), respectively. Conclusions: First-line tislelizumab plus chemotherapy was generally well tolerated and antitumor activity was observed in pts with advanced GC/GEJ cancer. Clinical trial information: NCT03469597.

Prognostic value of DNA repair gene based on stratification of gastric cancer. First Author: Jinjia Chang, Department of Oncology Fudan University Shanghai Cancer Center, Shanghai, China

Background: DNA repair genes can be used as prognostic biomarkers in many types of cancer. We aimed to identify prognostic DNA repair genes in patients with gastric cancer (GC) by systematically bioinformatics approaches using web-based database. Methods: Global gene expression profiles for 1,325 GC patients' samples from six independent datasets were included in the study. Clustering analysis was performed to screen potentially abnormal DNA repair genes related to the prognosis of GC, followed by unsupervised clustering analysis to identify molecular subtypes of GC. Characteristics and prognosis differences were analyzed among these molecular subtypes, and modular key genes in molecular subtypes were identified based on changes in expression correlation. Multivariate Cox proportional hazard analysis was used to find the independent prognostic gene. Kaplan-Meier method and log-rank test was used to estimate correlations of key DNA repair genes with GC patients' overall survival. Results: There were 57 key genes significantly associated to GC patients' prognosis, and patients were stratified into three molecular clusters based on their expression profiles, in which patients in Cluster 3 showed the best survival (P < 0.05). After a three-phase training, test and validation process, the expression profile of 13 independent key DNA repair genes were identified can classify the prognostic risk of patients. Compared with patients with high-risk score, patients with high risk score in the training set had shorter overall survival (P < 0.0001). Furthermore, we verified equivalent findings by these key DNA repair genes in the test set (P < 0.0001) and the independent validation set (P = 0.0024).

Conclusions: Our results suggest a great potential for the use of DNA repair gene profiling as a powerful marker in prognostication and inform treatment decisions for GC patients.
Tislelizumab in combination with chemotherapy for the treatment of Chinese patients (pts) with esophageal squamous cell carcinoma (ESCC): Results from one cohort of an ongoing phase 2 study. First Author: Nong Xu, The First Affiliated Hospital of Zhejiang University, Hangzhou, China

**Background:** Tislelizumab, a humanized IgG4 mAb with high affinity and specificity for PD-1, is specifically engineered to minimize binding to FcγRI on macrophages, thereby abrogating antibody-dependent phagocytosis, a potential mechanism of T-cell clearance and resistance to anti-PD-1 therapy. This phase 2 study assessed the safety and tolerability of tislelizumab combined with chemotherapy as first-line therapy with gastric cancer and ESCC. The results for the ESCC cohort are presented here. **Methods:** Chinese pts with inoperable, locally advanced ESCC were treated with tislelizumab (200 mg IV Q3W), cisplatin (80 mg/m² IV Q3W for up to six cycles), and fluorouracil (800 mg/m²/d, days 1-5 IV Q3W for up to six cycles). Safety/tolerability of the combination regimen was assessed by monitoring adverse events (AEs) per NCI-CTCAE v4.03 criteria. **Results:** As of 13 June 2018, 15 pts (median age, 61 yrs; male/female, 14/1) were enrolled. The median treatment duration was 108 days (range 21-201). The mean (Q3, Q2) dose intensity was 0.92 (0.91, 0.97) for tislelizumab, 0.91 (0.90, 0.98) for cisplatin, and 0.78 (0.72, 0.97) for 5-FU. Among the 15 pts, AEs occurring in ≥5% and possibly related to chemotherapy and/or tislelizumab are detailed in the table. One pt experienced grade 5 hepatic dysfunction (possibly from pro-

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<th>Grade</th>
<th>Decreased appetite</th>
<th>Nausea</th>
<th>Anorexia</th>
<th>White blood cell count decreased</th>
<th>Vomiting</th>
<th>Nausea without vomiting decreased</th>
<th>Hypoalbuminemia</th>
<th>Thrombocytopenia</th>
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**Conclusions:** Tislelizumab combined with chemotherapy was generally well tolerated in pts with advanced ESCC. Clinical trial information: NCT03469557.

Poster Session (Board #E4), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Zolbetuximab combined with EOX as first-line therapy in advanced CLDN18.2+ gastric (G) and gastroesophageal junction (GEJ) adenocarcinoma: Updated results from the FAST trial. First Author: Ugur Sahin, TRON - Translational Oncology at the University Medical Center of the Johannes Gutenberg Mainz, Mainz, Germany

**Background:** Physiologically, the tight junction protein CLDN18.2 is present only in the gastric mucosa. Upon malignant transformation, CLDN18.2 epitopes are exposed on the cell surface and accessible to targeted therapies. Zolbetuximab (formerly IMAB362) is a chimeric mAb that mediates specific killing of CLDN18.2+ cancer cells through immune effector mechanisms; single-agent activity has been reported in G/GEJ cancer. **Methods:** Patients (pts) with advanced HER2-negative (HER2-) G or GEJ cancer with CLDN18.2 expression of ≥2+ staining intensity in the anti-CLDN18 43-14A mAb in ≥40% tumor cells were eligible (NCT01630081). Patients were randomized 1:1 to receive first-line EOX + zolbetuximab (loading dose 800 mg/m², then 600 mg/m² Q3W). The study was extended in pts who achieved a complete response (CR) and continued EOX + zolbetuximab (EOX Q3W) (data not presented). Primary endpoint was PFS; secondary endpoints included OS, ORR, and safety/tolerability. **Results:** A total of 161 pts (G, n = 128; GEJ, n = 27; esophagus n = 6) were randomized to receive zolbetuximab (800/600 mg) + EOX (n = 77) or EOX alone (n = 84). In all, 45% of pts had diffuse type histology per Lauren classification. Median PFS was longer with zolbetuximab + EOX (7.5 mo) versus EOX alone (5.3 mo; P = 0.0005; HR 0.44; 95% CI 0.29, 0.67). Median OS (13 vs 8.4 mo; P = 0.0006; HR 0.56; 95% CI 0.40, 0.79) and ORR (39 vs 25%; P = 0.022) were also significantly higher with zolbetuximab + EOX versus EOX alone. Increased efficacy was more pronounced in pts with high CLDN18.2 expression (≥2+ staining intensity in ≥70% tumor cells). Zolbetuximab + EOX was generally well tolerated. Most AEs considered related to zolbetuximab and EOX (ie, nausea, vomiting, neutropenia, anemia) were of grade ≤2 severity; there was no significant increase in grade ≥3 events with the addition of zolbetuximab to EOX. **Conclusions:** Addition of zolbetuximab to first-line chemotherapy resulted in a clinically meaningful and clearly denoted increase in efficacy and manageable toxicity. A phase III trial is evaluating the combination of zolbetuximab plus mFOLFOX6 as first-line treatment of CLDN18.2+/HER2-negative, advanced/metastatic G or GEJ adenocarcinoma (NCT03504397). Clinical trial information: NCT01630083.

Poster Session (Board #E5), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Reliability of endoscopic biopsy compared with endoscopic submucosal dissection histopathologic diagnosis. First Author: Kyuwan Lee, Tae Ho Kim, The Catholic University of Korea College of Medicine, Gyeonggido, Korea, Republic of (South)

**Background:** Endoscopic biopsy is the most convenient and simple method for approaching gastric neoplasm. Aim of our study was to determine the diagnostic accuracy of biopsy during screening endoscopy compared to endoscopic submucosal dissection (ESD). **Methods:** 175 pts who underwent both screening endoscopic biopsy and ESD from 2015.01 to 2017.12 in Bucheon St. Mary’s Hospital were retrospectively reviewed. Among them, 175 pts had different histopathologic ESD findings compared with endoscopic biopsy. Among six endoscopic biopsies that showed atypia, four were diagnosed with adenocarcinoma and two maintained the results. 64 out of the 175 lesions showed low grade dysplasia by endoscopic biopsy. After ESD, two cases were diagnosed with high grade dysplasia and two cases were diagnosed with adenocarcinoma. Of 12 lesions which showed high grade dysplasia on endoscopic biopsy, four lesions turned out to be adenocarcinoma (three well differentiated, one moderately differentiated) after ESD. Of 91 adenocarcinoma cases, three lesions had discrepancy on differentiation level and one lesion turned out to be signet ring cell carcinoma after all. Patients who were infected with Helicobacter pylori (H. pylori) had tendency to have discrepancy between initial biopsy and ESD histopathology result. (OR 3.68, 95% CI 1.081-11.955, P = 0.018). **Conclusions:** Discrepancy between endoscopic biopsy and post-ESD histopathology were found. Possibility of coexistence or progression to high grade neoplasm should be considered regarding endoscopic biopsy results especially if infected with H. pylori and active ESD histopathological confirmation needs to be done if necessary.

Poster Session (Board #E7), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Feasibility study of diet counseling (DC) with oral nutritional supplements (ONS) for advanced esophageal and gastric cancer during chemotherapy (CT) or chemoradiotherapy (CRT): First report of ONS compliance from a prospective randomized controlled clinical study (DICON study). First Author: Yukiko Izawa, The Cancer Institute Hospital of JFCR, Tokyo, Japan

**Background:** Most advanced esophageal and gastric cancer patients(pts) experience fatigue, anorexia, and may arise malnutrition and sarcopenia, for which effective treatment has not been established. Nutritional support especially protein supplementations may prevent loss of body mass related with malnutrition and sarcopenia. We therefore, conducted a prospective randomized study to explore compliance and the best available ONS intake for pts undergoing CT or CRT. **Methods:** Eligibility criteria included: chemo-naive advanced gastric cancer or esophageal cancer; performance status (PS) of 0-1; pts who can eat more than as 50% as usual; age over 20 years. Pts were randomly allocated into four groups within each strata, i.e. esophageal or gastric cancer, Group A: DC only, Group B-1: DC and ONS 1 pack/day, Group B-2: DC and ONS 2 packs/day, and Group B-3: DC and ONS 3 packs/day. We use jelly type ONS which is easy to intake and include rich branched-chain amino acid. We assessed ONS compliance, the change of nutritional index (body weight, albumin, pre-albumin, and muscle mass), diet record (daily), and toxicity before CT or CRT and 14 days after administration of CT. **Results:** Among forty pts (11 in A, 11 in B-1 in B-2,10 in B-3) were enrolled from August 2017 to August 2018, median age was 64 years (range 46-81), median 0.81M was 20.6 (range 15-29), and 28 gastric cancer, 12 esophageal cancer. Median intake was 12 packs/2w (range 0-14), 15 packs/2w (3-28), 12 packs/2w (2-28), in B-1, B-2, and B-3 respectively. Mean compliance of ONS was 72.7%, 50.0% and 33.1%, in B-1, B-2, and B-3 respectively. There was a significant linear trend across the 3 groups (P = 0.0084). B-1 was significantly better than B-3 (P = 0.0270). There were no pts in group B-3 who could intake ONS for 14 consecutive days. Over 80% of pts in B-1 group were able to intake for 14 consecutive days. **Conclusions:** We found ONS 3 packs/ day was clear PFS and because of compliance. Choice of 1 or 2 packs/day should be determined by taking into account the total calories of foods. Clinical trial information: 000026705.
Incidence and prognosis of multiple organ involvement at gastric MALT lymphoma. First Author: Tae Hun Kwon, Seoul St. Mary's Hospital, Seoul, Korea, Republic of (South)

Background: MALT (mucosa-associated lymphoid tissue) lymphoma usually occurs in stomach but various MALT organs can be afflicted including salivary glands, parotid gland, lung, thyroid, and thymus. In this study, we aimed to evaluate the prevalence and characteristics of gastric MALT lymphoma with multi-organ involvement. Methods: We retrospectively analyzed a total of 174 consecutive patients who had been diagnosed with gastric MALT lymphoma at Seoul St. Mary's Hospital from January 2009 to May 2018. Clinical data were obtained from the medical records. At the time of diagnosis, neck, chest, abdominal CT, PET-CT and bone marrow biopsy were performed for the purpose of staging work-up. Organ involvement was identified by biopsy. Results: Nine out of 174 (5.2%) gastric MALT lymphoma patients were found to have multi-organ involvement. Three patients had biopsy proven lymphoma at lung, two patients had colon involvement, and two patients had ocular involvement. A patient with involvement at small bowel and duodenum were found, respectively. Seven patients were examined for Helicobacter infection. Two of them were positive for H. pylori infection and received eradication treatment. Except one patient treated with palliative care, eight patients underwent chemotherapy, in which two of them received additional radiation therapy and other two patients underwent bone marrow transplantation. Except one patient died of pneumonia during chemotherapy and one patient underwent palliative treatment, 7 patients had maintained complete remission. Conclusions: The overall prevalence of gastric MALT lymphoma with multi-organ involvement was 5.2%. The result suggests that the gastric MALT lymphoma patients require a careful investigation of other MALT organs.

Characteristics of gastric MALT lymphoma patients with multiorgan involvement.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Extra-gastric involvement site</th>
<th>H. pylori infection</th>
<th>H. pylori eradication</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>M</td>
<td>40</td>
<td>Lung</td>
<td>(-)</td>
<td>CTx, BMT</td>
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<tr>
<td>F</td>
<td>64</td>
<td>Esoph</td>
<td>(+)</td>
<td>CTx, BMT</td>
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<tr>
<td>F</td>
<td>60</td>
<td>Duodenum</td>
<td>(+)</td>
<td>CTx, BMT</td>
<td></td>
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<tr>
<td>M</td>
<td>36</td>
<td>Ocular adnexa</td>
<td>(+)</td>
<td>CTx, RT</td>
<td></td>
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<tr>
<td>M</td>
<td>53</td>
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<td>(+)</td>
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<tr>
<td>M</td>
<td>56</td>
<td>Duodenum</td>
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<td>CTx</td>
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Impact of intramuscular fat accumulation on survival in stage I/III gastric cancer. First Author: Yuhei Waki, Division of Gastric Surgery, Shizuoka Cancer Center, Shizuoka, Japan

Background: Intramuscular fat accumulation of skeletal muscle has been reported to be a prognostic factor in various cancers. To evaluate the impact of intramuscular fat accumulation of the intramuscular adipose tissue content (IMAC) measured by CT scan on survival, we investigated the impact of IMAC on survival in stage I/III gastric cancer (GC). Methods: A total of 383 patients with pathological stage I/III gastric cancers who underwent curative resection between January 2009 and December 2013 were included. IMAC was calculated by dividing the CT value of the multifidus muscles with that of the subcutaneous fat at the level of third lumbar vertebra. The IMAC cut-off values associated with cancer-specific survival (CSS) were separated by sex-based on the maximum values of Youden index (sensitivity + specificity -1). Patients were classified into normal or high IMAC group according to this cut-off value. Clinicopathological factors and survival outcomes were compared between the two groups. Results: The median values of IMAC were 0.327 (IQR: 0.404-0.250) in male and 0.239 (IQR: -0.335-0.114) in female. The cut-off values of IMAC were -0.345 in male and -0.126 in female. Patients were classified into normal IMAC group (n = 204) and high IMAC group (n = 179). There were significantly worse in the high IMAC group compared to the normal IMAC group. Interestingly, despite the fact that no significant differences were observed in the pathological findings between the groups, the overall survival and CSS were significantly worse in the high IMAC group than in the normal IMAC group (p < 0.001 and p = 0.035). Moreover, the high IMAC was identified as an independent prognostic factor not only for overall survival but also for CSS (HR: 1.440, p = 0.021; HR: 1.646, p = 0.008, respectively). Conclusions: The high IMAC was significantly associated with worse survival, suggesting that IMAC represents certain oncological implications in patients with GC. Therefore, IMAC could be used as a new prognostic factor in curatively resected GC.
Gastric cancer staging in the era of neoadjuvant therapy and its prognostic implications. First Author: Gina Kim, Montefiore Medical Center, Bronx, NY

Background: Increasingly patients are undergoing neoadjuvant therapy for gastric cancer. The relationship between stage-based prognostic information available prior to treatment (cStage), after surgery (ypStage), and difference between cStage and ypStage (delta) remains unclear. We aim to describe the relationship between cStage and ypStage as relates to survival for gastric cancer patients. Methods: Data from the National Cancer Data Base (NCDB) from 2004-2015 was used for the analysis. Patients with gastric adenocarcinoma who received neoadjuvant therapy then underwent surgery were included. Kaplan Meier curves were used to model survival. Harrell’s C-statistics obtained from Cox Regression models were reported. Results: 9,959 patients met our inclusion criteria. Increases in cStage, ypStage and delta (ypStage-cStage) were associated with worse survival. Median overall survivals for cStages 1-4 were: 53.8, 39.5, 29.2, 20.9 months (logrank test, p<0.0001). Median survivals for ypStage 0-4 were: 95.4, 89.7, 36.9, 23.4, 16.0 months (logrank test, p<0.0001). Survival was further stratified by delta. A representative table comparing cStage 2 and ypStage 2 is shown below. Acox regression model with cStage as predictor of survival yielded a Harrell’s C-statistic of 0.555; when delta was added to the model, the C-statistic increased to 0.638. Separately, a Cox-regression model with ypStage as predictor yielded a C-statistic of 0.632; when delta was added to this model, the C-statistic increased negligibly to 0.638.

Conclusions: Prognostic accuracy using cStage prior to treatment improved when tumor responsiveness was considered while this was not the case for ypStage. Pre-surgical prognostic information should be provided with a caveat that treatment response will influence survival. Post-surgery, the clinical staging is less relevant and ypStage can be used alone in providing prognostic information.

<table>
<thead>
<tr>
<th>cStage (delta)</th>
<th>ypStage cStage (%)</th>
<th>ypStage 2 (%)</th>
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<tr>
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<tr>
<td>-1</td>
<td>59.6</td>
<td>32.3</td>
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<tr>
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<td>38.0</td>
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<tr>
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<td>36.6</td>
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<tr>
<td>+1</td>
<td>2.8</td>
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Table: 5-year survival estimates of cStage 2 and ypStage 2 stratified by delta. Prognosis differed by tumor responsiveness for cStage 2 tumors, but not for ypStage 2 tumors.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Methods: Tumor tissue samples collected from 2005 to 2017 were procured from Yonsei Cancer Center (South Korea), Memorial Sloan Kettering Cancer Center (USA) and Aarhus University Hospital (Denmark). GEP score was derived from an 18-gene signature using extracted tumor RNA analyzed by NanoString nCounter; GEP high/intermediate (GEP-H/I) and low were defined by a cutoff of -1.540, consistent with pembrolizumab clinical trials. PD-L1 expression was assessed by PD-L1 IHC 22C3 pharmDX assay (Aptilent); positive was defined as combined positive score (CPS) >10, where CPS is the the number of PD-L1-positive cells (tumor cells, lymphocytes and macrophages) divided by the total number of viable tumor cells, multiplied by 100. Associations of GEP score and PD-L1 expression with clinicopathologic variables were analyzed by chi-square test and multiple logistic regression models. Overall survival (OS) from diagnosis date to death date/last follow-up was analyzed using Cox proportional hazards models adjusting for age, sex, stage, region and ECOG performance status (PS). Results: 294 samples with both PD-L1 and GEP data were analyzed. Median age was 65 y (range 33-88); 85% were from men, 58% were stage IV, 63% were esophageal adenocarcinoma (EAC) and 37% were esophageal squamous cell carcinoma (ESCC). Overall 36% of tumors were GEP-H/I; 46% in EAC vs 18% in ESCC. GEP was not associated with patient survival overall (aHR 0.99; 95% CI: 0.68-1.18) or in pts with EAC (aHR 0.93; 95% CI 0.68-1.27) or ESCC (aHR 0.76; 95% CI 0.40-1.44). 21% of tumors were PD-L1-CPS ≥10: 18% in EAC and 26% in ESCC. PD-L1 expression was associated with EOCPS (adjusted odds ratio 0.520; 95% CI 0.309-0.875; P = 0.04) but was not associated with OS overall (aHR 0.89; 95% CI 0.64-1.24) or in pts with EAC (aHR 0.97; 95% CI 0.63-1.49) or ESCC (aHR 1.33; 95% CI 0.73-2.34). Conclusions: Our results suggest that T-cell-inflamed PD-L1 and GEP-expression may not be prognostic in pts with EC who received SOC.

Disparities associated with the receipt of palliative care in patients with metastatic gastric cancer. First Author: Subhadeep Paul, Department of Surgery, University of Texas Southwestern Medical Center, Dallas, TX

Background: Metastatic gastric adenocarcinoma (mGA) is frequently associated with debilitating symptoms that negatively impact quality of life. We aim to determine the rate of palliative care (PC) use in mGA and the factors which are associated with OS overall (adjusted hazard ratio (aHR) -0.99; 95% CI: 0.68-1.18) or in pts with EAC (aHR 0.93; 95% CI 0.68-1.27) or ESCC (aHR 0.76; 95% CI 0.40-1.44). 21% of tumors were PD-L1-CPS ≥10: 18% in EAC and 26% in ESCC. PD-L1 expression was associated with EOCPS (adjusted odds ratio 0.520; 95% CI 0.309-0.875; P = 0.04) but was not associated with OS overall (aHR 0.89; 95% CI 0.64-1.24) or in pts with EAC (aHR 0.97; 95% CI 0.63-1.49) or ESCC (aHR 1.33; 95% CI 0.73-2.34). Conclusions: Our results suggest that T-cell-inflamed PD-L1 and GEP-expression may not be prognostic in pts with EC who received SOC.

Prognosis of gastric dysplasia after complete resection with endoscopic procedures. First Author: Junseok Park, Institute for Digestive Research, Digestive Disease Center, Division of Gastroenterology, Soonchunhyang University, Seoul, Korea, Republic of (South)

Background: Gastric adenomas are considered premalignant, and some can be interpreted as cancer according to different pathologic guidelines. The dysplastic lesions share histologic characteristics including mucin phenotype that are related that are related to prognosis. The prognosis of the lesions has been studied but tends to be researched separately. Moreover, the proposed prognostic factors are mostly derived from the study of surgical specimens, and most of them did not consider the anatomical changes after surgery. Previously researched prognostic factors of gastric dysplasia were evaluated on the recurrence after complete resection with endoscopic procedure. Methods: From 2005 to 2016, 1678 gastric dysplasia were endoscopically removed in Soonchunhyang university hospital, Seoul. They were followed up under endoscopy with a standardized protocol. For the 716 lesions were histologically evaluated including mucin phenotype with immunohistochemical stain of MUC5AC, MUC6, MUC2, and CD10. Recurrence of dysplastic lesions were analyzed for the 688 lesions with at least 1 year's follow-up. Results: Of five hundred and forty-three malignant lesions including in situ lesions were completely resected with endoscopic procedures. Endoscopic submucosal dissection was performed on 603 lesions and other lesions were removed with endoscopic mucosal resection. Submucosal invasion was on 83 lesions of carcinoma. The mucin phenotype of lesions was immunohistochemically evaluated. During median 40 months of follow-up, there was 89 cases of recurrence (12.9%). Kaplan-Meier analysis of the recurrence-free survival were estimated and the elderly over 65 years of age showed statistical significance (P = 0.0239). Conclusions: Completely resected early stage of gastric dysplasia showed relatively low recurrence rate. Previously proposed histologic features did not affect prognosis. However, the age of patient showed statistical significance on recurrence-free survival. Stratum surveillance on elderly patients is important to improve the clinical outcome of gastric dysplasia.

Cancers of the esophagus and stomach
and subsequent method of recurrence detection. There were no significant associations between baseline patient/tumor characteristics alone, 5.0 months when detected by imaging triggered by symptoms, and symptoms in 25 patients (38.5%), and symptoms alone in 6 patients (9.2%). Patients (47.1%) relapsed with a median RFS of 19.8 months. Recurrence was received neoadjuvant CRT. Median OS for entire cohort was 43.4 months. 65, 64, and 116 patients (84.1%) had adenocarcinoma. 111 patients (80.4%) received surgery with curative intent. 16.3% of GC patients received nutritional support along with 15.2% of surgical GC patients. Conclusions: Updated NACR data show long wait times for patients needing neoadjuvant or adjuvant therapies suggesting improvement in follow-up management. The low percentage of patients with nutritional support shows the need for supportive services. There should be strategies for earlier diagnosis given the low percentage of patients identified at early stages. Further directions include 2 and 5 year survival data and data on interdisciplinary care.

**Methods:** Surveillance for locally advanced esophageal and gastroesophageal junction (GEJ) cancers: Patterns of recurrence and methods of detection. First Author: Jubin Eghbali Matloubieh, University of Rochester Medical Center, Rochester, NY

**Background:** Tridomality treatment with neoadjuvant chemoradiation (CRT) followed by surgery is a standard treatment for esophageal/GEJ (E/GEJ) cancers. Following esophagectomy, there is no strong consensus about optimal surveillance and routine imaging. At our institution, patients have surveillance CT scans every 4-6 months for the first 2 years post-surgery and every 6-12 months for the next 3 years. Methods: An IRB-approved chart review was performed identifying patients who underwent surgical resection for locally advanced E/GEJ cancer between January 2011 and December 2015 at the University of Rochester. Study objectives were to describe timing of methods used to detect recurrence as well as their impact on patient outcomes. Recurrence-free (RFS) and overall survival (OS) were graphed via the Kaplan-Meier method. Results: 138 patients underwent surgical resection for E/GEJ cancer during the study period: 107 (77.5%) were male, median age was 64, and 116 patients (84.1%) had adenocarcinoma. 111 patients (80.4%) received neoadjuvant CRT. Median OS for entire cohort was 43.4 months. 65 patients (47.1%) relapsed with a median RFS of 19.8 months. Recurrence was detected by routine imaging in 34 patients (52.3%), imaging triggered by symptoms in 25 patients (38.5%), and symptoms alone in 6 patients (9.2%). Median OS post-relapse was 1.5 months when detected based on symptoms alone, 5.0 months when detected by imaging triggered by symptoms, and 13.5 months when detected by routine scans (Log-rank p = 0.046). There were no significant associations between baseline patient/tumor characteristics and subsequent method of recurrence detection. Conclusions: 47.1% of patients suffered local recurrence post-tridomality treatment for E/GEJ cancer, consistent with published literature. Almost half of these were detected based on symptoms despite routine imaging. Increased OS for patients with relapse detected by routine scans is likely related to lead time bias, but may be related to increased treatment intensity, or due to less aggressive tumor. Prospective randomized trials are needed to determine the true benefit of regular surveillance scans among esophageal cancer survivors.

**Methods:** Comparison of clinical and pathologic staging in esophageal cancer. First Author: Anthony Joseph Scholer, John Wayne Cancer Institute, Santa Monica, NJ

**Background:** Randomized trials have demonstrated improved disease-free survival for more advanced esophageal cancer treated with neoadjuvant chemoradiation (NCXRT). However, accurately treating a patient relies on the accuracy of pre-treatment T and N staging with endoscopy ultrasound and cross-sectional imaging, which is unknown, and can lead to over or under-treatment. Therefore, the objective of this study is to compare the clinical and pathologic staging in patients with early esophageal cancer that would be impacted by inaccurate clinical staging. Methods: Primary, non-metastatic esophageal cancer patients who had upfront esophagectomy without neo-adjuvant CRT between 2004 and 2013 were identified in the National Cancer Database. The Kappa index was used to determine patient and tumor characteristics that affected concordance between clinical and pathologic T and N staging (p > 0.05 shows discordance). Results: Of 1810, 43% of clinical T2 tumors were upstaged compared to 38% of T1 and 13% of clinical T2 were downstaged. Clinically positive N disease had the greatest concordance (91%) between clinical and pathologically staging, compared to clinical NO, where 57% were upstaged. Some patient groups significantly impacted the concordance rates of staging. T-Stage was less accurate (more discordant) in females (68%, kappa 0.41, p = 0.057) and Blacks (59%, kappa 0.22, p = 0.069) whereas overall N-stage was more discordant in Hispanics (83%, kappa 0.67, p = 0.165). Conclusions: Accurate staging for esophageal adenocarcinoma can significantly impact the course of treatment. Upfront surgical resection of clinical T1 lesions and node negative tumors are at risk for under-treatment due to poor concordance with pathological stage, which may lead to decreased survival compared to a regimen of NCXRT. Clinicians should be aware of patient and tumor characteristics that increase the likelihood of discordance between clinical and pathologic staging when discussing treatment options for patients with esophageal cancer.
The association of novel recurrent in-frame gene fusions with prognosis of diffuse gastric cancer. First Author: Hark K. Kim, National Cancer Center, Goyang, Republic of Korea

Background: Among the two histologic subtype of gastric cancer (GC), diffuse gastric cancer (DGC) is increasingly being considered distinct from intestinal type gastric cancer (IGC). Despite the relative importance of DGC, few whole transcriptomic analyses have been performed for this histologic subtype. We therefore conducted an RNA-sequencing study to search for novel driver fusions in DGC. Methods: We conducted a whole transcriptomic and targeted RNA sequencing study of 384 Korean DGCs to identify gene fusions that may be novel prognostic markers or therapeutic targets. Targeted DNA sequencing and SNP6.0 array analyses were conducted in parallel. Results: Whole transcriptomic analyses were conducted in 80 discovery dataset tumors collected from young patients with DGC who had not been treated with chemotherapy or radiation. Twenty-five in-frame fusions were associated with DGC, four of which were recurrent in 384 DGCs based on targeted RNA sequencing and RT-PCR sequencing analyses. Three of the four recurrent fusions contained a RhoGAP domain in their 3’ partner genes. Patients with one of these three fusions have a significantly worse prognosis than those without (HR, 2.8 [95% CI, 1.5–5.3]). The fusion that harbored a PAP2 domain in the 3’ partner gene was also identified as recurrent and poor prognostic in-frame fusions. Overall, RhoGAP and PAP2 domain-containing fusions were present in 7.5% of DGCs, but not in adjacent normal tissue, and clearly defined the worst prognosis subgroup. Their prognostic impact (adjusted HR 4.1 [95% CI, 2.1–7.9]) was higher than, and independent of, chromosomal instability (CIN) and CDH1 mutation, which we previously identified as the strongest adverse prognostic genomic abnormalities in DGCs (adjusted HRs, 2.5 [1.5–4.4] and 2.4 [1.3–4.4], respectively). Our comprehensive in-frame fusion screen also identified several clinically-actionable fusions amenable to ALK or FGFR inhibition, which had not been previously associated with gastric cancer. Conclusions: Our findings may provide novel genomic insights guiding future personalized strategies for managing DGCs, given the strong prognostic impact of RhoGAP and PAP2 domain-containing gene fusions.

Adjuvant therapy is associated with improved survival in pT1N1 gastric cancer in a heterogeneous western patient population. First Author: Matthew R. Porembka, Department of Surgery, University of Texas Southwestern Medical Center, Dallas, TX

Background: Two recent South Korean studies showed adjuvant therapy (AT) was not associated with improved survival in pT1N1 gastric adenocarcinoma (GAC). We aimed to establish the prognostic utility of lymph node status, determine the pattern of use of AT, and compare survival stratified by type of AT in pT1N1 GAC in a Western patient population. Methods: We identified patients with pT1N1 and pT1N1 GAC using the National Cancer Database from 2004 to 2017. Clinicopathologic variables, treatment regimens, and overall survival (OS) were compared. Results: We compared 4,516 (86.6%) pT1N0 to 514 (13.4%) pT1N1 patients. pT1N1 tumors were larger (median size 2.5 vs. 1.8 cm, p < 0.001), more often poorly differentiated (56.2% vs. 39.6%, p < 0.001), and had higher median retrieved lymph nodes (RLN) (14 vs. 12, p < 0.001) compared to pT1N0. pT1N1 was associated with worse median OS (6.9 vs. 7.9 years, 9.9 years for pT1N0, p < 0.001). pN1 was independently associated with worse OS (HR 2.79 [95% CI 1.84–2.56]). Increased RLN was associated with improved OS (HR 0.5 [95% CI 0.39–0.68], 0.35 [0.2–0.57]). Conclusions: pT1N1 tumors had an adverse prognosis compared to pT1N0. pN1 was an independent predictor of worse survival. RLN of ≥15 was associated with improved survival in pT1N1. ACT and ACRT were independently associated with improved survival in pT1N1 gastric cancer suggesting a valuable role in Western patients.

Effectiveness of laparoscopic surgery in patients with large gastric GIST (diameter > 5cm). First Author: Fei Li, Xuanwu Hospital, Beijing, China

Background: Recently, the application of laparoscopic or DaVinci surgery in relatively small gastrointestinal stromal tumors (GIST) has been increasingly recognized. However, the use in large stromal tumors, especially with a diameter greater than 5 cm, remains controversial for fear of tumor rupture. The aim of our study is to observe the effectiveness of laparoscopic approach in treatment of large gastric GIST. Methods: Patients who were diagnosed with gastric GIST (diameter > 5cm) at Xuanwu Hospital, China and underwent laparoscopic surgery from May 2011 to May 2018 were assessed. We set intraoperative tumor rupture as primary outcome. Secondly outcomes were conversion rate, operating time, estimated blood loss, length of postoperative hospital stay and recurrence rate at the end of the follow-up. Results: Forty patients were included in our study with tumor size (7.5±1.46 cm, range, 5.0–13.8 cm). There was no intraoperative tumor rupture occurred. The median duration of operation was (76.3±29.9) minutes with estimated blood loss (28±15.2) mL. The median time for length of postoperative hospital stay was (5.8±4.1) days. The follow-up period for all the patients was 23.1 months (range, 2.4–5 months). No local or distant recurrence was observed. Conclusions: Laparoscopic resection for large gastric GIST is feasible and effective. Laparoscopic surgery can substitute for open surgery as standard approach for gastric stromal tumors.

The Esophageal Online Patient Reported Outcomes (EsO-PRO) Questionnaire: Formal implementation and assessment of a combined clinical and research data collection tool. First Author: Shirley Xue Jiang, Princess Margaret Cancer Centre, Toronto, ON, Canada

Background: Systematic symptom monitoring improves quality of life, and possibly overall survival in cancer outpatients receiving chemotherapy. To reduce patient, staff, and resource burden, combining research surveys with electronic PRO assessments in a multidisciplinary academic esophageal cancer clinic may allow dual clinical-research goals to be met. Methods: EsO-PRO is a data collection tool directed at esophageal cancer outpatients created through expert feedback. Using the Canadian Institutes of Health research CIHR Knowledge-to-Action (KTA) framework, clinic flow and stakeholder maps were constructed. Facilitators and barriers were then identified, and responses were generated to address implementation barriers. Multiple iterations of the questionnaire were implemented; patient and clinic staff feedback was collected through key informant interviews, and major themes were described. Results: Creation of EsO-PRO included multiple validated tools: the FACT-E, modified Cancer Research UK esophageal cancer risk questionnaire, EQ-5D-5L, PRO-CTCAE for common esophageal symptoms, and baseline clinico-demographic data. Four iterations of the KTA cycle for pilot implementation identified specific key facilitators (clinician champions, staff engagement, resource-integration, and clinician-researcher synergy) and barriers (familiarity with technology, survey length, and communication barriers). Qualitative assessment also identified perceived importance of questions as key to patient completion, and role delegation, staff burden, clinic flow interrupion as critical issues to address. Splitting EsO-PRO into two separate visits for completion, allowing completion at home, and changing fill-in-the-blanks to check-off boxes were identified as potential solutions. Conclusions: The CIHR-KTA framework identified concrete methods for improved integration of a combined clinical-research survey tool for routine use in a multidisciplinary esophageal cancer outpatient clinic. Our process serves as an effective model for integration of innovations in multidisciplinary esophageal cancer clinics.
Preoperative factors predictive of pathologic upstaging in clinical stage I gastric cancer patients. First Author: Hayavadhan Thuppal, Department of Surgery, Montefiore Medical Center, Bronx, NY

Background: In patients with stage 1 gastric cancer, surgical resection without neoadjuvant therapy is offered as the first line treatment. However, some of these patients are found to have higher stage after resection and miss the opportunity for neoadjuvant therapy. Preoperative patient and tumor characteristics may be predictive of the likelihood of pathological upstaging in stage 1 gastric cancer patients who have not received neoadjuvant therapy.

Methods: The National Cancer Database was queried for patients diagnosed from 2004-2015 with clinical stage 1 gastric adenocarcinoma who had undergone surgical resection without neoadjuvant therapy. Univariate analysis and multivariable logistic regression were conducted to determine pre-operative factors associated with pathological upstaging. Candidate variables examined included age, sex, race, tumor size, histology, grade, tumor location, days to surgery, and lymphovascular invasion. Results: Analysis was conducted on 8,015 clinical stage 1 patients. Overall, 1,981 (25%) patients were upstaged. On multivariable logistic regression analysis, significant predictors of upstaging included increasing tumor size (ref: size < 1 cm; 1-2 cm aOR=3.8 (95% CI 2.3-6.1); 2-4 cm aOR=12.4 (7.9-19.5); > 4 cm aOR=25.9 (22.9-56.4)), younger age (ref: > 75, < 50 aOR=1.7 (1.4-2.1), 50-65 aOR=1.4 (1.2-1.6), 65-75 aOR=1.2 (1.1-1.5), male gender (aOR=1.6 (1.0-2.3)), presence of diffuse type gastric cancer (aOR=2.3 (1.7-3.2)), mucinous type (aOR=1.7 (1.2-2.5)), or signet ring cell histology (aOR=1.6 (1.3-2.0)) compared to intestinal histology, presence of lymphovascular invasion (aOR=6.0 (5.0-7.1)), and increasing grade (ref: grade 1, grade 2 aOR=12.4 (7.9-19.5); grade 3 aOR=49.3 (3.6-671)). Conclusions: A quarter of all patients thought to have stage 1 gastric cancer prior to surgery had higher pathological stage at time of resection. Patients with the above risk factors may be understaged with currently available diagnostic tools. The addition of neoadjuvant therapy could be considered when the above risk factors are present in clinical stage 1 patients.
43 Poster Session (Board #F13), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM and Poster Walks, Thu, 5:45 PM-6:30 PM
DNA methylation signature predictive of benefit from neoadjuvant chemotherapy in esophageal adenocarcinoma: Results from the MRC OE2 phase III trial. First Author: Raghav Sundar, National University Health System, Singapore, Singapore

Background: Platinum and 5-Fluorouracil (5FU) neoadjuvant chemotherapy followed by surgery is one of the standard approaches for patients with resectable EAC. To date, there are no predictive biomarkers of chemotherapy benefit. We hypothesize that DNA methylation of genes in key biologic and pathological EAC. To date, there are no predictive biomarkers of chemotherapy benefit. We hypothesize that DNA methylation of genes in key biologic and pathological pathways predict for chemotherapy benefit in EAC. Methods: In the OE2 trial, 802 patients with resectable esophageal carcinoma were randomised to surgery alone (S) versus two cycles of cisplatin and 5FU chemotherapy followed by surgery (CS). DNA was extracted from 213 EAC resection specimens (110 from the CS arm, 103 from the S arm). DNA methylation was analyzed at 1505 CpG sites within 807 genes using the Illumina GoldenGate platform. Cox proportional hazard analysis was performed to identify predictive markers of survival in (CS) arm; non-negative matrix factorization (NMF) was used to delineate methylation signatures. Results: Methylation status of 1505 CpG sites had no statistically significant difference between the (CS) and (S) arms. In the (CS) arm, 87 (5.7%) CpG sites were initially identified as promising candidates in univariate analysis (p < 0.05 cutoff). NMF generated a 4 CpG site signature which divided patients into poor risk and good risk. Genes involved in the signature include RUNX1T1, CCND2, MSTR1, and MMN1. Survival was significantly different between poor risk and good risk in (CS) arm (HR 0.32, 95% CI: 0.21 to 0.52, p = 0.0001). No difference in survival was detected in the surgery arm (HR 1.12, 95% CI: 0.76 to 1.80, p = 0.48), suggesting the signature served as a predictive and not prognostic biomarker. Methylation signature remained an independent predictor of survival in multivariate analysis with clinicopathologic factors (along with age and vascular invasion). Conclusions: Chemotherapy does not appear to change methylation status of EAC. Hypermethylation of RUNX1T1, CCND2 and hypomethylation of MSTR1 and MMN1 leads to significantly decreased benefit from chemotherapy in EA. We describe an epigenetic signature which may serve as a predictive biomarker for chemotherapy benefit using data form the largest bank of DNA methylation in EA reported to date.

44 Poster Session (Board #F14), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM and Poster Walks, Thu, 5:45 PM-6:30 PM
MSI-low is an intermediate type between MSI-high and MSS in 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: High level of microsatellite instability (MSI-high) is an actionable molecular status in oncology, informing tumor response to immune checkpoint inhibitor. However, little is known about MSI-low. The aim of this study is to unveil the characteristics of MSI-low tumor in esophagogastric junction (EGJ) adenocarcinoma. Methods: Using 372 cases with chemono-naive EGJ adenocarcinoma tissue, MSI-testing and Epstein Barr Virus (EBV)/DNA detection were performed by DNA fragment analysis (BAT25, BAT26, BAT-40, D2S123, D5S346, and D17S250) and real-time PCR, respectively. MSI-high was defined as having two or more unstable markers, MSI-low as one, and microsatellite stable (MSS) as none. MSI status was compared with clinicopathological and molecular status including epigenetic alteration in MLH1, LINE-1, and CpG methylator phenotype (CIMP), TP53 status (sequencing and immunohistological expression), Ki-67 index, intra-/peri-tumoral lymphocyte counts (CD8+ or FOXP3+), combined positive score (CPS) of PD-L1 expression. Results: We found there was a statistically significant difference (P < 0.05) in the frequency of recurrent mutations between US and China population. The US population was derived from The Cancer Genome Atlas (TCGA) PanCancer Atlas comprising 440 patients and the Chinese population from a University of Hong Kong study comprising 100 patients. Results: We found there was a statistically significant difference (P = 0.05) in the frequency of recurrent mutations between US and China population in 14 of the 25 most common genes mutations (t-test). Conclusions: This data suggests an underlying difference in the mutational profile of gastric cancers in the US as compared with Asia. These findings thus may help to describe the differences in incidence, histology, and outcomes that has been well described in the literature across these two regions of the world.

45 Poster Session (Board #F15), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM and Poster Walks, Thu, 5:45 PM-6:30 PM
Genomic profile of gastric cancer in the United States versus East Asia. First Author: Gregory A. Gilmore, UCSI, Fresno, CA

Background: Gastric cancer is the fourth most common cancer type and is the third leading cause of cancer deaths worldwide. Much heterogeneity exists in gastric cancer including geographic variation, with significantly higher incidence in Eastern Asia and a well-known but poorly understood relationship with Asian ethnicity. It has thus been hypothesized that differences in incidence and survival between United States and Asia may be related to a difference in the underlying tumor biology. Methods: We sought to compare the mutational frequencies by comparison of proportions of the 25 most frequent mutations between a US and Chinese population. The US population was derived from The Cancer Genome Atlas (TCGA) PanCancer Atlas comprising 440 patients and the Chinese population from a University of Hong Kong study comprising 100 patients. Results: We found there was a statistically significant difference (P = 0.05) in the frequency of recurrent mutations between US and China population in 14 of the 25 most common genes mutations (t-test). Conclusions: This data suggests an underlying difference in the mutational profile of gastric cancers in the US as compared with Asia. These findings thus may help to describe the differences in incidence, histology, and outcomes that has been well described in the literature across these two regions of the world.

46 Poster Session (Board #F16), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
Association between sarcopenia and gastric carcinogenesis: A health check-up cohort study. First Author: Young Min Kim, Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of (South)

Background: Insulin resistance which is a mechanism of metabolic syndrome has been known to promote carcinogenesis of various malignancies. In addition, metabolic syndrome is associated with sarcopenia. Thus, the aim of this study was to investigate the association between sarcopenia and gastric carcinogenesis including precancerous conditions: atrophic gastritis (AG), intestinal metaplasia (IM), and gastric adenoma. Methods: The study subjects were an adult population who underwent gastroendoscopy at Gangnam Severance Medical Center. AG and intestinal metaplasia were evaluated endoscopically. Gastric cancer based on muscle mass was defined as appendicular skeletal muscle (ASM) as a percentage of body weight that was less than 1 standard deviation below the sex-specific mean for healthy adults aged 20 to 39 years (cutoff point: 29.3% in male and 26.7% in female). Obesity was defined as body mass index (BMI) ≥ 25 kg/m2 according to the Asia-Pacific criteria. Sarcopenia obesity was a condition of combined sarcopenia and obesity. The association between sarcopenia and gastric lesions was evaluated. Results: 8,356 patients were enrolled this study. Among them, 12 (0.14%) and 3,552 (42.2%) patients were diagnosed as gastric cancer and precancerous conditions, respectively. 5 (41.7%) of 12 gastric cancer patients and 594 (16.9%) of 3,552 patients with gastric precancerous conditions were diagnosed with sarcopenia. Both diabetes mellitus (DM) (OR = 5.152, P = 0.002) and sarcopenia obesity (OR = 4.139, P = 0.016) were independent predictive factors for gastric cancer. And smoking, alcohol, DM, hypertension, dyslipidemia, Helicobacter pylori, and sarcopenia were significantly associated with gastric precancerous conditions. Conclusions: Sarcopenia and sarcopenia obesity were significantly associated with gastric carcinogenesis. Thus, sarcopenia may be one of the risk factors for gastric carcinogenesis.
Effect of surgical approach on node harvest in gastrectomy: Analysis of the National Cancer Database. First Author: Michael David Watson, Levine Cancer Institute, Carolinas Medical Center, Charlotte, NC

Background: Recent studies demonstrate significant surgical outcome advantages for patients undergoing minimally invasive versus open gastrectomy. Lymph node harvest at the time of gastrectomy is a key component of adequate surgical resection and greater harvest is associated with improved staging and patient outcomes. Our aim is to evaluate lymph node harvest based on surgical approach. Our hypothesis is that a minimally invasive approach, particularly robot-assisted, will be associated with higher lymph node harvest.

Methods: Patients undergoing gastrectomy for gastric adenocarcinoma in the period of 2010-2015 were identified using the National Cancer Database (NCDB). Data collected includes demographic data, institutional volume, approach, type of gastrectomy, tumor size, tumor location, pathologic T classification, year of diagnosis, Charlson-Deyo score and node harvest. Outcomes for patients undergoing open, laparoscopic, and robot-assisted gastrectomy were compared with univariate analysis and with a multivariate generalized linear mixed model (GLMM). Results: 19,555 patients were identified. There were 12,400 men (63.4%) and the mean age was 66.3 ± 12.5 years. 13,486 (69.0%) patients underwent open gastrectomy, 5,023 (25.7%) laparoscopic gastrectomy, and 1,046 (5.3%) robotic-assisted gastrectomy. Mean node harvest for open was 16.1 ± 11.5, laparoscopic was 15.1 ± 12.1, and robotic-assisted was 17.2 ± 13.3. Using a GLMM which controlled for the above listed covariates, robotic-assisted gastrectomy was associated with higher node harvest than both open (p = 0.041) and laparoscopic (p < 0.001) while open was associated with higher node harvest than laparoscopic (p < 0.001). There were 1582 operations with zero nodes harvested. In a sub-analysis of resections where at least one node was harvested (n = 17,973), the mean node harvest for open was 16.9 ± 11.1, laparoscopic was 17.5 ± 11.2, and robotic was 19.7 ± 12.3.

Conclusions: This data suggests that a robot-assisted approach is associated with increased node harvest compared to laparoscopic and open approach in gastrectomy.

Expression patterns of PD-L1 and other immune checkpoint molecules in gastric cancer. First Author: Kenichi Nakamura, Shizuoka General Hospital Cancer Center, Shizuoka, Japan

Background: Immune checkpoint inhibitors (ICPIs) have provided clinical benefit for various malignancies. A new approach was recently made to combine PD-1/PD-L1 inhibitors and other ICPIs. In order to establish a new strategy for ICPI combination therapy, we must first understand the expression patterns of PD-L1 and other ICPI molecules in gastric cancer. Methods: Seven ICP molecules (PD-L2, IDO1, CD80, ICOS, CTLA4, LAG3 and TIM3) were coexpressed with PD-L1 in the TCGA dataset. In our cohort, all of these molecules were also coexpressed (R > 0.5, p < 0.0001). Using a cluster analysis based on these gene expression profiles, patients were divided into Group A, characterized by the coexpression of PD-L1 and other ICP molecules, and Group B, characterized by the underexpression of PD-L1. In Group A, PD-L2 (R = 0.67) and IDO1 (R = 0.61) were particularly strongly associated with the PD-L1 expression. In Group B, elevated expressions of CTLA4 and ICOS were predominantly observed, and these expressions were strongly correlated with each other (R = 0.90). The tumor stage was significantly more advanced in Group B than in Group A (p = 0.02). Accordingly, Group A exhibited a better survival outcome than Group B. The immune landscape of Group A was particularly enriched for Th1, NK CD56dim and activated dendritic cells. Conclusions: PD-L1 and several immune checkpoint molecules tend to be coexpressed in gastric cancer. The combination of PD-L2/IDO1 and IDO1 target agents may be a new strategy for treating gastric cancer with PD-L1 overexpression. In contrast, the underexpression of PD-L1 might be an indication for the use of CTLA4- and/or ICOS-directed therapies.
Background: Gastric cancer (GC) is a heterogeneous disease. Cell-free DNA (cfDNA) has been a research hotspot in molecular tumor profiling. In advanced GC patients, malignant pleural effusion (MPE) and ascites provide a wealth of tumor cells that can be investigated. The aim of this study is to investigate fusion landscape in advanced GC. Methods: A multicenter study in China was initiated from Aug, 2016, and GC patients have been enrolled as of Aug, 2018. To determine the fusion frequency in GC, we analyzed data from 37 clinical GC cases, each of which had results from next-generation sequencing (NGS)-based 381 genes panel assay, analogous to the index patient.

Results: Of this entire cohort, 61 patients (16.44%) were identified with fusions, including TME45B-FFG3 (3), AXIN1-SMAD3 (3), BCL2L1-ERBB2 (2), ERBB2-LAMA3 (2), ERBB2-ACLY (2), TRIM24-BRAF (2), ARHGEF1-CD79A (2), FGFR4-UMCI3 (2), MSH2-TTCTA (2), SMARC4-LDLR (2), GONAL-TRITI (2), AKT1-CP5 (2), GATA6-COLEC2 (2), RICTOR-EFNA5 (2), KATEA-PLAT (2), ROCKI-CCDC17B (2), HBS1L-MYB (2), SLC35A2-ARID2 (2), MAPK1-ACTB (2), NOTCH3-UA1C (2), PIK3CB-KISSI (2), RICTOR-OSMR (2), FGFR2-MIR5694 (2), FGFR2-FGFR1 (2), MAN2A2-BLM (2), EGRF-MED15 (1), EML4-ALK (1), GORCP-ROSI1 (1), FXR2-TP53 (1), NPT1-PSMD11 (1), IRS2-PRKCI (1), FGFR2-KIAA1217(1), FGFR2-TACC2 (1), FGFR3-TACC3 (1), ERBB2, BRAF, EGFR, ALK and ROSI fusions were seen in 18.03% (11/61) of advanced Chinese gastric cancer fusion landscape patients. Conclusions: Advanced Chinese gastric cancer fusion landscape is rich. ERBB2, BRAF, EGFR, ALK and ROSI fusions are rare but potentially druggable in TCIs. Detection of ERBB2, BRAF, EGFR, ALK and ROSI fusions should be part of comprehensive profiling panels to determine TCIIs and direct appropriate combination therapeutic strategies.
High PGRN-expressing GISTs had more epithelioid/mixed histology (68% vs. 32%; p = 0.046), and (74%) had an exon 11 mutation, and D842V was observed in 3 patients (9%). Among the 34 patients whose tumors were genotyped, 25 patients (80%), respectively, and 27 patients (50%) had high PGRN-expressing tumors (RG group) and LG (LG group). Spindle histology was observed in 35 patients (65%). According to the modified NIH classification, 0; weak, 1+; moderate, 2+; strong, 3+. High expression was considered nohistochemical (IHC) analysis and semi-quantitatively categorized (no expression, 0; weak, 1+; moderate, 2+; strong, 3+). High expression was considered.

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Poster Session (Board #G7), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
Poster Session (Board #G8), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Comparison of HER2 expression by immunohistochemistry and HER2 copy number by digital PCR in tumor tissue during treatment with trastuzumab in the prospecto cohort of metastatic HER2-positive gastric cancer patients. First Author: Naoki Takahashi, Department of Gastroenterology, Saitama Cancer Center, Saitama, Japan

Background: Trastuzumab (Tmb) is an active molecular-targeted drug for HER2-positive gastric cancer (GC) patients. HER2 expression is known to change during the treatment of Tmb and HER2 amplification in blood is widely investigated as a new biomarker of the treatment candidate or the monitoring of HER2-target therapy. We evaluated the change of the HER2 expression by immunohistochemistry (IHC) and HER2 copy number by digital PCR during the treatment with Tmb in metastatic HER2-positive GC patients. Methods: Metastatic HER2-positive GC patients treated with Tmb were registered prospectively, and tissues were obtained by biopsy from primary lesions at the following points: (1) pre-treatment, (2) post-treatment, and (3) disease progression during chemotherapy with Tmb. Tissue paraffin-embedded sections were prepared, and the expression of HER2 copy number were scored by IHC and HER2 copy number were evaluated by digital-PCR. Results: Among 20 enrolled patients, HER2 expression was evaluated by IHC in all patients. HER2 copy number was evaluated by digital PCR in 15 patients. A patient was excluded because HER2 expression were not detected by re-evaluation. The median of HER2 copy number of 33 sampling points during the treatment was 6.37 (range: 2.12 - 85.8). The median of HER2 copy number of IHC 3+, IHC 2+; IHC 0-1 were 22.4 (3.37 - 85.8), 2.88 (2.65 - 3.6), 2.37 (2.12 - 3.85), respectively. High level of HER2 copy number was detected in tumor tissues of HER2 IHC 3+ compared with that of IHC ≤2+. HER2 expression by IHC was disappeared after treatment of Tmb in 42% of HER2-positive patients. Among these patients, HER2 copy number at pre-treatment was relatively low (2.63 - 3.6). Conclusions: High copy number of HER2 was detected in tumor tissues with HER2 IHC+ in HER2-positive GC patients during the treatment of Tmb. In addition, low copy number of HER2 in tumor tissues at pre-treatment may be associated with the loss of HER2 expression after treatment of Tmb. Further research by large number of patients to confirm our results is required.

CANCERS OF THE ESOPHAGUS AND STOMACH

Poster Session (Board #D6), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
Development of a liquid-biopsy-based technique for the supplementary diagnosis of highly advanced lymph node metastasis in patients with locally advanced gastric cancer. First Author: Takashi Oshima, Department of Gastrointestinal Surgery, Kanagawa Cancer Center, Yokohama, Japan

Background: The outcomes of patients with locally advanced gastric cancer who have highly advanced lymph node metastasis such as N3 remain poor despite radical resection. If the preoperative diagnoses of such patients improve, further improvement in treatment outcomes is expected to be obtained by means of personalized therapies such as preoperative chemotherapy; however, the accuracy of IHC remains undetermined. Therefore, exploratory proteome analysis using sera was performed with the aim of developing a supplementary liquid-biopsy-based technique to diagnose highly advanced lymph node metastasis in patients with locally advanced gastric cancer. We report the results obtained thus far. Methods: The subjects were 24 patients with pT4a gastric cancer (12 with pN0 disease and 12 with pN3 disease). Proteins that had significantly different (P<0.001) expression levels in the preoperative serum on exploratory proteome analysis by liquid chro-matography and mass spectrometry were identified. These proteins were verified by enzyme-linked immunosorbent assay (ELISA) using a different cohort (20 patients with pN0 disease and 13 with pN3 disease) from that described above. Results: In the exploratory proteome analysis, 2,357 kinds of proteome were identified and examined. Six these proteins were identified as candidate predictive markers of highly advanced lymph node metastasis. These proteins were verified using existing and newly developed ELISA kits, and reproducibility was verified for one protein (Protein V) (P = 0.0033).

Conclusions: The possibility of the supplementary diagnosis of highly advanced lymph node metastasis was similar or less than that of patients with locally advanced gastric cancer. Further evaluations by prospective studies are now in progress, with the ultimate goal of clinical application.
Conclusions: Numerous CTCs expressed N-cadherin but not CK. Perioperative and decreased postoperatively; C; no preoperative CTCs. The recurrence rates in function and pathway activation between patients with a poor response and Nevertheless, there is paucity of data regarding potentially involved cellular (LAEC). Former studies addressed the clinicopathological patterns of patients represents a key therapeutic strategy for locally advanced esophageal cancer Neoadjuvant chemoradiotherapy (NCRT) followed by surgery Petah-Tikva, Israel Proteomic analysis to identify markers for response to treatment in esophageal cancer. First Author: Oran Zlotnick, Rabin Medical Center, Petah-Tikva, Israel Background: Neoadjuvant chemoradiotherapy (NCRT) followed by surgery represents a key therapeutic strategy for locally advanced esophageal cancer (LAEC). Former studies addressed the clinicopathological patterns of patients who demonstrated good response to NCRT compared to patients with inferior response. Nevertheless, there is paucity of data regarding potentially involved cellular pathways that account for tumor response to NCRT. We performed a comprehensive proteomic analysis to identify the key differences in protein function and pathway activation between patients with a poor response and those with a favourable response to treatment. Methods: Patients diagnosed with LAEC who were treated with NCRT and operated at our institution were included in the study. Patients were defined as good responders (GR) upon the tumor regression grade (TRG) in the pathological specimen; GR defined as TRG 0/1 and no evidence of recurrence at 1-year post surgery. Bad responders (BR) were defined as TRG 2/3 and recurrence ≤1 year. Tumor was isolated from the surgical specimen and proteins were extracted and processed for mass spectrometry-based analysis. Clinical data of demographics, response to treatment, and survival was retrieved from electronic medical records. Difference in protein expression between GR and BR were analysed using validated gene expression pathways tools and correlated to clinical data. Results: Forty-four patients were included in the cohort. Mean age was 66.7 years, male predominance (33/44). Thirty-five patients had adenocarcinoma - 17 GR and 18 BR. Nine patients had squamous cell carcinoma - 6 GR and 3 BR. Protein expression patterns significantly differed between GR and BR regardless of histology, mainly in cellular pathways account for nucleic acid metabolism (p < 0.05), whereas BR had overexpression of these genes. Conclusions: Our study indicate that lack of response to NCRT may derive from overexpression of unique cellular pathways. Former studies imply these cellular pathways may play a role in resistance to cisplatin. Larger transcriptomic studies are warranted for future analysis to extend these observations.

Methods: Peripheral blood (7.5 ml) was taken from patients (n = 54) before curative resection, and at 7 days, 1 and 6 months postoperatively; CTCs were enriched using density gradient centrifugation and magnetic-activated cell sorting (negative selection). Cell suspensions were characterized by multi-immunofluorescence staining against cytokerin (CK) and N-cadherin, and by DAPI staining. CTCs were defined as nucleated cells expressing CK or N-cadherin. Threshold analysis identified 1 CTC/7.5 ml as an optimal cut-off value. The median observation period was 7.35 days. Results: CTCs were detected in seven patients (24%) with early cancer and 14 patients (56%) with advanced cancer (p < 0.05). Cells were identified as either N-cadherin+/CK−/CD45− or N-cadherin+/CK+/CD45−, but no N-cadherin−/ CK−/CD45− cells were observed. The median follow-up period was 24.5 months. After 2 years, postoperative recurrence was detected in nine patients, all of whom had advanced gastric cancer and N-cadherin+/CK−. postoperatively; B, preoperative CTCs and perioperative kinetics. Background: Circulating tumor cells (CTCs) have been shown to be heterogeneous. This study aimed to identify the prognostic significance of CTCs in patients with gastric cancer: Epithelial mesenchymal transition and perioperative kinetics. Prognostic significance of circulating tumor cells in patients with gastric cancer: Epithelial mesenchymal transition and perioperative kinetics. Conclusions: Twenty CDR mutations were tested by next-Generation Sequencing (NGS) with a 592-gene panel on a total of 1935 (709 EC; 831 GC; 355 GEJ) cancers. TMB was assessed by NGS, MSI by NGS or fragment analysis, and PD-L1 by IHC (22c3 for CPS or SP42). Results: GC had the highest TMB mutation rate compared to EC and GEJ (27% vs. 20%, p = 0.0005 and 17%, p = 0.0002, respectively). MSI-High (MSI-H) was significantly more common in the DDR mutated cohort (DOR-M) compared to non-mutated cancers (18% vs. 1%; p < 0.0001). TMB-High (≥ 10 mutations/megabase [mt/MB]) was higher in DDR-M (35% vs. 21%; p < 0.0001); in DDR-M cohort, GC had the highest TMB compared to DDR-M EC and GEJ (mean: 13.8 vs. 9.4 vs. 10 mt/MB, respectively; p < 0.0001). TMB mutations were more frequent in the PD-L1 combined positive score (CPS) ≥ 50 group than CPS 0 (42.9% vs. 24.4%; p = 0.037) and CPS 1-4 (42.9% vs. 20.6%; p = 0.05). ARID1A, ATRX, BRCA2, and Pten were the most prevalent DDR mutations. ARID1A defined as TRG ≤1 (17%, 22%, 25%, 24%, respectively); ARID1A, ATRX, BRCA2, and Pten were in TMB-High (74%, 7.7%, 6.7%, 6.8%); and ARID1A, BRCA2, RAD50, and WRN in PD-L1-high (CPS ≥ 10) (48.5% vs. 5.2% vs. 2.5% vs. 3.4%, respectively). Conclusions: DDR mutation rates were significantly more prevalent in the DDR-M cohort compared to non-DDR mutated cancers, most pronounced in GC. Alterations in ARID1A, ATRX, BRCA2, and Pten were correlated with MSI-H and MSI-low while ARID1A, BRCA2, RAD50, and WRN were correlated with increased PD-L1 expression. Our findings may help identify patients for tailored immunotherapy approaches in future clinical trials.

Prognostic significance of circulating tumor cells in patients with gastric cancer: Epithelial mesenchymal transition and perioperative kinetics. First Author: Yui Ishiguro, Department of Gastroenterological Surgery I, Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Methods: Peripheral blood (7.5 ml) was taken from patients (n = 54) before curative resection, and at 7 days, 1 and 6 months postoperatively; CTCs were enriched using density gradient centrifugation and magnetic-activated cell sorting (negative selection). Cell suspensions were characterized by multi-immunofluorescence staining against cytokerin (CK) and N-cadherin, and by DAPI staining. CTCs were defined as nucleated cells expressing CK or N-cadherin. Threshold analysis identified 1 CTC/7.5 ml as an optimal cut-off value. The median observation period was 7.35 days. Results: CTCs were detected in seven patients (24%) with early cancer and 14 patients (56%) with advanced cancer (p < 0.05). Cells were identified as either N-cadherin+/CK−/CD45− or N-cadherin+/CK+/CD45−, but no N-cadherin−/CK−/CD45− cells were observed. The median follow-up period was 24.5 months. After 2 years, postoperative recurrence was detected in nine patients, all of whom had advanced gastric cancer and N-cadherin+/CK−. postoperatively; B, preoperative CTCs and perioperative kinetics. Background: Circulating tumor cells (CTCs) have been shown to be heterogeneous. This study aimed to identify the prognostic significance of CTCs in patients with gastric cancer: Epithelial mesenchymal transition and perioperative kinetics. Prognostic significance of circulating tumor cells in patients with gastric cancer: Epithelial mesenchymal transition and perioperative kinetics. Conclusions: Twenty CDR mutations were tested by next-Generation Sequencing (NGS) with a 592-gene panel on a total of 1935 (709 EC; 831 GC; 355 GEJ) cancers. TMB was assessed by NGS, MSI by NGS or fragment analysis, and PD-L1 by IHC (22c3 for CPS or SP42). Results: GC had the highest TMB mutation rate compared to EC and GEJ (27% vs. 20%, p = 0.0005 and 17%, p = 0.0002, respectively). MSI-High (MSI-H) was significantly more common in the DDR mutated cohort (DOR-M) compared to non-mutated cancers (18% vs. 1%; p < 0.0001). TMB-High (≥ 10 mutations/megabase [mt/MB]) was higher in DDR-M (35% vs. 21%; p < 0.0001); in DDR-M cohort, GC had the highest TMB compared to DDR-M EC and GEJ (mean: 13.8 vs. 9.4 vs. 10 mt/MB, respectively; p < 0.0001). TMB mutations were more frequent in the PD-L1 combined positive score (CPS) ≥ 50 group than CPS 0 (42.9% vs. 24.4%; p = 0.037) and CPS 1-4 (42.9% vs. 20.6%; p = 0.05). ARID1A, ATRX, BRCA2, and Pten were the most prevalent DDR mutations. ARID1A defined as TRG ≤1 (17%, 22%, 25%, 24%, respectively); ARID1A, ATRX, BRCA2, and Pten were in TMB-High (74%, 7.7%, 6.7%, 6.8%); and ARID1A, BRCA2, RAD50, and WRN in PD-L1-high (CPS ≥ 10) (48.5% vs. 5.2% vs. 2.5% vs. 3.4%, respectively). Conclusions: DDR mutation rates were significantly more prevalent in the DDR-M cohort compared to non-DDR mutated cancers, most pronounced in GC. Alterations in ARID1A, ATRX, BRCA2, and Pten were correlated with MSI-H and MSI-low while ARID1A, BRCA2, RAD50, and WRN were correlated with increased PD-L1 expression. Our findings may help identify patients for tailored immunotherapy approaches in future clinical trials.

Proteomic analysis to identify markers for response to treatment in esophageal cancer. First Author: Oran Zlotnick, Rabin Medical Center, Petah-Tikva, Israel
Comprehensive molecular profiling of signet-ring-cell carcinoma (SRCC) from the stomach and colon. First Author: Alberto Puccini, USC Keck School of Medicine, Los Angeles, CA

Background: Signet ring cell carcinoma (SRCC) is a rare variant of adenocarcinoma, accounting for about 10% of gastric cancer (GC) and 1% of colorectal cancer (CRC). SRCC is associated with poor prognosis, however little is known about the underlying molecular characteristics. Herein, we aimed to characterize the molecular features of SRCCs, and to compare the molecular profile of SRCC to adenocarcinoma; further, we assessed the impact of tumor location on the molecular profile of SRCC. Methods: SRCCs were analyzed using NGS (MiSeq on 47 genes, NextSeq on 592 genes), immunohistochemistry, and in-situ hybridization. Tumor mutational burden (TMB) was calculated based on somatic nonsynonymous missense mutations, and microsatellite instability (MSI) was evaluated by NGS of known MSI loci. Chi-square and t-tests were used for comparative analyses. Results: A total of 8,500 CRC and 1,100 GC were screened for SRCC histology. Seventy-six SRCC were identified from the CRC cohort (<1%) and 98 from the GC cohort (9%). The most frequently mutated genes in CRC-SRCC were TP53 (47%), ARID1A (26%), APC (25%), KRAS (22%), RNF43 (16%), KMT2D (12%), CTNNB1 (11%), SMAD4 (10%) and BRAF (10%), while in GC-SRCC were TP53 (42%), ARID1A (27%), CDH1 (11%), BAP1 (7%), PIK3CA (7%), ERBB2 (5%). When compared to non-SRCC histology (N=3522), CRC-SRCC (N=37) showed more frequent mutation in BRCA1 (1% vs 0%, $P<0.001$) and less mutation in APC (19% vs 78%, $P<0.001$), KRAS (22% vs 51%, $P=0.001$) and TP53 (47% vs 73%, $P=0.001$). Among GC cohort, SRCC (N=54) had a higher frequency of mutations in CDH1, BAP1, and ERBB2, and a lower rate of amplification of MYB compared to non-SRCC (N=540), although none of these differences were statistically significant. When we compared GC-SRCC vs. CRC-SRCC, the mutation rate in APC (10% vs 25%) and KRAS (2% vs 22%) genes were significantly different (P < 0.01). Conclusions: Our research is the first to comprehensively characterize the molecular features of SRCC. Our data suggest that SRCCs harbor similar molecular profile, regardless the tumor location. On the other hand, significant differences were observed between SRCCs and non-SRCC tumors, therefore tailored therapy should be provided to these patients.

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Comprehensive molecular profiling of signet-ring-cell carcinoma (SRCC) from the stomach and colon. First Author: Alberto Puccini, USC Keck School of Medicine, Los Angeles, CA

Background: Signet ring cell carcinoma (SRCC) is a rare variant of adenocarcinoma, accounting for about 10% of gastric cancer (GC) and 1% of colorectal cancer (CRC). SRCC is associated with poor prognosis, however little is known about the underlying molecular characteristics. Herein, we aimed to characterize the molecular features of SRCCs, and to compare the molecular profile of SRCC to adenocarcinoma; further, we assessed the impact of tumor location on the molecular profile of SRCC. Methods: SRCCs were analyzed using NGS (MiSeq on 47 genes, NextSeq on 592 genes), immunohistochemistry, and in-situ hybridization. Tumor mutational burden (TMB) was calculated based on somatic nonsynonymous missense mutations, and microsatellite instability (MSI) was evaluated by NGS of known MSI loci. Chi-square and t-tests were used for comparative analyses. Results: A total of 8,500 CRC and 1,100 GC were screened for SRCC histology. Seventy-six SRCC were identified from the CRC cohort (<1%) and 98 from the GC cohort (9%). The most frequently mutated genes in CRC-SRCC were TP53 (47%), ARID1A (26%), APC (25%), KRAS (22%), RNF43 (16%), KMT2D (12%), CTNNB1 (11%), SMAD4 (10%) and BRAF (10%), while in GC-SRCC were TP53 (42%), ARID1A (27%), CDH1 (11%), BAP1 (7%), PIK3CA (7%), ERBB2 (5%). When compared to non-SRCC histology (N=3522), CRC-SRCC (N=37) showed more frequent mutation in BRCA1 (1% vs 0%, $P<0.001$) and less mutation in APC (19% vs 78%, $P<0.001$), KRAS (22% vs 51%, $P=0.001$) and TP53 (47% vs 73%, $P=0.001$). Among GC cohort, SRCC (N=54) had a higher frequency of mutations in CDH1, BAP1, and ERBB2, and a lower rate of amplification of MYB compared to non-SRCC (N=540), although none of these differences were statistically significant. When we compared GC-SRCC vs. CRC-SRCC, the mutation rate in APC (10% vs 25%) and KRAS (2% vs 22%) genes were significantly different (P < 0.01). Conclusions: Our research is the first to comprehensively characterize the molecular features of SRCC. Our data suggest that SRCCs harbor similar molecular profile, regardless the tumor location. On the other hand, significant differences were observed between SRCCs and non-SRCC tumors, therefore tailored therapy should be provided to these patients.

A novel patient derived orthotopic xenograft model of gastro-esophageal junction cancer: Key platform for translational discoveries. First Author: Omkara Lakshmi Veerani, MD Anderson Cancer Center, Houston, TX

Background: Mouse models of gastroesophageal junction (GEJ) cancer strive to recapitulate the intratumoral heterogeneity and cellular crosstalk within patient tumors to improve clinical translation. Current GEJ models have limited applications in tumor microenvironment, immune oncology and metastatic studies. Methods: A novel patient derived tumor orthotopic xenograft (PDXO) was established from GEJ cancer via surgical implantation. Patient tumor was compared to subcutanuently implanted PDX and PDXO by H&E, IHC, and next generation sequencing (12001 panel). Drug efficacy studies of 5-fluorouracil with and without radiotherapy are being performed. Results: Mechanical ablation of mouse GEJ prior to implantation of patient derived tumor in situ promotes tumor engraftment (100%, n = 6). Complete PDXO engraftment was observed with rapid intra and extra luminal tumor growth as evidenced by MRI. Patient derived stroma co-engrafts with tumor cells in GEJ-PDXO. PDXO contains fibroblasts, immune and inflammatory cells, vascular and lymphatic systems. Stromal hallmarks of aggressive GEJs were recapitated in GEJ-PDXO mouse model. PDXO demonstrates tumor invasio into vasculature. GEJ-PDXO is a clinically relevant model for metastases and immunological studies. Next generation sequencing with the T2001 revealed that the loss of heterozygosity of NOTCH3, TGFF, EZH2, and MLL3 are maintained with similar allelic frequency between the patient tumor and the xenografts. Additional somatic SNVs such as ARID1A, NDSI (CDSS17-1S8), NDSI (CDSS18-1S9), KDM6A, XPO1, MAPK1 and EGFR were found to be acquired in that order that were not present in the patient tumor. Drug and radiation efficacy studies are ongoing, tumor response to radiation was observed. Conclusions: A GEJ-PDXO model exhibits remarkable fidelity to human disease and captures the precise tissue microenvironment present within the local GEJ architecture facilitating it as a novel tool in translating to clinics. This model can be applied to address importance of tumor microenviro in metastatic and immunological studies, and to develop novel therapeutic approaches for the treatment of GEJ cancer.

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Activated interferon-γ (IFN-γ) pathway associated with clinical benefit to programmed cell death protein-1 (PD-1)/PD ligand 1 (PD-L1)-based therapy in esophageal squamous cell carcinoma (ESCC). First Author: Jhe-Cyuan Guo, National Taiwan University Hospital; Taipei, Taiwan

Background: Previous studies indicate a preexisting T cell response and the associated "adaptive immune resistance" are critical for the clinical efficacies of anti-PD-1/PD-L1 immunotherapy. The study explored the activated IFN-γ pathway and the expression of interferon regulatory factor 1 (IRF-1), as surrogate of preexisting T cell response, as potential biomarkers associated with clinical benefit (CB) for ESCC patients receiving anti-PD-1/PD-L1 therapy.

Methods: Thirty-one ESCC patients treated with PD-1/PD-L1 blockade antibody, alone or in combination, were enrolled. Tumor response evaluation was made according to Response Evaluation Criteria in Solid Tumours 1.1, and CB was defined as complete response, partial response or stable disease at least 6 months. Formalin-fixed paraffin-embedded tissues from 31 patients were analyzed for the expression of PD-L1 and IRF-1 by immunohistochemistry; 13 tissues were analyzed for the expression of immune-related genes by NanoString nCounter Human PanCancer Immune Profiling.

Results: Of 31 enrolled patients (M: F = 30: 1, median age of 58), 23 and 8 were of recurrent and de novo metastatic ESCC. Sixteen and 15 received PD-1/PD-L1 blockade alone and PD-1/PD-L1-based combination therapy, respectively; 13 had received at least 2 lines of systemic therapy for advanced disease. The response rate was 10%, and the CB rate was 16%. The median progression-free survival (PFS) and overall survival are 1.8 and 5.6 months, respectively. The 25-gene IFN-γ signature was significant higher in patients with CB than in patients without CB (P = 0.020). Neither PD-L1 expression on tumor cells (TC) nor immune cells (IC) was associated with CB (P = 0.489 and 0.646, respectively). However, the IRF-1 expression on TC or on IC was significantly associated with CB (P < 0.001 and 0.005, respectively). Conclusions: Activated IFN-γ pathway determined by 25-gene IFN-γ-sigature and high IHC-expression of IRF-1 were associated with CB in advanced ESCC patients receiving anti-PD-1/PD-L1-based therapy. (Supported by the grant of MOST 105-2314-B-002-186-MY3).

Survival of patients with metastatic HER2 positive gastroesophageal cancer treated with second-line chemotherapy plus trastuzumab or ramucirumab after progression on frontline chemotherapy plus trastuzumab. First Author: Justin Moser, University of Utah Huntsman Cancer Institute, Salt Lake City, UT

Background: Optimal second line treatment for patients with metastatic HER2 positive gastroesophageal cancer (Her2GE) is unknown. A retrospective study has suggested continuation of chemotherapy with trastuzumab (CT), as compared to chemotherapy alone, may improve outcomes. However, CT has never been compared to the current standard second-line treatment of chemotherapy plus ramucirumab (CR). Methods: The Flatiron Health EHR-derived database, a nationally representative database comprising patient-level structured and unstructured data, curated and technology-enabled abstraction from a nationally representative database comprising patient-level clinical data, was analyzed for the expression of PD-L1 and IRF-1 by immunohistochemistry; 13 tissues were analyzed for the expression of immune-related genes. Conclusions: The study explored the activated IFN-γ pathway and the expression of interferon regulatory factor 1 (IRF-1), as surrogate of preexisting T cell response, as potential biomarkers associated with clinical benefit (CB) for ESCC patients receiving anti-PD-1/PD-L1 therapy.

Methods: Thirty-one ESCC patients treated with PD-1/PD-L1 blockade antibody, alone or in combination, were enrolled. Tumor response evaluation was made according to Response Evaluation Criteria in Solid Tumours 1.1, and CB was defined as complete response, partial response or stable disease at least 6 months. Formalin-fixed paraffin-embedded tissues from 31 patients were analyzed for the expression of PD-L1 and IRF-1 by immunohistochemistry; 13 tissues were analyzed for the expression of immune-related genes by NanoString nCounter Human PanCancer Immune Profiling. Results: Of 31 enrolled patients (M: F = 30: 1, median age of 58), 23 and 8 were of recurrent and de novo metastatic ESCC. Sixteen and 15 received PD-1/PD-L1 blockade alone and PD-1/PD-L1-based combination therapy, respectively; 13 had received at least 2 lines of systemic therapy for advanced disease. The response rate was 10%, and the CB rate was 16%. The median progression-free survival (PFS) and overall survival are 1.8 and 5.6 months, respectively. The 25-gene IFN-γ signature was significant higher in patients with CB than in patients without CB (P = 0.020). Neither PD-L1 expression on tumor cells (TC) nor immune cells (IC) was associated with CB (P = 0.489 and 0.646, respectively). However, the IRF-1 expression on TC or on IC was significantly associated with CB (P < 0.001 and 0.005, respectively). Conclusions: Activated IFN-γ pathway determined by 25-gene IFN-γ-sigature and high IHC-expression of IRF-1 were associated with CB in advanced ESCC patients receiving anti-PD-1/PD-L1-based therapy. (Supported by the grant of MOST 105-2314-B-002-186-MY3).

KRAS amplification and mutation are independent events in gastroesophageal adenocarcinomas (GEA). First Author: Russell Madison, Foundation Medicine, Inc., Cambridge, MA

Background: KRAS mutations are common oncogenic events across cancers, but effective RAS-directed therapies are lacking. However, recent studies support use of PD-1 blockade in most subsets of lung cancer with KRAS short arm mutations (KRAS<sup>a</sup> codon 12/13, PMID: 29039262), and combination of MEK and SHP2 inhibition in KRAS amplified (KRAS<sup>SV</sup>) GEA (PMID: 30093730). We sought to explore the landscape of KRAS altered GEA and compare genomic profiles of KRAS-altered and KRAS wild-type (WT) cases for biomarkers of response to targeted therapies and immune checkpoint inhibitors. Methods: 6,667 tissue specimens from patients with advanced GEA were assayed using hybrid capture-based comprehensive genomic profiling. Tumor mutational burden (TMB) was determined on up to 1.1 Mbp of sequenced DNA and microsatellite instability (MSI) was determined on 95 or 141 loci. Descriptive statistics were used to compare among subgroups. Results: KRAS<sup>SV</sup> and KRAS<sup>a</sup> were identified in 11% and 5.8% of gastric adenocarcinoma (GA), respectively, and in 7.2% and 17% of esophageal adenocarcinoma (EA), respectively. KRAS<sup>SV</sup> and KRAS<sup>a</sup> were nearly mutually exclusive, co-occurring in only 4.4% of KRAS altered cases. ERBB2 alterations were less common in KRAS<sup>SV</sup> and KRAS<sup>a</sup> GEA (both 9%) as compared with KRAS<sup>WT</sup> GEA (99%) (P = 19E-16). EGFR<sup>a</sup> was less common in KRAS<sup>SV</sup> versus KRAS<sup>GA</sup> (9.3% vs. 9.1%, P = 2.6E-8), whereas PIK3CA<sup>a</sup> was more common in KRAS<sup>SV</sup> versus KRAS<sup>GA</sup> (56% vs. 50%, P = 1.5E-11), Mediant TMB for all groups was similar; however, KRAS<sup>SV</sup> GEA had a higher mean TMB (9.7 mut/Mb) as compared to KRAS<sup>SV</sup> GEA (9.5 mut/Mb, P = 5.0E-12) and KRAS WT cases (5.8 mut/Mb, P = 2.2E-7). KRAS code 12/13 accounted for > 80% of predicted pathogenic mutations. MSI-high was also more prevalent in KRAS<sup>SV</sup> (14%) versus KRAS<sup>GA</sup> (0.9%, P = 4.8E-5) and KRAS WT GEA (3.0%, P = 1.8E-25). MSI-high KRAS<sup>SV</sup> GEA was associated with older patient age (median 72 years) and with high TMB (median 40.9 mut/Mb). Conclusions: GA was enriched for KRAS mutation whereas EA was enriched for KRAS amplification. KRAS<sup>SV</sup> versus KRAS<sup>GA</sup> each presented distinct genomic profiles, KRAS<sup>SV</sup> in the absence of KRAS mutation exists in 11% of GA and warrants further exploration to inform combination treatment strategies.
Conclusions: The ratio (stratification for matched pairs) was 1.74 (95% CI: 1.04-2.90; p = 0.03). Three-year PFS was estimated at 40% (95% CI: 31-53%) for DM patients versus 50% (95% CI: 40-63%) for non-DM patients (p = 0.12). Hazard ratio (HR) was 3.43; p = 0.02. Three-year OS was estimated at 46% (95% CI: 37-57%) for DM patients versus 50% (95% CI: 40-63%) for non-DM patients (p = 0.02). The risk of death and progression is greater in DM patients as compared to non-DM patients.

Methods: We employed our Search Tag Analyze Resource (STAR-GEO) platform to conduct meta-analysis using the National Center for Biotechnology’s (NCBI) Gene Expression Omnibus (GEO). We tagged 151 tumor gene expression variations of EAC. We then analyzed the signature in Ingenuity Pathway Analysis, restricting genes that showed statistical significance (p < 0.05) and an absolute experiment log ratio greater than 0.15 between tumor and control. We identified a total of 269 (4.0%) FGFR2-altered cases consisting of FGFR2 amplified (amp; 209, 78% of FGFR2-altered), FGFR2 mutated (mut; 40, 15%), and FGFR2 rearranged (re, 37, 14%). There was a female predominance in FGFR2-altered cases (MF = 1:6) vs. patients without active treatment (WT) (2:8). Cases with FGFR2amp and FGFR2mut were exclusively MS-stable. The most common fusion partner was TACC2 (22%). FGFR2amp GEA had higher rates of TPS2 mutation versus either FGFR2mut or FGFR2amp cases (p = 4.4E-6). Co-occurring alterations in the other GEA RTK targets including EBRB2 (10%), EGF (8%) and MET (3%) were observed in all types of FGFR2-altered GEA. Co-occurring downstream alterations in MYC (17%), KRAS (10%) and PIK3CA (3.6%) were observed frequently in each class of FGFR2-altered GEA. The median TMB for FGFR2-altered GEA was 3.6 mut/mb, which was not significantly different from a median of 4.3 mut/mb seen in FGFR2 WT samples (p = 0.53). Conclusions: FGFR2-altered GEA is a heterogeneous subgroup with genetic activity, very little is known about the genomic landscape of FGFR2-altered GEA.

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75 Poster Session (Board #H5), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

A phase II, open-label, randomized study to evaluate the efficacy and safety of andequilliximab combined with nivolumab versus nivolumab alone in subjects with unresectable or recurrent gastric or gastroesophageal junction adenocarcinoma. First Author: Manish A. Shah, Weill Cornell Medicine/New York Presbyterian Hospital, New York, NY

Background: Andecliximab (ADX) is a monoclonal antibody that inhibits matrix metalloproteinase 9 (MMP9). Preclinical studies suggest that MMP9 inhibition relieves immune suppression and promotes T-cell infiltration to potentiate checkpoint blockade. Methods: Phase 2, open-label, randomized study of the efficacy and safety of ADX + nivolumab (NIVO) vs. NIVO alone in patients with pre-treated metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma. Patients were randomized to either ADX 800 mg IV + NIVO 3 mg/kg IV, or NIVO 3 mg/kg IV alone, and stratified by tumor PD-L1 status. Treatment was administered every 2 weeks. Re-staging CT scans were performed every 8 weeks to evaluate response. Primary endpoint: objective response rate (ORR). Secondary endpoints: progression-free survival (PFS), overall survival (OS), and adverse events (AEs). Results: Of the 144 patients randomized, 141 were treated, 109 (76%) completed tumor assessment. 81% of patients were white, with 69% male and a mean (SD) age of 59 (12) years. ORR (95% CI) was 11.1% (4.9-20.7%) in patients receiving ADX + NIVO, and 6.9% (2.3-15.5%) in those receiving NIVO alone, p = 0.6. Kaplan-Meier estimated median (95% CI) PFS was 18 (18.0-20.3) months in patients receiving ADX + NIVO, and 19 (16.7-19.0) months in those receiving NIVO alone. p = 0.2. Kaplan-Meier estimated median (95% CI) OS was 72 (52.9-93) months in patients receiving ADX + NIVO, and 59.9 (35.8-86.6) months in those receiving NIVO alone, p = 0.4. AEs leading to treatment discontinuation occurred in 1 patient in the ADX + NIVO group, and in 1 patient in NIVO-only group. PD-L1 and mismatch repair deficient subgroup analyses will be presented. Exploratory biomarker analyses will be submitted separately. Conclusions: Addition of ADX to NIVO did not improve ORR, PFS, or OS compared with NIVO alone in patients with pre-treated metastatic gastric or GEJ adenocarcinoma. Combination of ADX with NIVO had a favorable safety and tolerability profile. Clinical trial information: NCT02864381.

76 Poster Session (Board #H6), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Endoscopic features of submucosal invasion in undifferentiated type early gastric cancer sized less than 2 cm without ulceration. First Author: Su Jin Kim, Pusan National University Yangsan Hospital, Yangsan, Korea, Republic of (South)

Background: The prediction of invasion depth is important to decide the treatment modality for the undifferentiated type early gastric cancer (EGC) when size is less than 2 cm and had no ulceration. We aimed to identify the endoscopic features associated with submucosal invasion in the undifferentiated type EGC that meet the criteria of size and status of ulcer in the endoscopic submucosal dissection (ESD). Methods: A total of 120 patients with undifferentiated type EGC who received ESD or operation from August 2008 to December 2017 were enrolled in this study. All lesions met the ESD criteria except the invasion depth. We retrospectively reviewed endoscopic features of tumor before the resection and depth of invasion after resection. Results: In 120 undifferentiated EGCs, the mucosal and submucosal cancer were 97 and 23 lesions, respectively. In univariable analysis, discolor change, upper third location, the presence of deep/wide erosion were associated with submucosal invasion. Multivariable analysis revealed that upper/middle third location (odds ratio [OR] 8.0, 95% confidence interval [CI] 1.2-55.0), OR 7.9, 95% CI 1.8-35.1), erosion or polypoid (OR 41.8, 95% CI 4.1-427.9), and elevated type (OR 20.9, 95% CI 2.5-173.8) were significant risk factors. In 112 patients received gastrectomy with lymph nodes dissection, lymph node metastases were found in four cases (three mucosal cancer and one submucosal cancer). However, there was no lymph node metastasis in the lesions meeting the expanded ESD indication. Conclusions: The careful decision of treatment modality is needed for undifferentiated type EGC with erosion or elevated gross type located on the upper/middle third, although the tumor size and ulcer status meet the ESD indication.

77 Poster Session (Board #H7), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Long-term outcome of laparoscopic versus open total gastrectomy for advanced gastric cancer: A propensity score-matched analysis. First Author: Hayemin Lee, The Catholic University of Korea, Seoul, Korea, Republic of (South)

Background: Laparoscopic total gastrectomy (LTG) for advanced gastric cancer (AGC) is technically and oncologically challenging procedure for surgeons. The aim of this study is to compare technical safety and long-term oncologic feasibility of LTG for AGC patients compared to open total gastrectomy (OTG) using propensity score (PS)-matched analysis. Methods: Between 2004 and 2014, 185 patients (OTG: 127; LGT: 58) underwent total gastrectomy due to advanced gastric cancer. PS-matching was done using patients’ age, sex, American Society of Anesthesiologist (ASA) physical status, extent of lymph node dissection, presence of combined resection and pathological stage of disease. Results: A total of 4204 GC patients with NCT were included, 62% of them had additional neoadjuvant radiotherapy (NRT). NCRT and NCT improved pCR and R0 rates in GC without increase in postoperative mortality. The long-term OS benefit of NRT is likely secondary to higher pCR and R0 resection. NRT improved pCR and R0 rates in GC without increase in surgical morbidity/mortality. The long-term OS benefit of NRT is likely secondary to higher pCR and R0 resection.

78 Poster Session (Board #H8), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

The impact of neoadjuvant chemoradiation versus chemotherapy on short and long-term outcomes among gastric carcinoma patients. First Author: Basem Azab, Sentara Healthcare, Hampton, VA

Background: There is little consensus on the use of neoadjuvant chemoradiation (NCRRT) versus neoadjuvant chemotherapy (NCT) in gastric carcinoma (GC) patients. We sought to compare the outcomes of these two approaches in a large national cohort. Methods: National Cancer Data Base (NCDB) from 2004-2014 of GC patients who underwent NCRRT/NCT followed by resection were included. Primary outcome was overall survival (OS), secondary outcomes were pathological complete response (pCR), RD resection and postoperative mortality. Results: A total of 4204 GC patients with NCT were included. 62% of them had additional neoadjuvant radiotherapy (NRT). NCRRT had higher pCR and OR rates (551/2631 (21%), 2334/2561 (90%) than NCT group (148/1573 (9%), 1242/1543 (80%), p < 0.0001. Multivariate logistic regression showed similar higher odds of pCR (OR 2.8, 95% CI 1.65-4.60, p < 0.0001) and RD (OR 1.5, 95% CI 1.14-1.99, p = 0.004) among NCRRT versus NCT. There was no significant difference in length of hospital stay, 30-day readmission rate, 30- and 90-day postoperative mortality. Median, 3- and 5-year OS for NCRRT versus NCT were: (20.4 months, 24% and 11%) versus (18.3 months, 19% and 6%), p < 0.001. Univariate cox regression analysis showed superior OS with NRT (HR 0.9, 95% CI 0.80-0.91, p < 0.001). After adjusting for confounding variables, pCR (HR 0.2, 95% CI 0.18-0.24, p < 0.0001) and RD (HR 0.7, 95% CI 0.6-0.75, p < 0.001) had better OS, while NRT was not. Conclusions: NRT improved pCR and RD rates in GC without increase in surgical morbidity/mortality. The long-term OS benefit of NRT is likely secondary to higher pCR and RD resection.
CANCERS OF THE ESOPHAGUS AND STOMACH

79  Poster Session (Board #H9), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

The value of lymphadenectomy in esophageal cancer after neoadjuvant chemoradiation. First Author: Basem Azab, Sentara Healthcare, Hampton, VA

Background: There are conflicting reports on the value of the extent of post neoadjuvant chemoradiotherapy (NCRT) lymphadenectomy (LND) in locally advanced esophageal adenocarcinoma (E-ADC) and squamous cell carcinoma (E-SCC). We sought to study the impact of LND variables (positive and total lymph node (LN) number and LN ratio (LNR)) on oncological outcomes in these patients. Methods: The National Cancer Data Base 2004-2014 was queried for patients with NCRT followed by esophagectomy. The median examined LN number was used to divide the patients into a higher (> 12) and lower (<12) LND groups. The primary outcome was overall survival (OS) and secondary outcomes were 30- and 90-day postoperative mortality. Results: A total of 4708 patients were included. The median of positive, negative LN, and LNR were, respectively: (0, 11, 0%), and (12, 9, 1%). OS and 5-year OS for higher LND group were higher than the lower LND group (39 vs 32 months, 38% vs 34%), p < 0.0001. OS was not significantly different among E-SCC subset or among those who achieved pathological complete response (pCR). The higher LND group had better 30- and 90-day postoperative mortality rates (61 vs235 = 2.6, 141/2308 = 6.1%) than lower LND group (86/2262 = 3.8%, 184/2251 = 8.2%), p = 0.01 and 0.001, respectively. In multivariate Cox regression analysis, higher LND group (HR 0.88, 95% CI 0.81-0.96, p = 0.004) and LNR (per 10% increase: 1.11, 95% CI, 1.03-1.20, p = 0.029) were found to be independent predictors of poor survival. Conclusions: The LND (>12 examined LN) remains as a crucial treatment goal after NCRT with potential survival benefit, especially among E-ADC and those that did not achieve pCR.

80  Poster Session (Board #H10), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Randomized phase II/III study of 5-fluorouracil/leucovorin versus 5-fluorouracil/leucovorin plus paclitaxel in gastric cancer with severe peritoneal metastasis (JC061108/WJ007312G). First Author: Kensei Yamaguchi, The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan

Background: Oral fluoropyrimidine plus cisplatin is a standard treatment for advanced gastric cancer, but patients (pts) with severe peritoneal metastasis (PM) often cannot tolerate it. 5-fluorouracil (F), Leucovorin (L) and Paclitaxel (P) therapy (FLTXA) showed a promising activity in a feasibility study for such pts. We conducted a phase II/III (P/II) study comparing FLTXA vs FL. Methods: Eligibility criteria included: unresectable or recurrent gastric adenocarcinoma; 20-75 years; performance status (PS) 0-2; PM; massive ascites and/or inadequate oral intake; no prior chemotherapy. Pts were randomly assigned to receive FL (F 600 mg/m2, L 250 mg/m2; on day1, 8, 15, 22, 29 and 36 q4w), or FLTXA (F 500 mg/m2, L 250 mg/m2, P 60 mg/m2 on day8, 15 and 18 q4w). In the P-II, decision to proceed to the P-III was made based on the median survival time (MST) in both arms and treatment success rate at week 8 with the threshold of 30% in the FLTXA. Primary endpoint of the P-III was overall survival. Results: A total of 101 pts (51 in FL and 50 in FLTXA) were enrolled to the P-II, because of poor accrual, the protocol was amended for termination and the final analysis for the P-III was conducted. Treatment success rate at week 8 in FLTX was 66.7% (95% confidence interval (CI) 51.6-79.6). MST was 61.1 and 73.3 for FL and FLTXA, respectively (HR 0.79; 80% CI 0.60-1.05; p = 0.34). MST was 2.5 for FL and 5.1 for FLTX (HR 0.59; 95% CI 0.27-1.28) in pts with PS2 (n = 27); 6.5 and 8.6, respectively (HR 1.02; 95% CI 0.62-1.68) in pts with PS0/1 (n = 74). Median progression-free survival was 19.4 M for FL and 5.4 M for FLTXA (HR 0.64; 95% CI, 0.43-0.96; p = 0.029). Common adverse events of grade 3 were neutropenia (FL 30.0%, FLTXA 20.8%), and anorexia (FL 47.1%, FLTXA 31.3%). Conclusions: Although this study could not show a survival benefit of FLTXA over FL for pts with severe PM, FLTXA would be an option with longer PFS and feasible toxicity, especially for pts with PS2. Clinical trial information: UMIN000010949.

81  Poster Session (Board #H11), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM and Poster Walks, Thu, 5:45 PM-6:30 PM

A comparison of elderly versus nonelderly patients in the CRITICS gastric cancer trial. First Author: Astrid E Slager, Antoni van Leeuwenhoek/ Netherlands Cancer Institute, Amsterdam, Netherlands

Background: Although the proportion of elderly cancer patients (pts) increases, few randomized trials provide separate results on this group. Here, we present a sub-analysis of the CRITICS trial, comparing elderly with non-elderly pts. Methods: Preoperative (preop) chemotherapy (CT) included three cycles of epirubicin, cisplatin/oxaliplatin and capecitabine (ECCE/EOX); pts were upfront randomized between postoperative (postop) CT (3x ECCE/EOX) and chemoradiotherapy (CRT; 45Gy + cisplatin/capecitabine). Elderly pts were defined as age >70 years at the time of randomization. We present tolerability and outcomes for elderly versus non-elderly pts. Results: Details on baseline characteristics, preop treatment, surgery, postop treatment and survival are shown in Table 1. Tumor type and localization did not differ between both groups. Conclusions: Age had a significant impact on toxicity and tolerability of preop CT, but did not affect surgical resection rates and complications. Although less elderly pts started postop treatment and elderly pts received lower dose in de CT arm, there were no differences in treatment related toxicities. Survival was not significantly different. Clinical trial information: NCT00407186.

82  Poster Session (Board #H12), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Prognostic factor analysis in third-line chemotherapy for elderly patients with metastatic gastric cancer. First Author: Hiroko Hasegawa, Osaka National Hospital, Osaka, Japan

Background: Recently, the proportion of elderly patients (pts) with metastatic gastric cancer (mGC) has increased in Japan. Survival benefits of salvage treatment after second-line chemotherapy (CTX) for mGC were shown in several prospective studies. However, the role of salvage treatment in elderly pts remains controversial. Methods: We reviewed 185 pts with mGC who received palliative CTX aged ≥ 70 years at our institution between April 2007 and March 2018. Eligibility criteria were as follows: PS 0-2, refractory to first-line and second-line CTX. The purpose of this study was to evaluate the clinicopathologic factors that affected overall survival for elderly pts with mGC, univariate and multivariate analyses were performed on the baseline factors at the beginning of third-line CTX. Results: Of all, 71 pts were eligible. Median age was 75 years (71-85). Median progression-free survival (PFS) and overall survival (OS) for third-line CTX were 3.2 and 7.5 months, respectively and an overall response rate and disease control rate were 4.2% and 43.7%, respectively. In univariate analysis, the following four factors were identified to have prognostic significance: performance status (PS) (ECOG 0-1 or 2), serum albumin level (<3.5 or or 3.5 g/dl), serum LDH level (<240 or >240 IU/l), PFS under second-line CTX (<3 or >3 months). Multivariate analysis found three prognostic factors affecting poor survival following third-line CTX: PS of 2 (hazard ratio (HR) 8.89, 95% confidence interval (CI) 3.99-20.2; p = 0.001), serum LDH level >240 IU/l (HR 2.75, 95% CI 1.48-5.05; p = 0.002) and median PFS under second-line CTX <3 months (HR 1.80, 95% CI 1.01-3.43; p = 0.045). A prognostic index was constructed, dividing pts into low- (0 factor), intermediate- (1-2 risk factors), or high- (3 risk factors) risk groups. Median OS for each group were 12.6, 6.0 and 3.0 months, respectively (p = 0.045). A prognostic index was constructed, dividing pts into low- (0 factor), intermediate- (1-2 risk factors), or high- (3 risk factors) risk groups. Median OS for each group were 12.6, 6.0 and 3.0 months, respectively (p = 0.045). Conclusions: Although this analysis suggests that some clinicopathologic factors might be helpful in identifying the subgroup of elderly pts most likely to benefit from third-line CTX for metastatic gastric cancer.

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20
A retrospective analysis of third-line treatment in advanced gastric cancer. First Author: Yasunobu Ishizuka, Hirakata Municipal Hospital, Osaka, Japan

Background: As a result of ATTRACTION2, nivolumab was added to the third line treatment in advanced gastric cancer (AGC), but the response rate was about 10%. As there is no predictive biomarker and no comparison with cytotoxic regimen, it is difficult to choose the regimen. Therefore, we examined the treatment outcome of cytotoxic regimen in third line treatment in the real world retrospectively. Methods: We retrospectively evaluated efficacy and safety of cytotoxic regimen as third-line treatment in patients with AGC between July 2015 and December 2017. Results: Among 138 patients received chemotherapy as first line, 29 patients (21%) received third line therapy. The characteristics were as follows: the median age, 70 years old (range 34-80); male/female, 19 (66%)/10 (34%); performance status (PS) 0/1/2, 17/18/4. The overall response rate was 19% and the disease control rate was 38%. The median overall survival (OS) was 6.6 months and the progression free survival was 3.8 months. The most common grade 3/4 hematological toxicities were neutropenia (27%), followed by anemia (27%) and febrile neutropenia (13.7%). Grade 3/4 nonhematological toxicities included anorexia (27.6%), diarrhea (10%), nausea (10%). Conclusions: Cytotoxic regimen as third line showed acceptable activity, but only 21% of patients could received the third line chemotherapy. The further investigation of predictive biomarker of nivolumab is expected.

Impact of tumor growth rate during preceding treatment on tumor response to nivolumab or irinotecan in advanced gastric cancer. First Author: Kyoko Kato, Department of Clinical Oncology, Aichi Cancer Center Hospital, Nagoya, Japan

Background: Although nivolumab (NIVO) and irinotecan (IRI) are recognized as standard third-line and further treatments for patients (pts) with advanced gastric cancer (AGC), the drug that should be administered first remains unclear. Conversely, tumor growth rate (TGR) during preceding treatment was associated with tumor response to regorafenib or trifluridine/tipiracil in colorectal cancer. Methods: We retrospectively evaluated 212 pts with AGC treated with NIVO or IRI for the first time between January 2015 and June 2018 at three institutions. The main inclusion criteria were ECOG PS of 0-2, prior use of fluoropyrimidines and taxanes, and no prior use of NIVO or IRI. Pts were classified into slow (S) and rapid (R) growing groups according to TGR and presence or absence of new lesions (NL) during preceding treatment. TGR (Dn = CT1 - CT0, where CT1 is the date of CT at PD during preceding treatment, CT0 is the date of CT before CT1, and Dn is the sum of target lesion diameters at CT1, SG and RG were defined as NL – with low TGR and NL+ with high TGR or NL+, respectively). TGR cut-off value was defined as a median TGR of 0.30%/day. Results: A total of 117 pts (RG/SG, 72/45, NIVO/IRI, 32/85) were eligible. Almost all baseline characteristics were similar between the NIVO and IRI groups among the RG or SG, whereas the proportion of pts with peritoneum metastases was higher in the IRI group than in the NIVO group among the RG. The response rate (RR) was significantly higher with NIVO than with IRI (31% vs. 3%, odds ratio (OR): 13.8, p = 0.01) adjusted OR (aOR): 3.3, p = 0.002) among the SG, whereas it was comparable between both drugs (5% vs. 8%, OR: 0.68, p = 0.73; aOR: 0.94, p = 0.96) and RG. Pts with peritoneal metastases was highly in the IRI group among the RG, the RR was higher with NIVO than with IRI (31% vs. 3%, odds ratio (OR): 13.8, p = 0.01) among the SG, whereas it was shorter with NIVO than with IRI (mpfs 1.6 vs. 2.1 months, HR: 1.37, p = 0.28) in the RG. Conclusions: RR was higher with NIVO than with IRI among slow growing tumors, whereas it was comparable between both drugs among rapid growing tumors. TGR during preceding treatment might be helpful for drug selection in pts with AGC who are considered for treatment with NIVO or IRI.

Prognostic Nutritional Index as a predictive factor of survival in patients with gastric cancer in a Mexican population. First Author: Marytere Herrera, Instituto Nacional de Cancerología, Mexico City, Mexico

Background: Gastric cancer is a health problem that is gaining great relevance because despite the multidisciplinary treatment the clinical outcomes are not encouraging; with a diversified prognosis, considering that the results are not only influenced by tumor properties, but also by the patient's condition in an integral way, especially by the nutritional and immunological state. In this study we studied the prognostic nutritional index (PNI) as predictive value of survival in patients with gastric cancer. Methods: This is a observational study, 251 patients with diagnosis of gastric adenocarcinoma with locally advanced disease (confirmed by computed tomography (CT)) were analyzed from January 2010 to June 2016. Patients with locally advanced disease confirmed by laparoscopy were taken to radical surgery. Those patients who were taken to laparoscopy and who have been documented metastatic disease, were treated only in a palliative form (chemotherapy, radiotherapy, palliative care). Results: In the analysis of survival through the curves of Kaplan-Meier, and the log-rank, it was found that patients with a larger tumor size pathological (PT) 3/4/unclassifiable vs 1/2 had an average survival of 25.5 versus 55.5 months (p < 0.0001). With advanced pathological stages (EP) III/IV/non-classifiable vs. complete pathological response/I/II) reaching a survival average of 20.4 versus 59.1 months (p < 0.0001). In the multivariate analysis, it was found that the EP (Hazard ratio (HR): 1.54, confidence interval 95% [CI]: 1.32-1.810, p < 0.0001) and having received adjuvant chemotherapy (HR: 0.322, CI 95%: 0.217-0.508, p < 0.0001), were independently associated with the overall survival. Conclusions: This study demonstrates that low levels of PNI are associated with advanced diseases and, therefore, worse prognosis, with a tendency towards a decrease in overall survival.

Prospective evaluation of a developed S-1 dosage formula based on renal function. First Author: Takuro Mizukami, Department of Clinical Oncology, St. Marianna University School of Medicine, Kawasaki, Japan

Background: S-1 is an oral anticancer drug, containing tegafur (a prodrug of 5-FU), 5-chloro-2,4-dihydroxypyridine (CDHP, inhibitor of dihydoropyrimidine dehydrogenase) and potassium oxonate. Because CDHP is excreted in urine, impaired kidney function increases incidence of severe adverse drug reactions if the drug is not dosed based on renal function. AUC of 5-FU is increased with advancing renal impairment. Furthermore, in patients with AGC who are considered for treatment with NIVO or IRI. Pts with AGC who are considered for treatment with NIVO or IRI.

Methods: We retrospectively evaluated efficacy and safety of cytotoxic regimen as third-line treatment in patients with AGC between July 2015 and December 2017. Results: Among 138 patients received chemotherapy as first line, 29 patients (21%) received third line therapy. The characteristics were as follows: the median age, 70 years old (range 34-80); male/female, 19 (66%)/10 (34%); performance status (PS) 0/1/2, 17/18/4. The overall response rate was 19% and the disease control rate was 38%. The median overall survival (OS) was 6.6 months and the progression free survival was 3.8 months. The most common grade 3/4 hematological toxicities were neutropenia (27%), followed by anemia (27%) and febrile neutropenia (13.7%). Grade 3/4 nonhematological toxicities included anorexia (27.6%), diarrhea (10%), nausea (10%). Conclusions: Cytotoxic regimen as third line showed acceptable activity, but only 21% of patients could received the third line chemotherapy. The further investigation of predictive biomarker of nivolumab is expected.
Feasibility of endoscopic resection in early gastric cancer with lymphovascular invasion. First Author: Jun Haeng Lee, Samsung Medical Center, Seoul, Korea, Republic of (South)

Background: Lymphovascular invasion (LVI) is associated with the risk of lymph node metastasis (LNM) and poor survival in gastric cancer patients. However, it is unclear whether LVI is a noncurative criteria component in all patients. We evaluated the risk factors of LNM in LVI-positive early gastric cancer (EGC) patients and identified a subgroup with a negligible LNM risk to assess the feasibility of endoscopic resection in these patients. Methods: The clinicopathologic and survival data of patients undergoing surgery for gastric cancer were reviewed; LVI-positive EGC patients were selected. Logistic regression analysis was used to test the associations of potential risk factors with LNM; Kaplan-Meier analysis was used to compare survival curves. Results: LVI was detected in 1,243 (15.5%) patients. In the multivariate logistic analysis, larger tumor size (odds ratio [OR], 1.23; 95% confidence interval [CI], 1.16-1.31; P < 0.001), presence of ulcer (OR, 1.80; 95% CI, 1.15-2.82, P = 0.010), undifferentiated histology (OR, 1.64; 95% CI, 1.25-2.16; P < 0.001), submucosal invasion (OR, 2.28, 95% CI, 1.38-3.76, P = 0.001), middle (OR, 2.12; 95% CI, 1.26-3.55, P = 0.004) or lower third location (OR, 2.28; 95% CI, 1.32-3.60, P = 0.002), and younger age (OR, 0.98; 95% CI, 0.97-0.99; P = 0.002) independently predicted LNM in LVI-positive EGC patients. LVI-positive patients fulfilling the absolute endoscopic resection criteria did not have LNM, and there was no significant difference in the overall (P = 0.928) and disease-specific survival (P = 0.821) between these patients and those with LVI-negative EGC. Conclusions: Additional surgery after endoscopic resection might be unnecessary in LVI-positive patients meeting the absolute criteria for endoscopic resection.

Nutrition and exercise patterns in survivors of esophageal and gastroesophageal junction (EGEJ) cancers. First Author: Rishi Jain, Fox Chase Cancer Center, Philadelphia, PA

Background: While obesity is a risk factor for EGEJ, malnutrition is common at diagnosis (dx) and can be exacerbated by neoadjuvant therapy (NAT) and esophagectomy. Little is known regarding nutrition and exercise patterns of EGEJ cancer survivors. Methods: A survey of EGEJ survivors: > 12 months from esophagectomy was conducted. Pts were identified using institutional tumor registry. The Dillman mailed survey method was used. Questionnaires regarding health behaviors were employed: Godin Leisure-Time Exercise (GLTQ), Cancer Appetite and Symptom (CASQ), Nutritional Self-Efficacy (NSEQ). Chart review included demographics, pt characteristics and therapy received. Spearman correlation, Wilcoxon and Fisher's tests assessed relationships between groups or variables. Results: Forty one of 140 eligible pts (29%) returned questionnaires and had surgery between 1991-2004. Median age was 69 and 78% were male. Most (83%) had adenocarcinoma. On presentation, 73% had clinical stage II or III disease and 76% received NAT. Median time from dx was 5 years (range 2-25). Mean weight loss from dx to current was 38 lbs. Mean BMI (kg/m²) was 29.52 at dx and 24.15 at most recent clinic visit. Obesity was present in 37% of pts at dx, but only 7% of survivors. Mean health behavior scores (SD): GLTQ 22.10 (22.93), CASQ 31.74 (6.66), and NSEQ 11.39 (4.03). Age, marital status, gender, education, and income were not associated with GLTQ, CASQ or NSEQ. Sedentary lifestyle (SL) with GLTQ score < 14 was present in 46% of survivors and associated with overweight BMI (mean 26.7 for SL vs 23.7 for non-SL; P = 0.04). There was a significant positive correlation between current BMI and NSEQ score (r = 0.68; P = 0.003). Conclusions: Many EGEJ cancer pts present with obesity but subsequently lose weight after curative therapy. The mean CASQ score in our population is similar to other GI cancer populations, suggesting that residual symptoms persist years after treatment ends. There is a high prevalence of SL in survivors which is associated with being overweight. Higher levels of nutrition self-efficacy were also associated with a higher current BMI. Future studies should define strategies to optimize nutrition and exercise habits in EGEJ cancer survivors.
Phase I results from the phase 1/3 FIGHT study evaluating bemarituzumab and mFOLFOX6 in advanced gastric/GEJ cancer (GC). First Author: MohamedAldi Abdulaziz Tejani, University of Rochester Medical Center, Rochester, NY

Background: GC with FGFR2b overexpression or FGFR2b amplification is associated with a poor prognosis. Bemarituzumab (bema, FPA144) is a first-in-class humanized monoclonal IgG antibody that selectively blocks FGFR2b and triggers antibody-dependent cell-mediated cytoxicity. With favorable safety and activity as a single agent in 2L+ patients with FGFR2b+ GC, the global, randomized, double-blind, placebo-controlled FIGHT study (NCT03433449) is evaluating the front-line combination of bema with mFOLFOX6. We report here the results from the phase I evaluation of the combination. Methods: Patients (pts) with unresectable, locally advanced or metastatic gastroesophageal malignancy (irrespective of FGFR2b status) for whom mFOLFOX6 would be appropriate were eligible for the phase I. The main dose was bema 6 mg/kg and cohort 2 (Rolling-6) bema 15 mg/kg with one dose of 7.5 mg/kg on day 18. A dose-limiting toxicity was defined as any grade 3 toxicity except for the normal hematological toxicity window of 28 days was used for both cohorts. Results: Cohorts 1 and 2 treated 3 pts and 9 pts respectively with a median of 4 and 2 prior lines of therapy. As of the iDMC data-cut on July 24, 2018, the median duration of treatment was 15 wks, cohort 1 and 6 wks for cohort 2. 6/9 pts in cohort 2 continued on treatment. No DLTs were identified. No adverse events (AEs) led to treatment discontinuation. There were no newly identified bema-related toxicities and the only $\geq$ Gr 2 AE attributable to bema in cohort 2 was fatigue (1 pt/Gr 2). The most common AE overall were fatigue (65%/56%/nausea, vomiting and diarrhea (23%/23%/42%) each) and were generally attributed to FOLFOX or underlying disease. The $\geq$ Gr 3 AE present in $\geq$ 1 pt were fatigue and neutropenia (2 pts/Gr 3 each). mFOLFOX6 did not affect bema exposure and all evaluable pts in cohort 2 achieved the target $\geq$ 60 mg/mL trough concentration by day 15. 2/7 pts at the data-cut had FGFR-related GC. Conclusions: Bema in combination with mFOLFOX6 has acceptable safety to proceed with the cohort 2 dose to the phase III portion of the FIGHT trial in previously untreated patients with FGFR2b+ GC. Clinical trial information: NCT034334301.

Primary results of a randomized two-by-two factorial phase II trial comparing neoadjuvant chemotherapy with two and four courses of cisplatin/S-1 (CS) and docetaxel/cisplatin/S-1 (DCS) as neoadjuvant chemotherapy for locally advanced gastric cancer. First Author: Takaki Yoshihashi, The National Cancer Center Hospital, Tokyo, Japan

Background: Neoadjuvant chemotherapy is promising to improve the survival of resectable gastric cancer. Cisplatin/S-1 (CS) and docetaxel/cisplatin/S-1 (DCS) are both active for metastatic gastric cancer. Methods: We conducted a randomized phase II trial to compare two and four courses of neoadjuvant S-1/cisplatin (SC) and docetaxel/cisplatin/S-1 (SCS) using a two-by-two factorial design for locally resectable advanced gastric cancer. Patients with MO and either T3 or T4 were randomized to either 2 courses or 4 courses of neoadjuvant S-1/cisplatin (SC) and docetaxel/cisplatin/S-1 (SCS) using a two-by-two factorial design for locally resectable advanced gastric cancer. Patient with MO and either T3 or T4 were randomized to either 2 courses or 4 courses of cisplatin (60 mg/m$^2$ at day 8)/S-1 (80 mg/m$^2$ for 21 days with 1 week rest) or docetaxel (40 mg/m$^2$ at day 1)/cisplatin (60 mg/m$^2$ at day 1)/S-1 (80 mg/m$^2$ for 14 days with 2 weeks rest) as neoadjuvant chemotherapy. Then, patients underwent D2 gastrectomy and adjuvant chemotherapy for 1 year. The primary endpoint was 3-year overall survival. The planned sample size was 120 eligible patients in total so that the treatment group with the superior observed 3-year OS rate by more than 20% of the control group to be selected with a probability of 85% or higher. Results: Between October 2011 and September 2014, 132 patients were assigned to CS (n = 66, 33 in 2 courses and 33 in 4-courses) and DCS (n = 66, 33 in 2-courses and 33 in 4-courses). The 3-year OS was 58.1% (95% CI, 46.8-70.3%) in CS and 60.0% (95% CI, 48.7-71.9%) in DCS with a hazard ratio of 0.796 (95% CI, 0.475-1.335), while that was 53.1% (95% CI, 40.9-64.5%) in the two courses and 65.0% (95% CI, 53.2-76.8%) in the four courses with hazard ratio of 0.722 (95% CI, 0.429-1.216). In the survival analysis by duration in each regimen, the 3-year OS was 58.1% (95% CI, 45.8-70.3%) both for two and four courses in CS, while that was 48.5% (95% CI, 31.4-65.5%) for two courses of DCS and was 71.9% (95% CI, 56.3-87.5%) for four courses of DCS. Conclusions: Considering high 3-year OS, four courses DCS might be advantageous in a future phase III trial to confirm superiority of neoadjuvant chemotherapy for locally advanced gastric cancer. Clinical trial information: UMIN000006378.
Locally advanced gastric cancer (LAGC): Does histology suggest strategy in PAN-cancer Era?

First Author: Ina Valeria Zuriel, Fondazione Policlinico Universitario A. Gemelli - IRCCS - UOC Oncologia Medica, Roma, Italy

Background: Surgery is the only potentially curative treatment for LAGC. Evidences suggest that perioperative CT (pCT) plus surgery is superior to surgery alone, whereas studies on adjuvant CT (aCT) are controversial. Despite the arising of recent molecular classification, still far from modifying clinical practice, histology may predict a different benefit from CT administered in the two histology on the outcome of these different approaches. We hypothesized that diffuse LAGC. No trial has compared pCT and aCT or investigated the impact of fluences both survival and pathological response with worse prognosis among real-life many pts receive immediate surgery followed by aCT. Histology in- Guidelimes recommend a pCT approach in pts with stage II/III, nevertheless in surgery alone, whereas studies on adjuvant CT (aCT) are controversial. Evidences suggest that perioperative CT (pCT) plus surgery is superior to surgery alone, whereas studies on adjuvant CT (aCT) are controversial.

Methods: Eligible pts were advanced ESCC who had progressed after platinum or taxane containing chemotherapy. Between January 5, 2016 and May 22, 2018, a total of 165 pts from 13 centers in China were randomly assigned (in a 2:1 ratio) to anotinib arm (n=110), and placebo arm (n=55). Pts were given anotinib (12 mg/day) or placebo orally from day 1 to day 14 in a 2:1-day cycle until disease progression or had unacceptable toxic effects. The primary end point was progression-free survival (PFS). Results: Median PFS was 3.0 months with anotinib and 1.4 months with placebo (HR 0.5, 95% CI, 0.3-0.7, P<0.0001). Complete response was observed in 2 pts with anotinib and 0 pt with placebo. The objective response rates were 7% in the anotinib group and 4% in the placebo group (P=0.498), and the disease control rates (DCR) were 64% and 18%, respectively (P<0.0001). In anotinib arm, median duration of response was 5.8 months (range, 3.1-19.7+). Grade 3/4 treatment-related adverse events (TRAES) were reported in 36.7% and 11.0% of the two groups, and grade 5 TRAE were 2.8% and 0%, respectively. The most common grade 3/4 TRAE (>5%) in anotinib arm were hypertension (15.6%) and loss of appetite (5.5%). Median duration of survival were similar between the groups (6.1 months vs 7.2 months; HR 1.2, 95%CI(0.8-1.8, P=0.42). The ratio of pts received post study treatment studies was 41.2% (40/97) in anotinib arm and 72.7% (40/55) in placebo arm (P=0.0022), including chemotherapy (23.7% vs 54.6%), PD-1 inhibitors (4.3% vs 11.0%), and Apatinib, a VEGFR inhibitor (10.2% vs 20.0%), etc. Findings: In pretreated advanced ESCC pts, anotinib significantly improved PFS and DCR compared with placebo, with a manageable safety profile. Clinical trial information: NCT02649361.

Conclusions: This phase II study was designed to explore the antitumor activity of anotinib, a VEGFR inhibitor, in patients with ESCC who had progressed after first-line chemotherapy. The results showed that anotinib had a significant antitumor effect, with a median PFS of 3.0 months and a 7% objective response rate. The study also demonstrated a manageable safety profile, with a lower incidence of grade 5 treatment-related adverse events in the anotinib group compared with the placebo group. These findings support the further exploration of anotinib in ESCC.
Survival outcomes comparable between endoscopic resection and surgical resection for T1b esophageal adenocarcinoma. First Author: Samit Kumar Datta, Aurora Health Care, Milwaukee, WI

Background: Current guidelines recommend esophagectomy for submucosal T1b esophageal cancer. Data regarding efficacy of endoscopic resection (ER) of T1b esophageal cancer are limited. Our goal was to compare survival outcomes of ER as opposed to conventional surgical resection (SR) in a large cohort of patients with T1b cancers from a large national database.

Methods: Data were obtained from the large national database maintained by the Commission on Cancer. Patients with T1b esophageal cancers with clinical stage IA and IB who underwent ER and SR between 2010 and 2014 were identified using the American Joint Committee on Cancer (AJCC Version 7). Patients undergoing ER and SR were identified. Patients who underwent neoadjuvant therapy or had incomplete survival data were excluded. The primary outcome was survival for age and Deyo-Charlson comorbidity index. We also evaluated 30-Day and 90-Day Mortality outcomes. Results: There were 1071 patients with T1b esophageal cancer with complete mortality data. After selecting and excluding patients above, 141 patients were identified who underwent ERT and 286 who underwent esophagectomy. Average age was 71.5 years in the ER group and 64.5 years in the SR group (p < 0.001). In the group, 30-Day mortality after surgery was 1/33 (0.8%, 7 missing) compared to surgery with 30-Day mortality of 6/283 (2.3%, 3 missing) (P = 0.308). 90-Day mortality after surgery for the ER group was 3/33 (2.2%, 7 missing) compared to surgery with 90-Day mortality of 11/281 (3.9%, 5 missing) (P = 0.377). Adjusted for age and Deyo-Charlson comorbidity index, there was a HR of 1.051 (95% CI 0.695-1.589, p = 0.815) for mortality associated with surgery compared with ER. Mean follow-up of 42.6 months for the ER group and 55.7 months for surgery group. Conclusions: Based on the data from a large national cancer data base ER seems to be comparable to SR in terms of short-term (30 day and 90 day) mortality. Overall survival seems to be similar in both groups. Prospective done randomized studies comparing ER vs SR are desirable.

Real-world treatment patterns and clinical outcomes in patients receiving second-line (2L) treatment for advanced or metastatic gastric cancer (GC). First Author: Mayur Amonkar, Merck & Co., Inc., North Wales, PA

Background: Despite increased survival demonstrated for patients with advanced / metastatic GC due to 2L chemotherapy, different standard of care options exist. This study aims to describe RW treatment patterns and clinical outcomes in patients with advanced / metastatic GC receiving 2L treatment.

Methods: Retrospective chart review study conducted in Australia, Canada, Italy and UK. Patients diagnosed with metastatic / unsectable GC receiving 2L treatment between January 2013 and July 2015 were enrolled. Patient chart data (30 day and 90 day) mortality, Overall survival and complications were assessed.

Results: 280 patients were included (mean age 60.9 years, 68.9% male). Half of the patients (51.8%) received chemotherapy monotherapy in 2L. Among these, taxanes were most prescribed (69.0%) followed by irinotecan (22.1%). Doublet chemotherapy was the most common combination therapy in 2L (75.6%) with fluoropyrimidine + irinotecan (33.3%) being the most used, followed by fluoropyrimidine + platinum (17.8%). Less than a third of patients (29.3%) received subsequent third-line (3L) treatment; 62.7% received monotherapy (mainly taxanes (69.2%) or irinotecan (19.2%)). Most 3L patients who had combination therapy received a doublet (86.7%), most frequently fluoropyrimidine combined with irinotecan (53.3%) or platinum (20.0%). The majority of 2L patients (93.6%) had received combination therapy as first-line treatment, of whom 67.9% had received triplet chemotherapy, most commonly anthracycline + fluoropyrimidine + platinum (51.1%). Estimated median real-world progression free survival (PFS) and overall survival (OS) after 2L treatment initiation was 3.09 (95% CI: 2.76-3.68) and 6.54 (5.29-7.76) months, respectively, and estimated probability of overall survival (OS) and progression-free survival (PFS) at 12 months was 8% and 26%, respectively. Conclusions: The clinical management of advanced / metastatic GC patients in 2L treatment commonly involves taxanes or irinotecan as monotherapy, or irinotecan or platinum-based combinations with fluoropyrimidines. RW clinical outcomes for 2L treatment are similar to randomised controlled trials but remain poor.
105 Poster Session (Board #J15), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Comparison of real-world treatment patterns, persistence, healthcare resource utilization (HRU) and costs between octreotide and lanreotide for the treatment of neuroendocrine tumors (NET). First Author: Lynn Huynh, Analysis Group, Inc., Boston, MA

Background: There has been limited research assessing differences between somatostatin analogues (SSAs) as treatments for NET for the treatment pattern study aims to: assess treatment patterns, persistence, HRUs and costs among patients (pts) with NET receiving long-acting octreotide versus lanreotide.

Methods: Retrospective claims data from Symphony Health Solutions were analyzed for NET pts who initiated octreotide or lanreotide (index date) between 01/2015-11/2017 for ≥ 90 days. Pts with continuous clinical utilization of NET related HRUs and costs (provider charges for medical services and insurance payments for prescription drugs) using rate ratio (RR) and mean cost difference (CD) with 95% confidence interval (CI). Results: Among 2,043 NET pts identified, a balanced matched cohort of octreotide and lanreotide pts (N = 543 each) was achieved. In both cohorts, mean age was 65 years and baseline Charlson Comorbidity Index was 5.7. Approximately 80% of matched pts initiated monotherapy; others used SSAs in combination with chemo-, targeted or liver-directed therapy as first line therapy. Treatment patterns significantly differed between the two SSA cohorts: octreotide was more frequently used than lanreotide for the treatment of NET. Costs were also significantly higher in the octreotide cohort (NET related = 0.94 [0.86, 1.04]; all cause = 0.92 [0.84, 1.00]). Statistically significantly fewer NET related outpatient visits were observed among octreotide pts (RR [CI]: 0.87 [0.73, 1.02]). Octreotide pts also had lower proportions of related medical events and costs, including hospitalizations, emergency room visits, and ED visits.

Conclusions: This study demonstrated significant differences in treatment patterns and persistence between SSA cohorts. OCTreoTIDE appeared to be associated with less HRU and total costs compared with lanreotide.

106 Poster Session (Board #J16), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Efficacy of three-drug induction chemotherapy followed by preoperative chemoradiation in patients with localized gastric adenocarcinoma (GAC). First Author: Dilsa Mizrak Kaya, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Preoperative induction chemotherapy followed by chemoradiation yields better R0 resection rates, pathologic complete response (pCR) rates and improved survival for localized GAC. Previous studies with two-drug induction chemotherapy showed 70-90% R0 resection rates and 20-36% pCR rates. We report the effect of three-drug induction chemotherapy on a cohort of localized GAC patients. Methods: We identified 97 patients with localized GAC who received three-drug induction chemotherapy followed by preoperative chemoradiation therapy. We assessed various endpoints (overall survival [OS], recurrence-free survival [RFS], R0 resection and pCR rate). Results: The median follow-up time was 3.5 years (range; 0.4-16.7). Most of the patients were men (60.8%) and the median age was 60 years (range; 21-89). The induction chemotherapy regimen was a fluoropyrimidine and a platinum compound (cisplatin or oxaliplatin) with a taxane (docetaxel or paclitaxel) for 95% of patients. Seventy-three (75%) out of 97 patients underwent planned surgery. R0 resection and pCR rate were 93% and 21%, respectively. Pathologic partial response (<50% residual carcinoma) was 50.7%. The median OS was 6.43 years (95% CI 3.27-12.36) for the entire cohort and 11.1 years (95% CI 7.7-estimable) for patients that underwent surgery. The estimated 2- and 3-year OS rates were 72% (95% CI 62-80) and 54% (95% CI 43-64) for the entire cohort and 83% (95% CI 79-97) and 66% (95% CI 53-76) for patients who underwent surgery. Pathological lesser stage (stage I/II vs. stage III/IV) (p = 0.001) and R0 resection (p = 0.019) were independently associated with longer RFS in the multivariable analysis.

Conclusions: Our data show that three-drug induction chemotherapy is an effective therapy for providing substantial advantage in this setting of preoperative induction chemotherapy followed by chemoradiation and surgery.
Anatomical topography of the tumor is related to prognostic survival in adenocarcinoma of esophagogastric junction?: Multivariable analysis. First Author: Flavio Roberto Takeda, Instituto do Cancer do Estado de São Paulo, São Paulo, Brazil

Background: The adenocarcinoma of the esophagogastric junction (AJEG) is divided according to its anatomicopathological classification (Swietert classification) for the choice of surgical treatment. However, both the Swietert classification and the location of the AJEG are related to different prognoses reported in the literature. Objectives: To compare the survival of patients with AJEG admitted to Surgery according to different topographies in the esophagogastric junction. Methods: 147 patients were selected between 2000 and 2016. One hundred and thirty (88%) males, mean age 64 years. Analyzing the retrieved lymph nodes, affected and the relation of resected and affected. AJEG (E: esophagus, E/TEG: esophageal gastric and stomach transition, and E/TEG/G: esophagus, transition and stomach) were analyzed for global survival, free of disease, and after relapse. Results: In relation to epidemiological data, the mean age was 63.1 years. Of the 147 patients 90 (61.2%) were submitted to neoadjuvant treatment. There was no statistical difference between the groups regarding histological grade, pT, pN, tumor extension, lymphatic, venous and perineural invasion. The mean extension of the tumor was 5.4 cm. The mean number of retrieved lymphnodes were 32. Overall survival was E: 90%, E/TEG: 85%, E/TEG/G: 74%, TEG: 52%, TEG/G: 59% and E/TEG/G: 21%. (p <0.0001). Disease free of survival was E: 78%, E/TEG: 48%, TEG: 43%, TEG/G: 38% and E/TEG/G: 15%. (p <0.001). Conclusions: The survival of the AJEG varies according to the topography of the lesion, the tumors located closer to the stomach present worse survival than those located in the esophagus, except when the tumor is very extensive, from the esophagus to the stomach.

Subgroup analysis of JC0G0501 phase III study to confirm superiority of additional neoadjuvant chemotherapy with S-1 plus cisplatin to D2 gastrectomy with S-1 adjuvant chemotherapy for resectable type IV or large type III gastric cancer. First Author: Hitoshi Katai, National Cancer Center Hospital, Tokyo, Japan

Background: We previously reported that the superiority of neoadjuvant chemotherapy (NAC) with S-1 plus cisplatin was not demonstrated for scarhrous or similar macroscopic type (type 4 or large type 3) gastric cancer. However, overall survival (OS) in both arms was better than previous reports (3-year OS: 62.4% in gastrectomy plus adjuvant S-1 [arm A] and 60.9% in NAC followed by gastrectomy plus adjuvant S-1 [arm B]). Therefore, we explored whether histology and peritoneal cytology are associated with treatment effect. Methods: After staging laparoscopy, a total of 300 eligible patients with clinically resectable disease were randomized to arm A or arm B. In this report, treatment effect was explored in key subgroups such as histology and peritoneal cytology using the data from JC0G0501. Cox regression model was used to investigate the interaction between arms and subgroups. Results: Hazard ratio (HR) classified by histology (excluding one missing) was 0.868 (95% CI: 0.541-1.418) for non-signet type (n = 123) and 1.588 (95% CI: 0.805-1.666) for signet type (n = 176) (p = 0.098 for interaction). HR by peritoneal cytology was 0.870 (95% CI: 0.636-1.228) for the negative (n = 240) and 1.051 (95% CI: 0.598-1.845) for the positive (n = 60) (p = 0.513 for interaction). 3-year OS of signet ring cell histology was 63.2% (95% CI: 52.2-72.4) in arm A and 57.1% (95% CI: 40.9-63.5) in arm B, that of non-signet ring cell histology was 62.3% (95% CI: 48.9-71) in arm A and 74.2% (95% CI: 61.4-83.3) in arm B, and that of peritoneal cytology positive was 35.7% (95% CI: 18.9-53) in arm A and 25.0% in arm B (95% CI: 18.8-40.7), and that of peritoneal cytology negative was 68.6% (95% CI: 59.5-76.1) in arm A and 70.6% (95% CI: 61.5-77.9) in arm B. Conclusions: NAC might be beneficial for non-signet ring cell histology. Considering the survival results, primary surgery followed by S-1 could be recommended for this disease even though histology was signet ring cell type or peritoneal cytology was positive. Clinical trial information: UMIN00000279.

Endoscopic submucosal dissection versus surgery for undifferentiated-type early gastric cancer: A meta-analysis. First Author: Byung-Wook Kim, Catholic University of Korea, Incheon St. Mary's Hospital, Incheon, Korea, Republic of (South)

Background: It is still controversial to treat undifferentiated early gastric cancer by endoscopic submucosal dissection (ESD). Therefore, we aimed to perform a meta-analysis to investigate long-term outcomes of ESD and surgery for undifferentiated early gastric cancer. Methods: MEDLINE, PubMed, Cochrane Library, and EMBASE were used to search for relevant researches comparing endoscopic submucosal dissection and surgery for undifferentiated early gastric cancer. The methodological quality of the included publications was evaluated using the Risk of Bias Assessment tool for Non-randomized Studies. The overall survival rate, recurrence rate, adverse event rate, and complete resection rate were explored, and the odds ratio (OR) and 95% confidence interval (CI) were estimated. Results: This meta-analysis enrolled five studies, OS was 176 and 148 participants undergoing ESD and surgery, respectively. Overall survival rate did not show significant difference between ESD and surgery group (OR 0.57, 95% CI 0.18 – 1.83, P = 0.34). However, ESD was associated with higher recurrence rate (OR 11.57, 95% CI 5.07 – 26.39, P < 0.001) and lower complete resection rate (OR 0.69, 95% CI 0.51 – 0.99, P < 0.001). Adverse event rate was similar between two groups (OR 0.95, 95% CI 0.46 – 1.96, P = 0.88). Conclusions: Despite higher recurrence rate and lower complete resection rate, ESD demonstrated similar overall survival rate and adverse event rate in the treatment of undifferentiated early gastric cancer compared to surgery.

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The efficacy of splenic hilar lymph node dissection in advanced gastric cancer. First Author: Tetsuro Toriumi, Division of Gastric Surgery, Shizuoka Cancer Center, Shizuoka, Japan

Background: Total gastrectomy with splenectomy for splenic hilar lymph node (No.10LN) dissection has been a standard treatment for proximal advanced gastric cancer in Japan. The efficacy of No.10LN dissection with splenectomy for advanced gastric cancer without the greater curvature invasion was denied by a randomized controlled trial, JCOG0110. However, JCOG010 did not include the patients with greater curvature invasion. Therefore, we aimed to clarify the role of No.10LN dissection in patients with proximal advanced gastric cancer invading the greater curvature. Methods: A total of 273 patients with proximal advanced gastric cancer who underwent curative total gastrectomy with splenectomy from 2002 to 2013 were included. We reviewed esophagogastroduodenoscopy and upper gastrointestinal series for evaluation of clinical tumor localization and classified the patients into with greater curvature invasion group (G group, n = 108) or without invasion group (NG group, n = 165). The incidence and therapeutic value index (TVI) of No.10 LN were compared between the groups.

Results: Patients in the G group had more advanced T stage, undifferentiated histology, and larger tumor size than those in the NG group. However, there was no difference in survival between the groups; 5-year overall survival (OS) was 66.3% in the G group and 69.1% in the NG group (p = 0.570). The incidence of No.10 LN metastasis was significantly higher in the G group (10.2%) than that in the NG group (3.0%) (p = 0.028). TVI for No.10 LN dissection was higher in the G group (5.6%) than that in the NG group (0.6). The survival of the patients with No.10 LN metastasis tended to be better in the G group, although it did not reach statistical significance (5-OS: 54.5% in G group, although it did not reach statistical significance (5-OS: 54.5% in G, 52.9% in NG, p = 0.53). Conclusions: It is suggested that splenic hilar LN dissection has a favorable effect on survival in patients with proximal gastric cancer invading the greater curvature.

Endoscopic submucosal dissection using a novel endoscopic articulating knife for clinical staging of early esophageal neoplasia. First Author: Juan Genere, Mayo Clinic Rochester, Rochester, MN

Background: Clinical staging of early esophageal neoplasia traditionally involves histological confirmation and imaging with endoscopic ultrasound (EUS), CT, and PET which have low sensitivity and specificity for staging esophageal cancer (EC). Endoscopic submucosal dissection (ESD) therapy is traditionally used for treatment, but not diagnosis as it is felt to be technically challenging and have a high risk for complications. We applied a new articulating endoscopic knife that permits safe ESD (ESD-CC) to evaluate early neoplasia with potential curative resection. Methods: We performed a retrospective study of patients undergoing ESD to stage or treat suspected early EC (cT1-T2). Clinical stage was done by EUS, CT, and PET. Two expert GI pathologists reviewed all histology. Lesions were examined with high resolution white light endoscopy and narrow band imaging. ESD was done with 1:200,000 epinephrine and methylene blue dye injection for lifting and staining the submucosal space. A 5mm, scissors-like articulated knife was used to perform ESD and hemostasis. Complications during post-ESD observation or follow-up were recorded. Results: A total of 35 patients who underwent ESD-CC were included with median age 70 (IQR 12), 26 males (74%), and followed for a median 3.4 months (IQR 6.4). This group consisted of 32 potential adenocarcinomas and 3 squamous cell cancers. The clinical Pre-ESD diagnoses were cT1c (24, 69%), and suspected EC in Barrett’s esophagus (BE) (11, 31%). The cT1c EC cases had ESD staged at least T1b (5, 29%), T1a (11, 46%), and EC in situ (1, 4%), and dysplastic BE (7, 29%). The suspected EC cases had ESD staged at least T1b (1, 4%), T1a (2, 18%), and DBE (8, 73%). ESD-CC up staged 4 (11%), down-staged 10 (29%), and confirmed prior diagnosis in 21 (60%). No complications including bleeding, perforation, or stricture formation regardless of size of ESD, age of patient, or co-morbidities. Conclusions: Staging of early esophageal cancer can be improved using ESD with an articulating knife, without increase in complications. ESD may be used as a staging modality in early esophageal cancer.

Trastuzumab beyond progression in patients with HER2-positive advanced gastric adenocarcinoma: A retrospective real world study. First Author: Yang Chen, Chinese People’s Liberation Army General Hospital, Beijing, China

Background: Although the clinical trial WJOG112G was failed to prove weekly paclitaxel with trastuzumab in patients with HER2-positive gastric or gastro-esophageal junction (GEJ) cancer refractory to trastuzumab, it is believed that if paclitaxel alone, there are limited data concerning efficacy of continuing trastuzumab beyond first-line progression in the real world. Methods: This retrospective study included all consecutive patients with HER2-positive advanced gastric or GEJ adenocarcinoma who received chemotherapy with trastuzumab in first-line, or second-line, or third-line treatment between 2010 and 2016 in Chinese People’s Liberation Army General Hospital. Progression-free survival (PFS) and overall survival (OS) were estimated from the initial chemotherapy. Results: A total of 67 patients (median age, 59 years; male, 71.6%) with HER2-positive advanced gastric or GEJ adenocarcinoma treated with chemotherapy plus trastuzumab initially in first (n = 50), second (n = 13), or third (n = 4) line of therapy were included. The median OS of trastuzumab for first-line, second-line, or third-line treatment was 16.7 months, 14.2 months, and 13.2 months, respectively (p = 0.83). In patients initially using trastuzumab in first-line therapy, the continuation (n = 19) versus discontinuation (n = 31) of trastuzumab beyond first-line progression was significantly associated with an improvement of median PFS (3.4 versus 1.9 months; P = 0.02), but not OS (HR 19, 16.4 months; P = 0.13). In the multivariate analysis including the ECOG PS, number of metastatic sites and chemotherapy regimen, the continuation of trastuzumab beyond progression remained significant associated with longer PFS (HR 0.77; 95% CI, 0.41–0.93; P = 0.04), but not OS (HR, 0.85; 95% CI, 0.56–1.22; P = 0.24). Conclusions: This study suggests that HER2-positive advanced gastric or GEJ adenocarcinoma patients could benefit from trastuzumab no matter when they start receiving trastuzumab. The continuation of trastuzumab beyond progression has clinical benefit in patients with HER2-positive advanced gastric cancer for PFS, but not for OS. Large scale prospective randomized validation is warranted.

A retrospective analysis of neoadjuvant chemotherapy followed by surgery or definitive chemoradiotherapy in patients with advanced esophageal squamous cell carcinoma. First Author: Hiroshi Nakatsumi, Department of Cancer Chemotherapy, Hokkaido University Hospital Cancer Center, Sapporo, Japan

Background: The standard treatment of resectable esophageal cancer in Japan is neoadjuvant chemotherapy (NAC) followed by surgery, while definitive chemoradiotherapy (CRT) is considered as an alternative treatment. There are no randomized clinical trials comparing NAC and CRT in Japan. The aim of this study was to evaluate the efficacy of NAC or CRT in clinical practice. Methods: We retrospectively analyzed the clinical data of 43 patients (pts) with clinical stage IB/II/III thoracic esophageal squamous cell carcinoma (ESCC) who received NAC (n = 26) or CRT (n = 17) in Hokkaido University Hospital from January 2009 to December 2014. To compare NAC with CRT, Fisher’s exact test or Mann-Whitney U test was used in terms of pts’ characteristics, and Log-rank test was used in progression-free survival (PFS) and overall survival (OS). Results: Pts’ characteristics were as follows; Gender (male/female): 24/2 in NAC and 16/1 in CRT, median age (range): 65y (57-78) in NAC and 72y (57-80) in CRT, primary lesion (UL/M/L): 4/1/0 in NAC and 2/9/6 in CRT, clinical stage IB/II/III: 11/5 in NAC and 9/8 in CRT, Four pts (15.4%) in NAC and seven pts (41.2%) in CRT had multiple primary cancer. All pts in NAC and 15 pts in CRT received 5-FU+ cisplatin (CDDP), and two pts in CRT received 5-FU+ nedaplatin. RT dose in CRT was 50.4Gy in 11 pts, 59.4Gy in five pts, 60Gy in one patient. Four out of 10 pts in NAC with local recurrence received salvage surgery, and three out of 10 pts in CRT with local recurrence received salvage surgery. Median PFS was 21.6 months in NAC and 8.7 months in CRT (HR 1.282, 95% confidence interval (CI) 0.871-1.887, p = 0.203), and median OS was 50.4 months in NAC and 48.6 months in CRT (HR 1.151, 95% CI, 0.752-1.761, p = 0.516). 5-year OS rate was 49.7% in NAC and 48.3% in CRT. Conclusions: Definitive CRT showed comparable outcome to NAC followed by surgery in pts with resectable thoracic ESCC. Efficacy of NAC or CRT were not sufficient compared to clinical trials. Improvement in efficacy by development of optimal multimodality therapy was warranted.
A phase I/II study of crenolanib with ramucirumab (RAM)/paclitaxel (PTX) as second-line therapy (2L tx) for advanced esophageal adenocarcinoma (EAGA). First Author: Megan Greally, Memorial Sloan Kettering Cancer Center, New York, NY

**Background:** PTX/RAM as 2L tx for patients (pts) with EGA is a standard-of-care based on the RAINBOW trial (Lancet 2014;384:1224). Secondary benefit is modest. Upregulation of the platelet-derived growth factor (PDGF)-PDGF receptor-β (PDGFR-β) pathway causes resistance to VEGF inhibition. Crenolanib is a selective inhibitor of PDGFR-β. We report initial results of the dose escalation and expansion phase of a study of crenolanib plus RAM/PTX in pts with previously advanced EAGA. **Methods:** This phase I/II study is enrolling ECOG PS 0-1 EGA pts with progression on first-line chemo. PTX 80 mg/m²/ day on day 1, 8, 15 and RAM 80mg/kg q 14 days were administered with escalating doses of crenolanib (60, 100, 150 mg BID) after a 7 day “run-in” of crenolanib to assess crenolanib-related toxicities. The primary objective was to determine the maximum tolerated dose (MTD) of crenolanib plus RAM/PTX. Safety and preliminary efficacy were examined. **Results:** 15 pts were treated; 12 male, median age 58 (32-73), 66% were ECOG PS 1. Primary site was gastric in nine pts, GEJ in 4 pts and esophageal in two pts. Three pts each received crenolanib 60mg BID and 80mg BID, six pts received 100mg BID and three pts received higher doses. At data cutoff, eight pts continued on treatment. 12 pts have completed the DLT evaluation period across 3 dose levels (60 to 100 mg BID). Median treatment duration was 76 days (35-190). The combination was well tolerated, with no DLTs or serious adverse events (SAEs) attributed to study drug. Treatment related adverse events occurred in two pts (17%), all grade 1. These were fatigue, nausia, vomiting and hypertension. Disease progression was the most common reason for treatment discontinuation; no discontinuation was due to study drug related AEs. Nine pts were evaluable for response. One pt had objective response; the disease control rate was 78%. Median PFS and OS were 4.1 and 11.9 months respectively. **Conclusions:** Crenolanib plus RAM/PTX appeared well tolerated at a dose level of 100mg BID. Further escalation will be considered.

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**Impact of radiation dose during neoadjuvant chemoradiation on postoperative complications in esophageal (EC) and gastroesophageal junction cancers (GEJC).** First Author: Noah Kastelowitz, University of Colorado School of Medicine, Aurora, CO

**Background:** Neoadjuvant chemoradiation (nCRT) followed by resection is standard of care for operable stage III EC and GEJC; however, it can be associated with significant risk of postoperative complications (POC). The CROSS study was reported no increase in POC severity in pts with nCRT compared to surgery alone as defined by the Comprehensive Complication Index (CCI). We applied the CCI metric to evaluate the impact of nCRT radiation dose < 50 Gy vs. ≥ 50 Gy on POC rates and compared to the CROSS rates.

**Methods:** We retrospectively reviewed 84 pts (2004-2009) who underwent subsequent surgery. The study group reported no increase in POC severity with nCRT using 41.4 Gy compared to surgery alone as defined by the Comprehensive Complication Index (CCI). We applied the CCI metric to evaluate the impact of radiation dose < 50 Gy vs. ≥ 50 Gy on POC rates and compared to the CROSS rates.

**Results:** 15 pts were treated with < 50 Gy (range 39.6-46.8 Gy) and 53 (65%) were treated with ≥ 50 Gy (range 50.0-62.5 Gy) delivered using IMRT/VMAT (41%), 3D-CRT (46%), and conformal therapy were carboplatin/paclitaxel (59%), cisplatin/5-FU (17%), or other (24%). Resection was performed by Ivor Lewis esophagectomy (67%), esophagogastrectomy (14%), or other (19%). Rates of pulmonary complications were greater in the CROSS study. Rates of cardiac complications were greater in the CROSS study.

**Conclusions:** In highly selected EC and GEJC pts, definitive nCRT radiation doses do not appear to increase POC rates. Thus, 50 Gy can likely be delivered without increasing toxicity while also allowing a definitive dose for pts not able or willing to undergo subsequent surgery.
The preventive effect of neoadjuvant therapy on poor long-term outcomes of postoperative complications in patients with esophageal squamous cell carcinoma: A prospective cohort study. First Author: Masashi Takeuchi, Departments of Surgery, Keio University School of Medicine, Tokyo, Japan.

**Background:** Postoperative complications have a negative impact on survival after esophagectomy because systemic inflammation may induce residual cancer cell growth. A solution that could suppress micrometastasis is neoadjuvant therapy; however, to date, no study has shown that neoadjuvant therapy suppresses the proliferation of cancer cells due to postoperative complications after esophagectomy. To investigate the preventive effect of neoadjuvant therapy on poor long-term outcomes of postoperative complications in patients with esophageal squamous cell carcinoma. **Methods:** In total, 509 patients who underwent esophagectomy for primary esophageal squamous cell carcinoma were included in this prospective cohort study. We investigated the relationship between complications, such as pneumonia, and long-term oncologic outcomes with and without neoadjuvant therapy.

**Results:** Among all the patients, the 3-year overall survival (OS) rate was 68.4%, and the disease-free survival (DFS) rate was 58.1%. The patients were categorized into two groups: the neoadjuvant therapy (+) group (n = 227) and the neoadjuvant therapy (–) group (n = 282). Among patients not undergoing neoadjuvant therapy, the patients with pneumonia, atrial fibrillation, pyothorax, or chylothorax had significantly poorer OS and DFS than patients without these complications. However, among patients undergoing neoadjuvant therapy, there were no significant differences in long-term outcomes, regardless of the presence of complications. In multivariate analyses, pneumonia (p = 0.034) and chylothorax (p = 0.006) were identified as predictors of death in the neoadjuvant therapy (–) group. **Conclusions:** In patients with esophageal squamous cell carcinoma, the negative impact of postoperative complications can be reduced by performing neoadjuvant therapy.

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**Table: Univariate Odds Ratios for Cardiac Toxicity.**

<table>
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<th>Variable</th>
<th>OR</th>
<th>CI</th>
<th>P Value</th>
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<tbody>
<tr>
<td>FEVI % Predicted, per 10% decrease</td>
<td>1.1</td>
<td>0.81-1.5</td>
<td>0.45</td>
</tr>
<tr>
<td>DLCO % Predicted, per 10% decrease</td>
<td>1.1</td>
<td>0.91-1.3</td>
<td>0.39</td>
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**Methods:** A total of 2,254 patients were eligible for inclusion in the present study. One hundred seventy-five patients had IC group, while 2,079 patients had not. Operation time (p < 0.001), blood loss (p < 0.001) was significantly greater in the IC group. The incidence of postoperative inflammatory complication grade 2 or higher was 8.5% in which, pancreatic fistula (2.8%), anastomotic leakage (1.8%) were occurred. The mortality rate was 0.18%. The five-year OS rates of the IC and NC groups were 74.9% and 83.2%, respectively. The difference was statistically significant (p = 0.015). Multivariate Cox’s proportional hazard analyses demonstrated that the postoperative inflammatory complications were a significant prognostic factor for OS. **Conclusions:** Postoperative inflammatory complications have an obvious impact on the OS in curatively resected gastric cancer patients. It is necessary to reduce the incidence of postoperative complications.

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**Table: Univariate Odds Ratios for Pulmonary Toxicity.**

<table>
<thead>
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<th>Variable</th>
<th>OR</th>
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<tbody>
<tr>
<td>FEVI % Predicted, per 10% decrease</td>
<td>1.4</td>
<td>1.02-1.8</td>
<td>0.04</td>
</tr>
<tr>
<td>DLCO % Predicted, per 10% decrease</td>
<td>1.4</td>
<td>0.01-1.8</td>
<td>0.04</td>
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**Background:** Several studies have reported that postoperative complications such as anastomotic leakage affect long-term prognosis after gastric cancer surgery. This study aimed to determine whether or not long-term outcomes were affected by the postoperative inflammatory complications in patients who underwent curative resection for gastric cancer. **Methods:** The patients were retrospectively selected from the medical records of consecutive patients with adenocarcinoma of the stomach excluding patients with non-curative resection, unresectable stage IV GC and those who had undergone prior chemotherapy.**Results:** A total of 2,254 patients were eligible for inclusion in the present study. One hundred seventy-five patients had IC group, while 2,079 patients had not. Operation time (p < 0.001), blood loss (p < 0.001) was significantly greater in the IC group. The incidence of postoperative inflammatory complication grade 2 or higher was 8.5% in which, pancreatic fistula (2.8%), anastomotic leakage (1.8%) were occurred. The mortality rate was 0.18%. The five-year OS rates of the IC and NC groups were 74.9% and 83.2%, respectively. The difference was statistically significant (p = 0.015). Multivariate Cox’s proportional hazard analyses demonstrated that the postoperative inflammatory complications were a significant prognostic factor for OS. **Conclusions:** Postoperative inflammatory complications have an obvious impact on the OS in curatively resected gastric cancer patients. It is necessary to reduce the incidence of postoperative complications.
The hyperprogressive disease during nivolumab treatment or irinotecan treatment in patients with advanced gastric cancer. First Author: Masahiko Aoki, Division of Gastrointestinal Medical Oncology, National Cancer Center Hospital, Tokyo, Japan

Background: Nivolumab has demonstrated a survival benefit as a single agent in patients with advanced gastric cancer (AUC). However, not all patients benefit from nivolumab or irinotecan treatment. The frequency and outcome of HPD in AGC comparing between immunotherapy and cytotoxic agents are little known. The aim of this study was to clarify the prevalence and background of HPD in patients treated with nivolumab or irinotecan. Methods: The subjects of this retrospective study were AGC patients with measurable disease defined by RECIST version 1.1 who were treated with nivolumab or irinotecan at our institution between June 2009 and September 2018, and whose tumors were assessed at least 3 times (during prior therapy, immediately before and after initiating nivolumab or irinotecan). The tumor growth rates (TGR) both before and after nivolumab or irinotecan were calculated as reported (Stéphane Champliau, Clin Cancer Res 2017). HPD was defined as an increase in the TGR exceeding 50% after nivolumab or irinotecan compared with prior therapy. Results: 32 and 66 patients received nivolumab and irinotecan (20 patients received both nivolumab and irinotecan). There were more prior chemotherapy regimens before nivolumab than irinotecan (median: 3 vs 2). The median overall survival (MST) was 4.1 months (95%CI; 4.6-9.3 months) after nivolumab, and 7.0 months (95%CI; 6.3-9.3 months) after irinotecan. There were 9 patients showing HPD (28.1%) after initiating nivolumab and 9 patients (31.0%) after irinotecan (p = 0.0824). There were no differences in background between patients with and without HPD either after nivolumab or irinotecan. 9 patients with HPD showed shorter survival than those without HPD after nivolumab (median: 1.9 vs 6.4 months, p = 0.0007) while there was no such difference after irinotecan (median: 7.0 months, p = 0.3345). Conclusions: HPD was observed more frequently after initiating nivolumab compared with irinotecan, and was associated with a poor prognosis after nivolumab but not after irinotecan.

Hyperprogressive disease (HPD) during nivolumab (Nivo) or irinotecan (IRI) as salvage line in patients with metastatic gastric cancer (MGC). First Author: Naotoshi Sugimoto, Osaka International Cancer Institute, Osaka, Japan

Methods: We retrospectively compared tumor growth kinetics (TGK) on Nivo or IRI as salvage line and TGK on last treatment in patients with MGC in our hospital. The TGK ratio (TGKn/TGK0, ratio of the slope of tumor growth before treatment and the slope of tumor growth on treatment) was calculated. HPD was defined as a TGKn ≥ 2. Results: 51 patients have been treated Nivo (n = 31) or IRI (n = 20) as salvage line before Aug 2018 in our hospital. The median age was 67 years (range 37-81) in Nivo and 68 years (range 46-80) in IRI. 20 males and 11 females in Nivo and 16 males and 4 females in IRI. PS 0-1/2 score 19/72 in Nivo and 19/71 in IRI. Thirty-five patients (Nivo; IRI = 16/19) had target lesions according to RECIST 1.1 and performed CT pre, baseline and during treatment. HPD were observed in seven patients (44%) with Nivo. On the contrary, only one patient (5%) experienced HPD with IRI. Median PFS and OS (HPD vs. non-HPD) were 2.1 versus 3.5 months (HR: 0.29 (0.083-0.98); p = 0.046) and 5.3 versus 6.6 months (HR: 0.44 (0.078-2.5); p = 0.35) with Nivo. The rate of grade 3-4 irAEs were colitis (6%), interstitial pneumonia (6%), and myositis (3%) with Nivo. No treatment-related death and pseudo-progression were observed. Conclusions: HPD is more common with Nivo compared with IRI in patients with MGC as salvage line and associated with poor PFS in patients treated with Nivo. Further analysis will be warranted.

Neoadjuvant treatment in patients with locally advanced gastric cancer. First Author: Mahmut Gumus, Istanbul Medeniyet University, Faculty of Medicine, Department of Medical Oncology, Istanbul, Turkey

Background: Although neoadjuvant treatment has been standard approach in gastric cancer with the positive results of randomized controlled studies in recent years, neoadjuvant treatment approach rates are far below the expected to evaluate the neoadjuvant chemotherapy effect and the aim of this study is to explore the success rates of neoadjuvant treatment regimes in patients with advanced gastric cancer. Our study aimed to evaluate the results of neoadjuvant treatment protocols in patients with locally advanced gastric cancer. Methods: We evaluated characteristics and survival outcomes of 54 patients that were operated after neoadjuvant systemic treatment out of 1,143 gastric cancer patients recorded in our database. Results: The median follow-up was 12 months in this study. 38% of the patients were female and the median age was 61 (24-78). While 46 % of the tumors were located in gastro-esophageal junction and cardia, others were located distally. All of the patients treated with neoadjuvant treatment had positive lymph nodes. While lymphatic and perineural invasion were detected in 67% of the patients, vascular invasion was detected in 39 % of the patients after the operation. While 43 % of the patients had grade 3 tumors, others had grade 1-2 tumors. R0 resection was achieved in 91% of the patients and D2 dissection was done in 82% of the patients. FOLFOX/XELOX, DCF/DCX, EOX/ECF and FLOT were applied as neoadjuvant treatment in 19%, 50%, 21% and 11% of the patients respectively. The median chemotherapy cycle number was 3 applied pre and postoperatively. The disease control rate (response or stable disease) was achieved in 75,9 % of the patients after the neoadjuvant chemotherapy. In 13 patients progressive disease was detected and these patients were not operated. We found the median disease free survival was 25 months and overall survival was 41 months in survival analysis. Three year DFS was 29% and 3 year OS was 52 %. Conclusions: Neoadjuvant treatment approach is important both to facilitate operation procedure and to evaluate efficacy of systemic treatment. As the survival advantage was shown in a study last year, FLORT regimen is expected to be used more commonly. The patients are being evaluated and the treatment decisions should be made in a multidisciplinary tumor board including surgeon, radiologist, medical oncologist to provide optimal treatment benefit.
128 Poster Session (Board #K20), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
Comparative effectiveness of nivolumab (NIVO) relative to standard of care (SOC) for advanced/metastatic (adv/met) gastric or gastroesophageal junction cancer (GC/GEJC): A simulated treatment comparison (STC).
First Author: Ian Chau, Royal Marsden Hospital, London and Surrey, United Kingdom

**Background:** The prognosis of adv/met GC/GEJC among patients receiving third and later lines (L) of therapy is poor, and effective treatment options are limited. The study objective was to estimate the relative effect of NIVO versus SOC for overall survival (OS), in the US among adv/met GC/GEJC patients who received ≥3L therapy.

**Methods:** A STC was performed using individual patient data (IPD) from the single arm CheckMate 032 (CM032) trial, and the Flatiron Health (FH) database. Eligible patients had adv/met GC/GEJC and received NIVO (CM032) or SOC (FH) as ≥3L therapy; all patients met CM032 eligibility criteria. A regression model of OS was fit to CM032 data using prognostic factors and treatment effect modifiers identified through a systematic literature review. The regression model was used to predict OS for NIVO, using Flatiron patient characteristics as covariates, and to estimate the expected outcome if NIVO had been available in the Flatiron population. The observed and predicted OS for NIVO was compared against the observed OS for SOC to generate naive and adjusted hazard ratio comparisons of NIVO vs SOC.

**Results:** In total, 42 and 43 patients were included from CM032 and Flatiron, respectively. In the Cox model, 19 prognostic factors were considered and the final model adjusted for 6, based on data availability across the two sources: ECOG, alkaline phosphatase (ALP) and hemoglobin, prior surgery, and tumor location. Median OS was 8.97 months in the NIVO group and 5.61 months in the SOC group. The STC adjustment yielded a hazard ratio of 0.66 (95% CI: 0.41 to 1.06) for NIVO vs SOC compared to the naive estimate of 0.66 (95% CI: 0.31 to 1.46). Sensitivity analyses confirmed this result. Conclusions: In the absence of head-to-head data, this study suggests that NIVO may confer a benefit in terms of OS versus SOC for patients with GC/GEJC in ≥3L therapy in the US setting. Despite the inherent limitations of using non-randomized comparisons of clinical trial data and real-world evidence, these findings provide insight into the potential benefit of novel agents such as NIVO.

130 Poster Session (Board #L2), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
Endoscopic intratumoral injection of OBP-301 (telomelysin) with radiotherapy in esophageal cancer patients unfit for standard treatments.
First Author: Shunsuke Tanabe, Department of Gastroenterological Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

**Background:** OBP-301 (telomelysin) is an attenuated type-5 adenovirus with oncolytic potency that contains the human telomerase reverse transcriptase (hTERT) promoter. Supernatant viral replication, OBP-301 causes selective replication and lysis of a variety of cancer cells, and also inhibits the repair of radiation-induced DNA double-strand breaks, leading to radiosensitization. We investigated the feasibility and safety of treatment of esophageal cancer with OBP-301 and radiotherapy. Phase I dose-escalation study of OBP-301 with radiotherapy was conducted in 13 histologically confirmed esophageal cancer patients who deemed unfit to receive surgery or chemotherapy. Study treatment consisted of intratral injection of OBP-301 with radiotherapy. Treatment was administered concurrently over 6 weeks, beginning on day 4, to a total of 60 Gy. Virus administration was performed by intratumoral needle injection of the primary tumor through a flexible endoscope. The primary and secondary end points were incidence of dose-limiting toxicities and objective response rate.

**Results:** Of 13 patients, seven, three, and three patients were treated in the cohorts with 101, 105, and 107 virus particles of OBP-301, respectively. The patients comprised 10 males and 3 females, with median age of 79.7 years (range, 53 to 92 years). Common grade 1 and 2 toxicities included fever, esophagitis, pneumonitis, anorexia, constipation, and gastroesophageal reflux. All patients developed a transient, self-limited lymphopenia. Eight patients had local complete response (CR); all of them exhibited pathologically no viable malignant cells in biopsy specimens, and three had partial response. The objective response rate was 84.6%. The clinical CR rate was 80.0% in stage I and 66.7% in stage II/III, respectively. Histopathologic examination in post-treatment specimens showed massive infiltration of CD8+ cells in three partially-regressed tumors.

**Conclusions:** Multiple courses of endoscopic OBP-301 injection with radiotherapy were feasible and provided definite clinical benefits in patients with esophageal cancer. Clinical trial information: 000010158.

129 Poster Session (Board #L1), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
Phase I/II study of ramucirumab plus nivolumab in patients in second-line treatment for advanced gastric adenocarcinoma (NivoRam study). First Author: Hiroki Hara, Department of Gastroenterology, Saitama Cancer Center, Saitama, Japan

**Background:** Nivolumab (NIVO) showed a survival benefit in salvage line of advanced gastric cancer (AGC) patients in ATTRACTION-2 trial. Based on synergistic anti-tumor effects by simultaneous blockade of PD-1 and VEGFR-2, this phase I/II study was conducted to investigate the safety and efficacy of Nivo plus ramucirumab (Ram) in the second line chemotherapy for AGC.

**Methods:** AGC patients with measurable lesions, PS 0-1, disease progression on first line chemotherapy containing platinum were eligible. Patients received Nivo (3mg/kg, Q2W) and Ram (8mg/kg, Q2W) until unacceptable toxicity or disease progression. After feasibility was evaluated in six patients (phase 1 part), additional 40 patients were required in a phase 2 part with the primary analysis (expected 6-months progression-free survival (PFS) rate of 36%, threshold of 18%, one-sided alpha level of 10%, power of 90%). Secondary endpoints included overall response rate (ORR), disease control rate (DCR), PFS, overall survival (OS), and safety.

**Results:** 46 AGC patients (median age 66 years, PS 1 40%) were enrolled. No dose limiting toxicities were observed in the phase 1 part. With median follow up time of 10.2 months, 6-month PFS rate was 37.4% (90% confidential intervals: 25.7-49.2%), which met the primary endpoint of the phase 2 part. ORR/DCR were 26.7%/62.2%. Median PFS/OS were 2.9/7.0 months. Among all enrolled patients, grade 3 or 4 treatment related adverse events were hypertension (n = 2), diarrhea (n = 2), perforation at jejunum (n = 1), hemorrhage (n = 1), colitis (n = 1), pancreatitis (n = 1), liver dysfunction (n = 1), cholangitis (n = 1), hemoptysis (n = 1), neutropenia (n = 1) and proteinuria (n = 1). There were no treatment-related deaths.

**Conclusions:** Combination of Nivo and Ram showed promising antitumor activity and mild toxicity profile for second line AGC, which is worth evaluating in a further confirmatory study. Clinical trial information: NCT02999295.

131 Poster Session (Board #L3), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
A multicenter study of trimodality therapy for patients 75 years and older with esophageal cancer. First Author: Niamh Anna McDonnell, Mayo Clinic, Rochester, MN

**Background:** Trimodality therapy is the standard of care for patients with resectable cancer of the esophagus. However, patients ≥75 years have been underrepresented or excluded from landmark clinical trials to date. We investigated the feasibility of the treatment of esophageal cancer in patients ≥75 years. Trimodality therapy in patients ≥75 years. Methods: We performed a retrospective review of all patients ≥75 years who received trimodality therapy for esophageal cancer in 3 high volume tertiary cancer institutions from June 2007 to June 2013. All patients received neoadjuvant radiation with concomitant chemotherapy followed by esophagectomy. Toxicities and clinical outcomes were abstracted from the electronic medical record and primarily from a prospectively maintained database. Overall and disease-free survival were estimated using the Kaplan-Meier method. Results: Five hundred seventy patients were treated with trimodality therapy for esophageal cancer from 2007-2013. Of these, 38 patients (7%) were 75 or older at the time of diagnosis. At diagnosis, comorbidities included coronary artery disease (32%), atrial fibrillation (11%) and COPD (13%). The majority of patients (87%) received 50.4 Gy/28 fractions. 5-fluorouracil (5-FU)/cisplatin was the most common chemotherapy regimen (37%), followed by 5-FU/docetaxel (24%). A total of 13 patients (34%) developed acute grade ≥3 toxicity associated with neoadjuvant therapy. The most common acute grade 3 toxicities were hematological (10%), nausea (8%), esophagitis (5%) and fatigue (5%). Significant postoperative complications included respiratory (empyema, ARDS, pleural effusion) (39%), arrhythmia (32%), anastomotic leak (5%) and ileus (5%). There were 2 deaths (5%) within 90 days of surgery: one was secondary to empyema, the other developed DIC and sepsis. Median overall survival and disease free survival were 4.4 and 2.3 years respectively.

**Conclusions:** Trimodality treatment is a reasonable approach for management of carefully selected elderly patients with esophageal cancer, with similar rates of cancer outcomes, and treatment related morbidity and mortality as compared to younger patients.

Visit qicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Impact of peripheral neuropathy induced by platinum in first-line chemotherapy on second-line chemotherapy containing paclitaxel for advanced gastric cancer. First Author: Ryo Otsuka, Department of Pharmacy, National Cancer Center Hospital, Tokyo, Japan

Background: Chemotherapy-induced peripheral neuropathy (CIPN) is a common adverse effect of platinum and paclitaxel (PTX) persisting for long time. In the Gastric Cancer Treatment Guideline (Japanese Gastric Cancer Association, 2018), first-line chemotherapy with fluoropyrimidine plus platinum followed by taxane based chemotherapy is recommended. It is not well known how much CIPN in platinum in the first-line chemotherapy affects the tolerability of second-line chemotherapy containing PTX (second-PTX).

Methods: The subjects were advanced gastric cancer patients who received second-PTX after the platinum-containing first-line chemotherapy between March 2015 and June 2018. Patients were divided into two groups according to prior platinum: oxaliplatin (prior L-OHP) and cisplatin (prior CDDP) groups. CIPN was graded according to CTCAE ver.4. Severity of CIPN, dose reduction and discontinuation due to CIPN during the second-PTX were compared between the two groups. Results: 109 patients (50 prior L-OHP and 59 prior CDDP group) were included in this retrospective study. The severity of CIPN just before second-PTX was 46% for grade 1 and 12% for grade 2 in the prior L-OHP group, and 8.5% and 0% in the prior CDDP group. The median time to grade 2 neuropathy during second-PTX was 2.5 months in the prior L-OHP group and 8.6 months in the prior CDDP group (p = 0.004). CIPN-related dose reduction of PTX were 12.0% in the prior L-OHP group and 3.4% in the prior CDDP group (p = 0.177). Discontinuation of second-PTX due to CIPN were 10.0% in the prior L-OHP group and 5.1% in the prior CDDP group (p = 0.541). Conclusions: The severity of CIPN and tolerability of the second-PTX may be affected by prior platinum, L-OHP or CDDP, in the first-line chemotherapy for advanced gastric cancer.

Impact of double-flap technique for reconstruction after proximal gastrectomy. First Author: Kazuki Asanuma, Department of Surgery, Keio University School of Medicine, Tokyo, Japan

Background: Proximal gastrectomy (PG) has been performed for proximal early gastric cancer as a minimally invasive procedure. In PG, gastroesophageal reflux disease (GERD) becomes problem, thus several techniques have been reported to reduce GERD. So far, we have mainly performed the method of anastomosis based on double stapling technique (DST) using a trans-oral anvil delivery system for reconstruction after PG. For preventing GERD, we recently introduced double-flap technique (DFT) reported to be more physiological anti-reflux reconstruction which can prevent GERD. So, this study shows superiority of DFT compared to DST. Methods: Patients who have undergone PG for proximal gastric cancer during Jan, 2012 to Jul, 2017 in our hospital were reviewed as candidates. Operation time, blood loss, postoperative anastomotic complication, postoperative hospital stay, postoperative reflux symptom or endoscopic findings, intake of proton pump inhibitor (PPI) at 1 year after the operation, and postoperative nutritional status were retrospectively investigated. Results: DFT was performed in 26 patients whereas DST was performed in 38 patients. Average operation time and postoperative hospital stay was not significant in both groups (DFT group: 275.8±41.14 minutes, 13.6±8.9 days, DST group: 252.2±82.9 minutes, 15.2±7.2 days, respectively). As for postoperative complications higher than Clavien-Dindo Grade III, one case of suture failure was observed in DST group. Postoperative reflux symptoms and endoscopic findings of gastroesophageal reflux were significantly frequent in DST group compared to DFT group (Reflux symptoms, DFT group: 0 / 7 patients, p = 0.03). Conclusions: DFT is superior to DST as a reconstruction method after PG in terms of suppressing GERD.
Gastric cancer liver metastasis: Optimal management for oligo-metastatic disease. First Author: Hiromichi Ito, Japanese Foundation for Cancer Research, Tokyo, Japan

Background: The role of surgery for gastric cancer liver metastasis (GCLM) has not been established and particularly, the optimal management for liver-isolated, oligo-GCLMs remains controversial. The aims of this study were to review the outcomes for our patients with GCLM who underwent liver resection and to define the optimal selection criteria for resection. Methods: The medical records of patients who underwent liver resection for GCLMs with curative intent at our institution from 1993 through 2018 were reviewed. Our criteria for liver resection included absence of extraparenchymal disease, and the limited number of liver metastasis (often 3 or less). Results: Total 101 patients with GCLM (77 men [76%], median age 66 years) were included. Forty-seven patients (46%) had synchronous metastasis and all underwent simultaneous resection with the primary disease. Those with synchronous disease received neoadjuvant therapy more often than those with metachronous disease (63% vs 37%, p = 0.02). Median RFS and OS for the entire cohort were 11 months and 37 months, respectively, and 5-year-OS rate was 41%. Of note, 25 patients achieved survival longer than 5 years without any recurrence thereafter with median follow-up of 137 months. In the multivariate analyses, elevated CEA 50ng/ml or greater and nodal status of the primary were associated with shorter median follow-up of 137 months. In the multivariate analyses, elevated CEA 50ng/ml or greater and nodal status of the primary were associated with shorter OS (Table 1). Conclusions: For well selected patients with GCLM, liver resection is an effective therapy not only to prolong disease-free time, but also to achieve cure. CEA is useful to select patients with GCLM who unlikely benefit from aggressive surgery.

Safety and efficacy of dasatinib in patients with advanced gastrointestinal stromal tumors refractory to imatinib and sunitinib: A single arm, multicenters, phase 2 trial. First Author: Jian Li, Peking University Cancer Hospital, Beijing, China

Background: Regorafenib is recommended to treat advanced gastrointestinal stromal tumor (GIST) refractory to imatinib and sunitinib. However, the efficacy is not satisfied, other active agents need to be explored to advanced patients. Methods: In this single arm, multi-center, phase 2 trial, we enrolled patients aged 18 years and older with advanced GIST who had received previous imatinib and sunitinib treatment. Participants were treated with oral dasatinib 50mg twice a day for 2 weeks. If patients were tolerable, then they received dasatinib 70mg twice a day treatment, to tumor progression or intolerable toxicities. The primary endpoint was RECIST-based progression-free survival (PFS) in the intention-to-treat population. The secondary endpoints included response rate, overall survival (OS) and advent events. cDNA will be analyzed in some patients to explore the sensitive biomarker to dasatinib. Results: From May 2016 to June 2018, 58 patients from nine medical centers were enrolled in this study. Two patients had partial response and disease control rate was 62.0%. The median PFS was 3.0 months (95% CI, 2.6-3.4 months). There was no statistic difference of PFS in both subgroup with different primary mutations and in subgroup with different secondary mutations. The patients with wild type GIST had a trend of longer PFS of 5.5 months. In 4 patients with PDGFR A B42V mutation, two patients had stable disease. The median OS was 14.0 months (95% CI, 10.8-17.2 months). The most frequently observed grade 3 adverse events included anemia (10.3%), diarrhea (1.7%). The analysis of cDNA is ongoing. Conclusions: Dasatinib is an active treatment for patients with GIST who are refractory to imatinib and sunitinib. This study is registered with ClinicalTrials.gov, NCT02776878. Clinical trial information: NCT02776878.
Methods: Immune based therapy and in particular to PD-1 blockade when combined with chemotherapy in resected EC suggest early stage tumors may respond favorably to immunotherapy. Clinical trial information: NCT02734004.

Results: Forty pts were included in the safety and 39 in the efficacy analysis. Among 39 pts, median age was 57 yrs (range 28-77). Nineteen pts (48%) had a grade 3 AE; three pts (8%) had a grade 4 AE. Most common AEs were anemia, lipase increase, fatigue, dysphagia, hyponatremia, and alkaline phosphatase increase. Ten pts (25%) had immune-mediated AEs, most commonly rash. The ORR was 10%; two pts had complete response; two had partial response. Median DoR was 11.1 months. DCR at 12 ws was 26%. Further efficacy and biomarker data will be presented.

Conclusions: The combination of olaparib and durvalumab was well tolerated, with no unexpected AEs. All responses occurred after the addition of durvalumab and were durable, suggesting synergistic treatment effect of the combination in some pts. Furthermore, several pts with early PD showed unexpectedly long survival. DCR at 12 ws was below the target (70%) due to a high rate of early PDs following the olaparib run-in. To address the early treatment failures, an upfront addition of more aggressive therapies to the combination should be explored. Clinical trial information: NCT02734004.

Impact of antibiotic use on response to treatment with immune checkpoint inhibitors.

Methods: A number of factors can cause gut microbiome dysbiosis during immunotherapy (e.g., the use of antibiotics). We hypothesized that the use of antibiotics during immunotherapy can adversely affect the efficacy of CPIs. We explored the prevalence of ABX use amongst patients (pts) using CPIs, and whether the use of ABX influences the response to CPIs. Methods: We performed an analysis of an institutional retrospective database including all the pts treated with CPIs from 2/2015-3/2018. A patient was considered to have used ABX if he or she was prescribed ABX within 6 months before or after, initiating CPIs. Statistical analysis was done using logistic regression with overall response rate (ORR) (CR, PR and SD), as the outcome. 9 separate analyses were done: one for each temporality (30 days, 60 days, 6 months) and use-order (before, after, neither) combinations. Odds ratios for ORR as univariate analysis, and adjusted for age and sex; and adjusted for age, sex, and tumor type were calculated. Results: Out of 242 pts, 11 were lung, 36 bladder, 35 renal, 16 gastrointestinal and 44 other cancers. 50% (121) pts received ABX within 6 months, 46% (111) were lung, 36 bladder, 35 renal, 16 gastrointestinal and 44 other cancers. 50% (121) pts received nivolumab, 28% (68) pembrolizumab and 21% (52) atezolizumab. 75%, 46% and 32% of the pts received ABX within 6 months, 60 days and 30 days of starting CPIs. Only ABX use in the first 30 days had a significant effect on treatment outcome (p = 0.005 for 60-days). ABX use prior to initiation of CPI at any time point, or ABX use in the first 6 months of CPI use did not impact CPI efficacy, Table 1. Conclusions: ABX use within the first 60 days of starting CPI therapy is prevalent (32%). This study suggests that the use of ABX within 60 days following initiation of CPIs significantly negatively impacts the ORR. Unnecessary usage of ABX should be avoided, especially during the early phase of starting CPIs.

ABX Use in the first 60 days of CPI therapy

<table>
<thead>
<tr>
<th>ABX Use</th>
<th>ORR %</th>
<th>95% CI</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ABX</td>
<td>36.0%</td>
<td>[28.0, 44.0]</td>
<td>0.05</td>
</tr>
<tr>
<td>ABX within 60 days</td>
<td>29.0%</td>
<td>[21.0, 37.0]</td>
<td>0.05</td>
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</tbody>
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*During the same corresponding time period.
Evaluation of safety and tolerability of durvalumab (D) and tremelimumab (T) in combination with first-line chemotherapy in patients (pts) with esophageal squamous-cell carcinoma (ESCC). First Author: Dae Ho Lee, Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine Seoul, Seoul, Republic of Korea

Background: Platinum-doublet chemotherapy in first-line (IL) ESCC pts has reached a therapeutic plateau, and new therapeutic strategies are needed. Adding D (anti-PD-L1 mAb) and T (anti-CTLA-4 mAb) to IL platinum-based chemotherapy may improve outcome in pts with advanced/metastatic ESCC. Methods: In Part A of this Phase Ib study (NCT02658214), dose-limiting toxicities (DLTs) for D+T (D 1.5 g + T 75 mg on d1, q4w) and 5-FU+cisplatin chemotherapy may improve outcome in pts with advanced/metastatic ESCC. 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. Their 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 old and male were 301 (70.8%). Of these, 42 patients (9.9%) were diagnosed as pre-operative sarcopenia. Compared with non-sarcopenic group, pre-operative sarcopenia groups showed more female, higher BMI, less alcoholic, and less smoking. However, there was no significant difference in 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 un-differentiated tumor, lower hemoglobin level, less alcoholic, less smoking, and presence of diabetes mellitus. Furthermore, newly developed sarcopenic group showed more total fat area, especially more subcutaneous fat area and lower VFA / SFA ratio in the abdominal CT imaging. However, there was no significant difference in the 5-year overall survival and disease free survival among non-sarcopenic, sarcopenic and newly developed sarcopenic group (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.
Exploratory evaluation of baseline tumor biomarkers and their association with response and survival in patients with previously treated advanced gastric cancer treated with andealiximab combined with nivolumab versus nivolumab. First Author: Jean-Philippe Metges, Oncology & Haematology Institute, Brest University Hospital, Brest, France

Background: Andealiximab (ADX) is a monoclonal antibody that inhibits matrix metalloproteinase 9 (MMP9). Preclinical studies suggest that MMP9 inhibition relieves immune suppression and promotes T cell infiltration to potentiate checkpoint blockade. In the phase 2 study combining ADX with nivolumab (N) versus N monotherapy (NCT02864381), addition of ADX to N did not improve objective response rate, progression-free survival (PFS), or overall survival (OS).

Methods: Archival tumor samples were collected from all patients (n = 141). CD8 and PD-L1 (28-8 DAKO) were assessed by immunochemistry. CD8+ cell density was measured in the tumor area. PD-L1 was prospectively scored by a pathologist for tumor cell (TC) and associated immune cell (IC) positivity. IfNg, Teffector (Tf), and activated CD8+ T cell (ActT) gene signatures were assessed by RNA sequencing. Due to a small number of responders, treatment arms were combined to evaluate response. Cox proportional hazards models were used for survival analyses. Results: Baseline biomarkers of T cell infiltration and activation did not differentiate responders from non-responders (IfNg, Tf, ActT, CD8; p > .10). None of the evaluated biomarkers were associated with PFS or OS for all treated patients or per treatment arm (IfNg, Tf, CD8: p > .10). With the exception of CD8+ (PFS HR = 0.73, p = .021), none of the major baseline differences were positive for IC PD-L1 (1%; n = 36; 10%; n = 50; > 10-25%; n = 52; > 25%; n = 20) and negative for TC PD-L1 (H; n = 88; H < 1; n = 27; H = 1; n = 27). There was a trend toward an increasing hazard ratio for the PD-L1+ (TC + IC ≥ 1%) population (n = 102, HR = 0.62, p = 0.098), the TC < 1 group (HR = 1.46, p = 0.08) and the IC > 10-25% (HR = 0.66, p = 0.08).

Conclusions: Neither CD8+ cell density nor IfNg, Tf or ActT gene signatures were associated with response or survival to checkpoint blockade. While TC was low, IC intermediate and TC + IC ≥ 1% PD-L1+ groups trended toward better survival for the ADX+N arm, consistent with the hypothesis that ADX potentiates N activity; this did not translate into better outcome. Clinical trial information: NCT02864381.

Prognostic and predictive factors after failure of two drug lines for metastatic gastric adenocarcinomas: A French retrospective study. First Author: Benjamin Bousscac, Centre Antoine Lacassagne, Nice, France

Background: There is no therapeutic consensus after failure of two drug lines for metastatic gastric adenocarcinoma. The theoretical benefit of a third-line chemotherapy might be weighed with the potential toxicity it could generate. It is essential to have prognostic and predictive factors to better select the candidate patients for a 3rd line chemotherapy.

Methods: The medical records of patients (pts) treated in our institute from 2008 to 2018 who received at least two chemotherapy lines have been retrospectively analyzed. The main objective was to look for prognostic factors after failure of two chemotherapy lines. The secondary objectives were to look for predictive factors of progression-free survival, global survival, and RECIST response in 3rd line.

Results: Out of a total of 153 pts identified, 68 received at least 2 chemotherapy lines and 51 of the patients responded to the treatment. In multivariate analysis, a period of less than 12 months between the administration of the 1st line of chemotherapy and the failure of a 2nd line was associated with a Hazard Ratio (HR) for death of 2.7 (p < 0.001; 95% CI 1.44 - 5.2) and female patients who had a HR for death of 3.7 (p < 0.001; CI 95%: 1.97-7.3), and 2.8 (p < 0.001; 95% CI: 1.3-5.8) respectively. For patients who started a 3rd line: a PS ≥ 2 increased the risk of progression by 4.05 (p < 0.001; 95% CI: 1.15-17).

Conclusions: Predictive factors were able to identify a third-line chemotherapy. However, the benefit of this chemotherapy is low given the RECIST response rate, and the short overall and progression-free survival medians. Our results suggest that the administration of a third-line chemotherapy should only be considered for pts with 12 months or older ongoing metastatic lesions and whose general health condition is unaltered.

The combination of the changes and the value of neutrophil-to-lymphocyte ratio is useful for prediction of response for advanced gastric cancer treated with nivolumab: A multicenter retrospective study. First Author: Takatsugu Ogata, Department of Clinical Oncology, Kobe City Medical Center General Hospital, Kobe, Japan

Background: The ATTRACT-2 study showed that nivolumab is effective in treating advanced gastric cancer (AGC). Many studies have examined the changes in NLR (cNLR) was calculated by NLRpost/NLRpre. The association of NLRpre and cNLR with the disease control rate (DCR) and PFS were assessed.

Methods: Out of a total of 153 pts identified, 68 received at least 2 chemotherapy lines. The secondary objectives were to look for predictive factors of progression-free survival, global survival, and RECIST response in 3rd line.

Results: Out of a total of 153 pts identified, 68 received at least 2 chemotherapy lines. The secondary objectives were to look for predictive factors of progression-free survival, global survival, and RECIST response in 3rd line.

Conclusions: The combined use of NLRpre and cNLR seemed to be effective in predicting the response of AGC to nivolumab.
Predictive biomarkers for the efficacy of nivolumab as ≥ third-line therapy in patients with advanced gastric cancer (AGC): From a subset analysis of ATTRACTION-2 phase III trial. First Author: Jwa Hoon Kim, Department of Oncology, Asan Medical Center, University of Uisan College of Medicine, Seoul, Korea, Republic of (South Korea)

Background: ATTRACTION-2 phase III trial proved the clinical efficacy of nivolumab (Nivo) in AGC patients (pts) treated ≥ 2 previous chemotherapy regimens. However, the benefits of Nivo seem to be limited to a subset of pts and there is a need to identify predictive markers to select pts who would benefit from Nivo. Methods: Clinical data and tumor samples of AGC pts enrolled from Asian Medical Center in ATTRACTION-2 study were retrospectively analyzed. PD-L1 (+) was defined as combined positive score of ≥ 1%. EBV and MSI status were determined by EBV-encoded small RNA in situ hybridization and IHC for MLH-1, MSH-2, PMS-2, and MSH-6, respectively. Tumor mutation burden (TMB) was acquired by targeted next-generation sequencing using the NextSeq platform with OncoPanel. Results: A total of 45 pts (28/17 in Nivo/placebo arms) were eligible for the analysis. Baseline neutrophil-lymphocyte ratio (NLR) was median 2.9 and 7 pts had hyponatraemia (< 135). In 36 pts with available tissues, there were PD-L1 (+) (N = 13; 36.1%), EBV (+) (N = 6; 16.7%), and no MSI-high. TMB data could be acquired in 29 pts and median TMB was 8.2/Mb (0.0-21.3). With a median follow-up of 28.3 months (mo) in surviving pts, objective response rate, median progression-free survival (PFS), and overall survival (OS) were 16.0, 13.6, and 8.1 mo in Nivo arm and 0%, 1.6 mo and 6.5 mo in placebo arm. In Nivo arm with measurable lesions, PD-L1 (+) pts had significantly higher disease control rate than PD-L1 (+) pts (87.5% vs. 20%, p = 0.015). In multivariate model adjusted for important factors (age, sex, Nivo/placebo, treatment line, Na, and PD-L1), NLR ≥ 2.9 and PD-L1 (+) were significant factors for PFS (Hazard Ratio [HR] 0.47, p = 0.037 and HR 0.32, p = 0.006, respectively) and PD-L1 (+) was a significant factor for OS (HR, 0.44, p = 0.012). With adjusting these factors with TMB, PD-L1 (+) remained favorable for PFS and OS. Pts with NLR ≥ 2.9 or PD-L1 (+) or Na > 135 significantly favored Nivo compared to placebo in terms of PFS and OS. Conclusions: Baseline NLR and PD-L1 status may be relevant predictive markers to select pts with AGC who would benefit from Nivo.

Three different chemotherapeutic regimens as a postoperative adjuvant chemotherapy for curatively resected gastric cancer: A retrospective analysis. First Author: Shen Zhao, Department of Gastrointestinal Medical Oncology, Fujian Cancer Hospital, Fujian Medical University Cancer Hospital, Fuzhou, China

Background: Two double regimens, CAPEOX (CLASSIC trial) and docetaxel/capecitabine (5-FU (JACCRO GC-07), were standard treatment for curatively resected gastric cancer (GC) in Asia. However, the optimal postoperative adjuvant treatment remains unsatisfactory and the efficacy between oxaliplatin-based or taxane-based doublets is unknown. This study aimed to investigate if triplet improve survival compared with doublets and differences in toxicity between doublets and triplets. Methods: A total of 202 AGC patients was selected from our hospital. The POF consists of a three-hour infusion of paclitaxel 135 mg/m² for oxaliplatin of FOLFOX. We checked the overall operative adjuvant treatment remains unsatisfactory and the efficacy between oxaliplatin-based or taxane-based doublets is unknown. This study included 29 AGC pts and median TMB was 8.2/Mb (0.0-21.3). With a median follow-up of 28.3 months (mo) in surviving pts, objective response rate, median progression-free survival (PFS), and overall survival (OS) were 16.0, 13.6, and 8.1 mo in Nivo arm and 0%, 1.6 mo and 6.5 mo in placebo arm. In Nivo arm with measurable lesions, PD-L1 (+) pts had significantly higher disease control rate than PD-L1 (+) pts (87.5% vs. 20%, p = 0.015). In multivariate model adjusted for important factors (age, sex, Nivo/placebo, treatment line, Na, and PD-L1), NLR ≥ 2.9 and PD-L1 (+) were significant factors for PFS (Hazard Ratio [HR] 0.47, p = 0.037 and HR 0.32, p = 0.006, respectively) and PD-L1 (+) was a significant factor for OS (HR, 0.44, p = 0.012). With adjusting these factors with TMB, PD-L1 (+) remained favorable for PFS and OS. Pts with NLR ≥ 2.9 or PD-L1 (+) or Na > 135 significantly favored Nivo compared to placebo in terms of PFS and OS. Conclusions: Baseline NLR and PD-L1 status may be relevant predictive markers to select pts with AGC who would benefit from Nivo.

The effect of IMRT on acute toxicity in patients with gastric cancer treated with preoperative chemoradiation. First Author: Shalini Moningi, University of Texas MD Anderson Cancer Center, Houston, TX

Background: Two trials are currently investigating preoperative chemoradiation (CRT) for localized gastric adenocarcinoma. However, radiation therapy (RT) can be associated with relatively high rates of acute toxicity. Newer techniques, such as intensity modulated RT (IMRT), could reduce toxicity by reducing radiation dose to normal structures. Our goal was to compare rates of toxicity and toxicity-related events in patients treated with IMRT compared to 3D conformal RT (3DCRT).

Methods: The records of 202 gastric cancer patients treated with preoperative intent RT at our institution from 1998-2018 were retrospectively reviewed. Demographic data, treatment details, acute and late toxicities (CTCAE 4.0 criteria), progression and survival data were recorded. Patients who had stage IV disease were excluded. Statistical analysis included descriptive statistics, Cox regression analysis, and Kaplan-Meier survival. Results: 54% were male and the median age was 63. 82 patients received 3DCRT and 120 patients received IMRT (median 45.0 Gy, IQR, 45.0-45 Gy in each group). 78% of patients in the 3DCRT group and 91% of patients in the IMRT group received neoadjuvant chemotherapy prior to RT. 99% of patients received concurrent chemotherapy. The rate of grade 3-4 acute toxicity was significantly lower in patients treated with IMRT compared to 3DCRT (53% vs. 73%, p = 0.004). The composite rate of toxicity-related events (hospitalization, feeding tube, IV rehydration, or RT break) was also significantly lower in patients treated with IMRT compared to 3DCRT (80% vs. 91%, p = 0.031). 72% of patients who received 3DCRT and 68% of patients who received IMRT underwent subsequent surgical resection. The 3-year OS rate was 58.1% for patients receiving IMRT and 60.2% for patients receiving 3DCRT (p = 0.649). The 3-year PFS rate was 47.5% for patients receiving IMRT and 52.7% for patients receiving 3DCRT (p = 0.486).

Conclusions: Our study indicates a marked reduction in the rates of grade 3-4 acute toxicity and toxicity-associated events in patients treated with IMRT compared to 3DCRT. These findings suggest that IMRT should be considered as the radiation modality in patients treated with preoperative CRT for gastric cancer.
Conclusions: With survival compared to other Asian races (HR 1.48, 1.29-1.69), even after grade (HR 2.00, 1.92-2.08), and advanced stage (HR 5.71, 5.57-5.85) were poor 95% CI 1.92-2.03), lower income (HR 1.13, 1.11-1.16), more comorbidities (HR 1.59, 1.52-1.67), and timing increased 15.5%, 20.1%, 22.7%, and 25.8% p = 0.001. Response rate among the patients with target lesions was 18.8% (13/69), and disease control rate was 62.3% (43/69). On the other hand, response rate among the patients previously treated with nivolumab or pembrolizumab was 57.1% (4/7). Median overall survival (OS) for combination therapy and monotherapy was 10.8 months (95% confidence interval [CI] 7.1, 11.9) and 5.5 months (95% CI 0.89-9.5), respectively. Grade 3 or 4 neutropenia was more common with combination therapy than with monotherapy (53.1% vs. 11.9%). Of 69 patients who received ramucirumab plus paclitaxel as second or third-line chemotherapy, high NLR (> 3) was the significant factor for poor PFS (median PFS, 2.7 vs. 5.4 months, p = 0.00203), but didn’t show the difference about OS (median OS, 9.7 vs. 11.9 months, p = 0.27). Conclusions: In our analysis, efficacy data was comparable with previous reports. In subgroup analysis, good response was observed in the group of prior nivolumab or pembrolizumab. NLR was prognostic factor for PFS, while it wasn’t show the relevance to OS because of the influence of after ramucirumab therapy.

Background: Ramucirumab with paclitaxel or ramucirumab monotherapy have shown the efficacy and safety in second-line chemotherapy for advanced gastric cancer. The previous reports have shown that neutrophil-lymphocyte ratio (NLR) was the prognostic factor for progression free survival. Methods: We conducted a retrospective review of clinical data from patients treated with ramucirumab at our institution between April 2015 to August 2018. Results: Of 90 patients, 81 received ramucirumab plus paclitaxel, and 9 received ramucirumab monotherapy. There was a significant difference of treatment line between combination therapy and monotherapy (mean 2.5 vs. 3.9, p = 0.00027). Response rate among the patients with target lesions was 18.8% (13/69), and disease control rate was 62.3% (43/69). On the other hand, response rate among the patients previously treated with nivolumab or pembrolizumab was 57.1% (4/7). Median overall survival (OS) for combination therapy and monotherapy was 10.8 months (95% confidence interval [CI] 7.1, 11.9) and 5.5 months (95% CI 0.89-9.5), respectively. Grade 3 or 4 neutropenia was more common with combination therapy than with monotherapy (53.1% vs. 11.9%). Of 69 patients who received ramucirumab plus paclitaxel as second or third-line chemotherapy, high NLR (> 3) was the significant factor for poor PFS (median PFS, 2.7 vs. 5.4 months, p = 0.00203), but didn’t show the difference about OS (median OS, 9.7 vs. 11.9 months, p = 0.27). Conclusions: In our analysis, efficacy data was comparable with previous reports. In subgroup analysis, good response was observed in the group of prior nivolumab or pembrolizumab. NLR was prognostic factor for PFS, while it wasn’t show the relevance to OS because of the influence of after ramucirumab therapy.

Gastric adenocarcinoma prognosis in a multiracial population. First Author: Jared David Acoba, University of Hawaii Cancer Center, Honolulu, HI

Methods: We included 86,663 patients in our analysis. Gastric adenocarcinomas and N = 1203 (73%) squamous cell carcinomas, 7,858 (84.9%) were male and 1,398 (15.1%) female with a median age was 62 (24-88). R0 resections decreased as the NT-Surgery interval increased: < 6 wks, 6-12 wks, 2-6 mos, and > 6 mos at 93%, 94.1%, 94.1%, and 86.2% respectively p = 0.004. Additionally, the median lymph nodes harvested decreased as timing increased: 12, 10, and 9 p = 0.001 and the median nodes positive decreased as timing increased:15.1, 13.1, and 2.4 p = 0.01. The complete response rates increased as timing increased: 15.5%, 20.1%, 22.7%, and 25.8% p < 0.001. However, this improvement in cCR did not translate into an increase in median survival: < 6 wks 40.9 mos, 6-12 weeks 38.5 mos, 2-6 mos 34.8 mos, and > 6 mos 39.8 mos of survival, p = 0.94 90-day mortality increased as the timing from neoadjuvant therapy increased: 6.4%, 7.9%, 9.4%, and 16.0%, respectively p = 0.001. Conclusions: Our data demonstrates that patients who have a prolonged NT-surgery interval will have a substantial increase in 90-day mortality. While there was an increase in pathologic complete response rates, this did not translate into an improvement in survival. The current recommendations of a NT-surgery timing of 6-12 weeks should remain.

Cancers of the esophagus and stomach

Timing after neoadjuvant therapy predicts mortality in patients undergoing esophagectomy. First Author: Taylor Maramara, Florida State University College of Medicine, Sarasota, FL

Methods: Utilizing the National Cancer Database, we identified patients with esophageal cancer who underwent NT followed by esophagectomy. Patients were divided into 4 time intervals: < 6 wks, 6-12 wks, 2-6 mos, and > 6 mo. Mann-Whitney U, Kruskal Wallis, and Pearson’s Chi-square test were used as appropriate. Survival analyses were performed using the Kaplan-Meier method and p < 0.05 was considered significant. Results: We identified 9,256 patients who received NT followed by esophagectomy. There were 8,053 (87%) adenocarcinomas and N = 1203 (73%) squamous cell carcinomas, 7,858 (84.9%) were male and 1,398 (15.1%) female with a median age was 62 (24-88). RTD resections decreased as the NT-Surgery interval increased: < 6 wks, 6-12 wks, 2-6 mos, and > 6 mos at 93%, 94.1%, 94.1%, and 86.2% respectively p = 0.004. Additionally, the median lymph nodes harvested decreased as timing increased:15.1, 13.1, and 2.4 p = 0.01. The complete response rates increased as timing increased: 15.5%, 20.1%, 22.7%, and 25.8% p < 0.001. However, this improvement in cCR did not translate into an increase in median survival: < 6 wks 40.9 mos, 6-12 weeks 38.5 mos, 2-6 mos 34.8 mos, and > 6 mos 39.8 mos of survival, p = 0.94 90-day mortality increased as the timing from neoadjuvant therapy increased: 6.4%, 7.9%, 9.4%, and 16.0%, respectively p = 0.001. Conclusions: Our data demonstrates that patients who have a prolonged NT-surgery interval will have a substantial increase in 90-day mortality. While there was an increase in pathologic complete response rates, this did not translate into an improvement in survival. The current recommendations of a NT-surgery timing of 6-12 weeks should remain.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Efficacy of capecitabine and oxaliplatin versus S-1 as adjuvant chemotherapy in gastric cancer after D2 lymph node dissection. First Author: Kabsoo Shin, The Catholic University of Korea, Seoul St. Mary’s Hospital, Seoul, Korea, Republic of (South)

Background: The aim of this study is to compare capecitabine and oxaliplatin (XELOX) with S-1 based on disease-free survival, and to define the clinical impact of lymph node ratio to select a regimen. Methods: Patients who had curative resection and received either S-1 or XELOX as adjuvant chemotherapy for gastric cancer between Jan. 2011 and Dec. 2015, were analyzed using propensity score matching (PSM). Of the 412 patients enrolled, 301 received S-1 and 111 received XELOX and after PSM, the sample size of each group was 111 patients. And the groups were classified according to stage and lymph node ratio (0, > 0-0.1, > 0.1-0.25, > 0.25) and three-year disease-free survival (DFS) was evaluated. Results: In post-PSM analysis of all 222 patients, The three-year DFS rates in XELOX group was higher than in the S-1 group in all stage 3 (78% vs. 66.1%, p = 0.036), stage IIIC (64.1% vs. 42.0%, p = 0.038) and LNR > 0.25 (67.1% vs. 26.1%, p = 0.002). The hazard ratio of XELOX for recurrence compared with S-1 for stage IIIC and LNR > 0.25 was respectively 0.479 (95% CI 0.238-0.985, p = 0.046) and 0.351 (95% CI 0.162-0.758, p = 0.008). Conclusions: Adjuvant XELOX was more effective than S-1 for stage IIIC and LNR > 0.25 in gastric cancer after D2 dissection.

Characteristics of long-term survivors in stage III gastric cancer patients. First Author: Youn Jang, Korea University College of Medicine, Seoul, Korea, Republic of (South)

Background: Stage III gastric cancer patients had poor prognosis. This study aims to evaluate prognostic factor of stage III gastric cancer. Methods: We retrospectively studied 126 patients who were treated for stage III gastric cancer from Jan. 2007 to Dec. 2010 at Korea University Hospital and performed complete follow up for five years. Long-term survivor was defined more than five years survivor after gastrectomy. Results: Long-term survivor was 70 patients (55.6%). Tumor size, lymph node involvement, lymphatic invasion, venous invasion and neural invasion had prognostic significance on univariate analysis. But location of tumor, gross type, depth of invasion, TNM stage, combine resection, complication, histologic differentiation, type of operation and adjuvant treatment had no prognostic significance. The most common recurrence pattern was peritoneal recurrence (57.4%) according to analysis of recurrence pattern. The disease free survival according recurrence pattern was peritoneal recurrence (21.3 months), hematogenous recurrence (32.1 months), distant lymph node recurrence (12.0 months) and locoregional (12.0 months). The disease specific survival according recurrence pattern was peritoneal recurrence (9.2 months), hematogenous recurrence (11.3 months), distant lymph node recurrence (16.2 months) and locoregional (26.9 months). Conclusions: Lymph node involvement were the most significant prognostic factors on stage III gastric cancer after curative resection. Therefore, postoperative surveillance and adjuvant therapy were very carefully selected in stage III gastric cancer patient with extensive lymph node metastasis.
Impact of adjuvant therapy in patients with a microscopically positive margin after resection for gastroesophageal cancer. First Author: Lucy Xiaoou Ma, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada

Background: A microscopically positive (R1) resection margin following resection for gastroesophageal (GE) cancer has been documented to be a poor prognostic factor. The optimal strategy and impact of different modalities of adjuvant treatment for an R1 resection margin remain unclear. Methods: A retrospective analysis was performed for patients (pts) with GE cancer treated at the Princess Margaret Cancer Centre from 2006-2016. Electronic medical records of all pts with an R1 resection margin were reviewed. Kaplan-Meier and Cox proportional hazards methods were used to analyze recurrence free survival (RFS) and overall survival (OS) with and without adjuvant treatment as covariates in the multivariate analysis. Results: We identified 78 GE cancer pts with an R1 resection. 11% had neoadjuvant chemotherapy, 14% chemoradiation (CRT), 75% surgery alone. 28% had involvement of the proximal margin, 13% distal, 56% radial, 3% had multiple positive margins. By the American Joint Committee on Cancer 7th edition classification, 88% had a pT3-4 tumour, 66% pN2-3 nodal involvement, 64% grade 3, 68% with lymphovascular invasion. 3% were pathological stage I, 21% stage II and 74% stage III. Adjuvant therapy was given in 46% of R1 pts (24% CRT, 18% chemotheraphy alone, 3% radiation alone, 1% reoperation). Median RFS for all pts was 12.6 months (95% CI 10.3-17.2). Site of first recurrence was 71% distant, 16% locoregional, 13% mixed. Median OS was 29.3 months (95% CI 22.9-50) for all pts. The 5 year survival rate was 23% (95% CI 12%-43%). There was no significant difference in RFS (log-rank test p = 0.63, adjusted p= 0.14) or OS (log-rank test p = 0.68, adjusted p= 0.65) regardless of adjuvant therapy. Conclusions: Most pts with positive margins after resection for GE cancer had advanced pathologic stage and prognosis was poor. Our study did not find improved RFS or OS with adjuvant treatment and only one pt had resection. The main failure pattern was distant recurrence, suggesting that pts being considered for adjuvant RT should be carefully selected. Further studies are required to determine factors to select pts with good prognosis despite a positive margin, or those who may benefit from adjuvant treatment.

Survival benefit of gastric resection in the setting of metastatic gastric cancer. First Author: Trang Nguyen, John Wayne Cancer Institute, Providence Saint John’s Health Center, Santa Monica, CA

Background: Prognosis remains poor for metastatic gastric cancer. Gastrectomy in the setting of stage IV disease is typically reserved for palliation of symptoms such as bleeding or obstruction. The potential survival benefit of resection in this setting remains controversial. We aim to determine using the National Cancer Database (NCDB) whether there was an increase in overall survival in patients diagnosed with metastatic cancer who underwent a gastrectomy in addition to chemotherapy. Methods: The NCDB was queried between 2004-2014 for patients with metastatic gastric cancer (adenocarcinoma, mucinous adenocarcinoma, or signet ring carcinoma) who received chemotherapy. Kaplan-Meier analysis and multivariate Cox proportional hazards regression analysis was done using SAS software. Results: A total of 20,599 patients met inclusion criteria. A minority of these patients (2,508; 12.2%) underwent gastric resection in addition to chemotherapy. The median overall survival for those who underwent gastrectomy was 14.1 months compared to 8.6 months for chemotherapy alone (p < 0.0001). Other factors influencing survival included age, race, Charlson-Deyo co-morbidity index, year of diagnosis, primary tumor site, grade, and metastasis to multiple organs. Following multivariate analysis, patients who underwent gastrectomy and chemotherapy had a 36% lower risk of death compared to patients who had received chemotherapy alone (HR 0.64, 95% CI 0.48-0.80, P < 0.0001). Conclusions: In this population analysis, the addition of gastrectomy to chemotherapy was associated with improved overall survival for patients with stage IV gastric cancer and should be considered for patients that are surgical candidates. Patients who underwent gastrectomy had a 36% decreased risk of death compared to those who had chemotherapy alone. However, only a small proportion of patients in the United States received multimodality treatment.

Impact of preoperative treatment with chemoradiotherapy or chemotherapy in patients with locally advanced or irresectable gastric cancer (LAGC). First Author: C Diaz Romero, INCAN, Mexico, DF, Mexico

Background: The only curative treatment for gastric cancer remains surgery neoadjuvant chemoradiotherapy (NACRT) has shown decrease of staging and improve survival. La NACRT has been studied in esophagus cancer and gastrectomy, but this trials don't include this setting of gastric cancer. The aim of our study was to investigate the role of Chemoradiotherapy (CRT) and chemotherapy (CT) in the treatment of LAGC. Methods: We retrospectively reviewed the medical records of 108 patients who were treated between December 2010 and January 2015, with preoperative CRT or chemotherapy preoperative (CT). Evaluating parameters of resectability, pathological response complete, prognostic with 3-year follow-up. Results: 108 patients were analyzed, 61 man and 47 women, with median age 55 years, 83 (76.8%) with diffuse, 25 (23.2%) intestinal histology, however 83 patients (76.8%) had component of signet ring cells. Of the 108 patients, 41 (38%) received chemotherapy and 67 (62%) received CRT preoperative. RO radical surgery was possible in 41 patients of which 24.3% (10/ 41) were in the group of CT and 46% (37/67) CRT group. Radiological progression was documented in 8 (19.5%) patients with CT and 11 (16.4%) with CRT. 7 patients were considered inoperable and 17 unresectable at the end of the preoperative treatment. The carcinomatosis was documented during the surgery in 11 and 12 patients in the CT or CRT group respectively. 10 patients developed complications gastrointestinal and hematologic to the treatment with CT and 23 patients with CRT, which 4 patients in CRT needed reoperation post-surgery. Any patient in the chemotherapy group reached complete pathologic response while of the CRT group achieved 5 complete pathological responses. Medium-3 years follow-up survival rate was 11% in the group treated with CT and 23% with CRT. Conclusions: Our revision showed a high rate of pathologic response and survival in patients with LAGC that received CRT preoperative followed by gastrectomy. On the other hand, R0 resection has been reported to be a predictive factor for survival in this study were found more patients with resectable tumor after CRT preoperative.
Tumor regression grade in gastric cancer after preoperative therapy. First Author: Naruhiko Ikoma, University of Texas MD Anderson Cancer Center, Houston, TX

Background: The AJCC 8th edition updated ypStage TNM grouping for patients with gastric cancer due to the increasing use of preoperative therapy. We previously reported that nodal status after preoperative therapy ypN is most predictive for overall survival (OS). We intended to investigate if tumor regression grade (TRG) of the primary tumor scored by pathologists is helpful to predict survival of gastric cancer patients treated with preoperative therapy.

Methods: We reviewed an institutional database to identify patients with clinically non-metastatic gastric adenocarcinoma who underwent gastrectomy after preoperative chemothero-chemoradiation therapy. Pathology reports were reviewed, and TRG was classified into following categories: 0 (complete response), 1 (few clumps of viable tumor cells, E1-2%), 2 (significant response, viable cells £ 50%), 3 (minor or no treatment response, viable cells > 50%). Associations between TRG and clinicopathological factors were examined. Univariable and multivariable Cox regressions were performed to determine associations with OS. Results: We identified 356 patients who met study criteria, including 80 (23%) patients with GEJ tumors; 56% were white and 60% were male. Preoperative chemoradiation therapy was given to 268 (75%). Fifty-six (16%) had TRG 0, 57 (16%) had TRG 1, 128 (36%) had TRG 2, and 115 (32%) had TRG 3. There were no associations between TRG and pretreatment factors. TRG 2 or 3 was associated with advanced ypT and ypN categories (both p < 0.001), ypM1 (p = 0.004), and R1 resection (0.052). Of all patients, median OS was 6.6 years, and 5-year OS was 54.1%. TRG 3 was associated with worse OS than other groups (p = 0.015), while there was no significant OS difference among TRG 0-2 groups (p = 0.803) in univariate analyses. On multivariable analysis, TRG was not associated with OS after adjustment for ypT status. Conclusions: In patients with gastric cancer who underwent preoperative therapy, TRG 3 was associated with advanced ypT and ypN and R1 resection. Patients with TRG 3 had worse OS, due to associated advanced ypStage, particularly ypM1 status. Further studies are warranted to identify better definitions of treatment response and to identify the optimal modality for obtaining ypNO status.

Impact of clostridium difficile infection on gastrointestinal malignancies. First Author: Stuthi Perimbeti, Mount Sinai St. Luke’s and Mount Sinai West Hospital, New York, NY

Background: According to the Centers for Disease Control and Prevention, there were half a million documented cases with 83,000 resections and 29,000 deaths due to Clostridium difficile infection (CDI) in the year 2011. The influence of CDI on outcomes in gastrointestinal(GI) malignancies is not well described, although the incidence is known to be higher in this subgroup of patients. Methods: National Inpatient Sample 1999-2014 was analyzed to identify adult admissions (>18 years of age) using ICD-9-CM codes with a primary diagnosis of esophageal(EC), Gastric(GC), Colorectal(CRC), Small intestinal(SIC), Hepatobiliary(HCC) and Pancreatic(PIC) cancers. ICD-9 code 00845 was used to stratify these for the presence of CDI. We performed Chi-Square test to determine the in-hospital mortality percentage, and Cox Proportional Hazard model to control for confounders and determine the Hazard Ratio(HR) of death within 30 days of admission during hospitalization in patients with and without CDI. Results: See table. Conclusions: Despite controlling for potential confounders, patients with GI cancers and CDI are all an increased risk of death compared to those without CDI. Taking the more detrimental effects of CDI in this subgroup of patients into consideration, healthcare professionals should strive to avoid the inordinate use of antibiotics and strictly maintain current guidelines designed to prevent spread. It may be prudent to treat these patients as severe CDI, even if current criteria are not met. More scientific research is warranted in analyzing the specific outcomes of CDI in GI cancer patients and if more aggressive therapy for CDI is warranted, considering the limitations of this study.

Prognostic significance of malnutrition in metastatic esophageal squamous cell carcinoma. First Author: Kirsty Taylor, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada

Background: Disease related symptoms including anorexia, nausea and dysphagia lead patients with esophageal cancer to become malnourished. Malnourishment can result in systemic inflammation, reduced treatment tolerance, poorer quality of life and decreased overall survival. Currently, weight loss is the main clinical measure of malnutrition, and thus we set out to evaluate the prognostic utility of alternative screening tools of malnutrition. Methods: Patients with metastatic esophageal squamous cell cancer (MESCC) presenting to Princess Margaret Cancer Centre, between 1st January 2011 and December 2016, were identified from the institutional gastro-esophageal database. Nutritional Risk Score (NRS), Nutritional Risk Index (NRI) and Neutrophil Lymphocyte Ratio (NLR) were calculated and correlated with clinical-pathological variables and survival. Malnutrition was defined as NRS ≥ 3, NRI < 97.5 and NLR ≥ 3: Results: Of the 64 consecutive patients, 30 (47%) presented with de novo metastatic disease and 34 (53%) with recurrent disease. The median age was 62 years (range 40-85), 47 patients were ECOG 0 and 57 (16%) had TRG 1, 56 (16%) had TRG 0, 128 (36%) had TRG 2, and 115 (32%) had TRG 3. There were no associations between TRG and pretreatment factors. TRG 2 or 3 was associated with advanced ypT and ypN (NACR) using a large nationwide cohort.

Poster Session (Board #M20), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Utility of radiation after neoadjuvant chemotherapy for surgically resectable esophageal cancer. First Author: Francis Igor Macedo, Sylvester Comprehensive Cancer Center, University of Miami School of Medicine, Miami, FL

Background: Neoadjuvant chemotherapy (NAC) is the gold standard approach for locally advanced esophageal cancer (EC), however the addition of radiation remains largely controversial. We sought to investigate the role of radiation after neoadjuvant chemotherapy by comparing outcomes of patients who underwent neoadjuvant chemotherapy with (NACR) or without radiation (NAC) using a large nationwide cohort.

Methods: National Cancer Data Base (NCDB) was queried for patients with non-metastatic EC between 2010 and 2014. Kaplan-Meier, log-rank and Cox multivariable regression analysis were performed to calculate overall survival (OS). Logistic regression was used to identify factors associated with 90-day mortality and complete pathological response (pCR).

Results: A total of 12,546 EC patients who underwent neoadjuvant therapy were included: the majority were males (84%), Caucasians (90.3%), and had adenocarcinoma (81%). CT3 (60.6%) and C11 (49.1%), 11,269 (89.8%) patients had NACR, whereas 969 (7.7%), NAC alone.

Conclusions: This is the largest study comparing NACR versus NAC in resected EC. The addition of radiation to neoadjuvant chemotherapy is associated with improved pathological response rates, however it had deleterious effects in long-term and possibly, short-term survival. Our findings suggest that NAC without radiation may be the optimal neoadjuvant therapy in resectable EC, however further evidence with randomized clinical trials is warranted.

Poster Session (Board #N2), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Poster Session (Board #N3), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Poster Session (Board #N4), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Poster Session (Board #N1), Thu, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
Background: Genetic cancer is the fifth most common cancer, and is the third leading cause of cancer deaths worldwide. In patients with HER2/neu overexpressing gastric or gastroesophageal junction (GEJ) adenocarcinoma, we hypothesized that administration of IMU-131 in addition to single peptides into a hybrid peptide conjugated to CRM197 in conjunction with the advajant Montanide (P467-CRM-Montanide) improved formulation and stability of the vaccine. With the present Phase Ib/2 trial performed in patients with HER2/neu overexpressing gastric or gastroesophageal junction (GEJ) adenocarcinoma, we hypothesized that administration of IMU-131 in addition to chemotherapy is safe and immunogenic, and will prolong survival and may delay tumor progression and/or reduce tumor burden. Methods: This is an international open-label multicenter study performed in 16 Asian and Eastern European sites with a maximum of 18 patients enrolled in Phase 1b. The study is ongoing and is due to start in September 2018. RAMONA also includes translational research to identify predictive biomarkers, establish organoid cultures from tumor tissues and assess the utility of microbiome analyses for response prediction. Clinical trial information: NCT03416244.

TPS174
Trials in Progress Poster Session (Board #N6), Thu, 11:30 AM-10:00 PM and 5:30 PM-6:30 PM
Multicenter open-label phase II trial to evaluate nivolumab and ipilimumab for second line therapy in elderly patients with advanced esophageal squamous cell cancer (RAMONA). First Author: Nadja M Meinr-Benker, Universität Hamburg, Hamburg, Germany

Background: Advanced esophageal squamous cell cancer (ESCC) is frequently diagnosed in elderly patients (pts) and impact of 2nd line chemotherapy is poorly defined. In line with recent data demonstrating effectiveness of checkpoint inhibitors Nivolumab (Nivo) and Ipilimumab (Ipi) in squamous cell carcinoma pts, combined Nivo/Ipi therapy will be assessed as 2nd line therapy in advanced ESCC in elderly pts. Meds: Nivo (240 mg Q2W)+Ipi (1 mg/kg Q6W) combination therapy. The other pts will remain on Nivo only. The primary objective of this trial is to demonstrate a significant survival benefit of the Nivo/Ipi combination therapy in advanced ESCC compared to historical data of standard chemotherapy regimens. Primary endpoint is overall survival (OS); secondary endpoints are tumor response, PFS, quality of life (QoL). The trial has a 90% Power to detect a hazard ratio of 0.68 at a one-sided significance level of alpha = 0.05 under the assumption of exponential survival. This corresponds to an increase of the 1-year OS rate by a margin of 13% compared to historical controls. The trial is powered to have 80% power to detect a 17% improvement in 1-year OS with an estimated 17% OS in historical controls. At interim analysis, the trial will stop if either 2 pts demonstrate objective response, the trial will stop. Subjects are accrued for a period of 12 month. Follow-up continues for 24 month after the last subject is added. Including a sample size increase to compensate for uninformative drop-outs a total of n = 75 subjects will be recruited. The primary endpoint will be assessed using the log-rank test. A particular study objective is the evaluation of the tolerability of Nivo as single agent and in combination with Ipi in terms of QoL. Therefore time to QOL deterioration will be determined. 18 pts have been enrolled by mid of September 2018. RAMONA also includes translational research to identify predictive biomarkers, establish organoid cultures from tumor tissues and assess the utility of microbiome analyses for response prediction. Clinical trial information: NCT03416244.

TPS175
Trials in Progress Poster Session (Board #N7), Thu, 11:30 AM-10:00 PM and 5:30 PM-6:30 PM
A phase II study of M6620 and irinotecan in TP53 mutant gastric and gastroesophageal junction (GEJ) adenocarcinoma patients (pts) (NCT03641313). First Author: Satya Das, Vanderbilt University Medical Center, Nashville, TN

Background: Progressive metastatic or unresectable gastric/GEJ adenocarcinoma pts carry dismal prognoses with a significant need for novel systemic therapies. One avenue for drug development in this disease is targeting DNA repair mechanisms. TP53, a central gene to DNA damage repair (DDR), is mutated in 50% of gastric/GEJ cancer pts. Preclinical models from multiple cancer types demonstrate that cancer cells with TP53 mutations rely on the ataxia telangiectasia and Rad-3 related protein kinase (ATR) axis as a prial cell survival mechanism. DDR in the face of cytotoxic stimulus, such as irinotecan is typically triggered by single strand DNA breaks as such of generated by topoisomerase I inhibitors. Irinotecan is already known to be active in later line gastric/GEJ pts, thus, there appears to be an opportunity to combine the agent with the ATR inhibitor M6620 in TP53 mutant pts with the disease. Methods: Our trial is a single arm phase II study of M6620 plus irinotecan in progressive gastric/GEJ adenocarcinoma pts. Only pts with TP53 mutations in exon 2 and exons 4-11, as determined by next-generation sequencing from archival tissue, will be eligible. Pts will receive 180 mg/m²/2 of irinotecan immediately followed by M6620 every 2 weeks; the M6620 dose will be determined based on the recommended phase 2 dose from the ongoing phase I trial. CT scans will be repeated every 2 months to assess response. The primary endpoint of the study is overall response rate (ORR), with a pre-specified target of 35%. Correlative studies will be performed on fresh tumor tissue from the first 9 pts, obtained by biopsies on day 1 of cycle 1 post-irinotecan and day 2 of cycle 2, to assess dynamic changes in the biomarkers specified target of 35%. Correlative studies will be performed on fresh tumor tissue from the first 9 pts, obtained by biopsies on day 1 of cycle 1 post-irinotecan and day 2 of cycle 2, to assess dynamic changes in the biomarkers phosphorylated Poly (ADP-ribose) polymerase proteins 1 and 2 (PARP1/2) are involved in DNA damage repair, and their inhibition is cytotoxic for cells with HRD. Pamiparib is a selective PARP1/2 inhibitor that crosses the blood-brain barrier, has shown potent DNA-PARP trapping, and has demonstrated antitumor activity in preclinical models. In early phase clinical studies (NCT02361723; NCT03339915), pamiparib was generally well tolerated and showed preliminary antitumor activity; 60 mg oral twice daily (BID) was established as the recommended dose. Methods: This ongoing, global, double-blind, placebo-controlled, randomized, multicenter phase II trial (NCT03427814) is designed to compare the efficacy, safety, and tolerability of pamiparib vs placebo as maintenance therapy in ~540 patients with advanced GC who have responded to first-line, platinum-based chemotherapy. Patients who are ~8 years after their last dose of first-line platinum based chemotherapy will be randomized 1:1 to receive either pamiparib 60 mg BID or placebo in 28-day cycles. Patient randomization will be stratified by the presence of high grade dysplasia (HGD) or invasive disease. The primary endpoint will be overall survival, objective response rates, time to second subsequent treatment. Correlative biomarker analyses in tumor tissues and blood will be performed. Clinical trial information: NCT03427814.

TPS176
Trials in Progress Poster Session (Board #N8), Thu, 11:30 AM-10:00 PM and 5:30 PM-6:30 PM
A phase Ib/II open label study of IMU-131 HER2/Neu peptide vaccine plus cisplatin and either 5-fluorouracil or capcitabine chemotherapy in patients with HER2/Neu overexpressing metastatic or advanced adenocarcinoma of the stomach or gastroesophageal junction. First Author: Ursula Wiedermann, Medical University Vienna, Vienna, Austria

Background: Gastric cancer is the 5th most frequently diagnosed cancer and the 3rd leading cause of cancer deaths. HER2/neu is overexpressed in 15% to 25% of patients with gastric cancer and associated with a poor prognosis. Monoclonal antibodies against HER2/neu have been shown to be effective but alternative treatments are needed due to cost and global availability issues. IMU-131 is a B-cell peptide vaccine composed of 3 B cell epitopes derived from different non-overlapping tumor peptide domains. Polyvalent administration of B-cell peptides binding 3 separate regions (DIll, IV) of HER2/neu have been shown to elicit antitumor activity in vitro and a phase I study demonstrated safety and immunogenicity in Her-2 +/+ metastatic breast cancer patients. Fusion of the single peptides into a hybrid peptide conjugated to CRM197 in conjunction with the adjuvant Montanide (P467-CRM-Montanide) improved formulation and stability of the vaccine. With the present Phase Ib/2 trial performed in patients with HER2/neu overexpressing gastric or gastroesophageal junction (GEJ) adenocarcinoma, we hypothesized that administration of IMU-131 in addition to chemotherapy is safe and immunogenic, and will prolong survival and may delay tumor progression and/or reduce tumor burden. Methods: This is an international open-label multicenter study performed in 16 Asian and Eastern European sites with a maximum of 18 patients enrolled in Phase Ib. The study is ongoing and is due to start in September 2018. RAMONA also includes translational research to identify predictive biomarkers, establish organoid cultures from tumor tissues and assess the utility of microbiome analyses for response prediction. Clinical trial information: NCT03416244.
A phase Ib study of nivolumab plus trastuzumab with S1-capacitabine plus oxaliplatin for HER2 positive advanced gastric cancer (NI-HIGH study). First Author: Daiusuke Takahari, Department of Gastroenterology, Cancer Institute Hospital, Japan. Tokyo, Japan

Background: Trastuzumab (Tmb) with cisplatin and fluoropyrimidines improved the overall survival (OS) of patients (pts) with HER2 (+) advanced gastric cancer (AGC). Nivolumab (Nivo) is an anti-programmed death-1 (PD-1) antibody that demonstrated a survival benefit as third line or later of AGC. To date, most trials investigating anti-PD-1 antibody for 1st line treatment of gastric cancer (AGC). Based on these data, we have planned this phase Ib investigator-initiated trial to investigate the safety and tolerability of Nivo plus Tmb and either S1 or capecitabine (Cape) plus Oxaliplatin (Ox) for pts with HER2 (+) AGC. Methods: Histopathologically confirmed HER2(+)+ AGC with measurable lesions, age > 20 years, chemosensitive pts are enrolled in this study. Pts receive Nivo (360 mg/body; day 1) plus Tmb (course1, 8 mg/kg; course 2 onward, 6 mg/kg; day 1) and either S1 (40 mg/m² bid d1-14; cohort 1) or Cape (1000 mg/m² bid d1-14; cohort 2) plus Ox (130 mg/m²; day 1) every three weeks until disease progression or unacceptable toxicity. In the primary part, six pts for each part for each cohort will be assessed for tolerability. To estimate the objective response rate (ORR) in the analysis set, on our hypothesis that a true response rate is 80%, 20 pts are required for the 90% CI to be ± 20%. Therefore the expansion part for each cohort will be 12-15 pts. Primary endpoint is safety. Target sample size will be also analyzed using blood obtained during treatment. This study has just been initiated at four sites in Japan. Clinical trial information: UMIN000034222.

TPS179 Trials in Progress Poster Session (Board #N11), Thu, 11:30 AM-10:00 PM and 5:30-6:30 PM

bTMB-High Basket trial: A multicenter phase II trial of nivolumab monotherapy in patients with advanced gastrointestinal cancers with high blood tumor mutational burden (bTMB). First Author: Yoshiaki Nakamura, Department of Gastroenterology and Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa, Japan

Background: Tumor mutational burden (TMB) is an emerging biomarker for immune checkpoint inhibitors (ICis) in non-small cell lung cancer (NSCLC). Analysis of circulating tumor DNA (ctDNA) has been reported to effectively identify patients likely to respond to ICIs by non-invasively evaluating the TMB in the tumor in NSCLC and gastric cancer. Methods: We are conducting an investigator-initiated multicenter phase II basket trial to investigate efficacy of nivolumab monotherapy in patients with advanced gastrointestinal (GI) cancers with high bTMB identified by ctDNA analysis as part of the Nationwide Genome Screening Project (SCRUM-Japan GI-SCREEN). Eligibility criteria include histologically confirmed unresectable or recurrent GI malignancies; ECOG PS of 0 or 1 refractory or intolerant to standard therapies; and high bTMB identified by a 73-gene sequencing ctDNA panel (Guardant360) regardless of microsatellite instability status. Patients will be enrolled into one of four disease-specific cohorts (colorectal, gastric, esophageal, and other GI cancer cohort), and receive intravenous nivolumab monotherapy of 360 mg every 3 weeks. The bTMB score is calculated by adjustment of mutation count by tumor fraction, and tentative bTMB level cut-offs were determined according to objective response rate (ORR) reported for IC therapy for each tumor subtype in previous trials. The trial will utilize a two-stage design with a Bayesian hierarchical model, and tentative bTMB level cut-off will be re-assessed in the first stage. Primary endpoint in each stage is the disease control rate at 6 week and the ORR assessed by investigators per RECIST v1.1, respectively. Target sample size is determined as ≥ 20 in total so that the statistical power in each disease-specific cohort calculated based on a Bayesian posterior distribution attains 70 to 80% with one-sided alpha level in each cohort of approximately 10%. For biomarker analysis, ctDNA material and DNA will be serially collected and analyzed by whole-exome, transcriptome, and T cell receptor sequencing. This trial was initiated since September 2018. Clinical trial information: UMIN000033182.

TPS180 Trials in Progress Poster Session (Board #N12), Thu, 11:30 AM-10:00 PM and 5:30-6:30 PM

A phase II, multicenter, open-label study of [fam-] trastuzumab deruxtecan (DS-8201a) in subjects with HER2-expressing gastric cancer. First Author: Kohei Shihtara, National Cancer Center Hospital East, Chiba, Japan

Background: There is no HER2-targeted therapy for patients with HER2-positive gastric cancer (GC) who progressed on trastuzumab-based therapy. [fam-] trastuzumab deruxtecan (DS-8201a) is a novel HER2-targeted antibody-drug conjugate with a humanized HER2 antibody, forapertitumab vedotin, payload, cleavable peptide-based linker, and high drug-to-antibody ratio of approximately 8. In an ongoing phase I trial, [fam-] trastuzumab deruxtecan showed an acceptable safety profile and promising antitumor activity in salvage-line subjects with HER2+ GC who previously received trastuzumab (confirmed objective response rate [ORR] of 43.2% [9/44]; Iwata et al, ASCO 2018). Methods: The randomized, phase II, multicenter, open-label, DESTINY-Gastric01 study will assess the efficacy and safety of [fam-] trastuzumab deruxtecan in HER2-expressing GC. The primary cohort, HER2+ (IHC 3+ or IHC 2+/ISH+) GC subjects who progressed after ≥ 2 prior regimens and previously received trastuzumab, will be randomized (2:1) to [fam-] trastuzumab deruxtecan (6.4 mg/kg dose; over 3 weeks) or physician choice (R) treatment. The primary endpoint is the ORR assessed by investigators per RECIST v1.1, respectively, Target sample size is 150 with one-sided alpha level in each cohort of approximately 10%. For biomarker analysis, ctDNA material and DNA will be serially collected and analyzed by whole-exome, transcriptome, and T cell receptor sequencing. This trial was initiated in August 2017. As of Feb 18, 2018, 15 of 150 subjects have been enrolled. Clinical trial information: UMIN000032382.
Background: Neoadjuvant chemoradiation (CRT) followed by resection is the standard treatment for patients with stage II and III esophageal cancer. However, about 50% of patients develop recurrent disease after treatment completion. Patients with residual disease at the time of resection (~75%) and especially those with persistent lymph node involvement have the worst prognosis. Hence, novel strategies are needed to improve outcomes. A number of preclinical and clinical studies demonstrated synergism between radiation and immunotherapy. In esophageal cancers, CRT has been shown to alter tumor microenvironment with upregulation of PD-L1 expression and increase in CD8+ T lymphocyte infiltration. Immune checkpoint inhibitors have demonstrated promising activity in metastatic gastroesophageal cancer. Utilizing these agents in earlier disease stages and combining with chemoradiation may increase their efficacy by taking advantage of potential synergism with radiation. This trial will evaluate safety and efficacy of avelumab in combination with radiation may increase their efficacy by taking advantage of potential synergism with radiation. This trial will evaluate safety and efficacy of avelumab in combination with CRT in resectable esophageal cancer. Methods: This is a two-part phase I/II clinical trial evaluating safety and efficacy of perioperative avelumab plus CRT in patients with resectable esophageal cancer. Methods: This is a two-part phase I/II clinical trial evaluating safety and efficacy of perioperative avelumab plus CRT in patients with resectable esophageal cancer. This trial will enroll a total of 24 subjects with untreated resectable esophageal cancer (including gastroesophageal junction). Part 1 will be a run-in phase that enrolls 6 patients for safety evaluation. Part 2 will enroll 18 additional patients for efficacy and additional safety evaluation. The primary endpoint for the phase II component is the pathological complete response rate. Subjects will receive neoadjuvant radiation (41.4 Gy in 23 fractions) with weekly carboplatin (AUC 2) and paclitaxel (50 mg/m2). Three doses of avelumab (10 mg/kg, every 14 days) will be administered starting on day 29 of treatment, to coincide with the last chemotherapy dose. Esophagectomy will be performed ~8 weeks after CRT completion. Subjects will receive 8 doses of avelumab after resection. This study is actively enrolling patients at University of Wisconsin. Clinical trial information: NCT03490292.

Background: As second-line chemotherapy for gastric cancer, a survival benefit has been shown in several clinical trials. Irinotecan and taxanes are recommended as second-line regimen. However, therapeutic outcomes have remained unsatisfactory and more effective treatment are expected. Ramucirumab (RAM) is a fully human IgG1 monoclonal vascular endothelial growth factor receptor-2 (VEGFR-2) antibody that prevents ligand binding of VEGF-A, VEGF-C, and VEGF-D and the receptor-mediated pathway activation in endothelial cells, subsequently inhibiting neovascularization. In the REGARD study, RAM monotherapy for previously treated advanced gastric or gastro-esophageal junction adenocarcinoma improved median overall survival (mOS) compared with placebo. Moreover, in the RAINBOW study, RAM plus paclitaxel (PTX) versus placebo plus PTX, mOS showed significantly longer in RAM plus PTX group than in placebo plus PTX group. In contrast, there are no data on the efficacy of RAM and irinotecan in the second-line treatment for gastric cancer. The WJOG 4007 study demonstrated an equivalent efficacy between irinotecan and PTX. In this study, we propose to examine the efficacy of RAM plus irinotecan. Methods: This study is carried out as a multicenter, non-randomized, single arm, prospective, phase II study. The patients with metastatic or advanced gastric adenocarcinoma are randomized to laparoscopic PG with double tract reconstruction and laparoscopic TG with esophagojejunostomy. Patients are enrolled for two years and followed up for two years. Primary co-endpoints are prevalence rate of postoperative reflux esophagitis, morbidity and mortality, quality of life 2-year after operations, relapse-free survival, and overall survival. Nineteen investigators from 10 institutes participated in this trial. The first patient was enrolled on October 27, 2016 and we completed the patient enrollment on September 17, 2018. Clinical trial information: UMIN000030372.

**TPS181**

Phase I/II trial of perioperative avelumab in combination with chemoradiation in the treatment of stage II/III resectable esophageal cancer. First Author: Nataliya Volodymyrivna Uboha, University of Wisconsin Carbone Cancer Center, Madison, WI

**TPS183**

HGCSG 1603: Phase II study of ramucirumab and irinotecan combination therapy as second-line treatment in patients with metastatic or advanced gastric cancer. First Author: Atsushi Ishiguro, Teine Keijinkai Hospital, Sapporo, Japan

**TPS184**

Multicenter prospective randomized controlled trial of comparing laparoscopic proximal gastrectomy and laparoscopic total gastrectomy for upper third early gastric cancer (KLASS-05). First Author: Do Joong Park, Seoul National University Bundang Hospital, Seongnam-Si, Korea, Republic of (South)

**TPS185**

Clinical trial information: NCT02892643.
Randomized, open-label, perioperative phase II trial studying nivolumab alone versus nivolumab plus ipilimumab in patients with resectable HCC.

**Background:** In HCC, surgical resection is associated with high recurrence rate, and no established neoadjuvant or adjuvant therapies comparable to immune checkpoint inhibitors (ICI) exist. The basis of previous reports on the efficacy and safety of anti-PD-1 and anti–CTLA-4 antibodies against HCC, we initiated a randomized pilot trial of perioperative immunotherapy for resectable HCC.

**Methods:** This is a randomized phase II trial of nivolumab (Arm A) or nivolumab plus ipilimumab (Arm B) as perioperative treatment for patients (pt) with HCC who are eligible for surgical resection. Pt are given nivolumab 240 mg every 2 weeks (wk) for a total of 6 wk. Pt in Arm B are treated concurrently with ipilimumab 1 mg/kg every 6 wk. Surgical resection occurs within 4 wk after last cycle of therapy. Pt continue adjuvant immunotherapy for up to 2 years after resection. Primary objective is the safety and tolerability of nivolumab +/- ipilimumab. Secondary objectives include overall response rate, complete response rate and time to progression. Exploratory objectives include evaluating the pre- and post-treatment immunological changes in tumor tissues and peripheral blood.

**Results:** 9 pt were enrolled at the time of first interim analysis, and 8 pt were evaluable (5 in Arm A, 3 in Arm B). Pt were 60-69 yo, and males (78%). 5 pt were HCV-positive and 1 had chronic hepatitis B infection. 8 pt proceeded with resection as planned, surgical resection was aborted for technical reasons in 1 pt because of previous surgery. Pathologic complete response (pCR) was observed in 3/8 pt in Arm A and 3 (37.5%) pt in Arm B. 2 pt in Arm B and 1 in Arm A experienced grade 3 or higher toxicity which did not affect their resectability. No grade 4 or higher toxicities were observed. Immune analysis performed in the first case with a pCR in Arm A demonstrated that clinical response correlated with an increase in CD8+ T cell infiltration, notably an increase in two effector T cell clusters.

**Conclusions:** We report a pCR rate of 37.5% in the first interim analysis of a phase II pilot trial of perioperative immunotherapy for resectable HCC. Treatment was deemed safe and surgical resection was not delayed. The study is ongoing and results may contribute to a paradigm shift in the perioperative treatment of HCC.

**Clinical trial information:** NCT03222076.
**Background:** Despite improvements of postoperative adjuvant chemotherapy for resected pancreatic ductal adenocarcinoma (PDAC), its prognosis remains poor. A randomized controlled trial has been initiated to compare neoadjuvant chemotherapy using gemcitabine and S1 (NAC-GS) with upfront surgery (Up-S) for patients with PDAC planned resection. **Methods:** Patients were enrolled after a diagnosis of resectable PDAC with histological confirmation. They were randomly assigned as either NAC-GS or Up-S. In NAC-GS, gemcitabine was provided at a dose of 1g/m² on day 1 and 8 and oral S1 was administered at a dose of 40mg/m² twice daily on 1-4 days. Patients received 2 cycles of this regimen. S1 adminis-tered for 4 months was administered for the patients in current surgery and fully recovered within 10 weeks after surgery in both arms. The primary endpoint for the III part was overall survival (OS); secondary endpoints included adverse events, resection rate, recurrence-free survival, residual tumor status, nodal metastases, and tumor marker kinetics. **Results:** First, a total of 364 patients were enrolled in 57 centers (182 to NAC-GS and 182 to Up-S). Of these, two were excluded because of ineligibility, therefore 182 patients in NAC-GS and 180 in Up-S constituted the ITT analysis-set. The median OS was 36.7 months in NAC-GS and 26.6 months in Up-S; HR 0.72 (95% confidential interval 0.55-0.94; p=0.015 [stratified log-rank test]). Grade 3 or 4 adverse events frequently (72.8%) observed in NAC-GS were leukopenia or neu-ropenia. However, the resection rate, R0 resection rate, and morbidity of the operation were equal in the two groups. There was no perioperative mortality in either group. **Conclusions:** This phase III study demonstrated the significant survival benefits of NAC-GS treatment. Therefore, the results indicated that neoadjuvant chemotherapy could be a new standard for patients with resectable PDAC. **Clinical trial information:** UMIN000009634.
193

Poster Session (Board #A99), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Distribution of insulin growth factor-1 (IGF-1) binding proteins in hepatocellular carcinoma with and without cirrhosis. First Author: Ahmed Abdelkaheem, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Circulating insulin-like growth factor-1 (IGF-1) significantly decreases in patients (pts) with cirrhosis and hepatocellular carcinoma (HCC), reflecting damaged hepatocytes. The bioavailability of IGF-1 is controlled by insulin-like growth factor binding proteins (IGFBPs), which bind IGF-1. IGFBPs transcribe into cell specific, and are secreted mainly by the liver. Variations in circulating IGFBPs in HCC pts, especially those with non-cirrhotic HCC, has not been elucidated. We investigated the expression of these proteins in HCC with and without cirrhosis. Methods: Under Institutional Review Board approval, we measured plasma levels of seven IGFBPs in 489 cirrhotic HCC pts, 274 non-cirrhotic HCC pts, 75 pts with cirrhosis without HCC, and 200 healthy controls.

Also, we assessed variations in IGFBPs plasma level between early and advanced stage HCC in the presence and absence of cirrhosis. Levels of circulating biomarkers were summarized by descriptive statistics, and both Chi-square and ANOVA tests were used to compare levels between groups. Results: IGFBPs levels varied significantly between groups. Table: Moreover, IGFBP-3 was lower in HCC pts than in healthy controls (p < 0.001), and IGFBP-1, -2, -4, and -7 were higher in HCC without cirrhosis than in healthy controls (p = 0.001 for all). Additionally, in non-cirrhotic HCC pts, a similar pattern was observed in advanced stage HCC compared with early stage HCC. Conclusions: Levels of circulating IGFBPs may be associated with risk of non-cirrhotic HCC and could be used as markers for underlying liver damage.

Mean ± standard error of IGFBPs (ng/ml) by different groups of pts.

<table>
<thead>
<tr>
<th>Marker</th>
<th>HCC with Cirrhosis</th>
<th>HCC Without Cirrhosis</th>
<th>HCC Healthy Controls</th>
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</thead>
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<tr>
<td>IGFBP-1</td>
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<td>10.9 ± 10.8</td>
<td>9.8 ± 4.5</td>
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<tr>
<td>IGFBP-2</td>
<td>2091 ± 45.7</td>
<td>254.7 ± 17.2</td>
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<tr>
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<td>2568 ± 57.4</td>
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<td>634 ± 29.6</td>
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<td>IGFBP-5</td>
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<td>120 ± 2.5</td>
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<td>IGFBP-6</td>
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<td>5629 ± 30.4</td>
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<td>IGFBP-7</td>
<td>154 ± 3.4</td>
<td>176 ± 3.7</td>
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</table>

Where: N = 489, N = 274, N = 75, N = 200. P < 0.01.

194

Poster Session (Board #A10), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Peritoneal carcinomatosis (PC) in well-differentiated (WD) small-intestinal neuroendocrine tumor (SI-NET) patients (Pts) with mesenteric tumor deposits (MTDs). First Author: Satya Das, Vanderbilt University Medical Center, Nashville, TN

Background: Although WD SI-NETS are typically biologically indolent, they tend to metastasize. PC is a dreaded regional metastatic complication in pts with SI-NETs and contributes to significant morbidity and mortality. Risk factors for PC development in these pts are not well studied, however, one factor may be MTD presence. Our analysis is the first to suggest an association between MTD presence and PC in this pt subgroup. Methods: We performed a retrospective analysis on 191 WD SI-NET samples from Vanderbilt University Medical Center with mesenteric masses identified on gross pathology or radiographic review. Of 138 samples with suspected MTDs, 79 were confirmed definitively by detailed pathologic review and were considered likely based on descriptions from surgical pathology reports. We assessed whether pts in our cohort with MTDs had greater rates of PC compared to those without MTDs. We also assessed what other patient determinants were associated with PC and the prognostic role of these determinants. Results: Pts with suspected MTDs had an odds ratio (OR) of 3.9 for PC compared to pts without MTDs. Rates of PC in pts with definitive MTDs and those with likely MTDs were not significantly different (OR = 1.0). Although suspected MTD presence was not associated with poorer OS (p = 0.97), pts with confirmed MTDs had a trend toward a shorter median survival (OS) than pts with likely MTDs (p = 0.05). PC was a negative prognostic factor in all pts with regards to OS (p = 0.044).

Conclusions: SI-NET pts with MTDs appear to have significantly increased rates of PC compared to those without mesenteric deposits. We believe this observation merits prospective evaluation given its potential therapeutic implications. If confirmed prospectively, pts with MTDs could benefit from earlier use of cytoreductive therapies to hinder development of PC.

195

Poster Session (Board #A11), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Determination of 0-6-methylguanine-DNA methyltransferase by immunohistochemistry and pyrosequencing as a predictive factor of response to temozolomide in pancreatic neuroendocrine tumors. First Author: Roberto Escala, Department of Medical Oncology, Complejo Asistencial Universitario de Salamanca, Salamanca, Spain

Background: Temozolomide (TMZ) is an alkylating agent that has shown good results in the treatment of neuroendocrine and central nervous system (CNS) tumors. The presence of 0-6-methylguanine-DNA methyltransferase (MGMT) expression by pyrosequencing (PSQ) is a predictive factor of response to treatment with TMZ in high-grade gliomas. However, its predictive value in pancreatic neuroendocrine tumors (pNET) is controversial, and there is no consensus on how to best assess MGMT. The aim was to evaluate the objective response rate in pNET according to the state of MGMT, assessed by PSQ for evaluation of promoter methylation and immunohistochemistry (IHC). Methods: Patients with pNET who were treated with TMZ at the center between 2004 and 2014 were studied retrospectively. Ten patients were included in the study. A deficiency of MGMT was determined by IHC and MGMT promoter methylation by PSQ. For IHC, the cut-off was 10%, defined as negative < 10% of tumor cells positive in the tissue. For the PSQ, the cut-off was 8%, defined as methylated as presented > 8%. Results: A deficiency of MGMT was detected in five patients (50%) by IHC. An MGMT promoter methylation by PSQ was observed in three patients (30%). The IHC results were consistent with PSQ results in only six patients (60%); one patient with methylated MGMT had positive IHC, and three patients had unmethylated MGMT by PSQ unmethylated, IHC negative. PSQ had a high positive predictive value of response because the three patients with MGMT promoter methylation by PSQ presented objective responses (OR). Nevertheless, a low negative predictive power (57%) was observed because three of seven patients with unmethylated MGMT presented OR. Of the five patients with MGMT deficiency by IHC, four (80%) presented OR, suggesting positive predictive value of 80%; however, it also presented a low negative predictive power of 60% as other conclusions: Despite having 100% of the patients with MGMT promoter methylation showing OR in this series, the low negative predictive power suggests that the absence of MGMT deficiency by IHC or MGMT unmethylated by PSQ does not contraindicate the use of TMZ in pNET treatment.

196

Poster Session (Board #A12), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

The clinical implication of CD45RA+ naive T cells and CD45RO+ memory T cells in advanced pancreatic cancer: A proxy for tumor biology and outcome prediction. First Author: Junjie Hang, The Changzhou Second People’s Hospital Affiliated With Nanjing Medical University, Changzhou, China

Background: Naive and memory T cells play a pivotal role in solid tumor pathogenesis but their role in pancreatic cancer progression remains elusive. Thus, we aimed to investigate their clinical potential in advanced pancreatic cancer (APC). Methods: Flow cytometry was performed to evaluate the level of peripheral naive and memory T cells from APC patients. Interrelationships between naive, memory T cells and clinicopathological variables were evaluated using Pearson’s correlation. The prognostic impact of naive and memory T cells were assessed by Kaplan-Meier analysis and Cox regression. The correlation between naive/memory T cells and tumor progression was investigated by Student’s t test. Results: CD4+ naive/memory ratio showed close correlations with hemoglobin, red blood cell (RBC), absolute neutrophil count (ANC) and platelet while CD8+ naive/memory ratio was correlated with hemoglobin, RBC and CEA. Higher baseline level of CD4+CD45RO+/CD45RA+ was correlated with better overall survival (OS) (P = 0.036). Patients with CD4+ naive/memory ratio ≥ 0.36 had a poorer OS than those with CD4+ naive/ memory ratio < 0.36 (P = 0.021). In addition, CD4+ naive/memory ratio showed independent prognostic impact (HR 1.427, 95%CI 1.033-1.973, P = 0.031). Furthermore, poorer clinical response was correlated with higher level of CD8+ naive/memory ratio after the third cycle of chemotherapy (P < 0.01). Besides, patients with an low level of CD8+ naive/memory ratio had longer progression-free survival (PFS) (P = 0.028). Conclusions: We propose CD4+ naive/memory ratio as a novel prognostic biomarker for APC. In addition, CD4+ naive/memory ratio can be a candidate marker for predicting PFS and the change of its level may reflect the progression of APC.

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Development of a nomogram to predict overall survival in patients presenting with gastrointestinal neuroendocrine carcinoma (WHO G3). First Author: Zhenyu Lin, Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

**Background:** To evaluate the prognostic factors in patients with gastrointestinal neuroendocrine carcinoma (WHO G3), we developed a nomogram to predict 1-year overall survival (OS). **Methods:** We performed a retrospective analysis of 122 patients with GI-NEC. Nomogram for 1-year OS was created as visualizations of Cox proportional hazards regression models and internally validated by use of bootstrap and cross-validation. We assessed nomogram model performance by examining overall accuracy (Brier score), calibration (calibration plot), and discrimination (Harrell C index).

**Results:** The median survival was 9 months in 122 patients, and 51 (41.8%) patients died in the development cohort. A 1-year OS was chosen because 82% of the patients who died from disease did so within 1 year. Multivariable analysis identified prognostic factors including performance status, stage, Ki-67 index, and LDH, all of which were included in the final model. In the development cohort, the Harrell C index for overall survival was 0.887 (95% CI 0.810–0.964), and calibration curves showed adequate calibration (judged by eye) of the observed and predicted probabilities.

**Conclusions:** Prognostic factors were used to develop nomograms for 1-year OS for GI-NEC. The nomogram can be offered to clinicians to improve their abilities to assess patient prognosis, strengthen the prognosis-based decision making, enhance patient stratification, and inform patients in the clinic.

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Predictive factors for major complications after pancreaticoduodenectomy in patients aged 80 years or older. First Author: Naoya Takeda, Department of Surgery, Iioiga General Hospital, Niigata Federation of Agricultural Cooperative Associations, Iioiga, Japan

**Background:** As the population ages, elderly patients are being diagnosed with peripampillary tumors, and hence, it has been suggested that surgeons should consider the indications for pancreaticoduodenectomy (PD) in elderly patients. The aim of this study is to reveal risks and benefits of PD, and to identify prognostic inflammatory biomarkers for major complications after PD in patients aged 80 years or older. **Methods:** We retrospectively analyzed the cases of 161 consecutive patients who underwent PD between January 2000 and December 2015, and compared the patients aged ≥ 80 years (n = 22) with those aged < 80 years (n = 139). Postoperative results and preoperative conditions such as nutrition status using controlling nutritional status (CONUT) score, hemoglobin level and comorbidity were assessed. Correlations were evaluated between major postoperative complications (Clavien-Dindo grade III or higher) and 6 systemic inflammation-based prognostic score such as Glasgow prognostic score (GPS), modified-GPS, High sensitive-CMP, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio (PLR), and prognostic nutritional index in elderly patients. **Results:** There was no operative mortality. In elderly patients, postoperative hemoglobin level was lower and CONUT score was higher than in younger patients. The complication rates and the disease-specific survival did not differ significantly between the two groups. Ten patients (45%) experienced major complications in the elderly group. Among 6 systemic inflammation-based prognostic score, only PLR was revealed as predictor of major complications (p = 0.012) and optimal cutoff value was determined to be 145.3 (sensitivity = 33%, specificity = 100%, AUC = 0.842). **Conclusions:** PD could be performed safely in patients aged 80 years or older. The predictive PLR was a simple and useful predictor of major complications after PD in elderly patients.

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Baseline and longitudinal quantification of lean muscle mass using routine CT measurements prior to resection for pancreatic adenocarcinoma. First Author: Paul Elezzer Oberstein, New York University Perlmutter Cancer Center, New York, NY

**Background:** When compared to healthy populations subjects are defined as sarcopenic if they have severe loss of lean mass (LMM) and reduced muscle strength. Sarcopenia is associated with poor outcomes in some studies of pancreatic cancer (PDA) but the prevalence remains uncertain in resected patients and there is little data about changes in LMM during neoadjuvant chemotherapy. Muscle mass can be reliably quantified in cancer patients using routinely acquired imaging. We imaged a large cohort of patients undergoing surgery at a high-volume center to quantify LMM at baseline and with treatment, and to determine the association of sarcopenia with tumor histology and outcomes. **Methods:** We analyzed subjects undergoing surgery for PDA at the Pancreatic Center at Columbia University from 2011-2014. We used the images to measure cross sectional area of muscle at the L3 vertebral body (LMM in cm²) and used height to define a smooth muscle index (SMI-cm/m). Sarcopenia was defined based on SMI < 8.19 for females and < 5.54 for males. In subjects undergoing neoadjuvant chemotherapy, SMI was also calculated on post therapy scans. We collected information on clinical and pathological variables and performed statistical analyses using SAS 9.4 software. **Results:** Among subjects with available imaging (n = 106) sarcopenia rates at initial staging were high whether they were immediately resectable (52%) or locally advanced (63%). Rates of sarcopenia were higher in males than females (77 vs 38%, p < 0.001). Sarcopenic status was not correlated with survival, tumor stage or grade but was associated with age, gender, and BMI. Among locally advanced subjects who proceeded to surgery after neoadjuvant chemotherapy (n = 40) the prevalence of sarcopenia was 36% with no change in SMI or incidence of sarcopenia following treatment (median 171 days). **Conclusions:** Sarcopenia is highly prevalent at diagnosis in subjects undergoing surgery for PDA but was not associated with survival, tumor grade or staging in this cohort. Subjects who successfully completed neoadjuvant treatment did not experience significant loss in LMM despite extensive treatment suggesting that lack of change in LMM may assist in predicting favorable response to neoadjuvant therapy in PDA.

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Predictive factors for major complications after pancreaticoduodenectomy in patients aged 80 years or older. First Author: Naoya Takeda, Department of Surgery, Iioiga General Hospital, Niigata Federation of Agricultural Cooperative Associations, Iioiga, Japan

**Background:** As the population ages, elderly patients are being diagnosed with peripampillary tumors, and hence, it has been suggested that surgeons should consider the indications for pancreaticoduodenectomy (PD) in elderly patients. The aim of this study is to reveal risks and benefits of PD, and to identify prognostic inflammatory biomarkers for major complications after PD in patients aged 80 years or older. **Methods:** We retrospectively analyzed the cases of 161 consecutive patients who underwent PD between January 2000 and December 2015, and compared the patients aged ≥ 80 years (n = 22) with those aged < 80 years (n = 139). Postoperative results and preoperative conditions such as nutrition status using controlling nutritional status (CONUT) score, hemoglobin level and comorbidity were assessed. Correlations were evaluated between major postoperative complications (Clavien-Dindo grade III or higher) and 6 systemic inflammation-based prognostic score such as Glasgow prognostic score (GPS), modified-GPS, High sensitive-CMP, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio (PLR), and prognostic nutritional index in elderly patients. **Results:** There was no operative mortality. In elderly patients, postoperative hemoglobin level was lower and CONUT score was higher than in younger patients. The complication rates and the disease-specific survival did not differ significantly between the two groups. Ten patients (45%) experienced major complications in the elderly group. Among 6 systemic inflammation-based prognostic score, only PLR was revealed as predictor of major complications (p = 0.012) and optimal cutoff value was determined to be 145.3 (sensitivity = 33%, specificity = 100%, AUC = 0.842). **Conclusions:** PD could be performed safely in patients aged 80 years or older. The predictive PLR was a simple and useful predictor of major complications after PD in elderly patients.

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**201** Poster Session (Board #A17), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Hepatocellular carcinoma (HCC) survival by etiology: A SEER-Medicare database analysis. First Author: Gagandeep Brar, National Cancer Institute, Bethesda, MD

**Background:** HCC is the 6th most common occurring cancer worldwide and the 4th leading cause of cancer mortality, with a survival of 6-9 months. While survival varies by stage at diagnosis and treatment, the effect of HCC etiology on survival is unclear. We analyzed the SEER-Medicare database to evaluate whether HCC survival varied by etiology, after adjusting for stage, treatment, and survival. **Methods:** A total of 11,522 SEER-Medicare HCC cases (ICD-O-3 codes C22 for topography, B70-B775 for morphology) met criteria for the Cox proportional hazard analyses to assess survival differences among the risk factors for hepatitis C virus (HCV) infection, hepatitis B virus (HBV) infection, alcohol disorders, and metabolic disorders. These analyses were adjusted for covariates for gender, age at diagnosis, race, ethnicity, tumor size and extent of disease, a modified Charlson Index of comorbidities, and treatments that included resection, transplantation, ablation, arterial directed therapy and radiotherapy. Cases with multiple and unknown etiologies were included in analyses, however genetic disorders and primary biliary cirrhosis were excluded due to their rarity. **Results:** HBV associated cases had the highest proportion of single nodules (40% vs 33% overall), localized stage disease (57% vs 49%), treatment (40% vs 27%), and greatest frequency of resection (18.6% vs 9%). Non-Hispanic Asians/Pacific Islanders accounted for 66% of HBV infection-related HCC cases but only 16% of all cases. HBV associated cases had better survival than did HCC cases with other etiologies. Specifically, after adjusting for demographic and clinical attributes, compared to cases with HBV infection, the risk of death was highest for alcohol-related HCC (HR=1.69; 95% CI 1.40-1.64), metabolic disorders (HR = 1.32; 95% CI: 1.10-1.53), and HCC of unknown etiology (HR = 1.22; 95% CI: 1.04-1.43). **Conclusions:** Persons with HBV associated HCC had better survival than persons with HCC of other etiologies. Efforts to identify people with any etiologic risk factors for HCC, treat their conditions, and screen for HCC may improve survival overall.

**203** Poster Session (Board #A19), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

CA19-9 decrease and overall survival according to platelet level in patients with metastatic pancreatic cancer. First Author: Yang Chen, Chinese People’s Liberation Army General Hospital, Beijing, China

**Background:** Several studies have linked a decrease of carbohydrate antigen (CA) 19-9 to lengthened survival in pancreatic cancer. Experimental evidence supported that CA19-9 may be involved in platelet/tumor cell interactions. The objective of this study is to correlate CA19-9 with survival correlated to platelet level in metastatic pancreatic cancer. **Methods:** A retrospective analysis of patients with histologically diagnosed metastatic pancreatic cancer was performed. CA19-9 serum concentration and platelet level was measured at baseline and every 6 weeks. **Results:** Total 174 metastatic pancreatic cancer patients with baseline and week-6 CA19-9 measurements were analyzed. Median follow-up from initial chemotherapy was 29.2 months, and median survival from initial chemotherapy was 6.7 months. Multivariate analyses confirmed an early decrease in CA19-9 concentrations of 25% after two cycles of chemotherapy were associated with a favorable survival compared with patients who did not have a decrease of 25% (HR = 0.56 (95% CI: 0.40-0.78)). The association of CA19-9 decrease with overall survival differed by platelet level (PInteraction = 0.001). Multivariable adjusted hazard ratios for decrease in CA19-9 of 25% were 0.30 (0.18-0.49) in patients with low platelet level (PLT < 190 x 10^9/L) and 0.85 (0.53-1.35) in patients with high platelet level (PLT ≥ 190 x 10^9/L). **Conclusions:** In patients with MBC, 25% decrease at week 6 could be an early marker for prognosis. The association of CA19-9 decrease with pancreatic cancer survival is stronger in patients with platelet low tumors than platelet high tumors. Our findings suggest a differential prognostic effect of CA19-9 according to platelet level.

204 Poster Session (Board #A20), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Suggestion of new nomogram including inflammatory marker for predicting invasive carcinoma in intraductal papillary mucinous neoplasm of the pancreas. First Author: In Woong Han, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of (South)

**Background:** Previous studies have analyzed that inflammatory markers, such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and advanced lung cancer inflammation index (ALI), associated with the presence of invasive carcinoma in patients with intraductal papillary mucinous neoplasm (IPMN). This study aimed to evaluate the correlation between the inflammatory markers and the invasive carcinoma in IPMN and propose a nomogram including inflammatory markers for predicting the presence of invasive carcinoma in patients with intraductal papillary mucinous neoplasm IPMN. **Methods:** From 1995 to 2016, total 468 patients who underwent surgical resection at four institutions for histologically confirmed IPMN and the data were reviewed retrospectively. The patients with history of pancreatitis, other malignancies and without CA19-9 data or lymphocyte counts were excluded, the study cohort consisted of 365 patients. Variables with P < 0.05 in risk factor analysis were included in the nomogram. **Results:** Of 365 patients, 98 (26.8%) patients had invasive IPMN. In univariate analysis, high body mass index (BMI) (P = 0.037), pre-operative bilirubin level (P < 0.001), CA19-9 (P < 0.001), NLR (P = 0.019), PLR (P = 0.002), ALI (P = 0.001), main duct type (P < 0.001), the presence of solid portion (P < 0.001) and tumor size (P = 0.086) were identified as risk factors for invasive IPMN. In multivariate analysis, pre-operative bilirubin level (P = 0.033), CA19-9 (P = 0.002), main duct type (P = 0.034) and the presence of solid portion (P < 0.001) were independent predictive markers for invasive IPMN. The nomogram was developed including all factors of risk factor analysis. **Conclusions:** The inflammatory markers were the risk factors for the presence of IPMN-associated invasive carcinoma. This nomogram may be useful in identifying patients with IPMN at risk of malignancy and for selecting which patients should undergo surgery. Further validation studies are needed to assess the predictive ability of nomogram including inflammatory markers.
Role of central hypovascularity in the hepatic arterial phase of dynamic CT on mass-forming intrahepatic cholangiocarcinoma. First Author: Mitsuo Shimada, Tokushima University, Tokushima, Japan

Background: Intrahepatic cholangiocarcinoma (IHCC) is known as one of the most malignant cancers. Recently, the vascularity in the hepatic arterial phase (HAP) of dynamic CT has been reported as a possible prognostic marker in IHCC. The aim of this study is to elucidate the role of central hypovascularity in the HAP on mass-forming IHCC.

Methods: Forty patients who underwent initially hepatic resection for mass-forming IHCC were enrolled. The HAP was scanned 40 seconds after the injection of contrast agent. Vascular pattern was classified into three groups; hypervascularity (Hyper) group (n = 8), rim enhancement (Rim) group (n = 7) and hypovascularity (Hypo) group (n = 25) by a radiologist in reference to Fujiya, et al (Eur Radiol 2017). Hypoxxia-inducible factor1 (HIF-1) expression in the surgical specimen was evaluated by immunohistochemistry. The clinicopathological findings were compared among the groups.

Results: The advanced stage tended to be more frequent in Hypo group, however, no difference of tumor location (hilar or peripheral) was observed. Overall survival (OS) in Hypo group was worse than that in Hyper group. The OS in Rim+Hypo group, that means central hypovascularity in the tumor, was worse than that in Hyper group. Furthermore, Rim+Hypo group was an independent prognostic factor in OS (HR: 5.44). Regarding the HIF-1 expression, high HIF-1 expression in the central part of the tumor correlated with central hypovascularity in the HAP (25% in Hyper-group and 72% in Rim+Hypo group, respectively).

Conclusions: The central hypovascularity (Rim+Hypo group) was an independent prognostic factor, furthermore, high malignant potential of the tumor with central hypovascularity might be related to HIF-1 upregulation.

Quality-adjusted life years assessment using cabozantinib for patients with advanced hepatocellular carcinoma (aHCC) in the CELESTIAL trial. First Author: Ghassan K. Abou-Alfa, Memorial Sloan Kettering Cancer Center, New York, NY

Background: In patients previously treated for aHCC, cabozantinib (cabo) led to longer overall survival and progression-free survival vs placebo (pbo) in the randomized, phase 3 CELESTIAL trial (NCT01908426; N = 707). CELESTIAL showed longer overall survival and progression-free survival vs placebo (pbo) in the background.

Methods: First Author: Yasuke Yamamoto, Division of Hepato-Biliary-Pancreatic Surgery, Shizuoka Cancer Center, Shizuoka, Japan

Background: The objective was to clarify the prognostic impact of the 8th edition of AJCC/UICC staging system for intrahepatic cholangiocarcinoma (ICC).

Methods: ICC patients who underwent hepatectomy for ICC between 2002 and 2016 were enrolled. The survival impact of AJCC/UICC 8th edition was examined.

Results: A total of 103 resected patients were enrolled. The 5-year disease-specific survival (DSS) was 75.9% in T1a (n = 23), 88.9% in T1b (n = 10), 14.9% in T2 (n = 24), 52.5% in T3 (n = 11), and 15.2% in T4 (n = 35). The DSS was comparable among T2, T3, and T4 (p = 0.345, 0.295). The 5-year DSS was 87.5% in stage IA, 88.9% in IB, 18.1% in II, 66.7% in IIIA, and 15.0% in IIIB. The DSS rates of stage II and stage IIIB were comparable, and the DSS rate of stage II was worse than that of stage IIIB. A multivariate analysis identified multiple tumors (hazard ratio [HR]: 2.821), percutaneous infiltrating (HR: 2.439), perforation of the visceral peritoneum (HR: 1.850), and vascular invasion (HR: 1.872) as independent prognostic factors that were associated with the DSS.

Conclusions: The optimum tumor size with the greatest difference in the DSS was 2 cm (p = 0.019). A new T classification was developed as follows: T1, size ≤ 2 cm without other factors; T2, size > 2 cm without other factors; T3, vascular invasion or perforation of the visceral peritoneum; and T4, multiple tumors or percutaneous infiltrating. The HR of lymph node metastasis was similar to that of the low-HR factors, so lymph node metastasis was categorized as Stage IIIA. The 5-year DSS was 100% in T1 (n = 7), 76.6% in T2 (n = 28), 45.1% in T3 (n = 28), and 3.4% in T4 (n = 40). There were differences in the DSS between T2 and T3 (p = 0.035) and between T3 and T4 (p = 0.003). The 5-year DSS was 100% in stage I, 85.6% in stage II, 42.4% in IIIA, and 3.4% in IIIB (Fig. 2b). There were significant differences in the DSS between stage II and IIIA (p = 0.003) and between IIIB and IIIB (p = 0.026). Conclusions: T2, T3, and T4 of AJCC/UICC overlapped with regard to the DSS. The new staging can classify ICC patients with sufficient prognostic differences.

Investigating disparities: The effect of social environment on pancreatic cancer survival. First Author: David Madnick, Lewis Katz School of Medicine at Temple University, Philadelphia, PA

Background: Incidence rates of pancreatic adenocarcinoma (PAC) are higher in Black compared to White patients (pts). Beyond race, exposure to poor neighborhoods or social environments also contribute to cancer disparities. How does social environment impact PAC survival?

Methods: Social environments impact survival in a clinic population with metastatic PAC.

Results: PAC deaths occurred and median survival was 12m. 81% of pts were White; 39% resided in poor social environments (i.e. low SES or high RS). In multivariable analyses stratified by RS, median survival was lower in pts from high RS (11m) vs low RS areas (13m); however, this difference was not significant (p = 0.27). Variable effects differed by high/low RS. In high RS areas, sex, surgery, chemotherapy and neighboring SES were significant predictors of survival; in low RS areas, surgery, chemotherapy, radiation, PAC family history, tobacco use, Jewish ancestry and race were significant. Conclusions: While social environment did not appear to significantly affect survival time in metastatic pts, its potential moderating (interaction) effects may vary with PAC warrant further investigation.
Measurement of urinary kininogen (KNG) fragments as a noninvasive tool for early diagnosis of pancreatic cancer (PaCa). First Author: Izumi Ohno, National Cancer Center Hospital East, Kashiwa, Japan

**Background:** There is a clear need to identify a non-invasive biomarker for early diagnosis of PaCa, in order to improve the overall survival of PaCa patients. Secretion of large amounts of proteases is a hallmark of PaCa, which results in an abundance of protease-induced cleavage products being excreted in the urine. This has led to speculation that measurement of PaCa-specific fragments in the urine might be useful as a tool for discrimination between PaCa patients and healthy controls. Herein, we introduced urinary KNG fragments as a promising biomarker for early diagnosis of PaCa.

**Methods:** Urine samples were collected from PaCa patients and healthy volunteers, with the written informed consent, from January 2014 to July 2016. Urinary protein tryptic fragments derived from protein C-termini were measured using isobaric tags (iTRAQ) for their relative quantitation, and the diagnostic ability of the urinary levels of these fragments was evaluated by receiver operating characteristic (ROC) curve analysis. The fragments which showed an area-under-the-curve (AUC) of over 0.8 were selected as candidate fragments for further validation by the multiple-reaction-monitoring technique (MRM) combined with high-speed liquid chromatography. The urinary protein tryptic fragments derived from protein C-termini were quantified by MRM, and the diagnostic ability of the urinary levels of these fragments was evaluated by ROC curve analysis. The fragments which showed an area-under-the-curve (AUC) of over 0.8 were selected as candidate fragments for further validation by the multiple-reaction-monitoring technique (MRM).

**Results:** Urine samples of 39 PaCa patients (7 resectable, 32 unresectable) and 42 healthy controls were examined by iTRAQ to find 12,783 fragments. ROC curve analysis was carried out to select two candidate fragments (fragments A, B), both of which turned out to be KNG cleavage products. The urinary levels of the two fragments were measured in 23 resectable PaCa, 18 unresectable PaCa patients, and 42 healthy volunteers using high-speed-LC-/MRM. The AUCs of serum CA19-9 and urinary levels of fragments A and B for discriminating PaCa patients from healthy controls were 0.89, 0.81 and 0.70, respectively. **Conclusions:** Urinary KNG fragments showed favorable diagnostic capability and were considered as promising, noninvasively measurable biomarkers of PaCa.

210 Poster Session (Board #106), Fri, 11:30 AM-1:00 PM and 5:30-7:00 PM

**Prevalence of pancreaticobiliary cancer in Irish families with BRCA1 and BRCA2 mutations. First Author: Robert Power, Trinity College Dublin, Dublin, Ireland.

**Background:** Germline mutations in BRCA1 and BRCA2 genes are associated with pancreatic adenocarcinoma (PaCa), and more recently, associated with increased risk of biliary tract cancers (BTC). This study assessed the prevalence, age and gender distribution of PDAC/BTC in BRCA1/2 positive families, compared to those of the Irish population.

**Methods:** A review of all families referred to a national genetics clinic from 09/1997: 01/2016 was performed following institutional ethics board approval. Demographics including age, sex and BRCA mutation status was collected in each case of PDAC/BTC. The BRCA1/2A algorithm was used to estimate the penetrability that an untested relative of a known BRCA1/2 mutation carrier with PDAC or BTC was a carrier. Results: 3522 distinct family pedigrees were reviewed, of which 193 contained a proband who underwent testing for BRCA1/2 based on Manchester score ≥ 15. Among 150 BRCA2 positive families, 27 (21%) contained a 1r/2r/3r or 3r degree relative with PDAC, of 116 BRCA1 positive families, 11 (9%) contained a 1r or 2r or 3r degree relative with PDAC (male: female (f:m) = 1:0.9). Of these 38 families, 25 pts with PDAC had ≥ 50% likelihood of being a mutation carrier by BOICEA analysis. This cohort had a median age at diagnosis of 55 (33-75), with a mean (±55) significantly lower than that of 8364 unselected patients with PDAC identified through the National Cancer Registry Ireland (71; p < 0.0001). Six BRCA2 positive (5%) and 2 BRCA2 positive pedigrees (2%) contained an individual with BTC; median age at diagnosis was 65 (33-99, m:f=1:1). Additional pedigrees with Lynch Syndrome (n=3), FAP (n=1) and ATM (n=2) and PDAC were identified. **Conclusions:** PDAC and BTC are prevalent in Irish families with a BRCA1/2 mutation and are associated with early onset malignancy. This consolidates evidence of PDAC and BTC as BRCA-associated cancers in the Irish population and supports current guidelines recommending universal germline testing for PDAC patients.

**BRCA mutations in PDAC/BTC.

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211 Poster Session (Board #87), Fri, 11:30 AM-1:00 PM and 5:30-7:00 PM

**Multiplatform profiling of pancreatic neuroendocrine tumors (PanNETs) identifies novel co-occurring pathogenic alterations and associations with clinicopathologic factors. First Author: Michelle Guan, Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA.

**Background:** We correlated genomic, proteomic, and molecular pathway alterations with clinicopathologic factors and identified novel co-occurring pathogenic alterations of potential clinical relevance to PanNET management through multi-omic profiling. **Methods:** Perthera, Inc. deploys an IRB-approved registry that was utilized in partnership with PanCAN’s “Know Your Tumor” program. PanNETs having undergone molecular profiling for precision matched therapeutic purposes were screened. We performed correlation analyses by pairwise comparisons between pathogenic alterations or altered molecular pathways and clinicopathologic variables. Hierarchical clustering was used to visualize associations. The Kaplan-Meier method was used to estimate overall survival (OS) and survival differences across variables were assessed using log-rank test. **Results:** Out of 33 patients with predominantly locally advanced and metastatic PanNETs from 12/2014-1/2018, Chromatin remodeling pathway and MEN1 alterations by NGS were less associated with having high-grade PanNETs, while MEN1 alterations were also less associated with metastatic disease at diagnosis (all Fisher’s exact two-tailed p ≤ 0.05). Several molecular pathway or pathogenic alterations correlated with worse OS: DNA repair pathway (log-rank p < 0.0022), RBBP1 alterations by NGS (p = 0.018), and TP53 alterations by NGS (p = 0.01). There were several significant co-occurring alterations (Fisher’s exact p ≤ 0.05): ERCC1 expression by immunohistochemistry (IHC) and DAXX (NGS), RBBP1 (NGS) and DNA repair pathway (NGS), and TS (IHC) and cyclin-dependent kinase pathway (NGS). Having an altered chromatin remodeling pathway was less associated with having an altered receptor tyrosine kinase (RTK) signaling pathway (Fisher’s exact p ≤ 0.05). **Conclusions:** We identified several molecular signatures of potential clinical significance for therapeutic targeting and prognostication in PanNETs with actionable alterations. We found that pathogenic and expression generating and can inform larger molecular profiling efforts in PanNETs.

212 Poster Session (Board #88), Fri, 11:30 AM-1:00 PM and 5:30-7:00 PM

**Preoperative evaluation with computed tomography (CT) of the resectability of mesenteric lymph node metastases in small intestine neuroendocrine neoplasms (si-NENs): New criteria for clinicians and surgeons. First Author: Luigi Funicelli, European Institute of Oncology IRCCS, Milan, Italy.

**Background:** The 2016 European Neuroendocrine Tumor Society consensus guidelines update recommends resection of the primary tumor and all mesenteric lymph-nodes for all patients with si-NENs, both with curative and palliative purposes. Current resectability criteria are based on the degree of involvement of the superior mesenteric artery (SMA) by the metastatic lymph nodes. The aim of this work was to test these criteria for the evaluation of our patients: we included as additional criteria the degree of involvement of the superior mesenteric vein (SMV) and portal vein, two structures not considered by current literature. **Methods:** We retrospectively reviewed the pre-operative CT-scans of all patients with si-NENs operated at IEO (European Institute of Oncology) between 2008 and April 2018. A first analysis classified tumors as “resectable” or “unresectable” according to SMA involvement. A second analysis classified tumors as resectable or unresectable according to SMA involvement, SMV involvement (infiltration of the peripheral or proximal portion) and peritoneal involvement (presence or absence of fibrosis and retraction of the mesentery). We finally reviewed all surgery reports assessing radically and completeness of the operation. **Results:** Abdominal CT-scan were available for analysis in 42 out of 47 operated patients. According to the first analysis, all three tumors classified as unresectable underwent in complete resection, whereas out of the 39 tumors classified as resectable, six received an incomplete resection and 33 were completely resected. According to the second analysis, the nine tumors classified as unresectable underwent an incomplete resection, whereas 33 tumors classified as resectable were completely resected. **Conclusions:** Our retrospective analysis confirmed that SMA involvement may be useful to evaluate the resectability of the primary tumor and mesenteric lymph nodes. Furthermore, it suggested that the additional evaluation of the SMV and portal vein involvement can allow to identify further cases of tumors for which complete resection is not possible.
The impact of primary tumor site on outcomes of treatment with etoposide and cisplatin in grade 3 gastroenteropancreatic neuroendocrine carcinoma. First Author: Sang Eun Yoon, Samsung Medical Center, Seoul, Korea, Republic of (South)

Background: Gastroenteropancreatic neuroendocrine carcinoma (GEP-NEC) is a heterogeneous disease in terms of embryonic origin, aggressiveness, prognosis, and genomic profiling. Data regarding the efficacy of etoposide and cisplatin (EP) as a standard treatment of the primary tumor site in GEP-NEC are limited. Methods: We analyzed 64 patients with histopathologically confirmed metastatic GEP-NEC who received EP at Samsung Medical Center, Seoul, Korea, between January 2010 and January 2018. Based on primary tumor site, outcome of treatment with EP was evaluated. Results: Primary sites included 22 foregut-derived GEP-NECs (stomach, n = 6; duodenum, n = 4; pancreas, n = 12), 4 midgut-derived GEP-NECs, 5 hindgut-derived GEP-NECs of the rectum, 25 GEP-NECs originating from the hepatobiliary (HB) tract, and 12 GEP-NECs involving only intra-abdominal lymph nodes. No patient had a complete response (CR) and 17 had a partial response (PR), resulting in a 27.9% response rate (RR). When evaluating the efficacy of EP based on the primary tumor site, the RR was most favorable in GEP-NECs involving only intra-abdominal lymph nodes, followed by GEP-NECs originating from foregut, midgut, HB, and hindgut. However, no statistically significant difference was observed for RR based on primary tumor site (p = 0.82). Similarly, no significant differences were found for progression-free survival (PFS) among patients with GEP-NECs arising from various primary tumor sites. Conclusions: Results from this study showed that RR and PFS associated with EP treatment were not different based on the primary tumor site in patients with advanced or metastatic GEP-NEC.

Prevalence and molecular etiology of mismatch repair deficiency among gastrointestinal cancers. First Author: Navika Shukla, Stanford University, Palo Alto, CA

Background: In light of recent FDA approval of anti-PD1 therapy for microsatellite unstable (MSI-H) or mismatch repair deficient (dMMR) solid tumors, identifying patients with dMMR tumors has become increasingly important. While screening for dMMR and MSI-H patients with colorectal cancer (CRC) is recommended, this screening is less commonly done for extracolonic gastrointestinal (GI) tumors. At Stanford Comprehensive Cancer Institute (SCCI), all GI cancer patients have been universally screened for dMMR via immuno-histochemistry since January 2016. Methods: In this study, we undertook a retrospective review of all GI cancer patients screened for dMMR between January 2016 to December 2017. Data on patient characteristics, germline and tumor sequencing, and tumor characteristics were collected and reported. Results: A total of 1543 GI malignancies were screened for dMMR at SCCI during the study period. Colorectal (n = 711), pancreatic (n = 264), gastric (n = 159), and gastro-esophageal (n = 137) cancer were amongst the most frequently screened tumors. dMMR was detected in 7.1% of all GI malignancies. We detected the highest prevalence of dMMR in colorectal (69/711, 9.7%), followed by gastric (15/159, 9.4%), pancreatic (18/264, 6.8%), and gastro-esophageal cancer (6/137, 4.4%). Lynch syndrome was the most common etiology for dMMR in CRC patients (39.4%), double somatic (confirmed or possibly) mutations were most common in pancreatic cancer (44.4%), and somatic MLH1 hypermethylation was the most common etiology in gastric (73.3%) and gastro-esophageal cancer (100%). Conclusions: Given the relatively high incidence of dMMR in GI malignancies, we strongly recommend screening all GI malignancies. Of note, we found higher than previously reported rates of dMMR within pancreatic cancer. Our results also suggest that while rare, double somatic mismatch repair mutations may be a significant pathway causing dMMR in pancreatic cancer.

Early detection of pancreatic ductal adenocarcinoma using abnormal urinary fragmentation ratio of a liver-originated protein. First Author: Motoyasu Kan, National Cancer Center Hospital East, Chiba, Japan

Background: Non PDAC tissue-originated proteins are cleaved by proteases derived from PDAC, which can result in abnormal cleavage patterns in the urine of PDAC patients. Urinary proteomic analysis for quantifying the ratios of the abnormal protein fragments to the non-fragmented protein levels in the urine may be useful to distinguish early PDAC from healthy controls. This proof-of-concept study was planned to determine the usefulness of measuring the protein fragments from non PDAC tissue-originated proteins in the urine using the multiple-reaction-monitoring technique (MRM) for discriminating resectable PDAC from healthy controls. Methods: Urinary proteins were digested with trypsin, and resultant peptides were measured by MRM analysis and the ratio of the level of each fragment to the non-fragmented protein level (fragmentation ratio) was calculated. Fragments for which the fragmentation ratios were higher in the PDAC group than those in the healthy group were defined as abnormal protein fragments. The diagnostic capability of each abnormal protein fragment for discriminating cases of PDAC from healthy controls was evaluated by receiver operating characteristic (ROC) curve analysis. Results: A total of 21 patients with resectable PDAC and 30 healthy control subjects were enrolled in this study. All the PDAC patients were treated by pancreatic resection. Urine samples for this study were collected prior to the surgery from the PDAC patients. The non PDAC tissue-originated protein was determined as a liver-originated protein. The fragmentation ratios for six fragments were found to be higher in the PDAC group as compared to those in the healthy control group, and these fragments were determined as abnormal protein fragments. ROC curve analysis was performed for each of the abnormal fragments to determine the areas under the curve (AUCs) for discriminating cases of PDAC from healthy controls. The best AUC was 0.81 (95% CI, 0.68-0.91). Conclusions: The urinary fragments that showed the ability to discriminate cases of resectable PDAC from a healthy control group; abnormal fragmentation ratios may be promising, noninvasively measurable biomarkers of early PDAC.
Comparison of biomarkers among 34855 GI cancer samples shows heterogeneity of tumor types. First Author: Shaheenah S. Dawood, Mediclinic City Hospital, Dubai, United Arab Emirates

Background: Recent data indicate that biomarker driven use of targeted therapy and I/O-therapy among patients with GI cancer is associated with improved outcome. The presence of biomarkers varies broadly between different GI tumor types, highlighting the importance of comprehensive molecular profiling. To analyze the presence of various alterations in GI cancer samples of a large database, comparing congruency between various tumor types and also among various cancer sites. A retrospective data analysis of 34855 GI cancer patients profiled at CARIS Life Sciences obtained from Jan 1, 2010 till Sep 14, 2018 was performed. GI tumors were classified as CRC, esophageal/gastric/GIST, small intestine, pancreatic/hepatobiliary/liver. Technologies used to analyze the biomarkers: IHC for PD-L1, MMR and Her2, and DNA-NGS for EGFR, BRAF, KRAS, NRAS, MET-CNV, TMB, MSI, POLE and BRCAC1/2. Results: Median age was 61 range (18-89 years), 51.5% was CRC (n=18047), 15.9% was esophageal/ Gastric/GIST (n=5470), 3% was small intestinal cancer (n=886) and 30% was pancreatic/hepatobiliary/liver cancer (n=10452). Information on biomarkers was available from 2937 cases for MET amplification to 28536 for RAS mutation. Overall, the most common finding was a pathogenic RAS-mutation in 7650 cases (26.8%), the rarest one was a mutation in EGFR in 12 cases (0.06%). Higher rate of HER2 amplification was observed among cases with esophageal/gastric/GIST tumors (6.5%) in comparison to tumors at other GI sites (~1%). High TMB was seen among patients with CRC and small intestine tumors (~7%) while it was lowest among pancreatic cancer (1.8%). Compared to other GI sites lower MSI/MMR deficiency rates were observed in pancreatic f hepatobiliary tumors, significantly higher PD-L1 positivity was observed in gastroesophageal cancer types, increased MET-amplifications in gastroesophageal and small intestinal cancer types and lower RAS-mutation rate in gastroesophageal cancer. Conclusions: Molecular profiling analyzing drugable biomarkers can help identify patients with increased likelihood for benefit from immune-checkpoint-inhibitors and targeted therapies. Further investigations are needed to evaluate the different findings in various GI cancer types.

Circulating calprotectin, innate inflammatory protein, was decreased under disease control during first-line chemotherapy for advanced pancreatic cancer. First Author: Taro Shibuki, National Cancer Center Hospital East, Kashiwa, Chiba, Japan

Background: There is increasing evidence of a close link between inflammation and disease control in pancreatic ductal adenocarcinoma (PDAC). Damaged-associated molecular patterns (DAMPs) were inducers of inflammation in the innate immune system and were detected in PDAC tissue in recent reports. Calprotectin, one of DAMPs, is recognized as a potential mediator of the process of disease control in various tumors. In this study, circulating calprotectin is characterized on disease control in patients with 1st line chemotherapy for advanced PDAC. Methods: Patients with treatment-naive advanced PDAC were enrolled in this study. Patients with obvious infectious conditions were excluded. Serum levels of calprotectin and pro-inflammatory cytokines including interleukin-6 (IL-6) were measured at baseline and at one or two months after the start of 1st line chemotherapy. Disease control rate (DCR) was evaluated on the Response Evaluation Criteria in Solid Tumors ver. 1.1. Results: A total of 73 patients were evaluated. DCRs of gemcitabine group (GEM) (n = 57) and the patients with modified FOLFIRINOX or GEM + nab-paclitaxel (mFFX/GN) (n = 16) were 52.6% and 75.0%, respectively. In comparison of baseline-and-after data, circulating calprotectin levels were significantly decreased under disease control in GEM (baseline vs. after: 2.9 vs. 2.3 ng/ml in median, p = 0.001) and GEM/GN (2.7 vs. 0.5 ng/ml, p = 0.024). IL-6 was decreased in GEM/mFFX/GN (91 vs. 5.9 pg/ml; p = 0.095) but not in GEM (4.3 vs. 3.1 pg/ml; p = 0.303). There were no obvious changes under non-disease control in calprotectin (baseline vs. after: 6.2 vs. 5.7 ng/ml in GEM, 5.1 vs. 4.5 ng/ml in mFFX/GN and IL-6 16.5 vs. 25.6 ng/ml in GEM, 3.1 vs. 4.7 pg/ml in mFFX/GN). Conclusions: DCR related decrease of circulating calprotectin level during 1st line chemotherapy for advanced PDAC. Innate immune system plays a role in the chemotherapeutic efficacy in advanced PDAC.
Background: The impact of the distance from the root of the splenic artery to the tumor in patients with the pancreatic body/tail cancer is becoming unclear. **Methods:** Between 2008 and 2018, 98 and 17 patients who underwent distal pancreatectomy (DP) and DP with celiac axis resection (DP-CAR) for conventional pancreatic ductal carcinoma were retrospectively analyzed. DST (mm) was measured by preoperative CT scan images. The indications for DP-CAR are the following: tumor involvement of the common hepatic artery and/or the celiac artery or difficulty in keeping surgical margin at the stump of the splenic artery. **Results:** Patients with DST = 0 had longer operation time (p = 0.005), greater amount of blood loss (p = 0.036), and a higher morbidity rate (p = 0.010) than those with DST > 0. The rate of introducing adjuvant chemotherapy in the DST = 0 group was significantly lower than that in the DST > 0 group (50% vs. 82%, p = 0.012). The median survival time (MST) of the DST = 0 group was significantly worse than that of the DST > 0 group (20 vs. 56 months, p< 0.001). In contrast, there was no significant difference of MST between the groups of 0 < DST ≤ 10 and DST > 10 (p = 0.499). Multivariate analyses revealed that DST = 0 (HR 4.51, p = 0.001), preoperative CA19-9 > 40 U/mL (HR 2.91, p = 0.032) and preoperative neutrophil-to-lymphocyte ratio ≥ 2.3 (HR 2.49, p = 0.001) were independent prognostic factors. Regarding to the operative procedures, DP-CAR was performed 12 out of 14 procedure. which was a prognostic indicator. If surgical margin at the root of the splenic artery is narrow, then there was no difference of prognosis. DP-CAR are the following: tumor involvement of the common hepatic artery and/or the celiac artery or difficulty in keeping surgical margin at the stump of the splenic artery. **Conclusions:** Multidisciplinary treatment including DP-CAR should be warranted for patients with DST = 0, which was a prognostic indicator. If surgical margin at the root of the splenic artery is secured in patients with DST > 0, DP should be an acceptable procedure.

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1. **IGF-Child-Pugh score as a predictor of treatment outcome in Child-Pugh A, advanced hepatocellular carcinoma patients undergoing sorafenib therapy, First Author: Yehia I. Abugabal, University Of Texas MD Anderson Cancer Center, Houston, TX**

**Background:** Sorafenib is the first systemic therapy approved for advanced HCC treatment; with no accurate tool available to help predict survival and treatment outcome and to guide therapy decisions. Our novel blood-based IGF-Child-Pugh (CP) score comprises levels of IGF-1, bilirubin, INR, and albumin. IGF-CP score significantly improved the prediction of HCC survival in our recently published studies. The current prospective study aimed to compare the overall survival (OS) and progression-free survival (PFS) of 101 patients with CP-A HCC treated with sorafenib whose score is reclassified as IGF-A (AA) to that of patients whose score is reclassified as IGF-B/C (AB/AC). **Methods:** Between 2014 and 2018, after the approval of the institutional review boards and signing written informed consent, a total of 101 patients with HCC, CP-A were prospectively enrolled and started on sorafenib and followed until progression or death. **Results:** Sixty-three patients were evaluable. Patients who were reclassified by the IGF-CTP scoring system were better stratified by their new risk groups. Forty-two of patients were classified as IGF-CTP-A and had median PFS of 4.87 months (95% CI 2.3 to 6.84), and median OS of 15.43 (95% CI = 12.04 to 31.18 months), whereas 21 patients were reclassified as intermediate risk (IGF-CTP-B) and had significantly shorter OS of 7.6 months (p-value < 0.0001) and shorter PFS of 2.86 months (p-value < 0.0001). **Conclusions:** The results of this study confirms our biologically driven hypothesis: that among HCC patients with “old CP-A” class treated with sorafenib, some will be reclassified as “new CP-B/C” will have poorer prognosis in terms of shorter OS and PFS. Thus, our study provides an objective non-invasive strategy to better predict the outcome of HCC patients undergoing systemic therapy. Future validation of our IGF score may lead to adopting it as a stratification tool in trials to predict HCC outcome and guide therapy decision in routine practice.

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**Role of nonalcoholic steatohepatitis as a risk factor for intrahepatic cholangiocarcinoma and its role in patients’ prognosis: A case-control study, First Author: Stefania De Lorenzo, University Of Bologna - Department of Experimental, Diagnostic and Specialty Medicine - Unit of Oncology, Bologna, Italy**

**Background:** The prevalence of intrahepatic cholangiocarcinoma (ICC) is rising worldwide. The current epidemics of non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) might be partly responsible for this trend. **Methods:** Case-control study investigating the prevalence of histology-confirmed NASH in periportal liver of resected ICC patients and controls (pre-explant biopsies of liver donors). Controls were matched for age and sex in a 1:1 fashion. Correlates between NASH, tumor characteristics and overall survival (OS) were also explored in the ICC cohort. **Results:** Between 2006 and 2017, 84 ICCs were resected in our Institution. Sixty-two (74%) had no apparent risk factors for ICC. Amongst this group, the prevalence of NAFLD and NASH was 45.2% and 24.2% respectively, compared to 44.3 and 8.9% in the 124 matched liver donors (p = 1.000 and p = 0.007, respectively). The 5-year OS rate was 20.0% in NASH and 57.4% in ICC without either NASH and other risk factors (p = 0.017). Main tumor size, sex and NASH (hazard ratio 2.618 , 95% confidence interval 1.140-6.013, p = 0.023) were independent predictors of the OS at the multivariate Cox regression. **Conclusions:** NASH (but not NAFLD) acts as a risk factor for ICC and may affect its long-term outcome. A collaborative multicenter approach could confirm and strengthen these data.
Incidence and trends of pancreatic cancer (PC) in Girona: A population-based study from the Girona Cancer Registry (1994-2015). **First Author:** Adelaida García-Velasco, Hospital Dr. Josep Trueta, Institut Català d’Oncologia, Girona, Spain

**Background:** PC is the third leading-cause of cancer death in Spain. In this study, we aim to investigate PC’s incidence and trends from 1994-2015 in Girona.

**Methods:** Data were extracted from the population-based Girona Cancer Registry. Incident PC cases were classified using the ICD-0-3 Third Edition. Age-adjusted incidence rates (ASIR) to the European standard population and world standard population (ASWR) were obtained. Trends were assessed using the estimated annual percentage of change (EAPC) of the ASIR. **Results:** We identified 1590 PC incident cases, 45.8% females and 54.2%. Patients > 64 years old represented a 72.6% of cases. According to histology, epithelial tumors stand for a 44% of cases and neuroendocrine neoplasms represented only the 3% of all cases, being most of PC tumors histology non-specified. Cases detected only by death certificates (DCO) were 7.7% in males and 7.4% in females. For the whole study population, crude rate (CR) cancer incidence was 11.26 cases per 100,000 inhabitants/year (12.17 men; 10.34 women). Regarding the ASIR, results for the ASIR of 12.99 (95% CI 12.36;13.65) and ASIR of 5.58 (95% CI 5.83;655.9). Age-specific rates reflected a drastic increase with age, having the population over 85 years the highest rate (74.5 cases per 100,000 inhabitants/year). We also found a significant increase in incidence of PC cases over the study period, with an EAPC of 1.44% per year, present in both men (EAPC = 1.30%) and women (EAPC = 1.37%). **Conclusions:** Incidence rates of PC in Girona are within the European average, and likewise they have been increasing for the last two decades. There is an increase of incidence in the elderly population reflected in age-specific rates, reason whereby we believe there are a high proportion of unspecified histologies. These results can be used as baseline for further research.

**Plasma GH as a diagnostic and prognostic biomarker in HCC without cirrhosis.** **First Author:** Roberto Carmagnani Pestana, University of Texas MD Anderson Cancer Center, Houston, TX

**Background:** The association between the GH/IGF-1 axis and HCC was reported in patients (pt) with underlying cirrhosis. However, there is limited information about HCC pt without (w/o) cirrhosis. We herein investigated the role of GH as a diagnostic and prognostic biomarker for HCC. **Methods:** We prospectively enrolled 1267 newly-diagnosed HCC pt in a case control study at the MD Anderson Cancer Center (2000-2015). Controls were healthy individuals (n = 1104). Plasma GH and AFP were measured in 133 and 82 pt, respectively. We classified HCC pt into higher and lower GH values (cutoff for women, 3.7 µg/L; men, > 0.9 µg/L). **Results:** Most pt (74%) were male, with advanced BCLC staging (C, 74%) and 61% were older than 60y. Baseline GH was higher in HCC w/o cirrhosis (mean 3.3 µg/L) than controls (mean 0.4 µg/L; p < 0.001). ROC curve was plotted to assess diagnostic role. The AUC for AFP was 82.9 (p < 0.001) for GH 78.2 (p < 0.001). When only non-cirrhotic HCC pt with early stage (CLIP 0-2) and AFP < 20 ng/ml were compared to controls, the GH/IGF-1 ratio had high prediction of early stage HCC ~ AUC 83 (95% CI 78-89%) (p < 0.001). At a specificity of 90%, sensitivity of GH/IGF ratio was 67%. In addition, among HCC w/o cirrhosis, higher GH levels correlated with presence of vascular invasion (p < 0.001) and thrombosis (p = 0.04), tumor involvement of > 50% liver (p < 0.001), and more advanced BCLC (p < 0.001) and TNM staging (p < 0.001). Median overall survival (months) of HCC pt w/o cirrhosis with high GH levels was 13.1 (10.8-15.4) compared to 37.4 (19.8-55.0) of pt with lower plasma GH (p < 0.001). Multivariate cox regression analysis identified high GH as an independent risk factor for mortality (HR = 1.8; 95% CI, 1.3-2.4; p < 0.001). **Conclusions:** Our study demonstrates the diagnostic and prognostic role of plasma GH in non-cirrhotic HCC and identifies the GH/IGF-1 ratio as a promising diagnostic marker for early stage HCC w/o cirrhosis and low AFP. This analysis excludes the confounding effect hepatocyte impaired function by presence of cirrhosis. Further studies are warranted to assess the causes of the observed differences.
Differences in presentation and management patterns in patients with hepatocellular carcinoma (HCC): Data from HCC registry in Asia. First Author: Pierce K. H. Chow, National Cancer Center Singapore, Singapore, Singapore

Background: HCC is the 6th most common cancer worldwide with >70% of cases in Asia. There is limited real-world data on the disease aquired in Asian geographies: China, Singapore, South Korea, Japan, Taiwan, Australia, New Zealand, Hong Kong, and Thailand. We present initial data on diagnosis, etiology, stage at presentation, and treatment modalities of HCC from China [CN] (5 centers), Singapore [SG] (3 centers), South Korea [SK] (4 centers), and Japan [JP] (2 centers). Results: 657 patients (436 CN; 102 SG; 85 SK; 34 JP) were evaluated in August 2018. Patients from China were diagnosed at a younger age, while patients from Japan were diagnosed at an older age (mean age 51 years CN; 67 years SG; 58 years SK; 68 years JP). The highest proportion of regular alcohol drinkers were from Japan (16% CN; 24% SG; 50% JP) and occasional drinkers from China (20% CN; 17% SK; 15% JP). 77% had Hepatitis B across the 5 geographies, with the highest incidence in China (93%), followed by South Korea (68%). 27% were diagnosed using AASLD/APASL imaging criteria, with the highest utilization in Singapore (66% AASLD; 80% APASL) and South Korea (64% AASLD; 20% APASL). Later-stage patients (according to Barcelona Clinic Liver Cancer staging guidelines) were more predominant in Japan (Stage C: 28% CN, 16% SG, 8% SK, 41% JP; Stage D: 0/5% CN, 0% SG, 1% SK, 3% JP). Relative few radiofrequency ablations were carried out as the first-line therapy across the 5 geographies (2% CN; 5% SG; 2% SK; 0% JP). In China, liver resection was preferred in first-line HCC treatment (65% CN vs 28% SG, SK, and JP aggregated). Conclusions: There is considerable variation in presentation and management patterns between the 5 geographies. These data will benefit policymakers, companies and clinicians in improving policies and developing treatment strategies for HCC. (ClinicalTrials.gov: NCT03233360).

Epidemiology and characteristics of patients (pts) with hepatocellular carcinoma (HCC) and care in the United States. First Author: Yunes Doleh, AstraZeneca, Gaithersburg, MD

Background: The incidence of liver and intrahepatic bile duct cancer, with HCC accounting for 72.7%, has doubled from 1992 to 2014 in the U.S. This study examined the latest epidemiology of HCC by analyzing 2 large U.S. databases: MarketScan Commercial and Medicare Supplemental insurance (IBM-MS), and End Results-National Program of Cancer Registries (SEER-NPCR), databases. The incidence of VTE among pancreatic cancer and its possible risk factors among metastatic pancreatic cancer (mPC) treated at a single nonacademic center from 2010-16 was used to identify the factors correlating with VTE and Cox Proportional Hazard model was used to evaluate overall survival (OS) differences between those with VTE (Gp A) and those without VTE (Gp B). Results: Out of the 439 mPC pts (52% males, 86% with PS0-1, 63% with stage IV at diagnosis), 127 (29%) were in Gp A and 312 (71%) in Gp B. The groups were well balanced with respect to all factors except age (median age 67 Gp A; 65 in Gp B, p = 0.04). 2.3 % of pts in Gp A and 4.8 % pts in Gp B were on anticoagulation for reason other than VTE treatment. Within Gp A, 55% developed VTE after diagnosis of metastasis. A clear separation of the survival curves noted beyond the median OS (9 m, P = 0.01). Nine patients died within 30 days of VTE diagnosis, within 12 months from diagnosis of metastasis, and overall survival (OS) differences between those with VTE (Gp A) and those without VTE (Gp B) was used to evaluate overall survival (OS) differences between those with VTE (Gp A) and those without VTE (Gp B). Results: Out of the 439 mPC pts (52% males, 86% with PS0-1, 63% with stage IV at diagnosis), 127 (29%) were in Gp A and 312 (71%) in Gp B. The groups were well balanced with respect to all factors except age (median age 67 Gp A; 65 in Gp B, p = 0.04). 2.3 % of pts in Gp A and 4.8 % pts in Gp B were on anticoagulation for reason other than VTE treatment. Within Gp A, 55% developed VTE after diagnosis of metastasis. A clear separation of the survival curves noted beyond the median OS (9 m, P = 0.02), favoring Gp B. Statistically significant factors associated with risk of VTE included advanced stage at diagnosis (p = 0.004) and worse PS (P = 0.005). Treatment regimen used and CCI didn’t correlate with the risk of development of VTE. Conclusions: The incidence rate of VTE in our patients is lower than published literature, yet the diagnosis of VTE was associated with worse OS. Most cases occurred before the initiation of treatment. The use of anticoagulants for other medical causes may be contributing to a lower incidence of VTE in mPC. These findings need prospective validation.
Circulating tumor DNA may correlate with tumor size changes following therapy. First Author: John Chang, Banner MD Anderson Cancer Center, Gilbert, AZ

**Background:** Pancreatic cancer has significant mortality at five years, even in resectable disease. Recent effort has been dedicated to identify a more specific tumor marker for screening and assessing tumor response, in part because 10% of the population does not produce CA19-9. Detection and quantification of circulating tumor DNA (ctDNA) in the bloodstream is a novel concept for screening and treatment response assessment. This study examined possible correlations between ctDNA levels and various aspects of pancreatic cancer in a total of 17 patients receiving treatment at Banner MD Anderson Cancer Center. **Methods:** Present study is approved by our local IRB. Research was conducted according HIPPA regulation. Subjects on the present study were obtained from the list of patients participating in our ctDNA trial. A total of 17 subjects were identified from the list. Their ctDNA index levels were obtained from the sponsor (Chronyx) at baseline and following every cycle of the treatment. For each CT scan and each ctDNA study, they are considered the same time if they are obtained within 4 weeks of each other. The sizes of the primary tumor and the largest metastatic lesion were on a transverse image at the largest extent of the lesion. Data was analyzed with Spearman's correlation. **Results:** Baseline ctDNA levels did not correlate with patient demographic data (N = 17; gender, p = 0.63; age, p = 0.82), baseline size of primary mass on CT scan (N = 16; p = 0.85), baseline vessel involvement on CT scan (N = 17; p = 0.58), presence of metastasis on CT scan (N = 17; p = 0.78), size of largest metastasis on CT scan (N = 17; p = 0.85), presence of perineoplastic lymph nodes on CT scan (N = 17; p = 0.45) or overall survival (N = 8; p = 0.6). However, there is a trend toward correlating the change in ctDNA and change in size on CT scan following treatment (N = 7; p = 0.12). **Conclusions:** ctDNA at baseline appears to be secreted independent of the primary tumor size, location or presence of metastasis. However, changes in ctDNA does seem to correlate with changes in tumor size following treatment. Although our data was not statistically significant, this may be related to the low sample size. With larger sample size, it is expected that changes in ctDNA may prove to correlate with changes in tumor size.

Factors associated with biopsy diagnosis of hepatocellular carcinoma. First Author: Young soo Rho, University of Hawaii Internal Medicine Residency Program, Honolulu, HI

**Background:** Hepatocellular carcinoma (HCC) is one of the few cancers that can be diagnosed based on imaging findings. Although not always mandatory for diagnosis, biopsy (Bx) can confirm HCC and its histologic subtype. We have examined possible correlations between ctDNA levels and various aspects of pancreatic cancer in a total of 17 patients receiving treatment at Banner MD Anderson Cancer Center. **Methods:** Present study is approved by our local IRB. Research was conducted according HIPPA regulation. Subjects on the present study were obtained from the list of patients participating in our ctDNA trial. A total of 17 subjects were identified from the list. Their ctDNA index levels were obtained from the sponsor (Chronyx) at baseline and following every cycle of the treatment. For each CT scan and each ctDNA study, they are considered the same time if they are obtained within 4 weeks of each other. The sizes of the primary tumor and the largest metastatic lesion were on a transverse image at the largest extent of the lesion. Data was analyzed with Spearman's correlation. **Results:** Baseline ctDNA levels did not correlate with patient demographic data (N = 17; gender, p = 0.63; age, p = 0.82), baseline size of primary mass on CT scan (N = 16; p = 0.85), baseline vessel involvement on CT scan (N = 17; p = 0.58), presence of metastasis on CT scan (N = 17; p = 0.78), size of largest metastasis on CT scan (N = 17; p = 0.85), presence of perineoplastic lymph nodes on CT scan (N = 17; p = 0.45) or overall survival (N = 8; p = 0.6). However, there is a trend toward correlating the change in ctDNA and change in size on CT scan following treatment (N = 7; p = 0.12). **Conclusions:** ctDNA at baseline appears to be secreted independent of the primary tumor size, location or presence of metastasis. However, changes in ctDNA does seem to correlate with changes in tumor size following treatment. Although our data was not statistically significant, this may be related to the low sample size. With larger sample size, it is expected that changes in ctDNA may prove to correlate with changes in tumor size.

A blood-based assay for diagnosis of early-stage pancreatic cancer. First Author: Thomas Jens Ettrich, Ulm University, Ulm, Germany

**Background:** Pancreatic ductal adenocarcinoma (PDAC) has a dismal prognosis. Biomarker are needed to facilitate early and preferably noninvasive detection of PDAC, which directly may influence patients’ prognosis. Here we aimed to develop a novel biomarker combination for early PDAC, consisting of thrombomodulin-2 (THBS2), CA19-9 and circulating tumor DNA (ctDNA) analysis. **Methods:** Thirty-nine patients with histologically proven and clearly resectable PDAC (recruited from the NEONAX trial, NCT020247513) were enrolled. Fifteen patients with benign pancreatic disease (intraductal papillary-mucinous neoplasms, IPMN) served as controls. Blood samples were collected prior treatment. KRAS genotyping was performed after isolation of ctDNA from plasma (QiAamp MinElute ctDNA Kit, Qiagen) by digital droplet PCR (KRAS Screening Multiplex Kit; QX200 system, both: Bio-Rad). Clinical data and CA 19-9 levels were assessed by ELISA (Roche); THBS2 values were determined by Quantikine ELISA Human Thrombospondin-2 (R&D Systems). Statistical analyses were done using GraphPad Prism Version 7.00, GraphPad Software, Inc. **Results:** THBS2 had a c-statistic of 0.73 for all PDAC stages which was comparable to that of CA 19-9 (0.78). The c-statistic was improved to 0.94 by combining CA 19-9, THBS2 and total ctDNA amount. This marker combination performed best for all stages. C-statistics of defined PDAC stages was 0.93, 1.00 and 0.92 for stage I, stage II and stage III, respectively. Of note, the biggest improvement in sensitivity and specificity was seen for stage I PDAC. Here, c-statistic improved from 0.69 or 0.85 for CA 19-9 alone or the combination of CA 19-9 and THBS2, respectively, to 0.93 for the three-marker combination. **Conclusions:** These data underscore that CA19-9, THBS2 and ctDNA marker combination constitutes a composite liquid biomarker for non-invasive diagnosis of early-stage PDAC with a remarkable specificity. Larger studies are needed to examine the power of this approach.
The spectrum of activating EGFR mutations from cell-free DNA (cfDNA) in large pancreatic cancer cohort. First Author: Kristin Sedgwick Price, Guardant Health, Inc., Redwood City, CA

Background: Metastatic pancreatic cancer (mPC) is one of the deadliest cancers with a < 10% 5-year survival rate. Poor prognosis is well established with lack of response to or rapid progression on existing chemotherapy options. Targeted therapies, like EGFR-TKIs, have been shown to increase survival in other solid tumors like NSCLC with certain oncogenic drivers. Although treatment with the EGFR-TKI erlotinib, in combination with gemcitabine, is available for patients (pts) with mPC, the survival benefit is small in unselected patients. A better understanding of the spectrum of activating mutations in mPC may lead to improved therapy selection. Methods: We retrospectively reviewed genomic results from 2,938 consecutive mPC pt samples sent for cfDNA NGS analysis between 7/2014 - 9/2018 (Guardant Health, Inc.). All reported EGFR mutations were reviewed and activating mutations were determined based on literature review. Results: 19 EGFR activating mutations were identified in 16 unique pts (0.66% of total mPC pts with alterations detected). 3 mutations were identified in the extracellular domain and 16 mutations in the kinase domain (3 in exon 18, 3 in exon 19, 6 in exon 20, 4 in exon 21). Alterations in exon 20 included 5 T790M mutations; two of these were reported at allelic frequencies suggestive of germline origin. Analysis of co-mutations revealed 7 pts with EGFR mutations that appeared subclonal relative to other potential drivers (4 KRAS, 2 ERBB2, 1 GNAS). The median number of alterations per sample was 4 (range 2-170) with the latter pt exhibiting a hypermutator phenotype. Multiple pts had more than one activating EGFR alteration, including one who was found to have 4 EGFR sequence alterations (S768I, L861Q, T790M, p.Val769_Asp770met) plus EGFR amplification (plasma copy number 66.8). We will collect and report clinical details to characterize the treatment context for these pts. Conclusions: Activating EGFR mutations in mPC is common and may present unique opportunities for targeted therapy in this population. Further exploration is warranted to better understand the oncogenic activity of less common, subclonal, or co-occurring EGFR mutations and their sensitivity to EGFR-TKIs in mPC.

Leptomeningeal carcinomatosis in BRCA-mutated pancreatic cancer. First Author: Jessica Anne Stostad, Mayo Clinic, Rochester, MN

Background: Pancreatic adenocarcinoma is a rapidly fatal cancer with 5-year overall survival <5%. 5-10% of pancreatic cancers occur in patients with family history of disease, and 5-27% of these familial cancers are BRCA associated, with defects in Homologous Recombination Repair (HRR). In breast and ovarian cancer, BRCA mutations may be associated with increased risk for brain metastasis (BM). BM is rare in pancreatic cancer, but it is suggested HRR deficient pancreatic cancer patients may have an increased risk for BM/LC. Methods: We analyzed 3030 prospectively identified patients with pancreatic cancer and BRCA mutation status in our germline sequencing database (2000-2018) from the Mayo Clinic Pancreatic Cancer SPORE Registry. We used clinical databases (2000-2018) to assess the presence of BM or leptomeningeal carcinomatosis (LC). Unconditional logistic regression analysis, with Odds Ratio (OR) and 95% Confidence Interval (CI), assessed the association between HRR germline mutation carrier status and any BM. Results: Of 3030 total pancreatic cancer patients, 8 were diagnosed with clinically evident BM/LC (0.26%), confirming the very low incidence of this metastasis site (Table). Of these, all had BM, and 4 also had LC present. No patients had LC diagnosed without BM present. 175/3030 (5.8%) patients had a germline HRR gene mutation. Of these, 1 patient was a BRCA2 carrier (0.57% of HRR deficient patients). 7/2763 (0.25%) patients without germline HRR mutations had BM or LC (p = 0.44, OR 2.26; 95% CI: 0.27, 18.49). Conclusions: To our knowledge, this is the largest review of BRCA-associated pancreatic cancer patients with BM or LC. The incidence of BM is rare at 0.27%, with LC at 0.14%. Limitations include likely underdiagnosis given short clinical course and lack of availability of somatic HRR gene status. Our study suggests HRR germline carrier patients may have an increased risk of BM/LC development compared to non-carriers. Given rarity, larger studies should be explored.
High-income is a stronger predictor than race in understanding disparate survival outcomes in PDAC. First Author: Marcus A Alvarez, University of Tennessee Health Science Center, Memphis, TN

Background: Patients with pancreatic ductal adenocarcinoma (PDAC) from low income and minority racial groups have a lower reported long-term survival rates. It is unknown whether this is related to access to care, variations in genetic polymorphisms, or income status. We hypothesized that income status predicts survival better than race in PDAC. Methods: The pancreatic cancer data set of the National Cancer Database (NCDB) was studied for years 2011-15. Income groups were divided into top quartile (high income) or bottom three quartiles (non-high income) while racial groups were classified as Caucasian or non-Caucasian. Kaplan-Meier survival analysis and Cox proportional hazard models (CoxHR) were utilized. Analysis was controlled for established risk factors such as stage, grade, lymphovascular invasion, resection, and margin status. Results: Of the 164,631 patients meeting criteria, the average age was 68 ± 12 years, 51% were male, and 84% were Caucasian (the remaining patients were predominantly African American, 11%). Of patients with stage I or II PDAC who underwent resection, Caucasian patients had worse survival (CoxHR = 1.21, P < 0.0001) while high-income patients had better survival (CoxHR = 0.86, P < 0.001). To investigate only differences due to income or race, a survival model of highly selected, low risk patients (stage I or II lymph node negative well-differentiated tumors without lymphovascular invasion and in patients who underwent margin negative resection who received chemotherapy) found that high-income predicted survival similar to race (CoxHR = 0.89, P < 0.001 vs. CoxHR = 1.12, P < 0.005, respectively). On multivariable analysis, high-income was more impactful on survival (CoxHR = 0.83, P < 0.001) than Caucasian race (CoxHR = 1.16, P < 0.001). High-income, non-Caucasian patients had a median survival of 64 months while all other groups had a median survival of 40 months (P < 0.005). Conclusions: Caucasian PDAC patients have worse survival compared to non-Caucasian patients after selecting for patients with favorable tumor biology who received adequate therapy. The data suggests that high-income is slightly more important than race in understanding disparate outcomes in PDAC.

Aspirin and statin use and the risk of gallbladder cancer. First Author: Kritika Prasai, Mayo Clinic, Rochester, MN

Background: The risk factors for gallbladder cancer (GBC) are poorly understood and preventive therapeutic options have not been identified. The use of aspirin (ASA) and/or statin has been associated with reduced risk of several gastrointestinal cancers. In this study, we explore if the use of ASA or statin is associated with a reduced risk of GBC. Methods: We identified patients with GBC diagnosed between the years 2000 and 2016 at Mayo Clinic. We identified matched controls in 1:1 fashion for age, gender and country of residence from patients who underwent cholecystectomy at Mayo Clinic. We collected information on comorbidities and use of aspirin and statin by retrospective chart review. We compared baseline characteristics between cases and controls using Fisher’s exact test for categorical variables and Mann-Whitney U test for continuous variables. We used binomial logistic regression to calculate the odds of GBC. Results: We found that use of aspirin (ASA) (OR: 0.49) and 95% confidence intervals (CI) to estimate the association of ASA or statin use with GBC. The logistic regression model included history of cholelithiasis, diabetes, hypercholesterolemia (HCL), hypertension (HTN), hyperthyroidism, hypothyroidism, primary sclerosing cholangitis (PSC), inflammatory bowel disease (IBD), cirrhosis and statin or ASA use as covariates. Results: 633 cases and 1,266 controls were included in our final analysis. The median age at diagnosis of cases and controls was 67 years. The control group had a significantly (p < 0.05) higher proportion of patients with cholelithiasis, HCL, HTN, hyperthyroidism and liver cirrhosis compared to the cases. The case group, contrarily, had a significantly higher proportion of patients with PSC and IBD. In univariate analysis, ASA (OR: 0.47; 95% CI: 0.33-0.62) or statin (OR: 0.48; 95% CI: 0.38-0.60) use was associated with a lower risk of GBC (p < 0.001). However, in multivariate analysis, ASA use was associated with a lower risk of GBC (OR: 0.52; 95% CI: 0.41-0.67, p < 0.001) whereas statin use was not (OR: 0.76; 95% CI: 0.56-1.03, p = 0.08). Conclusions: Our study demonstrates that aspirin use is associated with a reduced risk of GBC, whereas statin use is not. Further studies on GBC are needed to confirm these results and to elucidate mechanisms that explain the risk reduction with aspirin.

Sorafenib versus transarterial chemoembolization as adjuvant therapies for patients with hepatocellular carcinoma and microvascular invasion. First Author: Xinyu Bi, Cancer Hospital, Chinese Academy of Medical Sciences, Beijing, China

Background: Microvascular invasion (MVI) is a risk factor for poor prognosis following curative resection in hepatocellular carcinoma (HCC). Currently, there is no standard of care for patients with HCC and MVI. The present study compared the effectiveness of sorafenib and transarterial chemoembolization (TACE) as adjuvant therapies following hepatic resection in patients with early and intermediate-stage HCC and MVI. Methods: This bi-center retrospective study examined 70 patients with HCC and MVI treated by hepatic resection between June 2009 and March 2018. Twenty-four patients received no postoperative adjuvant therapy (control), 19 received TACE and 27 received sorafenib. Recurrence-free survival (RFS) and overall survival (OS) were compared by the log-rank test. Results: Subjects consisted of 62 males and 8 females, with a median age of 53.5 (range, 29-82) years. The median follow-up was 26.0 (range, 4.1-103.3) months. RFS in the sorafenib group was significantly improved compared with the TACE group (P = 0.048), but not with the control group. OS in the sorafenib group was significantly improved compared with both TACE (P = 0.015; 2-year OS: 100% vs. 78.6%) and control (P = 0.023; 2-year OS: 100% vs. 80.0%) groups. Conclusions: Adjuvant sorafenib following hepatic resection improved OS in patients with HCC and MVI and might be a better choice than adjuvant TACE.
Epidemiological trends of small bowel tumors and changing incidence in Utah. First Author: Ramya Thota, Intermountain Healthcare, Murray, UT

Background: The incidence and prevalence of small bowel tumors in particular adenocarcinomas are thought to be rising but updated epidemiological data is lacking. Therefore, for this study we explored the evolving epidemiology of small bowel tumors. Methods: This is a retrospective population based study using Utah Cancer Registry (UCR) and Surveillance Epidemiology, and End Results program (SEER) conducted between 1973-2015. The age adjusted incidence and prevalence was determined. The incidence and prevalence rates were compared to other SEER residents diagnosed with invasive small bowel tumors using ICD codes C17.0 - C17.9. Results: The small bowel tumors have steadily increased from 1990 to 2015. In the UCR, the highest incidence of and small bowel tumors was reported 1.7 per 100,000 in 2015. The prevalence of small bowel tumors in the state of Utah from 1973 - 2014 was 616 including 41 adenocarcinomas, 327 with carcinoid tumors and 248 with other histology’s. There was 1.67% increase in incidence of small bowel tumors in SEER while in Utah we noted 2.81 % annual increase of incidence from 1990 to 2015. Especially, for small bowel adenocarcinomas, Utah has an annual increase of 2.43% from 1990-2015, and SEER had a smaller increase of 0.71% per year over the same time frame. Conclusions: The incidence of small bowel adenocarcinomas between 1995 and 2015 show a steady increase in both UCR and SEER databases. Despite the rarity of these tumors rising incidence warrants increasing awareness and need for better treatments to improve the survival outcomes of these under-studied tumors.

A systematic review and network meta-analysis of adjuvant therapy for curatively resected biliary tract cancers. First Author: Maxine Kish, Queen’s University, Kingston, ON, Canada

Background: Although recently completed randomized controlled trials (RCTs) have added high-quality data regarding adjuvant therapy in curatively resected biliary tract cancer (BTC), there is still no standard approach to manage these patients. We conducted a systematic review and network meta-analysis to compare the efficacy of adjuvant therapy regimens in curatively resected BTC to help guide clinical decision making and the design of future prospective trials. Methods: We conducted a systematic review of published studies and abstracts up to and including June 2018. Studies were included if they were phase III RCTs on patients with histologically proven BTC receiving adjuvant chemotherapy after a complete surgical resection (RO or R1). BTCs included gallbladder cancer, intrahepatic and extrahepatic cholangiocarcinoma. The endpoints of interest were overall survival (OS) and relapse-free survival (RFS). Network meta-analysis methods were used for indirect comparison between adjuvant therapy regimens. Results: Five RCTs were included in the qualitative synthesis and three RCTs (BILCAP, PRODIGE 12-ACCORD 18 and BCAT) included sufficient data to be included in the meta-analysis. Results from the indirect comparison demonstrated no significant difference in OS between any of the adjuvant therapy regimens, however there was a trend that favoured adjuvant therapy with capecitabine over gemcitabine or gemcitabine plus oxaliplatin (GEMOX), with hazard ratios (HRs) of 0.82 (95% CI, 0.53-1.27) and 0.86 (95% CI, 0.56-1.34), respectively. Similarly there was no significant improvement in RFS with capecitabine compared to gemcitabine or GEMOX with HRs of 0.82 (95% CI, 0.53-1.27) and 0.86 (95% CI, 0.56-1.34), respectively. Conclusions: Although capecitabine is considered to be standard of care in the adjuvant setting based on a single randomized phase III study, in this indirect comparison, we did not find a statistically significant improvement in OS or RFS with capecitabine compared to GEMOX or gemcitabine. Further prospective trials comparing adjuvant therapies to capecitabine are warranted.

Dissecting the spatial heterogeneity of single circulating tumor cells reveals immune evasion through MAX regulated CCL5 overexpression in hepatocellular carcinoma. First Author: Yun-Fan Sun, Department of Liver Surgery & Transplantation, Liver Cancer Institute, Zhongshan Hospital, Fudan University, Shanghai, China

Background: The transcriptional heterogeneity and immune evasion mechanisms of CTCs during systemic circulation are not well defined. Methods: Blood was drawn from 4 different vascular sites, including hepatic vein (HV), peripheral artery (PA), peripheral vein (PV) and portal vein (PoV) of 10 localized HCC patients. Single CTCs were isolated by negative enrichment and robotic micromanipulator, followed by single-cell RNA-sequencing (scRNAseq). After filtering, 132 CTCs with qualified data remained were subjected to further bioinformatics analysis. The scRNA-seq results were further validated in three independent cohorts of HCC patients. Results: Our scRNA-seq data revealed remarkable intra- and inter-vascular heterogeneity among CTCs from four vascular sites. We determined CTC transcriptional dynamics during transportation through consecutive vascular compartments and revealed their adaptation mechanisms under biomechanical stress during circulation. We further classified CTCs from different vascular sites into two subsets, namely dormant CTCs and activated CTCs. Dormant CTCs were associated with a non-cycling state and upregulation of EMT/angiogenic signatures and showed stronger prognostic ability for early recurrence than activated CTCs did. Furthermore, we discovered an immune escape mechanism by which CTCs recruited regulatory T cells (Tregs) via expression of CCL5, consequently promoting the formation of an immunosuppressive microenvironment favorable for their survival in the bloodstream and seeding in secondary organs. We proved that MAX, activated through the p38 pathway, was the key transcriptional factor regulating CCL5 overexpression, which was validated by CHIP, luciferase reporter gene and in vitro/vivo knockdown assays. And we further determined that Tregs-derived TGF-β1 can heighten MAX expression, thus amplifying the CCL5 expression in CTCs. Conclusions: Our findings reveal a previously unappreciated spatial heterogeneity of CTCs and a CTC immune-escape mechanism, which may aid in designing new anti-metastasis therapeutic strategies in HCC.

Soluble urokinase plasminogen activator receptor (suPAR) as a novel biomarker in patients undergoing resection of pancreatic adenocarcinoma. First Author: Sven H Loosen, University Hospital RWTH Aachen, Aachen, Germany

Background: Surgical resection represents the only potentially curative therapy for patients with pancreatic adenocarcinoma (PDAC), an aggressive malignancy with a very limited 5-year survival rate. However, even after successful R0 tumor resection, some patients are still facing an unfavourable prognosis underlying the need for better preoperative stratification algorithms. The soluble urokinase plasminogen activator receptor (suPAR) was recently described as a promising new biomarker for different clinical conditions including cancer. Here, we evaluated the potential role of circulating suPAR as a biomarker in patients undergoing resection of PDAC. Methods: Expression levels of uPAR, the membrane-bound source of circulating suPAR, were analysed in PDAC tissue samples using IHC. Serum levels of suPAR were measured by ELISA in an exploratory as well as a validation cohort comprising a total of 127 PDAC patients and 75 healthy controls. Results were correlated with clinical data. Results: Correlating with a high immunohistochemical expression of uPAR in PDAC tissue samples, serum levels of suPAR were significantly elevated in PDAC patients compared to healthy controls. Importantly, patients with high preoperative suPAR levels above a calculated cut-off value of 5.956 ng/ml showed a significantly reduced overall survival after tumor resection. The prognostic role of suPAR was further corroborated by un- and multivariate Cox-regression analyses including parameters of systemic inflammation, liver and kidney function as well as clinico-pathological patients’ characteristics. Moreover, high baseline suPAR levels identified those patients particularly susceptible to acute kidney injury after surgery. Conclusions: Our data suggest that circulating suPAR represents a novel prognostic marker in PDAC patients undergoing tumor resection that might be a useful addition to existing preoperative stratification algorithms for identifying patients that particularly benefit from extended tumor resection.
A phase Ib dose escalation study of vanticutumab (VAN) in combination with nab-paclitaxel (Nab-P) and gemcitabine (G) in patients with previously untreated stage IV pancreatic cancer. **First Author:** S. Lindsey Davis, University of Colorado Comprehensive Cancer Center, Aurora, CO

**Background:** Vanticutumab is a fully human monoclonal antibody that inhibits Wnt pathway by binding to FZD1, 2, 5, 7, and 8 receptors. A phase Ib study of VAN in combination with Nab-P and G was performed in patients with untreated stage IV pancreatic adenocarcinoma. **Methods:** Patients received VAN at escalating doses (3-7 mg/kg) in combination with standard dosing of Nab-P and G according to a 3+3 design. Due to fragility fractures occurring in this and other related clinical trials, dosing on an every 2 week schedule in cohorts 1 and 2 was transitioned to every 4 week dosing for cohorts 3 through 5. In these later cohorts, a minimum of six patients were treated at each dose level and additional data for maximum tolerated dose (MTD) integrating bone safety parameters were added. The bone safety plan was also revised for these cohorts. Sequential dosing of VAN followed by Nab-P and G was explored in cohort 5. **Results:** Thirty-one patients (52% male, 48% female) were enrolled in 5 dosing cohorts. Median age was 66. Most common study-treatment related adverse events were nausea (68%) and fatigue (52%). One dose limiting toxicity (DLT) event occurred in the study population—grade 3 dehydration in 1 of 9 patients in cohort 4 (5 mg/kg q4w). Fragility fractures attributed to VAN occurred in two patients in cohort 2 (7 mg/kg q2w). Once the dosing schedule was revised to every 4 weeks, the maximum administered VAN dose was 5 mg/kg. No fragility fractures attributed to VAN occurred in these cohorts; pathologic fracture not attributed to VAN was documented in 2 patients. The study was terminated due to lack of an acceptable therapeutic index. Partial response was documented in 13 patients (42%) and stable disease in 11 (36%). **Conclusions:** The MTD of VAN plus Nab-P and G was not determined, but the maximum administered dose (MAD) of VAN, 7 mg/kg every 2 weeks, was considered unsafe related to bone toxicity, a known effect of WNT inhibition. After the study was revised, the MAD was 5 mg/kg every 4 weeks, with no protocol-specified bone toxicity observed (n = 16). Clinical trial information: NCT02005315.

**Poster Session (Board #D9), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM**

**Dose intensity of nab-paclitaxel and gemcitabine chemotherapy in metastatic pancreatic cancer.** **First Author:** Alexander Lim, University of South Florida, Department of Internal Medicine, Tampa, FL

**Background:** Combination chemotherapy with nab-paclitaxel/gemcitabine is a standard of care option in metastatic pancreatic cancer management with increasing use due to an improvement in median overall survival of 1.8 months compared to gemcitabine alone. As the utility of this combination chemotherapy has grown, dose intensity (DI) in relation to survival outcome is an important measure for real world application. **Methods:** Fifty-five patients who were 18 years or older with metastatic pancreatic cancer treated with nab-paclitaxel/gemcitabine as first-line therapy from January 1, 2013 to December 31, 2014 at Moffitt Cancer Center were included in the analysis. The subjects were retrospectively reviewed, and demographic, treatment outcomes (survival and progression), and DI were collected. Overall survival was calculated with Kaplan Meier survival curves. Multi-Cox regression models estimated multivariable-adjusted hazard ratio with 95% confidence intervals. **Results:** There was no significant relationship between receiving a DI > 85% regimen in relation to independent variables of age > 65, sex, primary site, and known distant metastasis; however DI > 85% was significant for patients that received additional chemotherapy following nab-paclitaxel/gemcitabine (p = 0.044). The DI > 85% group compared to the < 85% group had a hazard ratio (HR) for all-cause mortality of 0.285 (0.106-0.764, p = 0.013). Six and 12-month survival were higher in the DI > 85% group (p = 0.009, p = 0.02 respectively). **Conclusions:** DI > 85% for nab-paclitaxel/gemcitabine compared to DI < 85% may have a lower all-cause mortality and higher 6 and 12-month survival.

**Poster Session (Board #D10), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM**

**Imaging findings of patients undergoing SBRT for HCC after prior TACE.** **First Author:** Aneliya Maleeva, Loyola University Medical Center, Maywood, IL

**Background:** Our purpose is to assess the treatment response using follow up MRI or CT in lesions treated with stereotactic body radiation therapy (SBRT) after transarterial chemoembolization (TACE). **Methods:** Twenty-six patients treated with liver SBRT at our institution in the period between 2015 and 2017. Of these we included patients who had lesions diagnosed as HCC (LR-5) or probable HCC (LR-4), and who had prior TACE with a residual/recurrent enhancing component on the pre SBRT images with adequate post SBRT imaging. One radiologist (5 year experience) evaluated all pre and post SBRT imaging and measured the lesion size and the size of the largest enhancing component. Lesion decrease or increased in size was assessed based on the mREIST criteria. Explant pathology results were collected for patients who received transplant. Necrosis > 90% on explant was considered full response to treatment. AFP (alpha-fetoprotein) values before and after SBRT were collected. **Results:** Eight patients with 9 lesions meet our inclusion criteria, 3 of which were LR-5 and 6 LR-4 prior to the TACE. At 1 month, 2 lesions had no residual enhancing component, 2 lesions decreased in size, 2 lesions increased in size, 3 lesions remain unchanged. After maximum available follow-up (ranging from 3 to 8 months), 3 lesions had no residual enhancing component, 2 decreased, 2 lesions increased in size, 2 lesions remain unchanged. Of the 3 lesions that were definitive HCC (LR-5): 1 lesion decreased in size, 2 lesions increased in size. 4 of 8 patients (4 lesions) underwent transplant, 3 of them showed only 50% necrosis on explant. 1 of 3 lesions showed no change in size by imaging, the other 2 lesions had no residual enhancing component. Only 1 lesion had full response on the transplant. This lesion was unchanged on 3 and 6 months follow up. The AFP was not helpful since the majority of the patient had low pre-treatment AFP. **Conclusions:** Patient with viable disease on imaging after TACE subsequently treated with SBRT demonstrated variable behavior on imaging. Close to half demonstrated resolution of the enhancing component, however, in the few that had explant, follow up there was no correlation between imaging findings and pathology.
Enhancement of the efficacy of radiofrequency ablation by neoadjuvant oncolytic virus therapy via antitumor immunity and the booster effect of immune checkpoint inhibitors. First Author: Tomoharu Yamada, The Institute of Medical Science, The University of Tokyo, Tokyo, Japan

Background: A third generation oncolytic herpes simplex virus type 1, G47Δ, destroys tumor cells selectively and induces a systemic antitumor immune responses. Radiofrequency ablation (RFA) is a standard local therapy for hepatocellular carcinoma (HCC). Here, we examined the efficacy of G47Δ used in combination with RFA and evaluated the antitumor immune responses. Methods: In A/J mice harboring bilateral fully immunogenic Neuro2a subcutaneous tumors, tumors on one side were treated with intratumoral injections with G47Δ (2×10⁶ pfu) on days 0, 2 and 4 followed by RFA treatment on day 6, which results in complete regression of the treated tumors. We further treated with an immune checkpoint inhibitor (ICi) in combination. Tumor infiltrating lymphocytes in contralateral tumors were analyzed with flow cytometric analysis. To examine the contribution of CD8+ T cells, CD8+ T cells were depleted by treatment with anti-CD8 monoclonal antibody. To mimic a remote recurrence, unilateral subcutaneous tumors were treated with G47Δ and RFA, and Neuro2a cells were implanted on the same day of RFA. In a separate experiment without rechallenge, antitumor immunity was evaluated using ELISpot assay on day 20. Results: The G47Δ+RFA treatment caused smaller volumes of contralateral tumors and increased infiltration of CD8+CD45+ T cells in the tumor, compared with RFA or G47Δ monotherapy. Without CD8- T cells, the antitumor effect on the contralateral tumors was completely abolished. When mice were rechallenged, those cured by G47Δ+RFA rejected the Neuro2a more frequently than those cured by RFA alone. ELISpot assay revealed that the number of Neuro2a reactive spleenocytes was significantly greater in the G47Δ+RFA group than the RFA group. The G47Δ+RFA+anti-PD-L1 treatment caused smaller volumes of contralateral tumors compared with G47Δ+RFA treatment, whereas anti-PD-L1 alone showed no effect. Conclusions: Intratumoral administration of G47Δ prior to RFA would enhance systemic antitumor immunity that is further enhanced by ICi.

255

Sunitinib in patients with pancreatic neuroendocrine tumors (panNETs): Exploratory pharmacogenomic analyses. First Author: Nicola Fazio, European Institute of Oncology, Milan, Italy

Background: In a phase IV trial (NCT01525550), median progression-free survival (PFS) was 13.2 mo in sunitinib-treated patients (pts) with well-differentiated panNETs. Objective response rate (ORR) was 24.5% and survival (PFS) was 13.2 mo in sunitinib-treated patients (pts) with well-differentiated panNETs. In a phase IV trial (NCT01525550), median progression-free survival (PFS) was 13.2 mo in sunitinib-treated patients (pts) with well-differentiated panNETs. Objective response rate (ORR) was 24.5% and survival (PFS) was 13.2 mo in sunitinib-treated patients (pts) with well-differentiated panNETs. In a phase IV trial (NCT01525550), median progression-free survival (PFS) was 13.2 mo in sunitinib-treated patients (pts) with well-differentiated panNETs. Objective response rate (ORR) was 24.5% and survival (PFS) was 13.2 mo in sunitinib-treated patients (pts) with well-differentiated PanNETs. Methods: Blood samples were collected at baseline and during treatment. Genotyping was performed using the Illumina Infinium Human SNP66 BeadChip. Pharmacogenomic analyses were performed using the Nextera Rapid Capture Exome Kit by Illumina on an Illumina HiSeq 2000/2500. The following criteria were used to define genetic variants: bidirectional, non-synonymous, clean mapping in IGV, IGV, 15X coverage, and an alternate allele frequency of 0.3 ≤ x ≤ 0.7. Results: All genetic PanNETs were classified as WHO grade G2/G3 based on their Ki-67 proliferation index. Each primary PanNET contained an average of 102 genetic variants while liver metastases showed an average of 124 genetic variants. MUFFINN and string analysis revealed that primary PanNETs contained enrichment for mutations involved in the PI3K/Akt and Ras signaling pathways. Conclusions: Potential associations between ORR and VEGFR1 rs9554320, VEGFR2 rs7692791, IL1B rs16944, KRAS G/A versus G/G (46.4% vs 4.5%; p = 0.001) in the combined group. Clinical trial information: NCT01525550.
The prognostic role of soluble transforming growth factor-β (sTGFβ) and soluble programmed death-ligand 1 (sPD-L1) in biliary tract cancer patients treated with binimetinib and cetuximab. First Author: Jin Won Kim, Seoul National University Bundang Hospital, Seoul, Korea, Republic of (South)

Background: Transforming growth factor (TGF)-β signaling is important for tumor growth, microenvironment, and tumor immune responses. Here, we evaluated the tumor response to programmed death-ligand 1 (PD-L1) blockade. This study aimed to evaluate a correlation between soluble TGF-β (sTGF-β) and soluble PD-L1 (sPD-L1) and its prognostic role in BTC. Methods: Study population consisted of 34 patients enrolled in phase Ib clinical trial of binimetinib (MEK inhibitor) with cetuximab in gemcitabine-pretreated BTC (ClinicalTrials.gov: NCT02773459). Blood samples at screening, after first cycle, after second cycle, and at disease progression were prospectively collected. Plasma sTGF-β and sPD-L1 values were measured by using an enzyme-linked immunosorbent assay. Results: In total 34 patients, 25 (73.5%) and 9 patients (26.5%) were second-line and third-line setting, respectively. Median progression-free survival (PFS) and overall survival (OS) were 4.1 and 7.8 months. The mean baseline sTGF-β and sPD-L1 were 18.7 ng/ml and 3.1 ng/ml. There was a positive correlation between sTGF-β and sPD-L1 (Pearson correlation = 0.596, p < 0.001). Mean baseline value was likely to be higher in best response of progressive disease, followed by stable disease and partial response. Similarly, higher baseline sTGF-β showed significantly shorter PFS (3.4 vs 5.1 months, p = 0.047) and OS (5.4 vs 9.7 m, p = 0.042). Higher baseline sPDL1 also had a trend for poor PFS and OS (PFS: 3.0 vs 4.3 m, p = 0.220; OS: 6.4 vs 9.7 m, p = 0.140). Regarding changes from baseline to after first cycle, sTGF-β change of >1.6 ng/ml demonstrated significantly shorter OS (5.9 vs 10.8 m, p = 0.020), although PFS did not show a significant change (p = 0.200). In contrast, OS did not differ according to sPD-L1 change (p = 0.190). sPDL1 change >-1.7 ng/ml even had longer PFS (5.1 vs 2.2 m, p = 0.005).

Conclusions: In BTC patients with binimetinib and cetuximab, there is a positive correlation between sTGF-β and sPD-L1 value and higher baseline sTGF-β and sPD-L1 indicate a worse prognosis. The early change of sTGF-β and sPD-L1 during treatment could predict the survival.

Gastrin vaccine and immune checkpoint antibody therapy for pancreatic cancer. First Author: Jill P Smith, Georgetown University, Washington, DC

Background: Pancreatic cancer is poorly responsive to therapy due to fibrosis in the tumor microenvironment and nonspecificity of treatments. The peptide gastrin stimulates growth of pancreatic cancer in an autocrine fashion. Polyclonal Antibody Stimulator (PAS) is a gastrin vaccine that in preclinical studies demonstrates neutralizing gastrin antibodies. We hypothesized that PAS also elicits a memory and T-cell response that would improve effectiveness of immune checkpoint antibodies. Methods: C57BL/6 mice were injected sc with syngeneic mT3 murine pancreatic cancer cells. Mice were randomized into 3 treatment groups: PBS (control); PAS (100 μg); or combined therapy with PAS100/PD-1. PAS was given ip at weeks 0, 1, and 3. Anti-PD-1 was given on days 0, 4, 8, 15 and 21. On day 31 spleens were collected for T-cell responses. –94.0) for censored cases, the median survival for all patients was 2 years, n = 4), while 11 patients died within 4 months. We show tumoral landscape of unresectable advanced pancreatic cancer and identified somatic mutations in known cancer related genes including KRAS (89%), TP53 (71%), SMAD4 (20%), CDKN2A (17%) and ARID1A (14%). We found that ARID1A mutation was mutually exclusive with TP53 mutation except for one tumor and had a significant correlation with survival outcomes. Among 9 patients who survived more than 2 years, 5 patients (56%) had ARID1A somatic mutation, whereas none (0%) had mutations in the remaining 26 patients who died within 2 years (p = 0.0004). The median overall survival was 47.7 months for 5 patients with ARID1A-mutated tumors and 8.9 months for 30 patients with ARID1A wild-type tumors (p = 0.0101). Conclusions: This is the first study to perform whole-exome sequencing in unresectable pancreatic cancer patients including very long-term survivors. We found that ARID1A mutations were associated with longer survival.
CANCERS OF THE PANCREAS, SMALL BOWEL, AND HEPATOBILIARY TRACT

261 Poster Session (Board #D19), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Circulating free tumor DNA copy number index (CNI) as a predictor of therapeutic response in pancreatic ductal adenocarcinomas (PDAC). First Author: Madappa N. Kundranda, Banner MD Anderson Cancer Center, Gilbert, AZ

Background: Cell-free tumor DNA (cfDNA) has potential to provide minimally invasive patient specific biomarkers to monitor tumor burden. Tumor-specific copy number instability (CNI) are used to quantify tumor-derived cfDNA in the plasma. We prospectively computed CNI Scores of cfDNA to compare with radiological and Ca 19-9 responses. Methods: In a laboratory blinded, prospective single-institution study, 119 plasma samples from 33 patients (pts) with PDAC were analyzed. Time-points were at baseline (C1), 2nd (C2) and 3rd (C3) cycle of systemic therapy. Tumor cfDNA was measured with a CNI scoring assay that quantifies cfDNA with somatic macro-alterations. CNI Score (CNI) of 31 was defined as ref. range (97.5 % - control group; N = 135), pts below this threshold were censored. Progression of disease (PD) defined as C3 NIs > 93 (3-fold threshold) and difference to the baseline > 31 (dispersion of reference population). Mutant KRAS in plasma was measured using ddPCR in a subset 22 pts. Pts with an increase of > 0.06% (critical difference) were classified PD. Radiologic imaging results were correlated with CNI and Ca19-9 changes from baseline to C3, respectively. Results: By standard radiological imaging 33 pts were classified as: 14 PR/CR, 10 SD, 9 PD. 27/33 pts (82%) were evaluable by CNIs which ranged from decrease of 2067 % increase of 64.5%. The C3 CNI classifier yielded a sensitivity of 86% for prediction of PD and 95% for SD/PR/CR. KRAS classification yielded an accuracy of 72%, and only 3/9 PD were accurately predicted (33%). 26/33 pts were secretors evaluable by Ca19-9. Only 2/8 PD pts showed increasing values in Ca19-9 and 6/8 of evaluable by CNI. 5/6 showed increasing increasing CNI scores. 3/20 deemed as SD on imaging with increasing values of CA19-9 were noted to have decreasing CNIs. CNI Score classification was significantly better than Ca19-9 (P = 0.001 and 0.63, respectively). Conclusions: Our evaluation of a comparative study on cfDNA and Ca19-9 versus imaging suggest that CNI quantification is potentially a more reliable blood-based marker for early assessment of efficacy to systemic therapy in PDAC. Furthermore, for patients not expressing CA19-9 it could serve as an alternative monitoring aid.

264 Poster Session (Board #E2), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Randomized phase II trial of the carboxyesterase (CES)-converted novel drug EDO-S7.1 in patients (pts) with advanced biliary tract cancers (BTC). First Author: Ulrich-Frank Pape, Department of Internal Medicine, Charité-Universitätsmedizin, Berlin, Germany

Background: The novel drug EDO-S7.1 (CAP7.1) is converted to active eoto- pes by CES allowing administration of higher doses, reducing resistance, and permitting treatment of advanced tumors. Methods: The primary ob- jective was to compare drug control rate (DCR) in 22 pts with respectable BTC randomized 1 to 3-week cycles of EDO-S7.1 (200 or 150mg/m2; iv) given on days (d) 1-5, or best supportive care (BSC) until progression (assessed every 4 weeks). Secondary objectives were progression-free survival (PFS), time to treatment failure (TTF), overall survival (OS), and safety. BSC pts could crossover to EDO-S7.1 upon progression. Results: DCR favored EDO-S7.1 (55.6% (CI 21.2, 86.3) vs BSC (20.0% (2.5, 55.6); treatment difference -12.80, 72.39)). More EDO-S7.1 treated pts achieved sustainable stable disease (SD) or partial response (PR) vs BSC. Progression-free survival (PFS) were significantly higher for cases versus controls (mean [SD]: $51,825 [70,423] vs $29,068 [56,454], respectively). Conclusions: This study revealed that CaHd is common among patients with CS both before and after initiating SAS treatment. Early diagnosis and control of CS is necessary to reduce the burden of CaHd.

265 Poster Session (Board #E3), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

The effect of hepatic stellate cells on hepatocellular carcinoma progression. First Author: Shuichi Iwahashi, Tokushima University, Tokushima, Japan

Background: The hepatic stellate cells (HSCs) localize at the space of Disse in the liver and have multiple functions. They are identified as the major contributor to hepatic fibrosis. Some manuscripts mentioned that activated HSCs predict prognoses of hepatocellular carcinoma. The aim of this study is to investigate the effect of HSCs and the role of IL-6 / STAT3 pathway on HCC progression. Methods: HCC cells (Hep G2 and Huh 7) were co-cultured with HSC (LX2 and Li90). The viability and migration ability of cancer cells were detected. Also, the expression of epithelial-mesenchymal transition marker (E-cadherin), stem cell marker (EpCAM and CD44), TGF-b and p-STAT3 of cancer cells were evaluated. Then the IL-6 neutralization was performed during HCC cells and HSCs co-culture. The viability and migration ability of cancer cells were detected. Also, the expression of epithelial-mesenchymal transition marker (E-cadherin), stem cell marker (EpCAM and CD44) and p-STAT3 of cancer cells were evaluated. Results: Co-culture with hepatic stellate cell increased cancer cell viability and migration ability. The expression of E-cadherin, EpCAM and CD44 of cancer cells also increased after co-culture with HSCs. The IL-6 expression and secretion of HSCs were elevated by cancer cell stimulation. The over-expressed IL-6 activated STAT3 of cancer cells and permitting treatment of advanced tumors. Conclusions: EDO-S7.1 demonstrated efficacy in pts with ad-
Deleterious alterations in DNA-damage repair (dDDR) genes as a predictive biomarker for platinum-based chemotherapy in metastatic pancreatic ductal adenocarcinoma (mPDAC), First Author: Sofia Palacio, University of Miami/Jackson Memorial Hospital, Miami, FL

**Background:** Germline genetic testing and somatic genomic profiling using comprehensive mutational panels are now routine in mPDAC. We aimed to test the hypothesis that dDDR is a predictive biomarker for response to first-line platinum-based chemotherapy. Methods: Utilizing the IRB-approved pancreatic cancer and genetic testing clinic database at the University of Miami, we identified all patients with mPDAC who had germline and/or somatic mutation testing. We performed a retrospective chart review to extract demographic and clinical characteristics including treatments received, response, and survival. Results: Between 2012 and 2018, 166 patients with mPDAC underwent germline (using InvivoGen) and/or somatic testing (using FoundationOne CDx). Among these, 40 received first-line therapy with FOLFIRINOX (95%) or gemcitabine/cisplatin (5%). The median age was 59 years and 15 (38%) were female. The majority (70%) were Hispanic, and 63% had de novo disease (treatment-naive). Germline testing revealed dDDR in 5 patients and somatic NGS found an additional 4 patients with dDDR (total of 9 (23%), including 5 with BRCA2, one each with BRCA1, RAD51C, ATM and MUTYH). The median progression-free survival (PFS) was significantly longer in patients with dDDR than without (17.3 vs 7.8 months, log-rank p = 0.01). The median overall survival (OS) was not statistically different between the two groups. Three patients with dDDR had complete or near-complete radiological and tumor marker responses to FOLFIRINOX and were treated chronically off-study. However, patient survival (BLOQ to death) and recurrent patients remained higher in dDDR free after 7, 12.4 and 13.6 months respectively. Conclusions: dDDR appears to define a subset of patients with mPDAC who may be more sensitive to platinum agents. There are currently no biomarkers for selection of first-line therapy in patients with mPDAC and we demonstrate that this composite biomarker which is easily done via commercially available assays may be able to inform treatment selection.

268 Poster Session (Board #E6), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

An open-label phase Ib/2 trial of TRC105 plus sorafenib in patients with advanced/metastatic hepatocellular carcinoma (HCC) (NCT019806064), First Author: Kanwal Pratap Singh Raghav, The University of Texas MD Anderson Cancer Center, Houston, TX

**Background:** TRC105, an endoglin antibody, potentiates the activity of sorafenib (S) in preclinical HCC models, and TRC105 + S demonstrated a 33% response rate. We aimed to explore the role of dDDR as a predictive biomarker for response to first-line platinum-based chemotherapy. Methods: Utilizing the IRB-approved pancreatic cancer and genetic testing clinic database at the University of Miami, we identified all patients with mPDAC who had germline and/or somatic mutation testing. We performed a retrospective chart review to extract demographic and clinical characteristics including treatments received, response, and survival. Results: Between 2012 and 2018, 166 patients with mPDAC underwent germline (using InvivoGen) and/or somatic testing (using FoundationOne CDx). Among these, 40 received first-line therapy with FOLFIRINOX (95%) or gemcitabine/cisplatin (5%). The median age was 59 years and 15 (38%) were female. The majority (70%) were Hispanic, and 63% had de novo disease (treatment-naive). Germline testing revealed dDDR in 5 patients and somatic NGS found an additional 4 patients with dDDR (total of 9 (23%), including 5 with BRCA2, one each with BRCA1, RAD51C, ATM and MUTYH). The median progression-free survival (PFS) was significantly longer in patients with dDDR than without (17.3 vs 7.8 months, log-rank p = 0.01). The median overall survival (OS) was not statistically different between the two groups. Three patients with dDDR had complete or near-complete radiological and tumor marker responses to FOLFIRINOX and were treated chronically off-study. However, patient survival (BLOQ to death) and recurrent patients remained higher in dDDR free after 7, 12.4 and 13.6 months respectively. Conclusions: dDDR appears to define a subset of patients with mPDAC who may be more sensitive to platinum agents. There are currently no biomarkers for selection of first-line therapy in patients with mPDAC and we demonstrate that this composite biomarker which is easily done via commercially available assays may be able to inform treatment selection.

269 Poster Session (Board #E7), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Mutational landscape by targeted next-generation sequencing in EBV-associated lymphoepithelioma-like cholangiocarcinoma. First Author: Nai-Jung Chiang, National Institute of Cancer Research, National Health Research Institutes, Tainan, Taiwan

**Background:** Lymphoepithelioma-like cholangiocarcinoma (LELCC) is a rare variant of intraductal cholangiocarcinoma, which is highly associated with EBV infection and abundant lymphoplasmytic cell infiltration. However, there’s limited data of genetic background in LELCC. Therefore, we want to explore the mutation profiles of LELCC, as well as copy number variations. Methods: Five patients’ tumor tissues diagnosed as LELCC, with positive EBV expression were retrospectively collected and microscopically dissected. Of them, two patients’ peripheral blood mononuclear cells served as background of germline mutations. Targeted next-generation sequencing was performed using the ACTOnco Comprehensive Cancer Panel (Ion AmpliSeq Comprehensive Cancer Panel, Life Technologies) to target all coding exons of 409 cancer-related genes for analysis of tumor tissue and blood. PD1-L1 immunohistochemistry staining with 22C3 antibody pharmDx was applied. Results: All EBV-associated LELCC showed positive expression of PD1-L1 staining, with combined positive score from 5% to 30%. Both somatic and germline mutations can be detected in LELCC tissue because diffuse infiltration of lymphocytes over tumor. After adjusting for background germline mutation frequency from peripheral blood, only mutations with allele frequency less than or around 10% were considered as somatic mutations. Overall, 10 non-synonymous somatic mutations were detected in 4 (80%) patients with a range of 1+ mutations per sample. Mutations were identified including BARD1, EPHAS, MUC6, TNAFAP3, CD19, PTCN, TET1, RECOL4, CD79B, and KDM5A. Copy number changes were rare in this special population. Interestingly, one patient with both tumor and peripheral blood for next-generation sequencing to identify truly somatic mutations in LELCC.
A pilot study of galunisertib (L12157299 monohydrate) plus stereotactic body radiotherapy (SBRT) in advanced hepatocellular carcinoma (HCC).  
First Author: Kim Anna Reis, University of Pennsylvania, Philadelphia, PA  
Background: TGF-β, the strongest known immunosuppressive cytokine, modulates the hepatic immune response to various antigens and to ionizing radiation. When activated, TGF-β blocks the effector T-cell response to cellular destruction and the release of tumor-specific antigens. Preclinical data demonstrate that neutralizing TGF-β during radiation effectively generates a CD8+ T-cell response to multiple endogenous tumor antigens, thereby generating an in-situ vaccine against a tumor. We hypothesized that the combination of TGF-β receptor inhibition plus SBRT would produce a potent and clinically effective antitumor immune response against HCC.  
Methods: Patients received galunisertib (L12157299 monohydrate) on days 1-4 of each 28 day cycle. SBRT was delivered in a single fraction of 18 Gy between days 15-28 of CI. Pretreatment and on-treatment biopsies were obtained, as well as serial blood collections for CTCs, cDNA and PBMCs.  
Results: 15 patients with advanced HCC and Child’s Pugh A cirrhosis were treated. 9/15 (60%) had a prior history of infectious hepatitis, three of whom had active viremia at time of enrollment. 6/15 (40%) had received prior systemic therapy for HCC and 12/15 (80%) had received prior liver directed therapy. The most common treatment-related toxicities were: fatigue (53%), nausea (47%), increased alkaline phosphatase (33%), abdominal pain (33%), vomiting (20%), decreased white blood cell count (20%). All drug-related toxicities were grade 1 or 2, with the exception of one patient who had grade 3 achalasia, thought possibly to be related to study drug. Median PFS was 5.68mo. There were two confirmed partial responses (PRs) and six additional patients had stable disease (SD) at least four months, resulting in a disease control rate (DCR) of 53%. Both PRs included shrinkage of lesions that had not been radiated. Transectional studies are currently underway.  
Conclusions: The combination of galunisertib with SBRT in patients with advanced HCC is a well-tolerated regimen. In this small pilot study, we observe a DCR of 53% including two PRs. These results warrant further study of this therapeutic combination in advanced HCC.  
Clinical trial information: NCT02906397.
The feasibility of hepatectomy for the super-elderly patients with HCC. First Author: Shogo Ohta, Tokushima University, Tokushima, Japan

Background: We previously reported the feasibility of hepatectomy for HCC patients who were above 80 years old (Yamada S, Shimada M, et al. Hepatology Res. 2012). However, there was the manuscript that it was important to assess the preoperative co-morbidity on hepatectomy in elderly patients. The aim of this study is to investigate the feasibility of hepatectomy in super-elderly patients over 85 years old focused on the postoperative complications.

Methods: Two hundred twenty-nine patients with HCC who underwent primary hepatectomy from April 2004 to October 2016 were enrolled in this study. Patients were divided into three groups; above 85 years old (super-elderly, n=6), between 75 and 85 years old (elderly, n=54) and below 75 years old (non-elderly, n=169). All of patients in this study did not underwent either preoperative treatment nor additional splenectomy. Clinicopathological data and outcomes after hepatectomy were compared between three groups.

Results: There were no significant differences between the super-elderly group and other two groups in the patients’ backgrounds and tumor factors. Regarding as the rate of total postoperative complications, there was no difference between three groups. However, in super-elderly group, the mortality was higher compared with other two groups (super-elderly 16.7%, elderly 0%, non-elderly 12%; p<0.01 One-way ANOVA, Turkey’s test). There was the one patient of liver failure in the super-elderly group, and he died due to the liver and respiratory failure. In long-term outcomes, there was no significant difference between the super-elderly group and other two groups.

Conclusions: The long-term outcome of super-elderly patients was similar to that of non super-elderly, however, the careful attention to the liver failure might be paid on super-elderly hepatectomy patients. Therefore, hepatectomy might be justified for selected super-elderly patients.
The impact of CDKN2A mutations on overall survival in pancreatic adenocarcinoma. First Author: Allison Doyle, Georgetown University School of Medicine, Washington, DC

Background: Pancreatic ductal adenocarcinoma (PDAC) is an aggressive disease with a five-year survival rate of only 9%. Analyses based on tumor DNA mutations indicate the presence of specific molecular subtypes of PDAC. Tumor genomic profiling could result in better treatment selection and improved overall survival. We performed a single institution analysis of PDAC mutations and correlated them with clinical outcomes. Methods: PDAC samples from patients (pts) seen at the Lombardi Comprehensive Cancer Center between 2014 and 2018 were profiled using next generation sequencing, including 592 whole-genome targets (Caris Life Sciences). Relevant clinical data was mined retrospectively and correlated with genomic data. Results: pts were evaluable: median age 62.6 years, female 63%, median tumor size 5.1 cm, 38% had stage IV disease. Seventy-seven percent developed metastatic disease with a five-year survival rate of only 9%. Stratification of OS based on single gene mutations did not significantly impact OS except for CDKN2A. Patients with CDKN2A mutations had significantly longer OS compared to wild type (22 vs. 35 months, P = 0.018). OS based on presence of co-occurring mutations only showed a negative OS impact when CDKN2A mutations were present (14 m vs. 35 m; P = 0.021). Conclusions: Our data demonstrate that the presence of CDKN2A mutations is a significant negative prognostic OS indicator for patients with PDAC. FGFR1 exhibited hypersensitivity to BGJ398.

Individual FGFR and pooled FGFR-3 RNA-ISH findings in patients with cholangiocarcinoma.

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280 Poster Session (Board #E18), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

A multi-institutional study assessing prevalence of deleterious germline mutations in pancreatic cancer. First Author: Meena Sadaps, Cleveland Clinic, Cleveland, OH

Background: Pancreatic cancer is being increasingly associated with germline implications. Some large single-center studies have reported results ranging from 9% of patients found to have germline variants (Shindo, JCO 2017; Lowery, JNCI 2018). Due to this wide range, we aim to further delineate prevalence of deleterious germline mutations in pancreatic cancer patients using a multi-institutional data set. We also aim to analyze predictive factors such as mutant allele frequency (MAF, in %) in germline versus somatic calls. Methods: We sequenced 23 genes in DNA prepared from clinical tissue and blood specimens submitted to Tempo Labs. Germline variants and somatic variants were separated separately. Germline variants were determined to be deleterious through the sum effect of a combination of in silico predictors, population databases, and internal evaluations. Tumor-normal comparisons were used to define somatic versus germline, and MAFs were calculated for each. Results: A total of 234 patient samples from 17 institutions were analyzed. Of these, 12 (5.1%) had predicted deleterious germline variants involving 8 different genes: BRCA1 (n = 3), CHEK2 (n = 3), ATM (n = 3), MLH1 (n = 1), MUTHY (n = 1), PALB2 (n = 1), SMAD4 (n = 1), TP53 (n = 1). For most somatic alterations, the MAFs were found to be greater than the germline deleterious alterations, with the latter approaching ~50% in most cases (Table). Conclusions: This multi-institutional study identifies 5% of patients with pancreatic cancer to have deleterious germline alterations. Somatic variant testing, particularly when paired with germline, can be used as a screening method for genetic counseling referrals, especially with MAF analyses of paired tumor-normal samples.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Ligand-inducible, prostate stem cell antigen (PSCA)-directed GoCAR-T cells in advanced solid tumors: Preliminary results from a dose escalation. First Author: Carlos Roberto Becerra, Baylor University Medical Center, Dallas, TX

Background: PSCA, a cell surface protein, is upregulated in many solid tumors and correlated with disease stage. PSCA is an auto-antigen, T-cell product engineered to contain a PSCA-CD3ζ CAR plus the small molecule rimiducid (Rim)-inducible MyD88/CD40 costimulatory domain. BPX601 is optimized for antigen-directed and independent T cell activation, proliferation and persistence, potentially enhancing efficacy in solid tumors versus traditional CARs. This first-in-human study assesses the safety, biological and clinical activity of BPX601 plus Rim in select PSCA-positive cancers. Methods: NCT02744287 is a two-part, open-label trial. Part 1 is an ongoing 3+3 dose escalation to identify the recommended BPX601 cell dose (Day 0) given in combination with a fixed, single Rim dose (0.4 mg/kg; Day 7). Eligibility criteria include previously treated metastatic pancreatic cancer (mPDAC) with measurable disease & positive PSCA expression. Results: Patients received only cyclophosphamide (CTX) for lymphodepletion (LD) within three days before BPX601 infusion. Nine adults have been treated across three cell dose levels (cells/kg): 1.25x10⁶ (cells only), 2.5x10⁶+Rim, 2.5x10⁶+Rim. All had mPDAC with ≥2 prior therapies. Common AEs were fatigue and nausea. No DLTs, related SAEs, neurotoxicity or CRS events were reported. Rapid cell engraftment by Day 4 was observed in all patients. No evidence of LD with CTX was seen. Of six patients that received Rim: two had cell expansion 10- to 20-fold within seven days; two had cell persistence > three weeks; all had elevated serum cytokines (IP-10, TNα) correlated with cell expansion. Best response after ≥ one scan was 4 SD ≥ eight weeks with two minor responses (not confirmed; one patient had matched CA19-9 decrease) and 2 PD. Disease control without new therapy was 16 and ≥11 weeks (ongoing) in one and two patients, respectively. Conclusions: BPX601 with single-dose Rim was well-tolerated and resulted in enhanced T-cell expansion and prolonged persistence in some patients despite lack of LD. Evidence of clinical benefit in this heavily pretreated mPDAC population was seen. Part 2 is planned to open soon and will include CTX/fludarabine LD to maximize engraftment as well as gastric and prostate cancers. Clinical trial information: NCT02744287.

Sequential gemcitabine (G), oxaliplatin (O), and irinotecan (I) based weekly metronomic chemotherapy (MC) regimens for the treatment of metastatic pancreatic cancer (mPC): A community cancer clinic experience. First Author: Ben M. Chue, Lifespring Cancer Treatment Center, Seattle, WA

Background: mPC has a poor prognosis with a median overall survival (mOS) ranging from 8.5 to 11.0 months (mo) with standard treatment, outlining the need for new innovative treatments. MC regimens utilize lower doses of chemotherapy that are administered more frequently which can maintain dose intensity while reducing toxicity. MC with paclitaxel (P) or nab-paclitaxel (N) may have effects on the tumor microenvironment. Methods: A retrospective analysis of treatment regimens and survival of patients (pts) with biopsy proven mPC who received treatment between August 2004 and August 2018 was performed. Results: 30 pts with biopsy proven mPC were identified. 14 pts received prior chemotherapy, mOS of this cohort was 18.9 mo after diagnosis and 14.2 mo after beginning MC. 70% of pts (21/30) survived longer than 12 mo, 37% (11/30) greater than 24 mo, and 27% (8/30) greater than 30 mo. All MC regimens were given on a weekly basis and included: P 60 mg/m² and G 600 mg/m² (PaG); P 60 mg/m², O 50 mg/m², folic acid (L) 20 mg/m², and 5-fluorouracil (5FU) 425 mg/m² (POLF); P 60 mg/m², I 100 mg/m², and cisplatin (C) 20 mg/m² (PIC) or P 60 mg/m², I 100 mg/m², L 20 mg/m², and F 425 mg/m² (PILF). 21 pts received N instead of P at some point during their treatment. PaG, POLF, and PIC or PILF were purposely switched before disease progression after a median length of 12, 11 and 12 mo, respectively. 16 pts received PaG as their first regimen. 12 of these 16 pts then received POLF as their second regimen, and 7 of these 12 pts subsequently received PIC or PILF as their third regimen. These 7 pts had a mOS of 21.7 mo after diagnosis and 13.6 mo after beginning MC. 10 pts were successfully able to receive PaG, POLF, or PIC/PILF more than once. Conclusions: Weekly MC regimens such as PaG, POLF, and PIC/PILF that are sequentially an effective treatment for mPC. Switching regimens may prevent the development of chemotherapeutic resistance, allowing for chemotherapeutic regimens to be used again in the future. There are limitations of retrospective studies so further investigation of this treatment strategy should be done with a large randomized clinical trial.

Defining DNA damage repair deficiency and replication stress in pancreatic cancer. First Author: Stephen Dreyer, Woffon Woff Cancer Research Centre, Institute of Cancer Sciences, University of Glasgow, Glasgow, United Kingdom

Background: Integrated multi-omic analyses revealed 24% of pancreatic cancer (PC) harbor defects in DNA damage response (DDR) and a subgroup demonstrate upregulation in replication stress pathways. DDR defective tumors are linked to DNA damage repair (DDR), and clinical data suggests that cell cycle inhibitors are seen in undefined subgroups, representing novel therapeutic strategies for PC. The aim of this study is to define and refine therapeutic segments for agents targeting DDR and replication stress in PC. Methods: We performed whole genome and RNA sequencing (RNAseq) on 48 patient-derived cell lines (PDCL) generated and characterized as part of the International Cancer Genome Initiative (ICGC). This identified increased replication stress in a sub-group of tumours, correlating with previously defined molecular subtypes of PC, irrespective of DDR status. Cytotoxicity assays were performed using agents targeting the DDR pathway and cell cycle checkpoints, including cisplatin, and inhibitors of PARP, ATR, WEE1, CHK1, CDK4/6 and PLK4. Subcutaneous patient derived xenografts (PDX) were generated to test therapeutic regimens in vivo. Results: DDR defective models, as defined by signatures of homologous recombination deficiency (HRD) were highly sensitive to cisplatin and PARP inhibitors. Replication stress predicted differential responses to cell cycle inhibitors of WEE1, CHK1, CDK4/6 and PLK4. A novel mRNA signature of ATR inhibitor sensitivity was generated and correlated with response. Response to cell cycle checkpoint inhibitors were independent of DDR status, but strongly associated with replication stress. Conclusions: This proof of concept data demonstrates DDR deficiency and increased replication Stress is an attractive target in PC. Therapeutic vulnerabilities extend beyond platinum chemotherapy and can be targeted with novel small molecule inhibitors, with independent biomarkers predicting response to agents targeting either DDR or cell cycle checkpoints. This is being used to develop and development of personalized clinical trials via the Precision Pan cancer platform targeting DDR and replication stress, and will allow clinical testing of signatures of HRD and replication stress.

MAPK pathway proteins expression and correlation with clinicopathological indices and long-term outcome according to the etiology of underlying chronic liver disease in hepatocellular carcinoma. First Author: Paulo Henrique Costa Diniz, Federal University of Minas Gerais, Belo Horizonte, Brazil

Background: Different etiologies of chronic liver disease (CLD) potentially lead to hepatocellular carcinoma (HCC) by multiple mechanisms that can be translated into clinicopathological and prognostic differences. We evaluated the expression of some proteins of MAPK pathway, an important signalling cascade in HCC, and correlated them to clinical and histopathological parameters, and long-term outcome, according to the etiology of the CLD. Methods: 90 patients (pts) who underwent orthotopic liver transplantation (OLT) for HCC at Universidade Federal de Minas Gerais, a referral center in Brazil, were randomly selected: 41 viral (V) (HBV or HCV infection), 39 nonviral (N) may have effects on the tumor microenvironment. 80 patients (pts) with underlying orthotopic liver transplantation OLT at Universidade Federal de Minas Gerais, a referral center in Brazil, were randomly selected: 41 viral (V) (HBV or HCV infection), 39 nonviral (NV) (alcohol abuse and cryptogenic) etiology. Clinical pre-OLT and histological data were retrospectively collected. Event (E) was defined as death or EFS. Results: V and NV groups were well balanced regarding clinicopathological indices, but alcohol was the main etiology in men (95%) and HCV in women (38.7%). Median E-free survival (EFS) was 74.5 months (range, 8.5-105), without difference between groups. Microvascular invasion (MIV) (p < 0.01) and age (p = 0.04) were independently associated with E. 11 pts (26.8%) of the V group had strong expression (SE) of K-RAS in tumor comparing to 0 (0%) in cirrhosis (p = 0.008) and to three (7.1%) in NV group HCC (p = 0.024). SE of K-RAS was seen in seven pts (17.0%) in V versus 11 (28.2%) in NV (p = 0.257), without difference from cirrhosis (p = 0.755). SE of MIV was not seen. Weak KRAS expression was more common in older pts (p = 0.04). The proteins expression was not related to E or EFS. Conclusions: SE of K-RAS, but not of BRAF and MEK, were more frequent in V group HCC than in cirrhosis and NV group tumors. It suggests that HBV and HCV can lead to HCC by different mechanisms comparing to NV etiology, and KRAS could be important to be considered as a diagnostic and prognostic marker in patients with HCC.
Clinical trial screening of CDKN2A genomic alterations in patients with pancreatic cancer and hepatobiliary cancers requires greater precision than somatic sequencing alone. First Author: Charles Joseph Vaske, Nanotomics, LLC, Santa Cruz, CA

Background: The TAPUR Study is a phase II multi-basket study that evaluates the anti-tumor activity of commercially available targeted agents in pts with advanced cancers with genomic alterations known to be drug targets. Results in two cohorts of PC and GBC pts each with CDKN2A loss or mutation were reported at ASCO 2018. The conclusion was that monotherapy with palbociclib is not associated with clinical activity in these patients. This may be a false conclusion if the genomic targets were absent in these patients.

Methods: A total of 158 GI pts (P = 123, GB = 20, Bile Duct = 15) with deep whole exome sequencing (WES) of tumor and blood samples, and whole transcriptome sequencing (RNA-Sequencing: ~200x reads per tumor) were available for this analysis from a commercial database. Variant calling was performed through joint probabilistic analysis of tumor and normal DNA reads, with germline variants of being determined by heterozygous or homozygous alternate allele fraction in the germline sample. Results: 26 somatic variants and 12 germline variants were detected, with one sample overlapping with a germline and a somatic variant (p.A148T and p.A766Rfs+4). Counting all 11 discrete germline variants as false positives, a total 37 of 158 samples would be positive for CDKN2A mutant status, a rate of 23% (17%-31% CI). However, if the 8 common germline variants are excluded, the call rate is 29.7% (12%-25% CI). The false positive rate is 4/158 = 14% (4%-31% CI). By RNAseq, the 8 common germline variants are excluded, the call rate is 29/158 = 18% (11%-27% CI). Total 37 of 158 samples would be positive for CDKN2A variant status, a rate of 23% (17%-31% CI). However, if the 8 common germline variants are excluded, the call rate is 29.7% (12%-25% CI). The false positive rate is 4/158 = 14% (4%-31% CI). By RNAseq, true somatic CDKN2A variants had significantly higher TPM counts than germline variants (T-test p = 0.0002). RB expression was not significantly different between the two groups.

Conclusions: The failure of palbociclib to show benefit in CDKN2A mutated PC and GBC patients in the 20 patient cohort of the TAPUR study could possibly be explained by patient selection rather than solely drug failure. It is unlikely related to RB loss.

Poster Session (Board #F7), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
Landscape of circulating tumor DNA profiling of advanced pancreatic cancer (PDAC). First Author: Kabir Mody, Mayo Clinic, Jacksonville, FL

Background: PDAC has limited treatment options. Genomic analyses have led to development of targeted therapies now in several clinical trials, and may enable the discovery of new treatment options. However, biopsy often yields limited tissue, thus hampering tissue-based profiling opportunities. Data regarding circulating tumor DNA (ctDNA) is a promising tool to be used in the clinical practice is limited.

Methods: We performed ctDNA NGS analysis in pts with advanced PDAC (December 2014-August 2018). ctDNA analysis was performed using Guardant360 (Guardant Health, CA), which detect single nucleotide variants, amplifications, fusions, and specific insertion/deletion mutations in up to 73 different genes. The mutant allele fraction (MAF) for the detection of alterations was calculated relative to wild type in ctDNA. Therapeutic relevance (TR) was defined as possible treatments within OncoKB levels 1-3B. Results: Among 171 pts and 206 total samples, ctDNA NGS revealed at least one genomic alteration in 150 pts (88%). Median diagnosis at 1, 2 and 3 years were estimated using Kaplan-Meier method. Results: Among 152 pts included in the study, 28% were normal weight, 40% were overweight and 32% were obese. The overall survival rate at 1, 2 and 3 years for normal weight pts with all stages combined was 54.1%, 35%, and 30.7%, respectively. The overall survival rate at 1, 2 and 3 years for overweight pts with all stages combined was 59.7%, 32.6%, and 25.4%, respectively. The overall survival rate at 1, 2 and 3 years for obese pts with all stages combined was 63.9%, 37.6%, and 26.7%, respectively (p = 0.8766). Multivariate analysis demonstrated no significant difference in overall survival for obese pts relative to normal or overweight pts (Table 1). Conclusion: Our findings showed, gender and CA19-9 were statistically significant predictors of overall survival, with males and pts with CA19-9 >100 doing worse (HR=1.65 (CI = 1.05, 2.61, p = 0.031) and HR 2.31 (CI = 1.49, 3.59, p < 0.001), respectively).

Conclusions: BMI did not make a significant impact on the overall survival though there may be a trend toward worse OS for pts with higher BMI. A larger, stage focused evaluation is warranted for further exploration of this trend.

Poster Session (Board #F6), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
Impact of obesity upon the survival of cholangiocarcinoma patients. First Author: Phani Keerthi Surapaneni, Mayo Clinic Florida, Jacksonville, FL

Background: Obesity is a risk factor for developing cholangiocarcinoma (CCA). However, the effect of obesity on survival of CCA is unclear. The primary aim of this study was to analyze the impact of obesity upon overall survival of CCA patients. Secondary aims were to analyze impact of obesity upon other disease characteristics such as tumor size, stage, age, sex, BMI and Ca 19-9. Methods: A total of 411 unique pts diagnosed with CCA at Mayo Clinic Florida between 2000 and 2018 were retrieved from our collective SDMS database. Variables evaluated included demographics, Body Mass Index (BMI), AJCC stage, tumor location and Ca 19-9. A total of 185 pts had all data available pertaining to these variables. We further restricted the analysis to pts with in-hospital CCA classified BMI as per CDC criteria (normal: 18.5-25kg/m²), overweight (25-29.9kg/m²), and obese (≥30 kg/m²), thus leaving a total of 152 pts. Continuous and categorical variables were compared across BMI groups using Chi-squared or Fisher's exact test. Overall survival rates after diagnosis at 1, 2 and 3 years were estimated using Kaplan-Meier method. Results: Among 152 pts included in the study, 28% were normal weight, 40% were overweight and 32% were obese. The overall survival rate at 1, 2 and 3 years for normal weight pts with all stages combined was 54.1%, 35%, and 30.7%, respectively. The overall survival rate at 1, 2 and 3 years for overweight pts with all stages combined was 59.7%, 32.6%, and 25.4%, respectively. The overall survival rate at 1, 2 and 3 years for obese pts with all stages combined was 63.9%, 37.6%, and 26.7%, respectively (p = 0.8766). Multivariate analysis demonstrated no significant difference in overall survival for obese pts relative to normal or overweight pts (Table 1). Conclusion: Our findings showed, gender and CA19-9 were statistically significant predictors of overall survival, with males and pts with CA19-9 >100 doing worse (HR=1.65 (CI = 1.05, 2.61, p = 0.031) and HR 2.31 (CI = 1.49, 3.59, p < 0.001), respectively).

Conclusions: BMI did not make a significant impact on the overall survival though there may be a trend toward worse OS for pts with higher BMI. A larger, stage focused evaluation is warranted for further exploration of this trend.

Mean Dose (Gy) Minimum Dose (Gy) Maximum Dose (Gy) D70 (Gy) D90 (Gy)
Average 99.9 20.6 302.3 66.9 43
Median 97 16 235 71 41
50% 99.9 17.8 267.1 40.3 27.8
Minimum 2.4 0.9 125 0 0.9
Maximum 298 78 1461 211 130
Background: Cholangiocarcinoma (CCA) has limited treatment options. Genomic analyses have led to development of targeted therapies now in clinical trials, and may enable discovery of new treatment options. However, biopsy often yields limited tissue, thus hampering tissue-based profiling opportunities. Comparative data regarding circulating tumor DNA (ctDNA) analysis and tissue based profiling in CCA are limited.

Methods: We performed ctDNA NGS analysis along with tissue based profiling in pts with advanced CCA (January 2015- February 2018). ctDNA analysis was performed using Ion Torrent (San Diego, CA) which detects single nucleotide variants, amplifications, fusions, and specific insertion/deletion mutations in up to 73 different genes and the majority of tissue based profiling using Foundation One. The mutant allele fraction (MAF) for detected alterations was calculated relative to wild type in ctDNA. Therapeutic relevance was defined as alterations within OncokB levels 1-3B and RT. The study was conducted in accordance with Mayo Clinic IRB requirements.

Results: Among 124 pts and 139 total samples, ctDNA NGS revealed at least one genomic alteration (excluding variants of uncertain significance and synonymous mutations) in 89% of pts. Median number of alterations per pt was 3 (range, 1-15), with a median MAF of 0.42% (range, 0.1%-96.4%). The total number of unique alterations was 321. The most commonly altered genes: TP53 (30%), KRAS (13%), FGFR2 (7%), APC, and PIK3CA (each 5%) and ARID1A (3%). Amplifications were noted in 14 genes: BRF, CCND1, CCND2, CCNE1, CDK4, CDK6, EGFR, ERBB2, FGFR1, FGFR2, MET, MYC, PDGFRα, and PIK3CA. Tissue-based profiling was available in 57 (46%) pts, with a median of 8.5 between ctDNA and tissue biopsy. IDH1, FGFR2, TP53 and KRAS were most common gene mutations found in pts who had both liquid and tissue biopsy done. (Comparative results to be shown). Conclusions: ctDNA plasma profiling of pts with advanced CCA is a feasible alternative method to gather comprehensive genomic-data. Further larger cohort studies comparing landscape of alterations seen on ctDNA versus tissue-based assays are needed.

Background: Pilot study of plasma KRAS as a prognostic biomarker in localized pancreas ductal adenocarcinoma (PDAC). First Author: Benjamin A. Krantz, New York University Langone Medical Center, New York, NY

Methods: In this pilot, 59% of localized PDAC patients had utility as a biomarker to predict the prognosis. Plasmatic plasma from a PDAC cohort at Memorial Sloan Kettering. Methods: 10 mL of whole blood was collected at diagnosis of localized PDAC and early interval CT scan (approx. 8 weeks). DNA was extracted using QIAamp DNA kits (Qiagen, Valencia, CA). Single nucleotide polymorphism (SNP) known, or multiple tumor inactivating, including KRAS, G12D mutation, 6 G12V and 9 unknown. Eight had gemcitabine-based treatment, 10 5-FU-based and 5 radiation. See table. mKRAS and CA19-9 at B were not associated with progression free survival (PFS) or overall survival (OS). mKRAS detection at I was associated with shorter PFS/OS (P < 0.001) was confirmed using IHC, validating the transcriptome analysis at protein level. Conclusions: These findings, combined with previously reported pathway analysis (Vijayvergia et al2017), highlight biological differences between PD and WD NETs and serve as a platform for future research. They also support investigation of novel drugs that inhibit activity of EZH2 (e.g. EPZ6438) in PD NETs and PAK3 (e.g. FRAX597) in WD NETs.
Characterization of the tumor mutation burden in hepatobiliary tumors. 

First Author: Ramya Thota, Intermountain Healthcare, Murray, UT

Background: Hepatobiliary 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 outcome of non-small cell lung cancer and tumor to predict the sensitivity to immune therapy. Herein, we explore the TMB as a potential biomarker of response to immune therapy in hepatobiliary tumors.

Methods: We retrospectively assessed all patients with hepatobiliary malignancies who have undergone next generation sequencing (NGS) between January 2013 and September 2018. We then analyzed the tumor mutation burden of these tumors and also identified frequency of patients with no clinically actionable mutations. Results: Of the 65 total patients with hepatobiliary tumors, 49 patients (75%) had at least one clinically actionable mutation while 16 patients (25%) had no clinically actionable mutations. Among 65 patients, 44 patients had hepatocellular carcinoma, 15 patients had cholangiocarcinoma and 6 patients had gallbladder carcinoma. The TMB data is available for 15 patients. The mean TMB reported was 2.7 (1.6 - 4.25), which suggests low mutation burden in general in all our HB tumors. Among the patients with available TMB, the underlying risk factor was noted as hepatitis C in 3, NASH in 1, others in 6, unknown in 5 patients. Conclusions: Our data suggests the TMB in hepatobiliary tumors is low in general irrespective of their underlying risk factors. Future larger studies are needed to evaluate TMB as a potential biomarker in hepatobiliary tumors to help select patients that will benefit from immune therapy.

Symptom burden at the end of life for neuroendocrine tumors: A population-based analysis of patient-reported outcomes. 

First Author: Julie I. Hallett, Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada

Background: How to best support neuroendocrine tumor (NET) patients remains unclear. While the peri-diagnostic period has been investigated, there are no studies on whether patients suffering a high symptom burden at the end of life, not previously described. This study examined symptom scores linked to provincial administrative datasets. Moderate-to-severe symptom scores were linked to provincial administrative datasets. Moderate-to-severe symptom scores in the 6 months prior to death were presented by 2-week intervals. Multivariable Poisson regression identified factors associated with moderate-to-severe symptoms scores. Results: Among 677 decedents, 2,579 symptom assessments prior to death were analyzed. Overall, moderate-to-severe scores were most commonly reported for tiredness (86%), well-being (81%), lack of appetite (75%), and drowsiness (68%) at any time. This proportion changed over time, progressively increasing closer to death: 56.8% to 83.9% tiredness, 50.5% to 73.1% well-being, 40.9% to 80.6% lack of appetite, and 41.5% to 68.8% drowsiness. The increase was steeper in the 8 weeks before death for lack of appetite, drowsiness, and shortness of breath. On multivariate analyses, the risk of moderate-to-severe symptoms was significantly higher in the last 2 months prior to death and with shorter survival from diagnosis (< 6 months). Women reported a higher burden of anxiety, nausea, and pain than men. There was no association between symptom burden and age or primary tumor site. Conclusions: N ET patients suffer a high symptom burden at the end of life, not previously described. The proportion of moderate-to-severe symptoms increases steeply as death nears, highlighting an opportunity for improved management. Combined with identified factors associated with moderate-to-severe symptoms, this information is important to improve patient-centred and personalized supportive care for NET at the end of life.
Outcomes of patients with borderline-resectable pancreatic cancer treated with FOLFIRINOX versus gemcitabine plus nab-paclitaxel. First Author: Shaina D’Lee Templeton, College of Medicine, University of Saskatchewan, Saskatoon, SK, Canada

Background: Pancreatic cancer is a major cause of cancer-related death. Less than 20% of patients have resectable disease at diagnosis. Patients with borderline-resectable pancreatic cancer (BRPC) are at high risk of incomplete resection with upfront surgery. Currently there is no standard induction chemotherapy regimen exists for BRPC. Both FOLFIRINOX (5-FU, irinotecan, oxaliplatin) and Gemcitabine/nab-paclitaxel have shown better efficacy than gemcitabine in advanced pancreatic cancer. The current study aims to assess outcomes of real-world patients with BRPC who received induction FOLFIRINOX or GnP. Methods: In this population-based multicenter retrospective cohort study patients with biopsy proven BRPC as defined by the pancreatic surgical team diagnosed from 2011-2017, in the province of Saskatchewan, Canada, who received FOLFIRINOX or GnP were assessed. Kaplan Meier methods and log rank tests were performed for survival analyses. Results: Of 161 patients with pancreatic cancer who received FOLFIRINOX or GnP during the study period, 20 eligible patients with BRPC, with median age of 65 yrs (54-79) and M/F 14:6, were identified. 85% had pancreatic head tumours with a median CA19-9 of 470 u/mL. Of eligible patients, 10 received FOLFIRINOX and 10 received GnP. No significant differences were found between the two groups, except more patients in FOLFIRINOX group had a WHO performance status of 0 (50% vs. 10%, p = 0.057) and had a higher body mass index (27.0 vs. 23.0, p = 0.027). Eleven patients showed partial response (5-FOLFIRINOX and 6-GnP), three progressed during treatment. Four patients (4-GnP) progressed and underwent curative surgery. Five patients (1-FOLFIRINOX, 4-GnP) had radiation and four underwent Nanoknife procedure (3-FOLFIRINOX, 1-Gnp). The median progression free survival was 17 months in FOLFIRINOX (95% CI 5.3-28.6) versus nine months (3.0-15) in GnP group (p = 0.26). The median overall survival was 32 months in FOLFIRINOX (not reach) versus 16 months (9.3-22.7) in GnP group (p = 0.15). Conclusions: The current study suggests that patients with BRPC who received FOLFIRINOX tends to have better outcomes. Future study are warranted to establish a preferred systemic therapy for BRPC.

Impact of renal function on the efficacy and safety of S-1 with concurrent radiotherapy for locally advanced pancreatic cancer. First Author: Satoshi Kobayashi, Department of Gastroenterology, Hepatobiliary and Pancreatic Medical Oncology Division, Kanagawa Cancer Center, Yokohama, Japan

Background: S-1 is an oral agent consisting of a mixture of tegafur which is a prodrug of 5-fluorouracil (5-FU), S-choro-2,4-dihydroxypropyridine (DHP) and potassium oxonate. Serum concentration of S-1 increases in case of renal dysfunction due to decrease of DHP excretion into urine. The aim of this study was to evaluate the influence of renal function to the efficacy and safety of S-1 with concurrent radiotherapy (RT) for locally advanced pancreatic cancer (LAPC).

Methods: This study was an integrated exploratory analysis of JCOG1106 and LAPC-S1RT, respectively. Median age was 65 years old (range: 20-80). Eligible pts were diagnosed with LAPC, and we should pay attention to renal function and consider for dose reduction. S-1 was received FOLFIRINOX tends to have better outcomes. Future study are warranted to establish a preferred systemic therapy for BRPC.

Clinical impact of preoperative biliary drainage on postoperative complications in pancreaticoduodenectomy. First Author: Hirohisa Okabe, Department of Gastroenterological Surgery, Kumamoto University, Kumamoto, Japan

Background: Biliary drainage is sometimes necessary for patients undergoing pancreaticoduodenectomy (PD) because of tumor invasion to the biliary tract. The current study aims to explore the clinical impact of preoperative biliary drainage (PD) on postoperative complications in PD.

Methods: One hundred sixty-six patients who underwent PD from 2012-2017 were enrolled in this study. Clinical impact of PD on clinical course was examined. Results: There were 66 patients (40%) undergoing PD. Patients with PD showed significantly higher infection rate of bile juice collected at surgery (p < 0.0001) and contamination rate of ascites collected from intraperitoneal drain on postoperative day 3 (POD3) (p < 0.0001) than patients without PD. Postoperative complication (Clavien Dindo ≥ IIb ) was associated with contaminated ascites on POD3 (p = 0.031), but not with PD. Among patients with PD, fifty-two patients (79%) received preoperative ERBD. Infection of bile juice at surgery was not associated with the procedure of PD (ERBD, ENBD or PTCO), but correlated with the duration of drainage. Receiver operating characteristic analysis revealed that patients with PD for more than 28 days occurs contamination of bile juice at surgery. Among patients with both the contaminated bile juice at operation and the contaminated ascites on POD3 (n = 24), both were consistent in 19 patients (79%). Although Enterococcus faecalis was the most species seen in their bile juice, patients with the contamination of other species of Enterobacter (36%) and Streptococcus (2%) showed higher severe postoperative complication rate than others (p = 0.049). Conclusions: PD was not directly associated with severe postoperative complications, but the duration of drainage for > 28 days was correlated with contamination of the bile juice. Contaminated ascites on POD3 caused by infectious bile juice at surgery was an only factor associated with severe postoperative complications and therefore needs careful management of the drain removal and selection of antibiotics after surgery.
Real-world outcomes among patients (pts) treated with gemcitabine (gem)-based therapy post-FOLFIRINOX (FFOX) failure in advanced pancreatic cancer (APC). First Author: Erica S Tsang, BC Cancer, Vancouver, BC, Canada

**Background:** Limited evidence exists for the selection of chemotherapy in APC after first-line (1L) FFOX. Gemcitabine/ nab-paclitaxel (GEMNAB) is published for second-line (2L) use in the provinces of Alberta (AB) and Manitoba (MB), but is not covered in British Columbia (BC). We compared population-based outcomes by region to examine the utility of 2L GEMNAB versus GEM alone.

**Methods:** We identified pts treated with 1L FFOX between 2013-2015 across BC, AB, and MB. Baseline characteristics and treatment regimens were compared between AB/MB and BC. Survival outcomes were assessed by the Kaplan-Meier, and compared with log-rank test. Results: 370 pts treated with 1L FFOX were identified (145 AB/MB, 225 BC), with a median age of 64y, 42% female, and 68% with metastatic disease (similar in both groups). Receipt of 2L therapy was 49% AB/MB vs 44% BC (p = 0.35), and time from diagnosis to 2L therapy measured 7.6 mos AB/MB versus 9.4 mos BC (p = 0.1). The distribution of 2L, gemcitabine use was: 72% GEMNAB, 23% GEM in AB/MB versus 27% GEMNAB, 66% GEM in BC (p < 0.001). Median overall survival (OS) from diagnosis was similar: 12.4 mos in AB/MB versus 10.9 mos in BC (p = 0.75). On Cox regression analysis, region was not significant. A secondary survival analysis by 2L regimen demonstrated a median OS of 18.0 mos with GEMNAB versus 14.3 mos GEM (p < 0.001). Conclusion: In our population-based comparison of APC pts treated with 1L FFOX, survival outcomes were comparable regardless of publicly funded access to 2L GEMNAB versus GEM. OS by regimen favored 2L GEMNAB, but patient selection may be largely responsible for this difference. Randomized trials are needed to demonstrate the benefit of GEMNAB post-FFOX in APC.

**Biliary tract cancers and the associated risk of venous thromboembolism.** First Author: Jasleen Khangua, USC Norris Comprehensive Cancer Center, Los Angeles, CA

**Background:** Venous thromboembolism (VTE) is a common cause of morbidity and mortality in cancer patients. Because biliary tract cancers (BTC) (cholangiocarcinoma and gallbladder GB) cancer are uncommon, the incidence of VTE in this population is not well-described.

**Methods:** We conducted a retrospective study of patients with BTC identified by the cancer registry at the Los Angeles County-University of Southern California (USC) Medical Center, USC Norris Cancer Center, and USC Keck Hospital between January 2011 to December 2016 to describe the incidence of VTE. 330 BTC patients’ medical records were reviewed for demographics, tumor characteristics, treatment history, and VTE events. 41 patients were excluded due to incomplete records/follow-up. Overall survival (OS) was calculated from date of diagnosis to date of death or last follow-up. Logrank test was used to evaluate the association of VTE with OS. Results: 289 patients with BTC were identified (177 cholangiocarcinoma, 112 GB) with a median follow-up period of 16.7 (3.3-89.0) months (mo). 169 (58%) were women. The median age at diagnosis of 66 years (range 22-89). 144 (59%) underwent cancer surgery and 274 (95%) received chemotherapy. 65 (22%) patients had VTE events: 22 pulmonary embolism [PE] with or without lower extremity (LE) deep vein thrombosis (DVT), 15 with LE DVT alone, three with upper extremity DVT, and 30 with visceral thrombosis (27 portal vein thrombosis [PVT]) with or without inferior vena cava thrombosis (IVC, 2 IVC thrombosis, two hepatic vein thrombosis). Five patients had both DVT/PE and visceral thrombosis. The median time from cancer diagnosis to VTE event was not met. Patients with a PVT or any visceral thrombosis had an inferior OS compared to those without (PVT: median OS 16.2 mo [95% CI 12.2-25.8] versus 7.5 [3.4-14.2], p = 0.01, visceral thrombosis: 17.0 mo [95% CI 18.8-25.9] versus 8.4 [95% CI 3.7-14.3], p = 0.30). There was a non-significant trend towards inferior OS in patients with any VTE event type (median OS 17.0 mo [95% CI 11.8-39.0] versus 11.4 [95% CI 7.2-18.4], p = 0.10). There was no difference in OS for patients with PE/DVT compared to those without. Conclusion: VTE is commonly observed in patients with BTC. Visceral thrombosis is associated with inferior survival in patients with BTC.

**Integrated population pharmacokinetic (PopPK) modeling of cabozantinib (C) in patients with various cancer types including hepatocellular carcinoma (HCC).** First Author: Linh Thuy Nguyen, Exelixis, Inc., South San Francisco, CA

**Background:** C significantly improved overall survival vs placebo in pts with advanced HCC from CELESTIAL and a prior phase 2 trial. Recently developed to characterize C concentration data from HV and pts with other cancers including hepatocellular carcinoma (HCC). Integrated population pharmacokinetic (PopPK) modeling of cabozantinib (C) significantly improved overall survival vs placebo in pts with advanced HCC from CELESTIAL and a prior phase 2 trial. Working Group (NCI-ODWG).

**Results:** Median OS, mo

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Median OS, mo</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCC</td>
<td>11.6</td>
<td>9.0-15.0</td>
</tr>
<tr>
<td>GB</td>
<td>11.6</td>
<td>8.4-14.8</td>
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</table>

**Conclusions:** Median OS was similar across cancer types. A 2-compartment model with first-order elimination provided a good description of C concentration data. Covariates included age, gender, race, body weight, cancer type, and liver dysfunction as defined by the National Cancer Institute Organ Dysfunction Criteria, had no discernable effect on C CL/F.

**A multicenter, open-label, phase I study of nivolumab alone or in combination with gemcitabine plus cisplatin in patients with unresectable or recurrent biliary tract cancer.** First Author: Masafumi Ikeda, National Cancer Center Hospital East, Chiba, Japan

**Background:** In Japan, biliary tract cancer (BTC) is the third leading cause of cancer death. First Author: Jasleen Khangua, USC Norris Comprehensive Cancer Center, Los Angeles, CA

**Methods:** In the monotherapy/recurrent BTC cohort, 30 patients with unresectable/recurrent BTC refractory or intolerant to gemcitabine-based treatment regimens received nivolumab monotherapy (240 mg, 2-week intervals). In the combined therapy cohort (N = 30), chemoradiative patients with unresectable recurrent BTC received nivolumab (240 mg, 2-week intervals) plus cisplatin-gemcitabine chemotherapy. The primary objective was tolerability and safety. Secondary efficacy endpoints included overall survival (OS), progression-free survival (PFS) and objective response rate (ORR) (central assessment). Results: The most frequently reported nivolumab-related adverse events were decreased appetite (5/30, 16%), fatigue (4/30, 13%), and pruritus (4/30, 13%) in the monotherapy cohort, and anemia (8/30, 27%) and decreased appetite (7/30, 23%) in the combined therapy cohort. Median duration of follow-up for efficacy (Table) was 5.1 months (mo; monotherapy cohort) and 8.2 mo (combined therapy cohort). In the monotherapy cohort, median OS and median PFS were longer in patients with programmed death-ligand 1 (PD-L1) ≥ 1% (including the patient who responded) than in those with PD-L1 < 1% (Table). In the combined therapy cohort, the ORR was higher, but median OS and median PFS were lower, in patients with PD-L1 ≥ 1% than in those with PD-L1 < 1% (Table). Conclusions: Nivolumab was well tolerated, with a manageable safety profile and signs of clinical activity, in this phase 1 study in patients with unresectable/recurrent BTC. PD-L1 expression status may predict clinical activity of nivolumab in advanced BTC. Clinical Trial Information: NCT0309068.
A phase I study of mesothelin-targeted immunotoxin LMB-100 in combination with nab-paclitaxel in patients with previously treated advanced pancreatic cancer. First Author: Christine Campo Akliewe, Center for Cancer Research, NCI, NIH, Bethesda, MD

Background: LMB-100 is a Pseudomonas exotoxin A-based immunotoxin that targets mesothelin (MSLN). MSLN is expressed by >75% of pancreatic adenocarcinomas (PDAC). LMB-100 kills MSLN-expressing cells by irreversibly modifying elongation factor-2 to halt protein synthesis. Phase I studies of LMB-100 defined the maximum tolerated dose (MTD) of 140 mcg/kg IV given on D1, 3 and 5 of a 21-day cycle. Development of anti-drug antibodies (ADAs) limited patient drug exposure beyond cycle 2. Our pre-clinical data showed that combination of LMB-100 with a taxane resulted in synergistic anti-tumor activity. Methods: We conducted a phase I single center study (standard 3+3 design) to determine the MTD of LMB-100 in combination with nab-paclitaxel in patients with previously treated advanced PDAC. LMB-100 was given on D1, 3 and 5 of a 21-day cycle, and nab-paclitaxel (125 mg/m²) on D1 and D8. Initial patients could receive a maximum of 4 cycles, but subsequently a 2-cycle maximum was employed. Results: Fourteen patients (median age 58) were enrolled. Two of 6 patients experienced DLTs at the 100 mcg/kg dose of LMB-100 (malignant 2 pts, fatigue: 1 pt, hypotension: 1 pt; all grade 3). One of 8 patients had DLT at the 65 mcg/kg dose (edema, urine output decrease; both grade 3). Other toxicities related to LMB-100 included hypoproteinemia, edema-associated weight gain, hypotension, fatigue, drug fever, infusion-related reaction, hypophosphatemia, nausea and anorexia. One patient died on treatment from complications of bowel perforation attributed to cancer. All patients achieved detectable serum levels of LMB-100 during the first cycle, even those with pre-existing ADAs, and 5 of 8 did so during cycle 2. One patient receiving the 65 mcg/kg dose had a confirmed partial response, and CA 19-9 dropped by >50% in 5 of 8 evaluable patients. Conclusions: MTD of LMB-100 is 65 mcg/kg given with nab-paclitaxel on this schedule. Anti-tumor activity was observed. A phase II cohort is currently being accrued. Clinical trial information: NCT02804187

Poster Session (Board #5), Fri, 11:30 AM-1:00 PM and 3:30 PM-6:30 PM

Single-shot celiac plexus radiosurgery in pancreatic cancer: Palliative and functional outcomes—Final results of a prospective clinical trial. First Author: Yaacov Richard Lawrence, Sheba Medical Center, Ramat Gan, Israel

Background: Pancreatic cancer is characterized by severe episodic/low back pain caused by infiltration of the celiac plexus. The celiac plexus is a network of nociceptive nerves, located along the abdominal aorta. Contempory treatments (surgical resections, celiac plexus neurolysis, chemotheraphy) are often inadequate. We hypothesized that ablative radiation targeted to the celiac plexus would alleviate pain. Here we report results for pancreatic cancer patients treated with a single fraction of radiation. Methods: We conducted a single institution single-arm prospective clinical trial. Eligible cancer patients had celiac-pain > 4/10 on Numerical Rating Scale (NRS) and completed treatment per protocol with at least one post-treatment visit. The celiac plexus was irradiated from D12 to L2. Radiation was given as a single-fraction 25 Gy. The primary endpoint was NRS pain 3 weeks post-treatment. Secondary endpoints were toxicity, pain at 6w, analgesic use, and pain interference with daily activities as evaluated by the ‘The Brief Pain Inventory’. Analgesia was not restricted. Total daily dose of opioids was measured in morphine milligram equivalents (MME). Results: Seventeen patients were evaluable, 65% female, median age 68 yr (range 51-79), three had undergone pancreatic resection, nine had liver metastases, median ECOG = 1. Sixteen patients reported 3-week outcomes, and 10 reported 6-week outcomes. At time of treatment subjects were a median of 8.2 months from diagnosis, and had received a median of one systemic treatment (range 0-3). Toxicity was limited to grade 1. Median baseline pain was 6/10 (IQR 5-7), was reduced to 2.3/10 (IQR 0-3.6) (p < 0.0005) at 3 w, and to 2.5/10 (IQR 0-3.1) at 6 w post-treatment, for both p < 0.0001. Median opioid consumption numerically decreased (baseline 52.9 MME, 3 w 43.9 MME, 6 w 37.5 MME, N.S). ‘BPI pain interference’ improved significantly: median baseline score 7.1 dropped to 1.1 at 3 weeks and 0 at 6 weeks (p < 0.01 for both time points). Conclusions: Single-shot celiac plexus radiation is safe and effective, and improves quality of life among patients with pancreatic cancer. A follow-up international trial is accruing. Clinical trial information: NCT02356406.

Poster Session (Board #56), Fri, 11:30 AM-1:00 PM and 3:30 PM-6:30 PM

Adjuvant gemcitabine versus 5-fluorouracil/folinic acid based on hENT1 immunostaining in curatively resected pancreatic adenocarcinoma: A biomarker stratified trial. First Author: Dong Woo Shin, Seoul National University Bundang Hospital, Seoul, Korea, Republic of (South)

Background: The human equilibrating nucleoside transporter (hENT1) protein transports gemcitabine into the cell. However, role of hENT1 as a predictive biomarker for gemcitabine responsiveness in pancreatic adenocarcinoma (PDA) is still needed to be elucidated, although several studies had been conducted. We investigated whether hENT1 has a predictable role on adjuvant chemotherapy responsiveness in PDA according to stratification of hENT1 immunostaining. Methods: The 44 patients who underwent curative surgery (R0 or R1) due to PDA at Seoul National University Bundang Hospital from May 2015 to June 2017 were enrolled prospectively. The hENT1 expressions were measured by immunohistochemical staining (SP20 rabbit monoclonal antibody, Ventana). According to hENT1 immunostaining, patients were stratified: (0-20% — < 50%), higher hENT1 group received gemcitabine [1,000mg/m² (day 1, 8, 15) x 4 weeks x 6 cycles] and lower hENT1 group received [5-FU 425mg/m² (day 1-5) plus folinic acid 20 mg/m² (day 1) x 4 weeks x 6 cycles]. Primary outcome was overall survival (OS) and secondary outcomes were toxicity and recurrence free survival (RFS). Results: Among 44 patients, 5 patients were excluded due to withdrew consent (3 patients) and toxicities (2 patients in 5FU/LV group). Eighteen patients in the higher hENT1 group and twenty-six patients in the lower hENT1 group were followed up for 24.3 months. Data showed OS was 97.4% at 12 months and 86.4% at 24 months. Moreover, RFS was 76.8% at 12 months and 64.2% at 24 months. Although it is preliminary data, it showed better OS and RFS compared to previous study (Neoptolemos JP et al., JAMA 2010) (OS, 61.3% at 12 months, 30.7% at 24 months; RFS, 58.7% at 12 months and 30.1% at 24 months). Conclusions: Adjuvant chemotherapy based on hENT1 immunostaining stratification provides excellent survival in resected PDA. Therefore, hENT1 immunostaining should be used for more rational decision for adjuvant chemotherapy remim in PDA. Clinical trial information: NCT02486497.

Poster Session (Board #7), Fri, 11:30 AM-1:00 PM and 3:30 PM-6:30 PM

Feasibility of SM-88 in PC after multiple prior lines and ECOG < 2. First Author: Marcus Smith Noel, University of Rochester. James P. Wilmot Cancer Institute, Strong Memorial Hospital, Rochester, NY

Background: Advanced PC patients with ≤ 3Ls of chemo or ECOG PS 2 are generally excluded from clinical trials. SM88 demonstrated no drug related AEs > grade 2 in an interim prostate phase 2 (3C01B 3665 P 17S). We sought to determine the feasibility of a trial in this vulnerable population using SM88. Methods: Propective randomized phase 2 of SM-88 (tyrosine derivative, CYP3A4 inducer, mTOR and oxidative stress catalyst) in patients with locally PD or mPC. ECOG PS ≤ 2 and ≤ 2 weeks from prior therapy. Results: Median age = 64.9 (range 45.6-84.1); 45.9% female, 93.1% white, 6.9% other; median prior lines = 3 (range 1-6); 12% had prior RT and 17% surgery. Median ECOG PS was 1 with 36.6% 0, 63.3% 1 and 0% ECOG PS 2. From April 2010 to this abstract, 36 patients initiated therapy, 39 failed screening and 17 remained in screening. Time from opening of trial to first patient consented was 51 wk; median time last regimen to consent was 6.7 wk; from consent to drug administration (CDO) = 1.7 wk. Subjects traveled up to 2600 miles to enroll at a site with an open slot. Median number of visits/site = 3 (151). Median time on trial was 52 days (122 wks). There were 15 unrelated SAEs among 36 randomized subjects; three subjects died after consenting but before receiving study drug (table). Grade 4 and 5 SAEs were more common before receiving drug or unrelated to drug (26/94) than at least possibly drug related (0/17) (Fisher p < 0.05). Efficacy using RECIST, PERIST and BIRC along with CTCs, NLR, PRos and other outcomes are being collected with high compliance. Conclusions: This prospective SM88 trial suggests that heavily pretreated PC patients with criteria that includes less than ideal ECOG can participate and gain access to novel therapies. This trial plans to enroll 99 additional subjects in under a year. Although ECOG 2 was allowed none have been consented to date and may reflect investigator bias on enrollment or PS assessment. Investigators need to meet the needs of this patient population by considering them for inclusion in future drug development trials. Clinical trial information: NCT03318756.

AEs on Trial (Unconfirmed)

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**Poster Session (Board #G9), Fri, 11:30 AM-1:00 PM and 5:30-6:30 PM**

**Predictive role of temporal changes in intratumoral metabolic heterogeneity during palliative chemotherapy in advanced pancreatic cancer patients: A prospective cohort study.** First Author: Shin Hye Yoo, Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea

**Background:** Metabolic intratumoral heterogeneity (ITH) is known to be related with cancer treatment outcome. However, information on the temporal changes in metabolic ITH during chemotherapy and the correlations between metabolic changes and treatment outcomes in patients with pancreatic cancer (PC) is sparse. We aimed to analyze the temporal changes in metabolic ITH and the predictive role of its changes in advanced PC patients who underwent palliative chemotherapy. **Methods:** We prospectively enrolled unresectable locally advanced or metastatic PC patients before initiation of first-line palliative chemotherapy. [18F]-Fluorodeoxyglucose positron emission tomography was performed at baseline (T1) and at the first response follow-up (T2). Standardized uptake values (SUVs), volumetric parameters, and textural features of the primary pancreatic tumor were analyzed. Relationships between the parameters at T1, T2, and changes in the parameters with response to therapy, progression-free survival (PFS), and overall survival (OS) were assessed. **Results:** Among 63 enrolled patients, the best objective response rate was 25.8% (95% confidence interval [CI], 14.6% to 37.0%). Sixteen (25.8%) patients who obtained partial response were classified as responders and 46 (74.2%) as nonresponders. The median PFS and OS were 7.1 months (95% CI, 5.1 to 9.7 months) and 10.1 months (95% CI, 8.6 to 12.7 months), respectively. Most of the parameters changed significantly during the first-line chemotherapy, in a way of reducing ITH. Metabolic ITH was more profoundly reduced in responders than in nonresponders. Multiple Cox regression analysis identified high baseline compacity (P = 0.023) and smaller decreases in SUVmax (P = 0.007) and entropyclpGM (P = 0.033) to be independently associated with poor PFS. Patients with a high CA 19-9 (P = 0.042), high pretreatment SUVmax (P = 0.008), and high cancer grading were classified as nonresponders. **Conclusions:** Reduction in metabolic ITH during palliative chemotherapy in advanced PC patients is associated with response to therapy and might be predictive of PFS and OS.

**Poster Session (Board #G1), Fri, 11:30 AM-1:00 PM and 5:30-6:30 PM**

**An updated retrospective review of the safety and efficacy of sorafenib for recurrent hepatocellular carcinoma post-liver transplantation.** First Author: Sophie Feng, Redcliffe Hospital, Queensland, Australia

**Background:** Orthotopic liver transplantation (OLT) is a potentially curative treatment for hepatocellular carcinoma (HCC). Despite an estimated recurrence rate between 15%-20%, there is currently no proven systemic therapy for the treatment of HCC relapse post OLT. Sorafenib has been a standard therapy for advanced HCC, however data is lacking for the safety and efficacy of sorafenib in the setting of concurrent immunosuppressive agents. **Methods:** A retrospective review was performed of patients who received sorafenib for HCC relapse after OLT. Data on patient characteristics, treatment toxicity and efficacy was collected. The primary objectives were to evaluate toxicity and safety of sorafenib when used in combination with immunosuppressive therapies such as calcineurin and mTOR inhibitors. **Secondary objectives** were objective response rate, progression free survival (PFS), and time on therapy. **Results:** 35 patients over the last 11 years received sorafenib for HCC recurrence following OLT. 54.3% of patients received concurrent immunosuppression with tacrolimus. Toxicity from sorafenib was as expected, with no cases of acute or chronic organ rejection whilst on treatment. The median maximum tolerated dose was 400 mg a day with 40% of patients requiring dose reductions. The incidence of any adverse events (AEs) was 88.6%, with 17.1% having Grade 3-4 toxicity. Incidence of Grade 3-4 liver dysfunction was higher than historical studies at 6%. The overall response rate was 2.8% with a median PFS of 2.8 months. Median time on sorafenib was 31.1 months. **Conclusions:** There is a paucity of evidence guiding treatment of HCC recurrence following OLT. This retrospective review is one of the largest in the literature and shows that sorafenib used concurrently with immunosuppressive therapy for organ transplant is safe, with no precipitation of acute or chronic rejection, although liver function should be monitored closely. The median PFS in our cohort was shorter than expected. The efficacy of other agents should be explored in this population.

**Poster Session (Board #G10), Fri, 11:30 AM-1:00 PM and 5:30-6:30 PM**

**Neoadjuvant chemotherapy followed by surgery versus upfront surgery in patients with borderline resectable and locally advanced unresectable pancreatic adenocarcinoma.** First Author: Junho Kang, Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Republic of (South)

**Background:** Although neoadjuvant chemotherapy (NACT) has been widely investigated, the magnitude of the clinical benefit and the potential risk of NACT followed by surgery compared with upfront surgery remains unclear for patients with locally advanced pancreatic cancer (LAPC). **Methods:** This retrospective, prospective cohort-based analysis included 135 patients who underwent NACT followed by surgery and 359 patients who received upfront surgery for LAPC between October 2005 and April 2017. Disease-free survival (DFS) and overall survival (OS) from surgery were compared between the two groups. **Results:** There were no significant differences in gender (male, 53% vs 56%) and age (median 60 vs 61 years) between the NACT followed by surgery group and upfront surgery group. As NACT, gemcitabine-based regimens and FOLFIRINOX were used in 69 (51%) and 66 (49%) patients, respectively. The NACT followed by surgery group showed significantly less advanced T-stage (T3-4, 93% vs 99%, p = 0.005) and N-stage (N+ 49% vs 71%, p < 0.001) than the upfront surgery group. NACT followed by surgery was significantly associated with better OS (median, 25.4 [18.6-32.2] vs 17.1 [15.5-18.7] months, p = 0.001) and DFS (median, 9.0 [95% CI, 6.8-11.2] vs 7.1 [6.4-7.8] months, p = 0.005) than upfront surgery. These results were consistent in the multivariable analysis for OS (adjusted hazard ratio [aHR], 0.73 [95% CI, 0.56-0.96], p = 0.02) and DFS (aHR, 0.72 [95% CI, 0.56-0.93], p = 0.01). There was no difference in length of hospital stay (median 13 vs 17 days, p = 0.96) or number of TS in the two groups, and the NACT followed by surgery group showed a significantly lower incidence of postoperative complications than the upfront surgery group (38% vs 27%, p = 0.03). **Conclusions:** The present study revealed that NACT followed by surgery may represent a survival benefit compared with upfront surgery in LAPC without causing significant safety issues.

**Poster Session (Board #G12), Fri, 11:30 AM-1:00 PM and 5:30-6:30 PM**

**Gemcitabine/nab-paclitaxel (G) alternating with 5-FU/euvoroin/irinotecan (FOLFIRI) in first-line metastatic pancreatic cancer (MPC): Updated results.** First Author: Vincent J. Picozzi, Virginia Mason Hospital and Medical Center, Seattle, WA

**Background:** Both gemcitabine- and 5-FU-based chemotherapy (chemoRx) have demonstrated efficacy in MPC. Alternating these two regimens may 1) decrease toxicity 2) slow emergence of resistant cancer biology, and 3) provide a broader platform for addition of other (non-chemotherapy) CT agents to the base regimen. The strategy using alternating G/A and FOLFIRI in MPC was first tested in the SEEN-A1 trial (Picozzi et al. GI Cancer Symposium 2017) and further suggested to be of benefit both at our own institution (Picozzi et al. ASCO 2018) and elsewhere (Assenat et al. ASCO 2018). We extend and update our observations here. **Methods:** Eligible patients (pts) had the following characteristics: 1) bx proven de novo MPC, 2) chemorX naïve, 3) ECOG PS 0/1, and 4) bi-dimensionally measurable disease. Treatment (Rx) consisted of 1) gemcitabine 1000 mg/m² and nab-paclitaxel 125 mg/m² d1(18,15) alternating every 8 weeks (2 cycles) with FOLFIRI. Pts were radiographically restaged every 8 weeks. Rx was continued for up to 48 weeks, at which time additional Rx was given per physician/patient decision. **Results:** As of 9/2018, 31 pts have been treated at our institution via this method. Median age is 67, ECOG PS 0/1 58/42%. Disease site involvement included liver, lung, peritoneum 79%, 39%, and 23% respectively. Toxicity is less than typical with either agents/ treatment approaches.

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Efficacy and safety of nivolumab in first-line or further treatment of advanced metastatic biliary tract cancer. First Author: Miaomiao Gou, PLA General Hospital, Beijing, China

**Background:** PD-1 inhibitors have improved efficacy in many cancers. There are few report of nivolumab for metastatic biliary tract cancer (MBTC). This study reviewed the efficacy and safety of nivolumab for MBTC to improve efficacy and survival. **Methods:** Thirty patients with MBTC were voluntarily treated with non-clinical nivolumab at the PLA General Hospital. Nivolumab 200 mg or 180 mg was administered according to patient tolerance. Progression-free survival (PFS), overall survival (OS) was evaluated by Kaplan-Meier and univariate analysis were carried out among clinical characteristics. Objective response rates (ORR), disease control rates (DCR), and treatment-related adverse events (AEs) were also evaluated. **Results:** The median treatment cycle is 4 cycles. One case was complete response (CR), 5 cases partial response (PR), 12 cases stable (SD). ORR was 20%, DCR was 60%. PFS was 3.1m (95% CI: 2.13–4.06 months). The AEs of nivolumab monotherapy were fatigue (3 cases), fever (2 cases), hypothyroidism (1 case), skin reaction (1 case). Nivolumab combined with chemotherapy related 1-2 hematologic toxicity (5 cases), thrombocytopenia (2 cases), and grade 3-4 were leucopenia (3 cases). Non-hematologic toxicity grade 1-2 were nausea and vomiting (4 cases), fatigue (4 cases), fever (3 cases), peripheral neurotoxicity (3 cases), and hypothyroidism (1 case). Univariate analysis showed that PFS was 4.20m in patients older than 53 years, slightly higher than those younger than 53 years (3.0 m, P = 0.047). PFS of nivolumab combined with chemotherapy was statistically significant compared with nivolumab monotherapy (3.1 m vs 2.5 m, P = 0.031). Patients with metastatic number > 2 had a shorter PFS than those < 2 (1.4 m vs 4.1 m, P = 0.05). PD-L1 expression positive have no better PFS compared with PD-L1 negative (3.6 m vs 3.1 m, P = 0.801). Multivariate analysis show nivolumab combined with chemotherapy was only independent for longer PFS in patients of condition that of SOR. The safety of nivolumab in MBTC is controllable. **Subgroup analysis suggests that further selection of superior populations is needed and sample size need to be expanded to improve the efficacy of nivolumab in MBTC.**

Neoadjuvant chemotherapy versus upfront resection in ampullary adenocarcinoma stratified by stage: A retrospective analysis using the National Cancer Database. First Author: Shivan Leonard-Murali, Henry Ford Hospital, Department of Surgery, Detroit, MI

**Background:** Outcomes of a neoadjuvant therapy (NAT) strategy to treat ampullary adenocarcinoma (AAC) are unclear. Upfront resection (UR) (typically pancreatoduodenectomy) has not been established as the treatment of choice for adenocarcinoma (CRC) patients who had not received any chemotherapy (Kudo M et al, Lancet 2018). NAT can improve several major outcomes for the first line systemic treatment of uHCC. The most common adverse events (AEs) in pts treated with LEN were hypertension and diabetes. In our study, the most common any-grade adverse events (AEs; 8-mg vs 12-mg) were hypertension (43% vs 42%), diabetes (35% vs 40%), decreased appetite (33% vs 35%), weight loss (29% vs 32%), and fatigue (28% vs 31%). Adjusted by treatment duration, AE rates (episodes/patient-year) were similar for 8-mg versus 12-mg hypertension (0.79 vs 0.78), diabetes (0.46 vs 0.39), decreased appetite (0.63 vs 0.59), weight loss (0.50 vs 0.51), and fatigue (0.52 vs 0.47). Pharmacokinetic profiles were similar between both groups. **Conclusions:** LEN efficacy was comparable between groups. Exposure to LEN did not increase for the 12-mg compared to 8-mg group. When AEs were adjusted by treatment duration, no notable differences in the AE profiles between the starting doses were observed. Altogether, these results support the 8-mg and 12-mg starting doses based on BW < 60 kg and > 60 kg, respectively, in REFLECT. Clinical trial information: NCT01761266.
Temozolomide in grade III neuroendocrine neoplasms (G3 NENs): A multicenter retrospective review. First Author: David Chan, Sunnybrook Odette Cancer Centre, Toronto, ON, Canada

Background: G3 NENs are aggressive, and optimal systemic treatment is unclear. Temozolomide (TEM)-based regimens have been used to treat grade 1–2 NETs, but their efficacy in G3 NENs (Ki-67 > 20%) remains undetermined. Aim: To evaluate the clinical efficacy of TEM-containing regimens in advanced grade III gastroenteropancreatic NENs (GEPNENs). Methods: A multicenter retrospective review (2008–2017) of patients with metastatic/unresectable G3 NENs who received a TEM-containing regimen. The primary endpoint was retrospective review (2008–2017) of patients with metastatic/unresectable G3 NENs. 57% were well-differentiated, 35% poorly-differentiated, and 18% were included (median age 55, 65% male, 15% functional, 75% pancreatic). The regimen used was CAPTEM in 93% and TEM in 7%. Best radiological responses were: complete response 9% and TEM in 7%. The most common adverse events (AEs) regardless of causality were thrombocytopenia (62%), neutropenia (52%), anorexia (38%), nausea (38%), diarrhoea (38%), and anaemia (33%); the most common (≥30%) all-grade adverse events were neutropenia (46%), thrombocytopenia (46%), and anaemia (33%). Conclusions: Varlitinib plus gem/cis was well tolerated in the 200 mg cohort; the 300 mg cohort is ongoing. Preliminary anti-tumour activity was observed. Data will be updated at the time of presentation. Clinical trial information: NCT02992340.

The role of perioperative systemic therapy in localized pancreatic neuroendocrine tumor. First Author: Hao Xie, Mayo Clinic, Rochester, MN, USA

Background: The role of perioperative systemic therapy (PST) is unclear in the management of localized pancreatic neuroendocrine tumor (pNET). We aim to evaluate the benefit of PST compared to surgical resection alone in localized pNET. Methods: We identified patients with stage I–III pNET who underwent curative-intent surgical resection in National Cancer Database from 2006 to 2014. Patients who underwent PST and surgical resection were matched with patients who received surgery alone by propensity score at 1:1 ratio with nearest neighbor method. Factors predicting the use of PST were identified from logistic regression. Survival was estimated with Kaplan-Meier method and compared with Cox proportional hazards regression. Results: 4991 patients were included in this study with median age of 60 years. 1397 (28%) patients had pNET at the head of pancreas. 2708 (55%) patients had pNET at pancreas body and tail. 334 (6.8%) patients received PST. Factors associated with significant more use of PST compared to surgery alone were age < 65 years, low income, community medical facilities, grade 3/4 tumor, tumor at the head of pancreas, T3-4 tumor and NL tumor. 310 patients in PST group were matched with 310 patients in surgery alone group, with no significant difference for all covariates after match. For those in PST group, 64 (21%) patients received neoadjuvant systemic therapy, 173 (56%) patients received adjuvant systemic therapy, 7 (2.3%) patients received both, and 66 (21%) patients received PST without clear sequence. In the matched cohort, PST group had significantly shorter overall survival (OS) compared to surgery alone group (median OS 9.1 months versus not reached, p = 0.04). This finding was confirmed by multivariable Cox proportional hazards regression in unmatched cohort with HR 1.5 (95% CI 1.2–1.9, p = 0.002). Subgroup analysis in patients with grade 3/4 tumor demonstrated PST group has a trend of shorter OS as compared to surgery alone group (median OS 34.1 months versus 54.4 months, p = 0.1). Conclusions: PST compared to surgery alone is associated with worse OS in patients with localized pNET. This finding suggests that PST in localized pNET in the absence of solid clinical trial data.
Sorafenib versus hepatic arterial infusion chemotherapy in patients with advanced hepatocellular carcinoma: A Japanese multi-center large cohort study. First Author: Sadahisa Ogasawara, Department of Gastroenterology, Graduate School of Medicine, Chiba University, Chiba, Japan

Background: Sorafenib, approved in Japan in 2009, is the first systemic therapy demonstrated to significantly improve overall survival (OS) in patients with advanced hepatocellular carcinoma (HCC). In Japan, hepatic arterial infusion chemotherapy (HAIC), which directly delivers high concentrations of cytotoxic agents to liver tumors, has been offered to patients with advanced HCC who were not approved by NCH. HAIC has been used in patients without extrahepatic metastases (EHM). This study aimed to compare the outcomes of patients with advanced HCC who received HAIC and sorafenib.

Methods: Consecutive patients with advanced HCC who received sorafenib or HAIC as the first-line systemic therapy were enrolled from 10 Japanese centers. The statistical analysis plan included pre-defined propensity score matching method and risk factors. All statistical analyses were performed by an independent biostatistician. Results: Between June 2009 and May 2016, 2006 patients were enrolled (sorafenib: 1344 patients, HAIC: 541 patients). The median OS of patients with macrovascular invasion (MVI) was not reached, and without EHM was significant longer in the HAIC group compared with the sorafenib group. After propensity score matching, there were 172 patients in each cohort. The OS was 9.1 months for the sorafenib group and 10.1 months for the HAIC group (hazard ratio [HR]: 0.668 [95% CI: 0.475-0.931], P = 0.018). There was no significant difference in OS between patients without both MVI and EHM. After propensity score matching, there were 76 patients in each cohort. The OS was 15.4 months for the sorafenib group and 12.2 months for the HAIC group (HR: 1.227 [95% CI: 0.699-2.153], P = 0.475).

Conclusions: HAIC might be a potential initial treatment for patients with advanced HCC with MVI (without EHM). Currently, several new drugs appear clinically beneficial for patients with advanced HCC. Although this study only focused on sorafenib as the chemotherapeutic agent, additional studies should be conducted to confirm the benefits associated with HAIC in a limited population of patients with advanced HCC.

Results from phase I study of the oncolytic viral immunotherapy agent caneraturev (C-REV) in combination with gemcitabine plus nab-paclitaxel for unresectable pancreatic cancer. First Author: Yusuke Hashimoto, Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital East, Kashiwa, Japan

Background: Caneraturev (C-REV, formerly HF10) is an oncolytic, spontaneous mutant Herpes Simplex Virus type 1, and is one of immunotherapies that combine direct tumor cell killing with immune modulation. The purpose of this study is to determine the recommended dose of C-REV in combination with chemotherapy (Gemcitabine + Nab-paclitaxel; G-nP) in Japanese patients with stage III or IV unresectable pancreatic cancer. We report the safety and antitumor activity in this study.

Methods: This study was a 3+3 dose escalation design with a 2-dose escalation scheme evaluating 2 doses of C-REV. The subjects received C-REV at 1x10^6 or 1x10^7 TCID50/mL (up to 2mL, depending on tumor size) intratumorally by EUS-guidance at a 2-week interval in addition to 1000mg/m^2 gemcitabine and 100mg/m^2 nab-paclitaxel by intravenous fusion on days 1, 8, and 15 of a 4-week cycle. The study treatment could continue up to 1 year if eligible for injection. The primary objective was Dose Limiting Toxicity (DLT); the secondary endpoints were adverse events (AEs) assessed per NCI CTCAE v4.0, Best Overall Response Rate (BORR) at 16-week by RECIST and progression-free survival. Results: Six patients (pts) were enrolled and treated: 33% (2/6) men, age range 63 to 72 yrs, disease stage 33% III, 66% IV. Of 6 safety evaluable pts, no DLTs were reported, 16% (1/6) pts had C-REV-related G3 AE and it was acute pancreatitis (G3). G-nP-Prerelated G3 AEs observed in more than 2 pts were neutropenia (50%), and the majority of G3 AEs were similar as the AEs previously reported in G-nP therapy. As of 01 Sep 2018, of the 6 efficacy evaluable pts, BORR at 16-week was 66% (4 PR), Disease control rate was 100% (2 SD), and 100% SD pts continues the study treatment. We will present the updated data. Conclusions: The recommended dose was determined as 1x10^7 TCID50/mL. The combination of C-REV and the standard chemotherapy demonstrated a favorable benefit/risk profile and encouraging antitumor activity in Japanese patients with unresectable pancreatic cancer. Clinical trial information: NCT02325820.

Chemotherapy-induced neutropenia as a prognostic factor in patients with unresectable pancreatic cancer treated with gemcitabine and nab-paclitaxel. First Author: Motoyasu Kan, National Cancer Center Hospital East, Chiba, Japan

Background: Chemotherapy-induced neutropenia (CIN) has been reported to be associated with a longer survival in patients with various cancers. The aim of our study was to assess whether CIN could also be a prognostic factor in patients with unresectable pancreatic cancer receiving treatment with gemcitabine (GEM) and nab-paclitaxel (nab-PTX).

Methods: We retrospectively analyzed the medical records of patients who had been treated with GEM and nab-PTX as first-line chemotherapy. CIN was categorized on the basis of the worst WHO grade during chemotherapy: absent/mild (≤ grade 2), or severe (≥ grade 3). The background characteristics and CIN as time-varying covariates (TVCs) were analyzed as potential prognostic factors using a Cox proportional hazards model. Results: We analyzed a total of 291 patients (absent/mild CIN: 116 patients; severe CIN: 174 patients). The median time to severe CIN was 14 days (interquartile range: 10–39 days). The median overall survival (OS) was significantly longer in the severe CIN group than in the absent/mild CIN group (9.2 vs. 13.3 months; p < 0.001). After adjustments, severe CIN was identified as an independent predictor of the OS (HR, 0.54; 95% CI 0.38–0.77; p = 0.001). In the TVC model also, severe CIN was identified as an independent factor (HR, 0.79; 95% CI, 0.68–0.92; p = 0.002).

Conclusions: Severe CIN was associated with a longer survival in patients with pancreatic cancer treated with GEM and PTX.

Ramucirumab (RAM) as second-line treatment in patients with advanced hepatocellular carcinoma (HCC) and elevated baseline α-fetoprotein (AFP): An analysis of AFP kinetics in the phase III REACH-2 study. First Author: Richard S. Finn, University of California Los Angeles Medical Center, Los Angeles, CA

Background: REACH-2 (NCT02435433) demonstrated a significant survival benefit with RAM vs placebo in the second-line treatment of patients with advanced HCC and AFP > 400 nmol/L. This analysis investigated changes in AFP during treatment, as well as potential relationships with survival or progression.

Methods: Patients were randomized (2:1) to RAM 8 mg/kg IV or placebo Q2W plus best supportive care until disease progression or unacceptable toxicity. Serum AFP levels were measured at baseline and every 3 cycles. Percent change in AFP from baseline was analyzed at each time point up to Cycle 12 with descriptive statistics and Wilcoxon rank sum test between treatment arms. AFP response was defined as ≥ 20% decrease from baseline.

Results: Changes in AFP during treatment. Clinical trial information: NCT02435433.
Checkmate-040: Nivolumab (NIVO) in patients (pts) with advanced hepatocellular carcinoma (aHCC) and Child-Pugh B (CPB) status. First Author: Masatoshi Kudo, Kindai University Faculty of Medicine, Osaka-Sayama, Japan

Background: Pts with aHCC and CPB liver status are often excluded from clinical trials of new therapies due to their poor prognosis (Green British Cancer 2005). Historical overall survival (OS) for these pts when treated with sorafenib (SOR) has ranged –3–5 mo in retrospective or descriptive studies (Abou-Alfa Gastrointestinal Cancer Res 21; Da Fonseca Mol Oncol 2015; Premo Ann Oncol 2013; Chuu Cancer 2013). No novel treatment options are needed for these pts. The PD-1 inhibitor NIVO is approved in the US, Canada, and elsewhere currently, for SOR-naive pts with aHCC based on results from CheckMate-040 (NCT01658878) (Eur. Immunol 2017). Here we report data from the CPB cohort of CheckMate-040, the first prospective study of immunotherapy in this pt group. Methods: Pts with CPB (B8-B7) aHCC who were SOR-naive (n = 25) or -experienced (n = 24) received NIVO 240 mg IV for 30 min Q2W until unacceptable toxicity or disease progression. Primary endpoints were objective response rate (ORR), investigator-assessed, and disease control rate (DCR). Safety was assessed in all treated pts using NCI CTCAE v4.0. Results: Of 49 analyzed pts, 28 (57.1%) had vascular invasion or extrahepatic spread. Safety was assessed in all treated pts using NCI CTCAE v4.0. No grade 3-4 treatment-related adverse events (AEs) were reported in 25 (51%) pts (of which 13.8% pts had prior hepatic TRAEs). TRAEs led to discontinuation in 2 pts (4.1%). NIVO safety profile in these pts appeared comparable to cohorts of pts with CPA aHCC. Comparison data for pts with CPA aHCC and extended follow-up for pts with CPB aHCC will be presented. Conclusions: Encouraging ORR and DCR were observed in pts with CPB aHCC treated with NIVO. AEs were manageable and did not lead to discontinuation compared with pts with CPA aHCC. NIVO showed promising efficacy and tolerability compared with historical data, supporting further investigation. Clinical trial information: NCT01658878.

Patterns of care and outcomes of definitive external beam radiotherapy and radioembolization for localized hepatocellular carcinoma: A propensity score-adjusted analysis. First Author: Danielle Sara Bitterman, Harvard Radiation Oncology Program, Boston, MA

Background: Hepatocellular carcinoma (HCC) is a leading cause of cancer mortality worldwide. Most patients with localized HCC are not surgically operable or transplantation candidates, thus there is an increasing role for nonsurgical locoregional therapies. Ablative external beam radiotherapy (XRT) and transarterial radioembolization (TARE) are two emerging radiotherapeutic treatments for localized HCC. However, there are little data comparing their efficacy. We therefore sought to evaluate their utilization and efficacy in a large nationwide cohort. Methods: Comparing their efficacy. We therefore sought to evaluate their utilization and efficacy in a large nationwide cohort. Conclusions: Radiotherapy may be safe and locally effective. Prospective study is needed to understand the optimal treatment of these patients.

328 Poster Session (Board #H6), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
External beam radiotherapy for hepatocellular carcinoma with right atrium tumor thrombus. First Author: Danielle Sara Bitterman, Massachusetts General Hospital, Boston, MA

Background: Hepatocellular carcinoma (HCC) with right atrium tumor thrombus (RATT) via progression through hepatic veins into the inferior vena cava is a challenging entity with limited treatment options. Given the significant clinical sequela of RATT, improved locoregional treatments are needed. We examined our experience with palliative right atrium-directed radiotherapy for HCC. RATT. Results: We conducted a retrospective study of 10 patients with HCC RATT treated with radiotherapy between 2011-2018. Patients with localized (n = 5) and metastatic (n = 5) disease were included. Clinical and treatment factors were collected. Results: Median follow-up was 3 mos. Baseline Childs Pugh score was A in 3 patients and B in 7 patients. The table below shows prescription and dosimetric data. No patients experienced grade ≥ 3 toxicity. The only major adverse cardiac event observed after radiotherapy was heart failure in 2 patients, and it was difficult to determine the contribution of treatment versus RATT. Three months post-radiation, 2 patients experienced a Childs Pugh score decline of ≥ 2 points. At last follow-up, 5 patients were deceased, 4 patients were alive without progression, and 1 patient was alive with progression. Median progression free and overall survival was 3 mos (0.5-7 mos) and 3.5 mos (range 0.5-13 mos), respectively. RATT progression occurred in 1 patient, hepatic progression outside the treatment field occurred in 1 patient, and distant progression occurred in 2 patients. Causes of death included RATT progression (n = 1), HCC progression elsewhere (n = 2), hepatic decompensation (n = 1), and aspiration (n = 1). Conclusions: This unique series suggests HCC RATT-directed radiotherapy may be safe and locally effective. Prospective study is needed to understand the optimal treatment of these patients.

329 Poster Session (Board #H7), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
Patterns of care and outcomes of definitive external beam radiotherapy and radioembolization for localized hepatocellular carcinoma: A propensity score-adjusted analysis. First Author: Danielle Sara Bitterman, Harvard Radiation Oncology Program, Boston, MA

Background: Hepatocellular carcinoma (HCC) is a leading cause of cancer mortality worldwide. Most patients with localized HCC are not surgically operable or transplantation candidates, thus there is an increasing role for nonsurgical locoregional therapies. Ablative external beam radiotherapy (XRT) and transarterial radioembolization (TARE) are two emerging radiotherapeutic treatments for localized HCC. However, there are little data comparing their efficacy. We therefore sought to evaluate their utilization and efficacy in a large nationwide cohort. Methods: Comparing their efficacy. We therefore sought to evaluate their utilization and efficacy in a large nationwide cohort. Conclusions: Radiotherapy may be safe and locally effective. Prospective study is needed to understand the optimal treatment of these patients.

330 Poster Session (Board #H8), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
A phase Ib study evaluating olaratumab in combination with nab-paclitaxel and gemcitabine in first-line treatment of metastatic pancreatic cancer. First Author: Uwe Pelzer, Charité - Universitätsmedizin Berlin, Berlin, BS, Germany

Background: Increased platelet-derived growth factor receptor alpha (PDGFRα) expression is linked to epithelial-mesenchymal transition in pancreatic cancer. Olaratumab (O) is a fully human monoclonal antibody against PDGFRα and has previously been reported in 25 (51%) pts (4.2% pts had advanced soft tissue sarcoma). Here, we report the initial safety and antitumor activity data of O in combination with nab-paclitaxel + gemcitabine (nPG) in first-line metastatic pancreatic cancer patients (pts). Methods: In this 3+3 dose escalation study, patient dose escalation (cohort 1: 3 pts; cohort 2: 7 pts) was conducted in a total of 10 pts treated in dose escalation (cohort 1: 3 pts; cohort 2: 7 pts) with no dose-limiting toxicities (DLTs) observed. Safety of 20 mg/kg O + nPG was confirmed in the expansion cohort: 1 of 12 pts (8.3%) experienced a DLT of grade 4 neutropenia. Most frequent adverse events (AEs) (≥ 25%) reported across all cohorts included fatigue (50%); neutropenia (50%); nausea (46%); thrombocytopenia (41%); and constipation (32%). Related grade ≥ 3 AEs reported in > 2 pts were neutropenia (N = 7; 32%), infusion-related reaction, and neuropathy (both N = 3; 14%). There were no deaths related to study drugs. Among pts evaluable for response, 2 of 15 pts had a partial response and 11 pts had stable disease as best response for an objective response rate of 13%. Notably, 2 of 3 pts in cohort 1 continue on treatment for more than 12 months as of the data cut-off. Updated data will be presented at the meeting.

Conclusions: Both dose levels were tolerated. Safety profile was similar to nPG chemotheraphy with most toxicity manageable through dose adjustments of nPG. Clinical trial information: NCT03086369.
Efficacy and safety of varlitinib, a reversible pan-HER tyrosine kinase inhibitor, in combination with platinum-based regimens in biliary tract cancers: A pooled analysis from three phase I studies. First Author: Aaron C. Tan, National Cancer Centre Singapore, Singapore, Singapore

Background: Varlitinib is a nanomolar inhibitor of EGFR, HER2, and HER4 and has shown promising activity in preclinical and early clinical models. During Phase (Ph) I development, significant tumor shrinkage was observed in biliary tract cancer (BTC) patients (pts). Tissue microarray analysis has revealed that ~70% of BTC pts exhibit HER overexpression, suggesting varlitinib could be beneficial in BTC. Methods: Data from BTC pts were pooled from 3 Ph1 trials of varlitinib (dosed 200-500 mg Bid) in combination with cisplatin and 5-FU/capcitabine (cape) (Study 002); oxaplatin and 5-FU/cape (Study 002SG); cisplatin and gemcitabine (Study 007). The depth of tumor response, disease control rate (DCR), and treatment-related adverse events (TRAES) were analysed. Results: As of 12 June 2018, 43 pts were recruited: 12 (27.9%); 10 (23.3%) and 21 (48.8%) from study 002; 002SG and 007 respectively. 002SG and 007 were still ongoing at data cut-off. 20 responses were defined as reduction from baseline >50%. With 55 pts per arm our study was powered to identify an ORR ≥25% (90% power, 5% α-error).

Results: We recruited 111 pts (55 panNETs/56 giNETs). Prior therapies were CHT 32%, SSAs 87%, everolimus (E) 70% and sunitinib (S) 30% for panNETs. ORR was 29%, 40% and 18.5% for panNETs and SSAs respectively. A median follow-up of 17 months (m), PFS for panNETs was 15.8 m (95% CI 10.8-23.6 m) and for giNETs, PD to TA was mandatory, regardless prior therapy with somatostatin analogs (SSAs) or chemotherapy (CHT), and for giNETs, PD on SSAs. Pts were treated with lenvatinib at 24 mg qd until PD or intolerable toxicity. The primary endpoint was ORR by central radiology review. Results was calculated by investigator assessment. Biochemical responses were defined as reduction from baseline >50%. With 55 pts per arm our study was powered to identify an ORR ≥25% (90% power, 5% α-error).

Conclusions: Varlitinib with platinum-based chemotherapy has a promising efficacy and safety profile in BTC. A Ph2/3 randomised study of varlitinib and cape in 2nd line BTC and a Ph3/2 study of varlitinib with platinum-based chemotherapy in 1st line BTC are ongoing. Clinical trial information: NCT02648425, NCT02435927, and NCT02992340.
Conclusions:
1. Surgery alone had worse overall survival.
2. There was no significant difference in overall survival between surgery vs Surgery + AT and NAT + Surgery in a large National Cancer Database.

Methods: We identified patients with surgically resected AJCC clinical stage 1, 1A, and 1B PAC between 2004-2014. Patients were stratified into 3 groups to assess outcomes. Exclusion criteria: those with incomplete survival and sequence of therapy data. Hazard ratios (HR) were calculated for evaluation of survival, as well as for 30-Day and 90-Day Mortality between the 3 groups. Results were adjusted for age and Deyo-Charlson comorbidity index.

Results: A total of 9684 pts with Clinical stage 1, 1A, 1B PAC between 2004-2014 were identified. Of these 2266 pts underwent surgery alone; 6222 had surgery followed by AT; and 1964 pts had neoadjuvant therapy followed by surgery. There was a HR of 0.995 (95% CI 0.935-1.058 p = 0.864) and 0.984 (95% CI 0.924-1.048, p = 0.617) for 30- and 90-Day mortality comparing upfront surgery to NAT, respectively, With AT as the reference group for survival, there was a HR of 1.362 (95% CI 1.286-1.443, p < 0.001) for surgery only and HR of 0.929 (95% CI 0.859-1.004, p = 0.064) for NAT.

Conclusions: 1. Surgery alone had worse overall survival. 2. There was no significant difference in overall survival when comparing AT and NAT. 3. A prospective randomized trial evaluating the differences in survival is needed.
Hepatocellular carcinoma and liver metastasis treated by hafnium oxide nanoparticles activated by SBRT: A phase I/II trial. First Author: Enrique Chajon, Centre Eugène-Marquis, Rennes, France

Background: Hafnium oxide nanoparticles, NBXTR3, were developed to increase the tumor-localized high energy density once activated by ionizing radiation such as stereotactic body radiotherapy (SBRT) and thus to increase tumor cell death compared to the same dose of radiation. NBXTR3 is characterized by a single intratumor/intralesional (IL) administration and fits into standard RT schedule with no change in patient's flow, treatment protocol or equipment. Herein the preliminary results of a phase I/II clinical trial evaluating this combination in patients (pts) with hepatocellular carcinoma (HCC) or liver metastasis (mts).

Methods: HCC and liver mets patients were treated with an IL injection of NBTXR3 followed by SBRT (15 Gy in 3 fractions). The phase I part of the trial follows a 3+3 dose escalation design at dose levels of NBTXR3 corresponding to 10%, 15%, 22%, 33% of the baseline tumor volume. This study aims primarily to identify the Recommended Dose and the incidence of early Dose Limiting Toxicities (DLTs) of NBTXR3 activated by SBRT. Secondary endpoints include assessment of global safety profile, liver function evaluated by Child-Pugh score (CPS), AST to Platelet Ratio Index (APRI), and response rate (mRECIST/RECIST 1.1).

Results: Enrolment is at the last dose level, 33%, and completed at 10% (6 pts), 15% (4 pts) and 22% (4 pts). So far, no early DLTs nor severe adverse events related to NBTXR3 were observed. Both CPS and APRI did not reveal important variations in accordance to NBTXR3 low toxicity. The best observed target lesions responses, among 7 evaluable HCC pts for response (mRECIST), were: 3 complete responses, 3 partial responses (PR) and 1 stable disease (SD) and among 3 evaluable liver mets pts: 1 PR, 3 SD and 1 progressive disease (RECIST 1).

Conclusions: NBTXR3 is well tolerated at the 22% dose level with an overall positive safety profile. This innovative approach might constitute a valuable solution for pts with liver tumors beyond standard treatment lines. NBTXR3 was successful in a phase II/III in soft tissue sarcoma (NCT02379845) and is currently evaluated in head and neck (NCT01946867; NCT02901483), prostate (NCT02805894) and rectum cancers. Clinical trial information: NCT02720565.

Phase II trial of preoperative modified FOLFIRINOX (mFOLFIRINOX) followed by postoperative gemcitabine (GEM) in patients (pts) with borderline resectable pancreatic ductal adenocarcinomas (BR-PDAC). First Author: Changhoon Yoo, Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Republic of (South)

Background: mFOLFIRINOX and GEM are standard chemotherapy for metastatic and resected PDAC, respectively. This phase 2 trial assessed the efficacy and safety of perioperative chemotherapy consisting of preoperative mFOLFIRINOX and postoperative GEM in pts with BR-PDAC. Methods: Pts with histologically proven and radiologically confirmed BR-PDAC as defined by NCCN criteria were eligible. Pts received 8 cycles of preoperative mFOLFIRINOX (oxaliplatin 85 mg/m², irinotecan 180 mg/m², 5-FU 2,400 mg/m² plus either anti-cytotoxic T lymphocyte antigen 4 (30.4%) or tyrosine kinase inhibitors (TKIs) (54.5%), or both (15.1%). We reviewed their liver function tests and HIRAEs onset was related to time to treatment failure (TTF).

Results: Overall, 12 patients (30%) developed grade ≥ 3 hepatitis according to Common Toxicity Criteria for Adverse Events v. 4.03, resulting in 4 cases of grade 2 drug-induced liver injury per DILL Working Group criteria. Time between therapy initiation and hepatitis onset was 1.4 months (0.4-2.8) and median peak aminotransferase (AT) level was 258 U/L (85-869). Of 6 permanent treatment discontinuations due to adverse events (AEs), 4 were linked to hepatitis. Higher AT median levels at baseline were significantly linked to grade ≥ 3 hepatitis compared with lower grades (95 U/L vs. 36 U/L, respectively; p = 0.008). Etiology, age, treatment, did not predict HIRAEs onset. TTF in patients in patients with grade ≥ 3 hepatitis was shorter than in the whole 1 (1 vs. 0.09 months, p = 0.049), while overall survival did not differ (p = 0.125).

Conclusions: We observed a 30% incidence of clinically significant HIRAEs. HIRAEs represent the most frequent AEs leading to treatment discontinuation in patients with HCC undergoing treatments with immune checkpoint inhibitors. Baseline AT levels may identify patients at increased risk of grade ≥ 3 hepatitis.

Effect of neoadjuvant chemoradiotherapy on prognosis in resectable and borderline resectable pancreatic cancer with venous involvement. First Author: Minako Nagai, Nara Medical University, Kashihara, Japan

Background: The efficacy of neoadjuvant treatment for pancreatic cancer (PC) remains to be established. In this study, we have retrospectively evaluated the impact of neoadjuvant chemoradiotherapy (NACRT) on peripancreatic or peritoneal disease of PC. Methods: One hundred eighty one patients who preoperatively received full-dose gemcitabine (1000mg/m²) with concurrent radiation of 54 Gy between 2006 and 2017 were analyzed. One hundred forty nine patients who proposed upfront surgery were served as controls.

Results: Among the 181 patients treated with NACRT, 23 (13%) couldn't undergo pancreatic resection after NACRT because of distant metastasis in 10, tumor progression in 7 and poor PS in 6. While among the 149 patients who proposed upfront surgery, 10 (7%) couldn't undergo pancreatic resection at laparotomy, because of distant metastasis in 8 and tumor progression in 2. In overall survival analysis of all patients with resected and un-resected tumors, patients treated with NACRT had a better prognosis than those without (median survival time: 37.0 vs. 27.1M, P = 0.049). According to tumor resectability status including R (resectable), BR-P (borderline resectable with venous involvement) and BR-A (borderline resectable with arterial involvement) PC, in the R and BR-P group, overall survival was significantly better in the patients with NACRT (45.7 vs. 33.8M, P = 0.049, 61.7 vs. 14.6M, P = 0.022). Also only for resected tumors, patients treated with NACRT had a better prognosis than those without in the R and BR-P group (53 vs. 36.5M, P = 0.033, 61.7 vs. 14.6M, P = 0.002), while NACRT had no significant impact on prognosis in the BR-A group. The rate of pancreatic fistula, delayed gastric emptying and abdominal abscess were lower in the NACRT group than the control group. Furthermore, the lymph node metastasis rate, R0 resection rate and pathological stage were favorable in the NACRT group (P < 0.001, P < 0.005, P < 0.001). The completion rate of adjuvant chemotherapy was also increased in the NACRT group (80%). Conclusions: NACRT had a variety of favorable impact in PC treatment. In particular, it significantly improved the prognosis in the R and BR-P, but not BR-A.
Multicenter retrospective analysis for efficacy and safety of liposomal irinotecan (nal-IRI) plus 5-FU/leucovorin (5-FU/LV) after progression on gemcitabine-based therapy in Korean patients (pts) with metastatic pancreatic ductal adenocarcinoma (mPDAC): A study by Korean Cancer Study Group (KCSG), First Author: Changhoon Yoo, Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Republic of (South)

Background: Nal-IRI plus 5-FU/LV has demonstrated efficacy in mPDAC pts associated with median OS. Despite heavily pretreated patients were included, efficacy and safety outcomes in our cohort were consistent with the results of previous NAPOLI-1 trial.

Methods: Multicenter retrospective case design. First Author: Andrea Grace Bocobo, UC San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA

Results: A total of 86 patients entered into this NPP among 10 Korean institutions. Median age was 61 years (range, 37-79) and 52 pts (60%) were male. Liver (n=49, 57%), peritoneum (30%, 35%), and lung (27, n=31%) were the most common metastatic sites. All patients had ECOG performance status 0-1 and previously received gemcitabine-based therapy. Prior to nal-IRI plus 5-FU/LV, 35 (41%) and 51 (59%) patients received c and 2 lines of chemotherapy for unresectable/metastatic disease, respectively. Best response was complete response (n=2, 2%), partial response (7, 8%), stable disease (38, 44%), and progressive disease (32, 37%), indicating overall response rates of 10% and disease control rate of 25%. Median follow-up duration was 6.4 months, median progression-free survival (PFS) was 3.5 months (95% CI 1.3-5.7) and median overall survival (OS) was not yet reached. The 6-month PFS and OS rates were 37.5% and 65.1%, respectively. Most common grade 3-4 toxicities were neutropenia (n=32, 37%), nausea (9, 10%), vomiting (8, 9%), anemia (7, 8%), and diarrhea (4, 5%). Febrile neutropenia occurred in 7 (8%) patients. Conclusions: Nal-IRI plus 5-FU/LV was well tolerated and effective for mPDAC patients who progressed on gemcitabine-based therapy. Multicenter retrospective study for efficacy and safety of liposomal irinotecan (nal-IRI) plus 5-FU/leucovorin (5-FU/LV) in Korea. This analysis is multicenter, prospective, pre-approval access of nal-IRI in Korea. This analysis is multicenter retrospective study for patients who received nal-IRI plus 5-FU/LV under the NPP.

Poster Session (Board #J2), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Changes in alpha-fetoprotein (AFP) and systemic therapy outcomes in advanced hepatocellular carcinoma (HCC): A multicenter retrospective analysis. First Author: Andrea Grace Bocobo, UC San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA

Background: AFP is elevated in 70% of HCC and is associated with poor prognosis. The role of AFP as a biomarker of response to systemic treatments has not been established; though small, retrospective studies show association between AFP and outcome and survival on sorafenib for HCC. The relationship between AFP changes and response to immune checkpoint inhibitors (ICI) has not been reported. This study examines AFP changes on treatment for association with outcomes on first-line (IL) Sor and any subsequent CPI in a contemporary, multicenter, retrospective, pooled analysis. Methods: Design: Multicenter retrospective case series. Key eligibility: Received IL Sor or Sor-based combination for advanced HCC; ≥1 post-treatment AFP value available; enrolled on NCI-approved registry. Objectives: associate AFP changes within 3 months of start of treatment with overall survival (OS) and time on treatment (TOT) on IL Sor and any subsequent CPI; associate baseline AFP with OS and TOT for Sor and CPI; relate baseline AFP and changes on treatment to clinical covariates. Results: 152 patients were identified from two centers. Baseline characteristics: M/F 132/20; HBV/HCV/nonviral 40/71/41; Child Pugh A/B 128/23; BCLC 25.0 (OR 6.41) and R1 resection (OR 3.97). There was no significant difference of survival between two groups divided by FLRV/Wt ratio (0.5) in Kaplan-Meier analysis. There was significant difference of survival according to PHLF. In univariate analysis, predictors of PHLF (p = 0.043) were resection major postoperative complications (Dindo III to IV). Results: Combined Portal vein resection was performed in 18.8%, PHLF incidence was 13.6% and 90-day mortality was 3.5%. On multivariate analysis, predictors of PHLF (< 0.05) were FLVR/Wt ratio < 0.5 (odds ratio (OR) 9.45, 4.5IC RIS < 15 (OR 3.72), BMI > 25.0 (OR 6.41) and RI resection (OR 3.97). There was no significant difference of survival between two groups divided by FLVR/Wt ratio (0.5) in Kaplan-Meier analysis. There was significant difference of survival according to PHFL. In univariate analysis, predictors of PHFL (p = 0.043) were resection major complications (Dindo III to IV), BMI (> 25) and RI resection is associated with PHLF for patients with PHCC. We confirmed that PHLF is also associated with OS improvement in patients with high BMI and RI resection. Preoperative assessment to patients with PHCC should be optimized to minimize the risk of PHLF.

Poster Session (Board #J6), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Risk factors of hepatic failure after liver resection for perihilar cholangiocarcinoma: Importance of future liver remnant volume, body weight ratio, and impact on long-term survival. First Author: Jong Woo Lee, Asan Medical Center, Seoul, Korea, Republic of (South)

Background: Hepatic resection for perihilar cholangiocarcinoma (PHCC) is associated with high postoperative mortality. Future liver remnant to total liver volume ratio has been used to anticipate the risks associated with liver resection for PHCC. We sought to investigate the independent determinants of hepatic failure associated with postoperative hepatic failure (PHLF) and assess predictive value of future liver remnant volume - body weight (FLVR/Wt) ratio after resection for PHCC. Methods: This study included 287 patients who underwent major hepatectomy for PHCC between 2008 and 2015, including caudate lobectomy with bile duct resection for PHCC between 2008 and 2015 in single center. FLVR were calculated with CT volumetry and perioperative clinical and operative data were analyzed to identify independent determinants of PHLF (grade B/C mortality) and major postoperative complications (Dindo III to IV). Results: CombinedPortal vein resection was performed in 18.8%, PHLF incidence was 13.6% and 90-day mortality was 3.5%. On multivariate analysis, predictors of PHLF (< 0.05) were FLVR/Wt ratio < 0.5 (odds ratio (OR) 9.45, 4.5IC RIS < 15 (OR 3.72), BMI > 25.0 (OR 6.41) and RI resection (OR 3.97). There was no significant difference of survival between two groups divided by FLVR/Wt ratio (0.5) in Kaplan-Meier analysis. There was significant difference of survival according to PHFL. In univariate analysis, predictors of PHFL (p = 0.043) were resection major complications (Dindo III to IV), BMI (> 25) and RI resection is associated with PHLF for patients with PHCC. We confirmed that PHLF is also associated with OS improvement in patients with high BMI and RI resection. Preoperative assessment to patients with PHCC should be optimized to minimize the risk of PHLF.

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The clinical outcomes of combination chemotherapy in elderly patients with advanced biliary tract cancer: An exploratory subgroup analysis of JCOG1113. First Author: Nivethan Vela, Cancer Institute, Tokyo, Japan

Background: JCOG1113 is a randomized phase III trial to confirm the non-inferiority of gemcitabine plus S-1 (GS) to gemcitabine plus cisplatin (GC) for advanced biliary tract cancer (BTC) in terms of overall survival (OS). In the final analysis, OS demonstrated non-inferiority to GC in OS and was considered as a new option of standard of care for advanced BTC. However, there are few reports on the efficacy and comparison of combination chemotherapy in elderly patients with advanced BTC. Therefore, this study aimed to explore the clinical outcomes of combination chemotherapy in elderly patients with advanced BTC.

Methods: Among all enrolled patients in JCOG1113, ≥ 75 years old patients were included in this exploratory subgroup analysis. Cox regression analysis was performed to investigate the influence of age at baseline on OS and PFS. Clinically relevant adverse events (AEs) were defined as any of grade ≥ 2 or more fatigue, appetite loss, nausea, vomiting, oral mucositis, and diarrhea, and were compared using Fisher’s exact test. Results: Among all enrolled patients, 195 patients in GC and 139 patients in GS were included in ≥ 75 years old cohort and 20 patients in GC and 40 patients in GS were included in ≥ 75 years old cohort. The HR of ≥ 75 years old cohort to < 75 years old cohort for OS was 0.96 (95% CI 0.71-1.30) in all enrolled patients. The HR of ≥ 75 years old cohort to < 75 years old cohort for OS was 1.26 (95% CI 0.77-2.04) in GC, and 0.84 (95% CI 0.56-1.24) in GS. The HR of ≥ 75 years old cohort to < 75 years old cohort for PFS was 1.01 (95% CI 0.63-1.61) in GC, and 0.78 (95% CI 0.54-1.12) in GS. Clinically relevant AEs were 36.6% in ≥ 75 years old cohort and 25.3% in ≥ 75 years old cohort in GC, 45.3% in ≥ 75 years old cohort and 32.5% in ≥ 75 years old cohort in GS. Conclusions: The clinical outcomes of combination chemotherapy in elderly patients were comparable to non-elderly patients. Clinical trial information: 000010667.

Survival and cost associated with chemotherapy and chemoradiotherapy among resected pancreas cancer patients. First Author: Ikuhiro Yamada, Japanese Foundation for Cancer Research, Tokyo, Japan

Background: Pancreas cancer is expensive to treat, and the effectiveness of adjuvant chemotherapy (CT) and chemoradiation (CRT) following resection is debated. We compared both survival and healthcare costs by adjuvant therapy after curative-intent pancreaticoduodenectomy (PD) for pancreas adenocarcinoma (PC). Methods: All patients with resected PD in Ontario, Canada, diagnosed 2004-2014 were identified and linked to administrative healthcare databases. Stratified Kaplan-Meier survival curves and log-rank test compared survival across treatment groups. Costs were assessed from the perspective of Ontario’s single-payer healthcare system, and compared between CT and CRT. A one-year time horizon was used from the date of surgery. Results: 677 PC patients met all inclusion/exclusion criteria and underwent curative-intent PD. Among all enrolled patients, 155 patients in GC and 139 patients in GS were included in ≥ 75 years old cohort, and 25 patients in GC and 40 patients in GS were included in 50-74 years old cohort. The HR of 75 years old cohort to 50-74 years old cohort was 1.37 (95% CI 0.97-1.92) in GC, and 1.96 (95% CI 1.25-3.07) in GS. Other clinic and healthcare costs by adjuvant therapy after curative-intent pancreaticoduodenectomy (PD) and 0.84 (95% CI 0.56-1.24) in GS. The HR of 75 years old cohort to < 75 years old cohort for OS was 1.26 (95% CI 0.77-2.04) in GC, and 0.84 (95% CI 0.56-1.24) in GS. The HR of ≥ 75 years old cohort to < 75 years old cohort for PFS was 1.01 (95% CI 0.63-1.61) in GC, and 0.78 (95% CI 0.54-1.12) in GS. Clinically relevant AEs were 36.6% in ≥ 75 years old cohort and 25.3% in ≥ 75 years old cohort in GC, 45.3% in ≥ 75 years old cohort and 32.5% in ≥ 75 years old cohort in GS. Conclusions: The clinical outcomes of combination chemotherapy in elderly patients were comparable to non-elderly patients. Clinical trial information: 000010667.

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Provider-volume associated with variable receipt of therapy and outcomes for noncurative pancreas adenocarcinoma: A population-based analysis. First Author: Julie I. Hallet, Odette Cancer Centre, Toronto, ON, Canada

Background: While high-volume providers for pancreatic adenocarcinoma (PA) surgery yield better outcomes, variation in practice and the role of provider-volume has not been investigated for systemic therapy. We examined a population-based practice and outcomes in the management of non-curative PA based on medical oncology provider-volume. Methods: We conducted a population-based retrospective cohort study of non-resected PA over 2005-2016 by linking administrative healthcare datasets. High-volume (HV) medical oncology providers were defined as the 5th quintile of number of PA seen per year. Outcomes were receipt of chemotherapy and overall survival. Results: Among all enrolled patients, 155 patients in GC and 139 patients in GS were included in ≥ 75 years old cohort, and 25 patients in GC and 40 patients in GS were included in 50-74 years old cohort. The HR of 75 years old cohort to 50-74 years old cohort was 1.37 (95% CI 0.97-1.92) in GC, and 1.96 (95% CI 1.25-3.07) in GS. Other clinic and healthcare costs by adjuvant therapy after curative-intent pancreaticoduodenectomy (PD) and 0.84 (95% CI 0.56-1.24) in GS. The HR of ≥ 75 years old cohort to < 75 years old cohort for OS was 1.26 (95% CI 0.77-2.04) in GC, and 0.84 (95% CI 0.56-1.24) in GS. The HR of ≥ 75 years old cohort to < 75 years old cohort for PFS was 1.01 (95% CI 0.63-1.61) in GC, and 0.78 (95% CI 0.54-1.12) in GS. Clinically relevant AEs were 36.6% in ≥ 75 years old cohort and 25.3% in ≥ 75 years old cohort in GC, 45.3% in ≥ 75 years old cohort and 32.5% in ≥ 75 years old cohort in GS. Conclusions: The clinical outcomes of combination chemotherapy in elderly patients were comparable to non-elderly patients. Clinical trial information: 000010667.

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Background: Sorafenib is indicated for the treatment of HCC. This study captures and describes real-world use of IL therapy for advanced unresectable or metastatic HCC across Canada and Europe. Methods: A retrospective, non-interventional survey of 278 physicians in Canada (7.5%) and Europe (92.5%) (France, Germany, Italy, Spain and UK) was conducted between Feb-Mar 2018. Clinical and treatment data were collected from medical charts for patients aged ≥18, who initiated and completed systemic IL treatment for HCC within 2 years of data collection, and a Child-Pugh [CP] A/B at IL initiation. Descriptive statistics compared 1L systemic therapy, sorafenib vs. other.

Results: 706 patients were included in = 504 sorafenib; n = 202 other (83% chemotherapy; 10% targeted therapy; 7% checkpoint inhibitors) with a mean age at IL of 62.7 = 9.3y and 79% males. Comorbidities did not differ by sorafenib vs. other for alcoholism (33%), Hepatitis C (14%), and non-alcoholic steatohepatitis and/or non-alcoholic fatty liver disease (9%) but did for Hepatitis B (12% vs. 6%) and cirrhosis (31% vs. 18%) (both p < 0.05). At diagnosis, more patients treated with sorafenib vs. other had portal vein invasion (56% vs. 35%, p < 0.001). At IL initiation, sorafenib patients had better performance status (PS) (ECOG 0-1: 80% vs. 67%, p < 0.05) and preserved liver function (CP A: 58% vs. 47%, p < 0.05). The results indicated that sorafenib was used less compared to other systemic therapies among those with poor performance (ECOG 2-4) and poor liver function (CPB) (71% vs. 83%, p = 0.068). Median treatment duration was shorter for sorafenib (2 vs. 4 months, p < 0.001). The most common grade 3 adverse events were fatigue (9%), diarrhea (5%), and hand/foot skin reaction (4%). Conclusions: In this real-world chart survey of Canadian and European physicians, sorafenib remains the most commonly used IL systemic therapy for advanced HCC. Patients treated with sorafenib were more likely to have cirrhotic liver disease, portal vein invasion, better PS and preserved liver function, but sorafenib use was not limited to CP A. Understanding determinants of IL therapy is important as the treatment landscape of HCC is evolving to address unmet need.
CANCERS OF THE PANCREAS, SMALL BOWEL, AND HEPATOBILIARY TRACT

357 Poster Session (Board #J15), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Racial disparities in the receipt of adjuvant chemotherapy in patients with resected stage I-III pancreatic adenocarcinoma. First Author: Nina Niu Sanford, University of Texas Southwestern Medical Center, Dallas, TX

Background: Adjuvant chemotherapy for resected pancreatic adenocarcinoma is a category 1 NCCN recommendation, however studies have shown that many patients do not go on to receive chemotherapy after definitive surgery. Whether racial disparities exist for receipt of adjuvant chemotherapy is unknown.

Methods: The National Cancer Database was used to identify 28,255 patients with non-metastatic pancreatic adenocarcinoma who underwent definitive surgery between 2005-2014. Multivariable logistic regression defined adjusted odds ratio (AOR) and 95% confidence intervals (CI) of receipt of adjuvant chemotherapy by race. Additional variables included in the model were age, sex, stage, node positivity, comorbidity index, facility type and insurance. Among those receiving chemotherapy, multivariable logistic regression assessed odds of treatment with multicast chemotheraphy and among those not receiving chemotherapy, predictors of chemotherapy refusal were assessed.

Results: Compared to whites, black patients were less likely to receive adjuvant chemotherapy (AOR 0.74, 95% CI 0.64-0.85, p < 0.001) and multigant adjuvant chemotherapy (AOR 0.80, 95% CI 0.72-0.88, p < 0.001). The disparities were limited to patients with comorbidity score of 0 and persisted when analyses were restricted to only academic cancer centers.

Conclusions: In this nationally representative study, black patients were less likely to receive NCCN-guideline concordant treatment for resected pancreatic adenocarcinoma; this disparity did not appear to be driven by increased refusal of treatment by black patients. Given that differences in quality of care may contribute to disparities in cancer survival, our findings suggest that outcomes for black patients could be improved by increasing the proportion receiving guideline-concordant adjuvant chemotherapy. Further investigation is needed to identify factors leading to the observed differences in this study, such that appropriate interventions can be undertaken to mitigate this disparity.

358 Poster Session (Board #J16), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Real world usage of gemcitabine and nab-paclitaxel in older adults with metastatic pancreatic cancer: A single institution experience. First Author: Arthur Winer, Fox Chase Cancer Center, Philadelphia, PA

Background: The median age at diagnosis for metastatic pancreatic cancer (mPC) is 72. Gemcitabine and Nab-Paclitaxel (GA) is often the preferred chemoremo regimen in this population due to presumed reduced toxicity compared with FOLFIRINOX. While the traditional GA schedule (TDS) includes treatment on days 1, 8, and 15 of a 28-day cycle, it can cause side effects and patients often require dose reductions. There is data for a modified dosing schedule (MDS) treating only day 1 and 15 and therefore, we retrospectively analyzed our older adults treated with GA using the TDS versus the MDS and compared tolerability and outcomes between the two groups.

Methods: We identified pts with mPC >64 y/o treated with GA at Fox Chase Cancer Center between 1/2010-7/2018 and collected their demographic, disease and treatment information. We analyzed discrete variables using Fisher’s exact test and continuous variables using Wilcoxon tests. Overall survival (OS) was analyzed by the Kaplan-Meier method and Cox proportional hazards regression. Results: Fifty-six pts were identified with a median age at diagnosis of 71 (range: 64-90) and 67.8% with metastatic disease at presentation. 57% received GA in the first line. 44% were treated with TDS while 56% received a MDS; an older median age was seen in the MDS group (73 vs 69 y/o, p<0.001). Up front dose reductions of GA were seen in 24% in the TDS vs 48% in MDS, and they were more common with nab-paclitaxel (26% in MDS vs 10% in TDS) than with gemcitabine (two pts in TDS vs one pt in MDS). Of pts who began with TDS only 11% (of all pts) were able to tolerate it without adjustment throughout treatment; 14 (25%) transitioned to the MDS. More pts suffered grade 3 toxicity with the TDS vs. MDS (68% vs. 51%; p=0.27) and more required a dose reduction (TDS 72% vs. MDS 48%; p=0.1). 58% required an additional GA dose reduction over the course of treatment. Median OS among GA treated pts in the front line (n=32) was not significantly different (MDS: 17.7 mo vs. TDS: 13 mo; p=0.3).

Conclusions: These results demonstrate tolerability and similar efficacy of the GA MDS among older adults with mPC. Given the limited sample size, further studies are required to help establish the appropriate therapy for older patients.

359 Poster Session (Board #J17), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Update result of HGCSG 1403: Phase I trial of oxaliplatin/irinotecan/S-1 (OX-IRIS) as first-line chemotherapy for unresectable pancreatic cancer. First Author: Shintaro Nakano, Department of Gastroenterology and Hepatology, Hokkaido University Hospital, Sapporo, Japan

Background: FOLFIRINOX has become one of the standard treatments for unresectable pancreatic cancer with distant metastasis. OX-IRIS is the combination therapy of oxaliplatin (L-OHP), irinotecan (IRI) and S-1. It is the useful combination therapy of oxaliplatin (L-OHP), irinotecan (IRI) and S-1 orally. For establishing OX-IRIS therapy as a new standard treatment, we planned this study for evaluating dose limiting toxicity (DLT) and maximum tolerated dose (MTD).

Methods: This study was carried out as a multicenter phase I trial. Chemotherapy-naive patients with unresectable pancreatic cancer were included. L-OHP and IRI were administered on day 1 and 15, and S-1 orally. For establishing OX-IRIS therapy as a new standard treatment, we planned this study for evaluating dose limiting toxicity (DLT) and maximum tolerated dose (MTD).

Results: Between January 2016 and August 2017, 13 cases were enrolled. The patients’ backgrounds were median age 62; male / female, 9/4; the primary tumor sites head /body and tail, 8/5; ECOG PS 0/1, 7/6; UIR-LA (U+R-M, 4/9). Two of five enrolled in level 0 (L-OHP: 85 mg/m2, IRI: 100 mg/m2, S-1: 80 mg/m2) had DLT. One of six in level 1-L-OHP: 65 mg/m2, IRI: 100 mg/m2, S-1: 80 mg/m2) had DLT. At level 1, 100% of cases had anemia and fatigue, 80% anorexia, diarrhea, peripheral sensory neuropathy, 60% platelet count decrease. At level 1, 100% had anemia, 75% nausea and fatigue, 63% anorexia. Response rate was 10% and disease control rate was 70% in ten cases with evaluable lesion. Median PFS was 4.1 months (95% CI: 0.0-8.6 months). Median OS was 13.7 months (95%CI: 5.9-21.5 months).

Conclusions: In this study, MTD was estimated to be level 1, and recommended dose level is level 1 for the planned future study. We are going to evaluate efficacy and safety in a phase II study. (UMIN ID: 000017002) Clinical trial information: 000017002.

360 Poster Session (Board #J8), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Is rising BMI associated with an increased rate of clinically relevant pancreatic fistula after distal pancreatectomy for pancreatic adenocarcinoma? First Author: Evan Scott Glazer, Moffitt Cancer Center, Tampa, FL

Background: Clinically relevant pancreatic fistula (CR-POPF) following distal pancreatectomy (DP) remains a clinical challenge. Prior studies investigating the relationship between body mass index (BMI) and CR-POPF have yielded conflicting results. We examined this relationship utilizing our institutional database and hypothesized that BMI is associated with CR-POPF in patients having DP for pancreatic ductal adenocarcinoma (PDAC).

Methods: Patients who underwent DP for PDAC at a single institution from 2007 to 2018 were retrospectively reviewed. A CR-POPF was defined as ISGPS grade B or C fistula. Uni-and multivariable logistic regression analysis to assess factors associated with CR-POPF following DP was performed, controlling for factors such as gland texture, operative drain placement, gender, and smoking status.

Results: 78 patients met the inclusion criteria. 51% were female, 51% were Caucasian, and the average age was 59 ± 15 years. The median BMI was 26 (interquartile range 24 to 29). Overall, 19% (n = 15) of patients had a CR-POPF. With a mean follow up 28 ± 2.5 years, the presence of a CR-POPF was not associated with long-term survival (P = 0.17). On univariable logistic regression, older age was associated with a decreased risk of CR-POPF (OR = 0.95, P = 0.015) while increasing BMI was associated with an increased risk of CR-POPF (OR = 1.1, P = 0.044). After controlling for multiple factors on multivariable logistic regression analysis, BMI (OR = 1.12, P = 0.035) was the only factor associated with development of a CR-POPF while older age (OR = 0.94, P < 0.001) was slightly protective of CR-POPF development.

Conclusions: For patients undergoing DP for PDAC, increasing BMI is associated with increased risk of CR-POPF development. These findings should be considered during preoperative counseling. Although there is no specific cut-off for the association between BMI and CR-POPF, efforts to diminish the risk of CR-POPF should be focused on patients with higher BMI based on this data.

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Outcomes of tyrosine kinase inhibitors (TKI) after immunotherapy in unresectable or advanced hepatocellular carcinoma (HCC) patients. First Author: Thomas Cheung Yau, Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong, China

Background: The outcomes of tyrosine kinase inhibitor (TKI) treatment after immune checkpoint inhibitor (ICI) therapy in advanced/unresectable HCC population is largely unknown. Methods: Retrospective analysis of advanced HCC patients treated with immune checkpoint inhibitors (ICIs) followed by TKI therapy at Queen Mary Hospital, Hong Kong were reviewed for the outcomes. Results: From January 2016 to July 2018, 30 HCC patients (83% of HBV, 80% of Child Pugh A, 83% of ECOG 0-1, and adequate hepatic and renal function). Enrolled in extrapulmonary poorly-differentiated neuroendocrine carcinomas (EP-PDNECs). In small cell lung cancer, promising antitumor activity of pembrolizumab (PEM)-based therapy in biomarker-unselected patients was reported. In the current study, we aimed to establish in extrapulmonary poorly-differentiated neuroendocrine carcinomas (EP-PDNECs). Background: Immune checkpoint inhibitor (CPI) efficacy has not been established in extrapulmonary poorly-differentiated neuroendocrine carcinomas (EP-PDNECs). In small cell lung cancer, promising antitumor activity of pembrolizumab (PEM)-based therapy in biomarker-unselected patients was reported. In the current study, we aimed to establish the efficacy and safety of pembrolizumab (PEM)-based therapy in biomarker-unselected EP-PDNECs. Methods: Open label, multicenter, phase 2 study of PEM-based therapy in patients (pts) with EP-PDNECs, excluding Merkel cell carcinoma and well differentiated grade 3 NET, with progression on first-line systemic therapy, ECOG 0-1, and adequate hepatic and renal function. Enrollments were via an adaptive Simon’s 2-stage design. Plan for 14 pts treated with PEM alone (Part A Stage 1) 200 mg IV every 3 weeks. If > 2 of 14 pts respond by week 18, then 21 additional pts enroll in Part A Stage 2, corresponding to H0 10% vs. H1 26% response rate (RR) at type I error 0.05 with power 0.80. Otherwise, study proceeds to Part B: PEM plus chemotherapy (dealer’s choice of weekly irinotecan or paclitaxel). Primary endpoint is objective RR (ORR) by RECIST 1.1. Secondary endpoints include safety, overall survival, and progression-free survival (PFS). In March 2016 at 14 sites in Japan were registered. Tumour assessments in accordance with RECIST v1.1 modified RECIST were done using repeat CT or MRI within the original trial and without omitting responses that were included outside the trial. Median progression free survival (PFS) was 3.7 m (95% CI: 2.0-5.7) with mOS of 11.6 m (95% CI: 6.14-15.7). 16 pts (67%) experienced disease control (response to or stable disease). Grade 3 or 4 HT occurred in 11 pts (46%), and 9 (38%) were supported with granulocyte colony-stimulating factor at some point duringtx. 6 pts (25%) required hospitalization for any reason, mostly common toxicity criteria (CTC) grade 3 pts, and 10 (42%) stopped PEM due to toxicity, most commonly fatigue (6 pts). Conclusions: In this single-center retrospective analysis of 24 unresectable PC pts age 75 or older given FOLFIRINOX, OS outcomes were similar to those reported by Conroy et al. and the original trial which excluded patients younger than 75. In our review, tumours including incidences of grade 3 or 4 HT were similar to those reported in the initial study. These data indicate that the use of modified dosing FOLFIRINOX in advanced PC pts older than 75 appears to maintain similar efficacy and toxicity when compared to younger pts.
Conclusions: Patients with HLMR had significantly increased OS (MST: 7.1 mos vs 3.8 mos; HR = 0.86). Median OS was 7.1 mos (95% CI 3.0-15.3) for SECOX vs 12.5 mos (95% CI 7.2-15.4) for sorafenib (p=0.29). The HR of GS to GC for progression-free survival (PFS) was 0.91 (95% CI 0.5-1.7; p=0.77; predetermined futility boundary HR = 0.94) in the low CCr group. Grade 3-4 AEs of white blood cell count restoration instead of 5-FU, that can be more feasible than FOLFIRINOX. The aim of this study was to evaluate the clinical impact of CS after SOXILI treatment for patients with unresectable pancreatic cancer. Furthermore, it may be a potent first-line treatment when considering conversion surgery. Clinical trial information: UMIN000014339.

The effect of lymphocyte-to-monocyte ratio on efficacy of sorafenib for recurrent hepatocellular carcinoma after curative resection. First Author: Hideki Yokoo, Hokkaido University Graduate School of Medicine, Sapporo, Japan

Background: Sorafenib, an oral multikinase inhibitor, is approved for advanced hepatocellular carcinoma (HCC) treatment. Predictive biomarkers of sorafenib are needed due to its frequent adverse effect. Lymphocyte to monocyte ratio (LMR) has been reported as a prognostic or predictive biomarker of chemotherapy in cancer. However, clinical significance of LMR are unclear as predictive biomarker of sorafenib. To investigate the efficacy prediction value of LMR in patients who received sorafenib for recurrent HCC after curative resection.

Methods: Clinicopathological data of 59 patients who received sorafenib for recurrent HCC after surgical treatment between 2009 and 2017 were retrospectively analyzed. Sorafenib was administered at a dose of 400mg or 800mg. Survival outcomes were estimated using the Kaplan-Meier method and compared by the log-rank test. Univariate and multivariate analyses were performed to evaluate the predictive impact of LMR and other clinicopathological factors for efficacy of sorafenib on overall survival (OS) and progression-free survival (PFS).

Results: The optimal cutoff value of LMR for response evaluation was 3.1, which resulted in the most appropriate sensitivity of 60.5% and specificity of 71.4%, with the area under the curve (AUC) of 0.641 (95% CI: 0.515-0.806). All patients were divided into either a low (< 3.1) LMR (LLMR) group (n = 27), or a high (> 3.1) LMR (HLMR) group (n = 32). Patients with HLMR group had significantly increased OS (MST: 20.0M vs 8.0M, P = 0.001) and PFS (MST: 10.2M vs 5.1M, P < 0.001) compared to those with a LLMR group. Multivariate analyses indicated that a HLMR was a significantly independent predictor of superior OS (P = 0.006) and PFS (P < 0.001). Conclusion: LMR in pre-administration of sorafenib was demonstrated to serve as an independent efficacy prediction factor of sorafenib in recurrent HCC patients after curative resection.
Background: The first-in-class recombinant fusion protein IPA blocks WNT function tests, were comparable between arms prior to subsequent treatment. Kaplan-Meier analysis, multivariate analysis, and preliminary efficacy. Results: Twenty-six pts in four dose escalation cohorts were enrolled, five in the cohort one and seven each in cohorts 2-4. Median age was 61.7 years and a majority were male (73%). Reported IPA-related AEs of any grade occurring in pts receiving IPA in cohorts 1-4 were: asthenia and anemia (53%); nausea (29%); vomiting (23%); anorexia and pyrexia. IPA-related AEs grade ≥ 3 included 2 events of AST elevation, and 1 each of nausea, maculopapular rash, vomiting and WBC decrease. No dose limiting toxicities or fragility fractures were observed. Of 26 evaluable pts (9.4%); most of postoperative patients) had a partial response (PR) or complete response (CR). No dose limiting toxicities were observed. Disease control rate was 90.2% (95% CI 84.7-94.1). Among these pts, mOS was 21 vs 17 mo and ORR was 27.6% vs 8.7% for LEN and SOR, respectively. In a subset analysis of LEN responders who subsequently received SOR (n = 35), mOS was 26 mo (95% CI 18.2-34.4). Conclusions: IPA can be safely administered with Nab-P and G in pts with mPC. Additional studies targeting the WNT pathway in pancreatic cancer are warranted. Clinical trial information: NCT02050178.
Prosp ective trial of functional liver image-guided hepatic therapy (FLIGHT) with hepatobiliary iminodiacetic acid (HIDA) scans and update of institutional experience. First Author: David Long, Indiana University Department of Radiation Oncology, Indianapolis, IN

Background: Functional liver image-guided hepatic therapy (FLIGHT) is a novel stereotactic body radiation therapy (SBRT) planning technique. A functional map, generated from hepatobiliary iminodiacetic acid (HIDA) scans, is used to maximize the functional residual capacity of liver volume receiving <15 Gy (FRC15HIDA). We present initial results of a prospective trial evaluating FLIGHT vs standard planning and update our institutional experience. Methods: Eligible patients were ≥18 with or without liver malignancy and Child-Pugh ≥B. Liver function was assessed with HIDA and blood chemistry at baseline, mid-treatment, and 3, 6, and 12 months post SBRT. Both standard and FLIGHT (optimized to avoid high functioning liver) plans were generated for each patient. The primary endpoint was to show >5% increase in FRC15HIDA in 3/75 pts. Secondary endpoints included the rate of FLC15HIDA and other liver function tests. Prior institutional experience included 27 pts with FLIGHT planned retrospectively. Paired t-test was used to compare in HIDA and blood chemistry at baseline, mid-treatment, and 3, 6, and 12 months post SBRT. Both standard and FLIGHT (optimized to avoid high functioning liver) plans were generated for each patient. Treatment MDs were blinded to planning technique before selecting the treatment plan. The primary endpoint was to show >5% increase in FRC15HIDA in 3/75 pts. Secondary endpoints included the rate of FLIGHT plans and were selected and changes in HIDA and other liver function tests. Prior institutional experience included 27 pts with FLIGHT planned retrospectively. Paired t-test was used to compare dosimetric endpoints for FLIGHT vs. standard plans, including: FRC15HIDA, mean liver dose, effective uniform dose (EUD), and functional EUD (FEUD).

Results: Fifteen pts were enrolled. The primary endpoint was met, as 4/15 pts had >5% improvement in FRC15HIDA (mean 5.2%, range -2.3-19.8%). Notably, the FLIGHT plan was selected in 11/15. The mean improvements in FRC15HIDA (5.2 vs 5.0%), mean liver dose (19.5 vs 13.0%), EUD (5.1 vs 5.2%), and FEUD (6.9 vs 7.1%) were similar between prospective and retrospective cohorts (p > 0.5). In the entire cohort (n = 42), FLIGHT improved FRC15HIDA, mean liver dose, EUD, and FEUD (p ≤ 0.001). There were >5% improvements in FRC15HIDA in 15, mean liver dose in 31, EUD in 19, and FEUD in 27.

Conclusions: FLIGHT with HIDA led to improvements in all analyzed dosimetric parameters. The extent of benefit was similar in both cohorts, and there was individual variation in the extent of benefit. Longer follow-up is required to determine the effect of FLIGHT on post-SBRT liver function. Clinical trial information: NCT0338062.

Interaction of race and pathology for neuroendocrine tumors: Epidemiology, natural history, or racial disparity? First Author: Rachel M Lee, Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA

Background: The prognostic value of pathologic variables is not consistent for gastroenteropancreatic neuroendocrine tumors (GEP-NETs). We previously demonstrated a limited prognostic role of lymph node (LN) positivity in small bowel NETs (SBNET) compared to pancreatic NETs (panNET). Although minority race is often associated with worse cancer outcomes, the interaction of race with pathologic and oncologic outcomes of pts with GEP-NETs is not known. Methods: Pts with GEP-NETs who underwent curative intent resection at 2 institutions of the US NET Study Group and a single institution were analyzed. Given few pts of other races, only Black and White race pts were analyzed. Results: Of 2,182 pts, 1,143 met inclusion criteria. Median age was 58 yrs, median follow up was 3 yrs, 48% were male, 14% (n = 157) were Black, and 90% (n = 1,266) were White. Median follow-up was 48 months (range 3-132). First Author: Alejandro Recio Boiles, University of Arizona Cancer Center, Tucson, AZ

Poster Session (Board #K14), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

An analysis of the safety and efficacy of rivaroxaban (Riv) and low molecular weight heparin (LMWH) in gastrointestinal cancer-associated venous thromboembolism (GICA-VTE). First Author: Alejandro Recio Boiles, University of Arizona Cancer Center, Tucson, AZ

Background: CAVTE has a significant morbidity and mortality burden, with higher incidence and bleeding complications of anticoagulation (AC) in GICA. Current guidelines prefer LMWH, and recently added Riv, as an alternative to LMWH standard after the SELECT-D trial (S-D). There is a paucity of data comparing the safety and efficacy of other DOACs in pts with GICA. We indirectly compared the safety and efficacy of Riv vs LMWH of our pts with active GICA-VTE at the University of Arizona Cancer Center (UACC) to the S-D GICA population. Methods: Pts with biopsy proven GICA, symptomatic or incidental VTE, and 6 months or more treatment with Riv or LMWH at UACC from 11/2013-12/2017 were retrospectively reviewed. S-D GICA data was extracted. Primary efficacy outcome was recurrent deep vein thrombosis (DVT), nonfatal pulmonary embolism (PE), or fatal PE. Safety outcomes for major bleeding (MB) include Hgb drop ≥ 2 g/dL, transfusion of ≥ 2 units PRBC, bleeding in critical site, or bleeding contributing to death. Fisher exact test was used for p-value < 0.05. Results: Our review included pts on Riv (n = 40) and Riv (n = 37). In the entire cohort (n = 42), FLIGHT improved FRC15HIDA, mean liver dose, effective uniform dose (EUD), and functional EUD (FEUD).
Duodenal neuroendocrine tumors: Somewhere between the pancreas and small bowel? First Author: Adriana Carolina Gamboa, Division of Surgical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA

Background: While small sub-2 cm pancreatic neuroendocrine tumors (NETs) are often observed given their indolent behavior, small bowel NETs are usually resected with a regional lymphadenectomy regardless of size due to their malignant potential. Considering this variability, our aim was to define the natural history of duodenal D-NETs and determine the role of resection. Secondary aim was to define clinicopathologic factors associated with overall survival (OS) in pts who undergo resection. Methods: All pts in the National Cancer Database (2004-14) diagnosed with non-metastatic, non-functional D-NETs were included. Local resection (LR) was defined as local excision, polypectomy, or excisional biopsy. Anatomic resection (AR) was defined as removal with radical surgery. Tumor size was divided into three categories (< 1 cm, 1-2 cm, ≥ 2 cm). Propensity score weighting analysis was used to create balanced cohorts between resection and no-resection pts; this was maintained in all three size categories. Primary endpoint was OS. Results: Among 5,502 pts, median age was 65 yrs; 52% were male. Median 1/f was 51 mos. Median tumor size was 0.8 cm. Resection was performed in 72% (n = 3954) of which 61% were LR and 39% were AR. At least one lymph node (LN) was retrieved in 67% had high income. 21% lived in an area where 56% had Medicare, 33% private insurance, 7% Medicaid, and 4% were uninsured. 67% had high income. 21% lived in an area where 20% of adults did not finish high school. NH-B and Hispanic pts had more unfavorable SEF including less education, lower income, lower education, non-academic facility, location outside the Northeast, higher Charlson-Deyo score, worse grade, larger tumor size, and higher stage were all associated with decreased OS (all p < 0.05). Conclusions: All pts with non-metastatic non-functional D-NETs should be considered for resection regardless of tumor size. Given their lack of prognostic value, the type of resection and extent of LN retrieval should be tailored to the patient’s clinical picture and safety profile.

Impact of initial imaging with gallium-68 dotatate PET/CT on diagnosis and management of patients with neuroendocrine tumors (NETs): A sequential case series. First Author: Hagen F. Kennecke, Virginia Mason Hospital and Medical Center, Seattle, WA

Background: Somatostatin analogue functional imaging with Ga-68 Dotatate PET/CT has demonstrated superiority in lesion detection in patients with NETs. The effect of this novel imaging modality on US clinical practice and its usefulness in different types of NETs is not well described. We describe the impact of initial NETSPOT imaging on diagnosis and management in NET patients at a large urban medical center. Methods: Consecutive patients diagnosed with NETs and referred to our institution who received an initial Ga-68 Dotatate PET/CT between 07/2017-09/2018 were included. Imaging was reviewed and compared to prior available CT, MRI, and/or 111 Pentetetoxide scans. Results: Among 101 patients, 51/50 were female/male, tumor origins were gastroenteropancreatic (GEP) (75%), Unknown Primary (UP) (13%), lung (8%), thymic (2%), and other (2%). All tumors were histologically well/moderately differentiated and 37/51/3/10 were G1/G2/G3/Unknown, respectively. Initial imaging with Ga-68 Dotatate PET/CT revealed additional metastatic disease in 37 of 77(48%) patients with prior evidence of metastatic disease. Most common sites were distant lymph nodes (18), bone (15) and liver (9), peritoneal/pleural (4). A previously UP tumor was identified in 3 patients. No patients with metastatic lung carcinoids (6 atypical, 2 typical) or thymic NETs (2 atypical/2 typical) NETs had evidence of Ga-68 Dotatate PET/CT uptake above reference liver SUV levels. Results of imaging altered patient management as follows: 14 initiated systemic therapy due to documentation of progression, in 6 surgical therapy was altered, in 4 biopsy/other management was changed. In 11 patients with no Ga-68 Dotatate uptake, decisions about use of PRRT and somatostatin analogues was altered. Conclusions: In this series, Ga-68 Dotatate PET/CT altered diagnosis and management in 35/101 NET patients. Among GEP and UP NETs, Dotatate imaging diagnosed primarily new nodal, bone, liver and pleural/peritoneal metastases missed by other imaging modalities. These results support the use of Ga-68 Dotatate PET/CT in the care of patients with advanced and early stage NETS.
Conclusions: The efficacy of nal-IRI plus 5-FU/LV in our study is encouraging and outperforms CI 0.18-0.98; mOS 9.31 months versus 6.16 months, p=0.0386, HR 0.43, 95% CI 0.18-1.02). Significantly improved mPFS and mOS, when treated with nal-IRI plus 5-FU/LV compared to gemcitabine based chemotherapy was 4.49 months while treatment with oxaliplatin plus fluoropyrimidines in previous gemcitabine. Prospective randomized trials are urged to validate our observation.

Background: No established second-line treatment (2L) is available for patients (pts) with advanced biliary tract cancer (ABC) failing gemcitabine/ platinum from first-line chemotherapy (1L CT). However, 20-40% of pts are offered 2L CT in daily practice. We evaluated the impact of clinical and biochemical parameters on survival of ABC in order to identify factors aiding in 2L treatment selection. Methods: Medical records of consecutive ABC pts treated with 2L CT between 2005 and 2018 at the Modena Cancer Centre were reviewed. Log-rank test and multiple Cox proportional hazard regression were performed to assess the prognostic significance of covariates on OS. A prognostic score was developed from the multivariate model. Results: A total of 98 pts were identified and included in the analysis. Median (m) age was 63 years, 52% of pts were female, 75% had ECOG PS of 0-1. 72% of pts received first-line gemcitabine/platinum combination. In the 2L setting, 70% of pts received a doublet and the most common regimen was FOLFIRI (26%), followed by TOLFLEX (20%) and fluoropyrimidine monotherapy (19%). Disease control rate was 39%, with 7% of objective responses. mOS and mPFS were 7.2 months and 3.5 months, respectively. At both univariate and multivariate analysis ECOG PS > 0 (P = 0.002), peritoneum involvement (P < 0.001), LDH > 430 U/L (P < 0.001), albumin < 3.5 g/dL (P = 0.001), gamma-GT > 100 U/L (P = 0.001), Pts to first-line < 6 months (P = 0.025), Na+ < 140 mEq/L (P = 0.010), absolute lymphocyte count < 1000/μL (P = 0.030) were significantly associated with shorter OS. By assigning to each of the 8 variables weight = 1, three different risk groups were identified: low-risk group (3-4 factors), intermediate-risk group (4-5 factors) and high-risk group (5-8 factors). mOS was 18, 9, 4, and 2.9 months in the low-, intermediate-, and high-risk group, respectively (P < 0.001). Conclusions: Our 2L study confirms the prognostic value of ECOG PS, PFS to first-line and peritoneal carcinomatosis, identifies novel biochemical prognosticators and proposes a readily-available and inexpensive score to risk stratify patients both in daily practice and clinical trials.
Methods: regimens in Japanese pts (Iguchi, ASCO 2015). The study was subsequently followed by a separate cohort that received D+T with additional pts enrolled if responses were seen in a dose escalation phase evaluating various D doses and T doses. This Phase 1 study (NCT01938612) evaluated D (anti-PD-L1 mAb) and tremelimumab (T) in patients (pts) with biliary tract cancer (BTC).

Background: After decades of minimal to no therapeutic options, Gemcitabine, docetaxel, and capecitabine (GTX) as a first-line regimen in metastatic pancreatic adenocarcinomas (mPAC) has emerged as the only safe & effective frontline regimen for mPAC. A 3-drug combination regimen, GTX, first optimized by Fine et al in 2009 showed improved progression free (PFS) & median overall survival (mOS) based on a multicentric prospective phase II study. It didn’t receive much wider acceptance likely due to lack of phase III data and emergence of newer regimens such as Gemcitabine plus nab-Paclitaxel (GA) and FOLFIRINOX (FFX). We reviewed our institutions experience with GTX and other regimens in mPAC patients. Methods: We performed a retrospective review of clinical outcomes in patients diagnosed with mPAC between January 2005 and December 2015 and treated at our institution. Attempts were made to include all eligible patients to reduce any selection bias. Results: Fifty patients with mPAC were analyzed for mOS and toxicities with different regimens. 50% patients received GTX while remaining received – FTX (22%), Gemcitabine (14%), GA (4%), FOLFIRINOX (4%) & other (6%) regimens. The mOS for all the patients was 7.67 months (95% CI 5.98-10.81). The mOS was significantly improved in patients who received GTX as first line regimen compared to patients who received non-GTX regimens (9.45 vs 6.08 months; P=0.0157). GTX also showed non-statistically significant improvement in mOS compared to FXX (9.45 vs 6.08 months; P=0.1436). Compared with FXX, GTX was associated with fewer grade 4 (40 vs 45.5%; p = 1.00) and hematologic (20 vs 36.4%; p = 0.40) toxicities. Conclusions: GTX significantly improved mOS and had fewer severe toxicities compared to non-GTX regimens. Limitations include the retrospective and non-randomized nature of the study and the small sample size. However, GTX may be considered an alternative first line regimen in mPAC patients who are unable to tolerate aggressive regimens such as FXX and in whom the need to balance quality of life with efficacy is particularly important.

Characteristics

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Evaluated 47 patients with neuroendocrine tumors. A pooled analysis was conducted to assess the safety profile of high-specific-activity I-131 metaiodobenzylguanidine (HSA-I-131 MIBG) (AZEDRA) in PPGL and neuroblastoma. Methods: Safety data were pooled from four clinical studies with 118 subjects who received HSA-I-131 MIBG. Adverse events (AEs) were described by age, gender, race, number of HSA-I-131 MIBG doses, temporal association of AEs within 12 weeks after therapeutic dose 1, vital signs, laboratory values, hematological events of Grade 3/4, and serious AEs, and changes in mean hematology values over a period of 12 months. Results: Of 118 subjects, mean age was 47.0 ± 18.9 years (range 3-76); 57.6% were males and 47.6% were white. A total of 102 (86.4%) subjects had at least one AE assessed as treatment-related. The incidences of most AEs were similar among both genders and all racial groups. The most common toxicities associated with HSA-I-131 MIBG were gastrointestinal disorders, with nausea the most prevalent. The incidences of nausea and painful gland pain showed decreasing trends with age while dyspnea, asthenia, and peripheral edema showed increasing trends. The second most common toxicities were hematologic. Following each therapeutic dose, mean hemoglobin, leukocytes, neutrophils, and platelets decreased. Most hematological AEs resolved within 12 weeks, and recovery to pre-therapeutic dose values was apparent 6 months after each therapeutic dose. After therapeutic dose 1, higher percentages of subjects experienced AEs in the first 2 weeks, and the incidence decreased beyond 6 weeks. No notable changes were observed in clinical chemistry tests. The incidence of Grade 3/4 AEs was similar following each therapeutic dose. Conclusions: HSA-I-131 MIBG was safe and well-tolerated among subjects with iobenguane scan positive cancers. No trends were observed between baseline characteristics and AEs. Hematology results reflected toxicity profile expected in a population of subjects administered a radiopharmaceutical. Clinical trial information: Pooled Safety.
Combination chemotherapy for pancreatic cancer in older adults: Efficacy and safety analysis of patients at a majority-Hispanic NCI-designated cancer center. First Author: Emily Henkel, UT Health San Antonio Cancer Center, San Antonio, TX

Background: Pancreatic cancer (PCa) is more frequent in older adults, but older patients are underrepresented in clinical trials. There is limited data on efficacy and safety of regimens such as FOLFIRINOX or nab-paclitaxel/gemcitabine (nab-gem) in older adults, especially Hispanics. Therefore, we compared the efficacy and safety of first-line PCa regimens in older adults.

Methods: Retrospective analysis of stage IV PCa at our Hispanic-majority NCI-designated cancer center from 2000-2017. mPFS and mOS estimated from KM curves and groups were statistically compared with the log-rank test.

Results: Forty-eight pts, mean age 71.7 years, median 69.2 (range 65-90), 31% Hispanic; 50% Male. First-line treatment: FOLFIRINOX (n=9), nab-gem (n=11), gem (n=11), other (n=9), supportive care (2). Baseline ECOG 0: 100%, 94%, 45%, 100%, 1% (p=0.004). Baseline albumin: 3.4, 3.4, 3.1, 3.2, 2.5 (p=0.06). mOS 7.1 months (95% CI 5.9-10.1), mPFS 5.6 months (95% CI 5.3-9.4), mOS by group: 6.6 mo, 7.1 mo, 3.2 mo, 2.9 mo, not available (p=0.95). Most patients had grade 0-2 toxicities (See Table). Grade 3-4: fatigue n=2, neutropenia n=1, neuropathy n=1, mucositis n=1.

Conclusions: Combination systemic chemotherapy is tolerated in older adults with PCa; however, in our cohort, survival was lower than historic phase 3 clinical trials with these regimens. Patients receive 2+ drugs had higher ECOG and albumin at baseline. Prospective studies with geriatric assessments are needed to determine patients who benefit from combination chemotherapy.

390
Dose intensity of neoadjuvant FOLFIRINOX (FFX) in borderline and locally advanced pancreatic cancer (LAPC): A comparison to the adjuvant benchmark. First Author: Janet E. Murphy, Massachusetts General Hospital, Boston, MA

Background: Optimal timing and duration of FFX for resectable, borderline resectable, and LAPC has not been established. The PRODIGE 24/CCTG PA.6 study utilized a FFX regimen that included b5FU and irinotecan at 180mg/m2 demonstrating superior DFS (21.6 mo) over gemcitabine (12.8 mo). However, only 48% of patients (pts) received 70% of intended chemo dosing, and 66.4% of pts completed all doses due to postoperative tolerability. We conducted total dose analysis (TDA) to evaluate dose intensity (DI) of FFX in LAPC and Borderline pts. TDA includes all pts that received at least 2 cycles of FFX during the initial 92 pts were studied: Borderline n = 43, LAPC n = 49. Sixteen of 92 (17.3%) patients discontinued chemotherapy prior to 8 cycles due to: withdrawal of consent (2), chemotherapy toxicity (6), progression (4), and disease-related complications (4). 82.6% of patients completed 8 doses. 61.4% of all bFU was given at the intended dose of 400 mg/m2. The mean relative dose intensity of bFU (the actual cumulative dose relative to the planned cumulative dose over 8 cycles) was 72%. 65.5% of patients required a reduction in bFU over eight cycles. Data for all chemotherapy are presented in Table 1. Overall, 71 of 92 patients (77.2%) had > 70% dose of FFX, with mean relative dose intensity of 81.2%. Among surgically resected patients, mPFS was 21.3 months in LAPC (n = 34) and 48.6 months in Borderline (n = 33). Compared to adjuvant therapy, dose intensity was reduced in a higher proportion of participants with TNU, utilizing a FFX regimen that included bFU and irinotecan at 180mg/m2.

Relative dose intensity: 61.0% of bFU, 79.2% of 5-FU, 61.8% of oxaliplatin, 52.8% of irinotecan. Mean mPFS: 9.4 months in LAPC and 23 months in Borderline.

Conclusions: TDA allows for comparisons of dose intensity for FFX in LAPC and Borderline pts. Despite lower toxicity and withdrawal of consent in LAPC, pts received adequate dose intensity of FFX. Further studies are needed to establish optimal duration/dose intensity of FFX in LAPC.

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Clinicopathological features and outcomes of fibrolamellar hepatocellular carcinoma. First Author: Sakti Chakrabarti, Mayo Clinic, Rochester, MN

Background: Clinicopathological features and the outcomes of patients with fibrolamellar hepatocellular carcinoma (FLHCC) are not clearly defined.

Methods: Data were collected by retrospective chart review on 42 patients with FLHCC treated between November 2014 and September 2017 at the Mayo Clinic. Clinicopathological characteristics, response to treatment, recurrence pattern and survival were analyzed.

Results: Of 42 patients (17 males and 25 females; median age at diagnosis 22 years, range 15 to 39); 10 patients (23%) had stage I disease and 32 patients (77%) had stage II to IV disease. All 10 patients with stage I disease and 21 of 32 patients with stage II-IV disease underwent resection at presentation. In stage I patient group, 6 patients experienced recurrence with a median time to recurrence of 30.5 months, resulting in a 5 year overall survival (OS) of 86%. Patients with stage II to IV disease who underwent resection (n=21) at presentation had a median OS of 32.5 months and 5 year OS of 44%. In the upfront surgery group, 71% of the patients experienced recurrent disease. The median OS of patients with unresectable disease (n=11) was 10 months. Systemic therapy was given to 17 patients which included sorafenib, FOLFLOX (5-fluorouracil/leucovorin and oxaliplatin), gemcitabine plus oxaliplatin, single agent adriamycin or gemcitabine, capcitabine plus interferon alfa, gemcitabine plus cisplatin, cisplatin plus adriamycin and nivolumab. Sorafenib was given to 9 patients and 4 patients achieved stable disease (SD) with duration ranging from 5 months to 5 years. One programmed cell death receptor positive-1 patient had a durable complete response after 2 months of therapy with nivolumab.

Conclusions: In FLHCC, surgical resection was associated with prolonged OS; however, recurrences were common after the surgery. Limited benefit was derived from the systemic treatment. In rare cases, therapy with a checkpoint inhibitor may provide a viable treatment option.

395 Poster Session (Board #L15), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
The correlation between the proportion of patients with pancreatic ductal adenocarcinoma who received neoadjuvant therapy and overall survival between 2004 and 2015. First Author: George Molina, Dana-Farber Cancer Institute/Brigham and Women’s Hospital, Boston, MA

Background: Neoadjuvant therapy (NAT) for pancreatic ductal adenocarcinoma (PDAC) is associated with improved overall survival (OS), and this has led to its rising use. The aim of this study was to evaluate the correlation between use of NAT and OS among patients with PDAC. Methods: This population-level study evaluated the Spearman correlation between the annual proportion of patients receiving NAT and the annual 1-year and 5-year OS, respectively, using the 2004-2015 National Cancer Database. Annual 1-year and 5-year survival was calculated from year of diagnosis using Kaplan-Meier survival analysis. All patients with a confirmed diagnosis of PDAC (histology code 8500), without any metastasis, and who underwent an RO or R1 resection were included. Results: A total of 18,852 patients (median age 67 (IQR 60-74); 49.4% female) with PDAC underwent an RO/R1 resection from 2004 to 2015. Among these patients, there was a significantly positive correlation between the proportion of patients who received NAT (12.1%; n = 2,133) and 1-year OS (Spearman’s rho = 0.909; P = 0.0000) and 5-year OS (Spearman’s rho = 0.7833; P = 0.01), respectively. Patients who underwent R0 resection (n = 14,547; median age 67 (IQR 60-74); 49.9% female) had a significantly positive correlation between those who received NAT (13.1%: n = 1,773) and 1-year OS (Spearman’s rho = 0.8818; P = 0.00003) and 5-year OS (Spearman’s rho = 0.7333; P = 0.02), respectively. Among 9,142 patients who had upfront resectable disease with RO resection margin status (median age 68 (IQR 60-75); 49.8% female), there was a significantly positive correlation between those who received NAT (11.9%: n = 781) and 1-year OS (Spearman’s rho = 0.7273; P = 0.01) and 5-year OS (Spearman’s rho = 0.8000; P = 0.0096), respectively. Conclusions: Between 2004 and 2015 there has been an increase in the use of NAT for patients with PDAC. Concurrently, the OS has also increased during this time period. This study demonstrates that there is a statistically significant and positive correlation between the proportion of patients who received NAT and 1-year OS and 5-year OS, respectively.

396 Poster Session (Board #L16), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
A network meta-analysis of adjuvant systemic therapy in resected pancreatic cancer. First Author: Jorge Chaves Porras, Sunnybrook. Health Sciences Centre, Toronto, ON, Canada

Background: Multiple randomized controlled trials (RCTs) have established several systemic therapy regimens as adjuvant therapy treatment options for resected pancreatic cancer. The aim of this study is to conduct a network meta-analysis of comparisons from the results of randomized controlled trials. Methods: We identified all phase III RCTs involving 3,394 patients and 6 regimens (5-flourouracil and folinic acid, Gem, gemcitabine and erlotinib (GemErl), GemCap, mFFX and S1) were identified. Hazard ratios (HR) and 95% confidence intervals (CI) of OS and DFS of selected comparisons from the results of the NMA are shown in the table. Results: Nine phase III RCTs involving 3,394 patients and 6 regimens (5-flourouracil and folinic acid, Gem, gemcitabine and erlotinib (GemErl), GemCap, mFFX and S1) were identified. Hazard ratios (HR) and 95% confidence intervals (CI) of OS and DFS of selected comparisons from the results of the NMA are shown in the table.

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Incidence of and risk factors (RFs) for development of non-alcoholic fatty liver disease (NAFLD) after pancreaticoduodenectomy (PD) for pancreatic cancer: A single institutional review.

First Author: Amy McGhee-Jez, Thomas Jefferson University Hospital, Philadelphia, PA

Background: PD may increase the risk of development of NAFLD, a precursor for non-alcoholic steatohepatitis and cirrhosis. Studies have not clearly identified consistent RFs for NAFLD, but patients with post-PD NAFLD do not appear to have the traditional RFs for NAFLD such as metabolic syndrome. The primary objective of this study was to identify the incidence of and RFs for post-PD NAFLD.

Methods: Retrospective chart review was done on 425 patients who underwent PD for a cancer diagnosis at our institution from 2007 to 2017 and had at least 6 months of postoperative follow up. Cox proportional hazards model was used to examine multiple potential pre-operative RFs for NAFLD including body mass index, BMI, estimated surgical blood loss, LFTs, hemoglobin, albumin, age, sex, comorbidities, and tobacco use as predictors of time to develop post-PD NAFLD. Patients without post-PD NAFLD were considered censored at the time of last follow-up. The proportional hazard assumptions were validated. Post-PD NAFLD was identified by review of radiology reports.

Results: Sixty (14%) of the 425 patients had post-PD NAFLD. The male to female ratio was 236:189 and median follow up time was 1 year. Median age was 65 years with median time to NAFLD development of 7 months. Multivariate Cox Proportional Hazard Model identified higher BMI and female sex as RFs for the development of post-PD NAFLD. Each 1 point increase in BMI implied an 8.4% increase in the hazard of fatty liver (HR = 1.083, 95% CI: 1.012-1.136; p = 0.001). Females had 89.7% higher hazard of fatty liver compared to males (HR = 1.897, 95% CI: 1.084-3.319; p = 0.025).

There was statistically significant association between post-PD NAFLD and pre-operative characteristics studied. Conclusions: Female sex and higher BMI may be RFs for the development of NAFLD post-PD. No other pre-operative RFs were identified. In conclusion, patients with higher BMI and female gender may need closer monitoring for earlier detection and management of NAFLD.

Multivariate cox proportional hazard model

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Treatment sequencing in MPC, insights from a 3rd care center.

First Author: Ivan Barrera, Jewish General Hospital, McGill University, Montreal, QC, Canada

Background: Since 2011, options for treatment of metastatic pancreatic cancer (mPC) have improved with the use of nab-paclitaxel plus gemcitabine (n-PGEM) or FOLFIRINOX (FFX) as first line treatments (1LTx). In 2016, Nanoliposomal irinotecan plus 5FU (n-IRI-5FU) demonstrated efficacy in FFX resistant patients. To date, n-IRI-5FU has not been confirmed in a randomized trial. The primary objective of this study was to confirm previously published, retrospective cohort study results. We evaluated oncologist-selected TX algorithms and resultant progression free & overall survival (PFS, OS) for pts with mPC from 2010 and 2018 at the Jewish General Hospital, Toronto, ON. This retrospective study included 203 pts with post-1LTx PFS >12 months (33 to 89 years, 54% male). Results: PFS1 included 66 pts on FFX, 60 pts on n-PGEM, and 66 pts on single-agent Gem. The remaining pts received Cavitopac (CAP) or another TX (N = 11). Mean PFS in FFX, n-PGEM, and Gem groups was 5.07, 5.52, and 4.10 months, respectively (progression was 1 or 2 disease progression or a change of a Tux due to adverse events or intolerance). Only the FXX and Gem groups were significant when compared (p = 0.049).

Conclusions: Forty 3.8% of pts (N = 89/203) advanced to 2LTx most receiving Gem (N = 27), n-PGEM (N = 21), or FFX (N = 11). FXX 3.87, 7.04, and 2.30 months, respectively, FXX and n-PGEM groups were significant when compared (p = 0.011). CAP and n-IRI-5FU were 2LTx options for 25.8% (N = 23/89) and 7.9% (N = 7/89) of pts, respectively. For 30 pts in 1LTx, TXs included: n-IRI-5FU (N = 8), clinical trials (CT) (N = 7), Gem (N = 5), FXX (N = 4), n-PGEM (N = 2), CAP (N = 2) and Irinotecan (IRI) (N = 2). Only 7 pts received 4LTx: Gem (N = 3), CAP (N = 2), CT (N = 1), and RIR (N = 1). Median OS from start of 1LTx for pts in FXX (N = 60), n-PGEM (N = 41), and Gem (N = 60) groups was 11.42, 9.50, and 6.23 months, respectively. (Excluding pts on ongoing tx and other censored data points).

Gem tx was a significant prognostic factor for shorter OS, Gem versus FXX, HR 1.673 (1.652 to 1.70, p = 0.0053), Gem versus n-PGEM, HR 1.51 (1.012 to 2.258, p = 0.0347). No difference in survival was seen between FXX and n-PGEM groups, HR 0.903 (95% CI 0.605-1.045, p = 0.6966). Conclusions: Though the FXX and n-PGEM are considered mainstays of 1LTx, Gem was chosen by physicians in 1/3 cases despite reduced PFS. Pts on FXX or n-PGEM had better OS compared to Gem alone, as expected. Further investigation into Tx sequencing in this and larger cohorts, is needed.
Outcomes of stereotactic body radiotherapy for unresectable hepatocellular carcinoma. First Author: Yizhou Zhao, BC Cancer Surrey Centre, Surrey, BC, Canada

Background: Stereotactic body radiotherapy (SBRT) is an emerging curative treatment for hepatocellular carcinoma (HCC). We report toxicity and efficacy of all patients treated in British Columbia, one of the largest series to date.

Methods: From 2011 to Jan 2018, 99 patients underwent SBRT to 128 HCCs. Fiducials were placed and 4D CT (78.4%) and respiratory gating (19.6%) were used for motion management. Local control (LC), progression-free survival (PFS) and overall survival (OS) were analyzed by Kaplan-Meier, Cox regression identified outcome predictors. Results: Median Child-Pugh Score (CPS) was A5 (65%), B5% (18%), A6, 12% B7, 5% B8 (1%) and median Albumin-Bilirubin (ALBI) score was -2.55, grade 2 (48%) q1, 45% q2, 6% q3. Most (87.7%) had either Hepatitis B or C and 73.7% had prior HCC treatment, with 47.5% going-on to further HCC treatment post SBRT and 42.4% deceased at the time of analysis. The median tumor size was 2.8 cm (range 0.8 – 11). The median prescribed biologically effective dose (BED10) was 125 Gy, with 45 Gy in 3 fractions (BED10,125 Gy) in 56.9% of cases and 45 Gy in 5 fractions (BED10, 85.5 Gy) in 30.4%. Median follow-up was 18.5 months (range 2.2 - 73.5). At 3 months, 12 (11.8%) patients had a rise in CPS of ≥ 2, and 26 (25.5%) patients had increased ALBI grade (median change in score of +0.16). Excluding laboratory findings, 14 (14.1%) patients developed CTCAE V5 grade 3 / 4 toxicities (ascites n = 12, hepatic failure n = 4, hepatic pain n = 1, nausea n = 1, GI bleed n = 1). The 1-, 2- and 3-year LC were 94.3%, 86.6% and 80.2%. The median PFS was 14.8 months, respectively 53.7%, 39.5% and 23.8% at 1, 2 and 3 years. The median OS was 14.8 months, respectively 80.3%, 63.5% and 55.2% at 1, 2 and 3 years. Univariate factors predicting improved LC were mean dose (Dmean) to GTV (p < 0.01), lower CPS (p = 0.04) and lower ALBI score pre-SBRT (p = 0.01), no liver directed therapy post-SBRT (p = 0.01), smaller tumor size (p < 0.01), lower Child-Pugh Score (p = 0.01), lower age (p < 0.03), and favorable ECOG (p < 0.01). Conclusions: SBRT achieves excellent LC, with low rates of toxicity and can be included with or without other therapies in HCC treatment.

Impact of adjuvant hepatic arterial chemoinfusion using high-dose 5-fluorouracil with systemic gemcitabine for pancreatic cancer: A propensity score–matched analysis. First Author: Kota Nakamura, Nara Medical University, Kashihara, Japan

Background: The aim of this retrospective study was to evaluate the efficacy of adjuvant hepatic arterial infusion chemotherapy (HAI) using high-dose 5-fluorouracil with systemic gemcitabine on prognosis of resected pancreatic cancer. Methods: Between January 2006 and April 2016, 298 patients underwent elective pancreatic resection for resectable or borderline resectable pancreatic cancer at Nara Medical University Hospital. Patients who received adjuvant HAI plus systemic gemcitabine after surgery (HAI group) were compared with those who received systemic chemotherapy alone (control group). Patients were propensity score matched for age, sex, ASA score, CA19-9, NCCN resectability status, neoadjuvant treatment, surgical procedure, portal vein invasion, T stage, N stage, and margin status. Results: 224 patients with resectable or borderline resectable pancreatic cancer were enrolled in this study; 151 patients in the HAI group and 73 patients in the control group were included. Propensity score matching analysis was used to identify 63 well-balanced patients in each group for overall survival comparison. The estimate overall survival (OS) for patients treated with HAI was longer than patients without HAI in both the whole cohort (median OS, 54 vs. 24 months, respectively; P < 0.001) or matched cohort (median OS, 58 vs. 26 months, respectively; P = 0.003). The liver was only resected in one patient in the control group (p = 0.03). In the multivariate analysis, adjuvant chemotherapy without HAI were independently associated with worse outcome in the whole cohort. A total of 127 patients in the HAI group (84%) had completed the planned dosing of HAI. The remaining 24 patients stopped treatment before the end of the planned cycle due to catheter-associated complications in 9 (6.0%) and development of liver abscess in 2 (1.3%). No treatment-related deaths occurred. Conclusions: The efficacy of hepatic arterial chemoinfusion as adjuvant treatment for resectable pancreatic cancer should be revisited.

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405 Poster Session (Board #M5), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Oral chemotherapy as second-line treatment option for gemcitabine-refractory advanced pancreatic cancer with poor performance status. 
First Author: Se Jun Park, Seoul St. Mary’s Hospital, The Catholic University of Korea, Seoul, Korea, Republic of (South)

Background: There is few data for effective second-line treatment in advanced pancreatic cancer, and most patients have poor performance status after progressive disease. We evaluated the efficacy, toxicity, and median dose intensity of oral chemotherapy, capecitabine, or TS-1 in gemcitabine-refractory advanced pancreatic cancer for second-line treatment.

Methods: Patients who have progressive disease after first-line gemcitabine-based chemotherapy were retrospectively analyzed between Jan, 2011 and Nov, 2017. These patients were treated with capecitabine or TS-1 as second-line treatment. Capecitabine were administered as 2,500 mg/m² divided dose on day 1-14, followed by one week rest. In TS-1 group, TS-1 was taken orally based on patient’s BSA (60mg twice daily in BSA > 15, 50mg twice daily in BSA 12.5-15, and 40mg twice daily in BSA < 12.5) through 28 days, by two week rest. Median dose intensity was compared by calculating a percent of target dose achieved in the average cycle for each patient. 

Results: Of the total 62 patients, 41 patients were treated with capecitabine and 21 patients were treated with TS-1. The median age was 61 years for the capecitabine group compared with 62 years for the TS-1 group. In capecitabine group, males were 56% and in TS-1 group, males were 66%. 29% of capecitabine group received prior fluorouracil base therapy, and 47% of TS-1 group were received prior fluorouracil base therapy. The objective response rate was similar in the two groups: 12.2% with capecitabine and 4.8% with TS-1 (p = 0.358). There was no difference in median progression free survival between capecitabine and TS-1 (2.1 months vs. 2.7 months, p = 0.102). However, TS-1 group showed better median overall survival time than capecitabine group (6.9 months vs. 4.6 months, p = 0.048).

Most of the adverse events were similar in both group, except that grade 3 or 4 mucositis was more common in TS-1 group. There was no significant difference in median dose intensity between two groups. (Capecitabine 91.5% vs. TS-1 90.1%, p = 0.216).

Conclusions: Oral agents such as TS-1 or capecitabine can be second-line treatment for advanced pancreatic cancer patients with poor performance status after progression to gemcitabine-based regimen.

406 Poster Session (Board #M6), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Prognostic factors and disease course in patients enrolled onto clinical trials of second-line therapy for hepatocellular carcinoma. 
First Author: Nicola Personeni, Humanitas University, Pieve Emanuele, Italy

Background: Prognostic factors of survival and disease course in patients with hepatocellular carcinoma (HCC) and preserved liver reserves, enrolled onto clinical trials of second-line treatments after sorafenib, are unclear.

Methods: This single-center database analysis included all patients with Child-Pugh A score and ECOG performance status (PS) 0 - 1 participating between 2012 and 2017 in clinical trials of second-line systemic treatments for advanced HCC. Patients received first-line sorafenib and experienced either disease progression (PD) to sorafenib or were sorafenib-intolerant. Their clinicopathologic characteristics were correlated with overall survival (OS), calculated from the day of first-line treatment to death or last visit available, and post-treatment survival (PTS, calculated from the date of end-of-treatment to death or last follow-up).

Results: Ninety-nine patients (21 sorafenib-intolerant, 78 progressors) were enrolled onto trials of checkpoint inhibitors (CT, 23 patients), tyrosine kinase inhibitors (TKI, 44 patients) versus best supportive care (BSC, 24 patients), open-label TKI (8 patients). Overall, median OS was 9.4 months (9.6, 9.8, and 8.0 months for CPI, TKI and BSC, respectively; p = 0.493). Median time-to-treatment failure was 3.5, 4.4, 3.7 months for CPI, TKI and BSC, respectively (p = 0.561). In multivariable analyses, worse OS was linked to high neutrophil/lymphocyte ratio (Hazard Ratio, HR = 1.13; p = 0.005) and macrovascular invasion (MVI), HR = 2.59; p < 0.001). Second-line treatment discontinuation due to liver failure independently conferred worse PTS than adverse events (HR = 2.32; p = 0.111) or PD (HR = 3.44; p = 0.002), as did ECOG PS > 1 at EOT (HR = 3.05; p = 0.003). Death rate within 30 days of end-of-treatment was 4.2% on placebo versus 10.5% on IO versus 22.9% on TKI. Conclusions: In this homogeneous cohort of compensated HCC patients pre-treated with sorafenib, MVI and NLR at start of second-line trial are prognostic factors. Besides ECOG PS > 1 at EOT and liver failure, further predictors of subsequent PTS in treatment options beyond second-line were not identified.

407 Poster Session (Board #M7), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Dynamical changes of treatment patterns and outcomes of unresectable pancreatic cancer patients in real-life practice. First Author: Kazuki Nagai, Department of Gastroenterology, Ishikawa Prefectural Central Hospital, Kanazawa, Japan

Background: Several new combination therapies, including GEM plus nab-paclitaxel (GnP) and FOLFIRINOX (FFX) has been developed for treating pancreatic ductal adenocarcinoma (PDAC) in these ten years. We investigated trends in characteristics, treatment patterns, and outcomes of unresectable patients with unresectable PDAC in real-life practice in Japan. Methods: We retrospectively reviewed the medical records of 1917 patients diagnosed as having unresectable or recurrent PDAC in multiple centers in our local area between January 2009 and April 2018. Results: The median age was 74, and 53.1% were men; 27.2% had locally advanced and 67.2% metastatic disease, and 5.6% had recurrences. Oncological therapy was administered to 1295 patients (67.6%); chemotherapy (n = 1161), chemo-radiotherapy (n = 117), or radiotherapy (n = 17); the remaining patients were treated with best supportive care. Of 100 patients diagnosed in 2009, 62.0% received GEM as first-line chemotherapy; whereas 56.8% of the 266 patients diagnosed in 2017 or 2018 received GnP, 20.3% GEM, and 15.4% FFX. The objective response rates of patients treated with GnP, FFX, and GEM were 16.8%, 17.6%, and 5.1%, respectively. The median time to treatment failures were 3.9, 3.6, and 2.8 months, and the overall survivals were 11.5, 11.7, and 6.5 months after GnP, FFX, and GEM, respectively. Grade 3 or greater any hematological toxicity occurred in 53.7%, 64.7%, and 34.6% of the patients treated with GnP, FFX, and GEM, respectively. The treatment discontinuation rates due to adverse events were 17.2%, 14.9%, and 22.9% in the patients treated with GnP, FFX, and GEM, respectively. Conclusions: Chemotherapeutic protocols changed dramatically between 2009 and 2018 in Japan. GnP and FFX are tolerable and effective in real-life practice despite high frequent adverse events.

408 Poster Session (Board #M8), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Halo 110-101: Early safety results of pegvyhydroxandiole alfa (PEGPH2O; PVHA) + cisplatin (C) + gemcitabine (G) = atezolizumab (ATZ) in patients (pts) with locally advanced or metastatic cholangiocarcinoma (CCA) and gallbladder cancer (GBC). First Author: Do-Youn Oh, Seoul National University Hospital, Seoul, Korea, Republic of (South)

Background: Standard of care for CCA/GBC is C-G therapy. MABs (ATZ, pembrolizumab) targeting PD-1/L1 show promise in treating CCA/GBC. Hyaluronan (HA), which may impede drug and immune cell access, is high (67%) in CCA/GBC tumors. PEGPH2O enzymatically degrades HA. HALO 110-101 (NCT03267940) evaluates safety and activity of PEG-C-G ATZ or PEG-C-G versus C-G in CCA/GBC pts with unresectable CCA/GBC with or without liver metastases. PEGPH2O + C + G was evaluated in a dose-escalation phase (ES) and a phase 2 study. Results: A total of 182 patients (n = 91 in CCA and 91 in GBC) were enrolled on a 3 + 3 design, 6 pts at each dose level. In CCA, the median age was 68 (58-73) years, 64% were male, and 19% were Karnofsky 80 or less. The most common AE was nausea (57%). The most common treatment-related AEs grade > 3 were nausea (38%), fatigue (29%), diarrhea (18%), and vomiting (11%). Conclusions: The overall safety profile of PEGPH2O + C + G = ATZ is acceptable and consistent with safety observed for the individual components. There were no DLTs resulting in a dose reduction or discontinuation of PEGPH2O + C + G. The recommended starting dose (RSD) was 3 mg/kg in the ES phase. Clinical trial registration: NCT03267940.
Multi-agent neoadjuvant chemotherapy improves response and survival in patients with resectable pancreatic cancer. First Author: Taylor Maramara, Florida State University College of Medicine, Sarasota, FL

Background: Neoadjuvant therapy (NT) for resectable pancreatic adenocarcinoma (PAC) continues to be debated. We sought to establish the impact of single-agent (SAC) versus multi-agent chemotherapy (MAC) with or without radiation (RT) on survival in patients with resectable pancreatic cancer.

Methods: Utilizing the National Cancer Database we identified patients with PAC who underwent up front surgery (UFS), SAC, or MAC ± RT followed by surgery. Patient characteristics and survival were compared with Mann Whitney U, Pearson’s Chi-square, and the Kaplan-Meier method. Multivariable analysis (MVA) was developed to identify predictors of survival. All tests were two-sided and α < 0.05 was significant.

Results: We identified 26,563 patients of which, 23,877 (89.9%) UFS, 1,482 (5.6%) NT+RT (SAC+RT 768, MAC+RT 560), and 1,204 (4.5%) chemo only (SAC 262, MAC 864) with a median age of 66 (25-90). The median tumor size was smaller, p = 0.003 and Charlson/Deyo score, tumor size, grade, margin status, facility volume, and MAC were predictors of survival.

Conclusions: Multi-agent chemotherapy with or without radiation improves overall survival, RT resection rates, and complete pathologic response rates in patients undergoing neoadjuvant therapy for resectable pancreatic cancer.

Effect of FOLFIRINOX with PEG-G-CSF for unresectable/recurrent pancreatic cancer. First Author: Ichiro Moriyama, Shimane University Hospital, Izumo, Japan

Background: FOLFIRINOX (FFX) is a standard therapy for unresectable/recurrent pancreatic cancer, but it is associated with a high frequency of severe adverse events, especially blood toxicity. Human pegylated granulocyte colony-stimulating factor (PEG-G-CSF) can reduce the outpatient toxicity in the chemotherapy of patients with other malignant tumors, but there are few reports on the effectiveness of PEG-G-CSF in preventing febrile neutropenia during FFX. We retrospectively investigated the usefulness of PEG-G-CSF in reducing blood toxicity.

Methods: From June 2014 to January 2017, 40 patients with pancreatic cancer were enrolled. On univariable analysis, age, Charlson/Deyo score, tumor size, grade, margin status, facility volume, and MAC were predictors of survival.

Results: The median patient age was 68 years (range: 30-92), including 27 patients (68%) with resected pancreatic cancer. Response rates of the patients who had measurable lesion according to RECIST v1.1 was 17% (9/54), and disease control rate was 70% (32/46). The progression-free survival rate between the two groups is not significantly different. The median overall survival (OS) of NLR ≥ 3 group was 11.8 months, while OS of NLR < 3 group was 29.2 months. The overall survival rate in the NLR ≥ 3 group was significantly lower than that in the NLR < 3 group (p = 0.0339). Conclusions: Our study confirmed that high NLR is associated with worse OS and PFS, and suggested it may be a predictive marker for GC chemotherapy in patients with BTC.

Hypofractionated radiation therapy for unresectable/localy recurrent inhepatocellular cholangiocarcinoma. First Author: Alicia Smart, Harvard Medical School, Boston, MA

Background: Our objective was to evaluate outcomes for patients with unresectable/localy recurrent inhepatocellular cholangiocarcinoma (IC) treated with hypofractionated proton or photon radiation therapy (HF-RT).

Methods: We retrospectively identified 66 patients with inresectable IC who were treated with HF-RT from 2008-18. Patients had inresectable disease only, and 15 patients had inresectable disease at time of RT but received RT for biliary control. Median age at RT was 76 years (range: 30-92), including 27 patients (41%) with extrahepatic disease. Median RT dose was 55 Gy (range: 37.5-67.5), delivered in 15 daily fractions. 32 patients received proton RT, and 34 patients received photon RT. Rates of local control (LC), progression-free survival (PFS), and overall survival (OS) were calculated by the Kaplan-Meier method.

Results: Median follow-up times from diagnosis and RT start were 21 and 14 months, respectively. In total, 5 patients (7.6%) developed local failure. Only 1 patient developed isolated local failure. The 2-yr outcomes were 93% LC, 37% PFS, and 55% OS. Among the 51 patients treated with definitive intent, the 2-yr LC was 96%, PFS 35%, OS 60%. Receipt of protons was significantly associated with younger age (p = 0.02), but not gender, race, ECOG status, metastatic disease at presentation, mean liver dose, cumulative GTV, or number of lesions. There were no significant predictors of LC or PFS, including RT dose. On UVA for OS, younger age, female gender, prior chemotherapy, prior surgery, and proton RT were associated with improved OS (p = 0.05). On MVA, female gender (HR: 0.33, p = 0.001), prior chemotherapy (HR: 0.38, p = 0.002), and proton vs. photon RT (HR: 0.50, p = 0.05) remained significantly associated with OS. Conclusions: HF-RT yields high rates of local control and is an effective modality to optimize biliary control for unresectable IC. HF-RT should be considered for elderly patients who are considered medically inoperable. Proton RT and chemotherapy may further improve outcomes.
Clinical characteristics and predictors of outcomes in patients with fibrolamellar carcinoma: An eleven-year analysis of the National Cancer Database (NCDB). First Author: Hussein Assi, University of Oklahoma Health Science Center, Oklahoma City, OK

Background: Fibrolamellar carcinoma (FLC) is a very rare liver tumor, comprising only 1% of all primary liver tumors in the United States. There is no standard of care for unresectable disease. Current practices are based on small retrospective studies and case series. We aim to analyze the clinicopathologic factors and treatment modalities affecting overall survival (OS) in FLC.

Methods: Using the National Cancer Data Base (NCDB), we identified 496 patients diagnosed with FLC between 2004 and 2015. Simple descriptive statistics were created for all covariates. Survival data was available on 461 patients. Kaplan Meier Survival analysis was used for unadjusted results, and Cox proportional hazards model was used for multivariable analysis. The objective of the study is to identify predictors of survival in FLC.

Results: The median age at diagnosis was 32 (range 18-90) years. Fifty-six percent were males. Stage distribution included IIA (31.2%), IIIB (11.8%), IIB & IVA (24.3%) and 120 (32.8%) patients for stages I, II, III and IV, respectively. Median follow-up was 24 months. Surgery of the primary site was performed on 282 (56.9%) of patients, 146 (51.2%) of which had regional lymph node dissection. Seventy (47.9%) patients had pN+ disease. Among patients with available serum alpha fetoprotein (AFP) data, 146 (42.5%) had abnormal AFP levels (＞20 ng/mL). Median OS by stage were 78.5, 87.2, 18.6, and 10.6 months for stages I, II, III and IV, respectively. Multivariate analysis showed that age (HR 1.01, < p < 0.0001), pN+ (HR 2.31, p = 0.0003), and abnormal AFP (HR 1.69, p = 0.0003) were negative predictors of survival. Among metastatic patients, 57 (11.4%) had metastectomy. Metastectomy improved overall survival in stage IV FLC, HR 0.51 (95% CI 0.29-0.89). Conclusions: Independent predictors of decreased OS in patients with FLC include age, pN+ and abnormal AFP. Metastectomy improved OS, FLC is a rare disease entity that warrants further investigations to better delineate optimal treatment approaches.

Pathologic outcomes of systemic therapy followed by stereotactic body radiation therapy (SBRT) for pancreatic cancer (PC) in a novel lateral decubitus treatment position. First Author: Ethan Song, USF Health Morsani College of Medicine, Tampa, FL

Background: Outcomes of multi-fraction stereotactic body radiation therapy (SBRT) for PC report low rates of toxicity and high local control, improving feasibility for combination with more aggressive systemic therapy. However, SBRT in the ablative range poses risk to adjacent normal structures, excluding this option for tumors within 1 cm of a mucosal organ. In this study, we report our initial experience with treatment in the lateral decubitus position. Methods: An IRB retrospective query identified patients with pancreatic body adenocarcinoma treated with systemic chemotherapy followed by SBRT in the lateral decubitus position. SBRT was delivered to the entire gross disease with 30 Gy in 5 fractions with focal dose escalation up to 40 Gy to the tumor/vessel interface (TVI) as long as constraints were met. Patients were excluded if they had a prior history of SBRT, were pregnant or nursing, or had prior vascular procedures. The primary endpoints were pathologic response and margin status. Descriptive analysis was performed with SPSS 24.

Results: The median age of the cohort was 68.6 (range, 50-83 yrs), with a white (94%) and male (59%) predominance. Initial staging of the 17 patients who met criteria included 10 (59%) patients diagnosed with borderline resectable disease (BRPC) and 7 (41%) with locally advanced disease (LAPC). 7 (41%) patients were treated with FOLFIRINOX, 5 (29%) with gemcitabine/nab-paclitaxel, 4 (24%) with gemcitabine/oxaliplatin/docetaxel, and 1 (6%) with gemcitabine/paclitaxel preceding SBRT. A median dose of 40 Gy (range, 33-40 Gy) was delivered to the TVI for all patients. 5 BRPC (29%) and 2 LAPC (12%) patients went to surgery, with 6 of these patients undergoing an R0 resection (86%) and 1 BRPC patient with an R1 resection. Pathologic tumor regression grades by the College of American Pathologists guidelines were 14% Grade 1, 71% Grade 2, and 14% Grade 3. Conclusions: Lateral decubitus treatment expands in- clusion of pancreatic body patients for SBRT with focal TVI dose escalation leading to margin negative resection and significant partial tumor response, warranting future studies exploring ablative dosing in this position.
Impact of hospital volume and type on survival in hepatocellular carcinoma: Results from the National Cancer Database. First Author: Johannes Uhlig, Section of Interventional Radiology, New Haven School of Medicine, New Haven, CT

Background: To assess the impact of hospital volume and type on survival in patients with hepatocellular carcinoma (HCC), we analyzed patients with histopathological or imaging-based diagnosis of HCC were identified from the 2003-2015 National Cancer Database (NCDB). First-line treatment was stratified as liver transplant, surgical resection, interventional oncology (IO) and chemotherapy. Hospital volume was stratified as high (ranking among top 10% in case numbers) and low volume, separately for each treatment modality. Hospital type was categorized as academic and non-academic. Overall survival was assessed using multivariable Cox proportional hazards models.

Results: A total of 63,877 patients were included (transplant n = 10,596; surgical resection n = 11,332, IO n = 12,286, chemotherapy n = 29,863). Of 1,261 hospitals systems which treated HCC, 226 (17.9%) were academic centers and 1,035 (82.1%) were non-academic centers. Mean number of cases treated annually was higher in academic centers (55.2; 34.6; 40.7; 79.9) versus non-academic centers (10.7; 6.25; 6.6; 19.9 for transplant; surgical resection; IO and chemotherapy; p < 0.001, respectively). Young African American patients and those with private insurance, high income and education were more likely to receive treatment at academic centers. Geographical difference were evident among US regions, with highest proportion of HCC treated at academic centers in New England states (83.6%) and lowest in South Atlantic states (48.6%). Overall survival was superior for academic versus non-academic centers (HR = 0.89, 95% CI: 0.87-0.9, p < 0.001) and high versus low volume centers (HR = 0.79, 95% CI: 0.77-0.81, p = 0.001), after multivariable adjustment for potential confounders. These effects were evident among all HCC treatment modalities. Conclusions: HCC treatment in academic centers shows distinct patterns according to patient demographics and US geography. Among all treatment modalities, both academic setting and hospital volume independently affected HCC outcomes, with highest patient survival observed in high-volume academic centers.

The Impact of histology (adenocarcinoma vs. SCC) on outcomes in non-metastatic pancreatic cancer. First Author: Joshua Gruhl, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT

Background: Outcomes in squamous cell carcinoma (SCC) of the pancreas are generally thought to be poor compared with adenocarcinoma; however, this has not been sufficiently demonstrated in prior studies. This is the first NCI SEER analysis to examine the prognostic role of histology in non-metastatic pancreatic cancer. Methods: We analyzed patients with non-metastatic pancreatic cancer using the National Cancer Database (NCDB) diagnosed between 2006-2014. Patients were analyzed according to histology-only adenocarcinoma, adenosquamous carcinoma, or SCC were selected for. The primary endpoint was overall survival (OS) from the time of diagnosis. Kaplan-Meier and Cox proportional hazard models were used to analyze OS. Results: A total of 94,928 patients were included; 94,016 in the adenocarcinoma group, 757 in the adenosquamous group, and 155 in the SCC group. There was a statistically significant decrease in median OS for patients with SCC (MS = 8.67 months, 95% CI: 7.23-9.92 months), compared to patients with adenocarcinoma (MS = 12.7 months, 95% CI: 11.9-13.7 months) and adenosquamous carcinoma (MS = 14.0 months, 95% CI: 13.6-14.06 months, p < 0.001). On multivariable Cox regression, both adenocarcinoma and adenosquamous carcinoma were associated with a longer OS compared with SCC for adenocarcinoma, HR 0.45, 95% CI: 0.31-0.66, p < .001; for adenosquamous carcinoma, HR 0.60, 95% CI: 0.39-0.92, p = 0.02). On subgroup analysis, this OS improvement for adenocarcinoma histology was seen for patients with resectable/borderline resectable disease (HR 0.50, 95% CI: 0.32-0.79, p = 0.003) and for those with unresectable disease (HR 0.39, 95% CI: 0.19-0.77, p = 0.001). Conclusions: In patients with non-metastatic pancreatic cancer, there was a statistically significant detriment in OS for those with SCC histology compared with adenocarcinoma or adenosquamous carcinoma. On subgroup analysis, this difference persisted for those with resectable/borderline resectable disease and for those with unresectable disease.

Histology | 6-mo OS (%) | 12-mo OS (%) | 18-mo OS (%) | 24-mo OS (%) | 30-mo OS (%)
---|---|---|---|---|---
SCC | 61.7 | 36.2 | 23.8 | 16.3 | 12.9
Adenosquamous Carcinoma | 83.9 | 53.0 | 36.2 | 28.4 | 24.2
Adenocarcinoma | 83.7 | 56.5 | 39.3 | 28.9 | 22.5

Outcomes following liver SBRT for metastatic pancreatic cancer. First Author: Oluwadamilola Temilade Oladeru, Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

Background: Traditionally, the role of localized therapy for metastatic pancreatic cancer (MPC) has been limited. However, with more effective systemic therapies, recent studies have explored a potential role for local therapies. We aimed to report outcomes following SBRT (stereotactic body radiation therapy) for liver metastases (LM) in setting of MPC and to identify predictors of response. Methods: 41 patients who underwent ablative RT to LM for MPC (2005-17) were retrospectively identified. Median RT dose was 50 Gy (range: 8-60 Gy), delivered in 5-6 fractions. Kaplan Meier method was used to calculate local control (LC), progression-free survival (PFS) and overall survival (OS). Univariate (UVA) and multivariate (MVA) Cox proportional hazards models were used to identify predictors of clinical outcomes. Results: Median follow up was 14.6 months. This cohort included 19 men and 22 women. 61% of pts had metachronous LM, 39% had synchronous LM. At time of RT, the treated lesion was stable (response to chemotherapy (CTX) in 36.6% of pts; 46.3% were progressing with mixed response; 17% were off- CTX. Median number of prior CTX regimens was 2 (range: 0-5). Median number of LM was 1 (range: 1-4). Median pre-RT CEA was 7.9 mg/L, median pre-RT CA19-9 was 354 U/ml. The 12-month outcomes were 75.8% LC, 16.5% PFS, and 36.3% OS. 8/41 (20%) patients were off CTX for ≤ 4 months. On UVA for LC, pre-RT CA19-9 (log10 scale) was associated with LC (HR 2.28, p = 0.03). Timing of RT, LC of LM, response of LM, number of lesions, RT dose and CEA did not predict LC. On UVA for PFS, extrapancreatic disease at time of RT was associated with worse PFS (HR = 2.42, p < 0.001), and response to CTX (HR = 0.04, p < 0.001) was associated with stable or responding) approached significance (HR 1.83, p = 0.10). On UVA for OS, lower pre-RT CEA (HR 1.009, p = 0.03), lower pre-RT CA19-9 (HR 1.67, p = 0.01), and response to CTX (HR 6.42, p < 0.001) were associated with improved OS. On MVA for OS, response to CTX at time of liver RT remained significant for OS. Conclusions: SBRT of LM for MPC offers high rate of LC. In a small subset of patients, SBRT to LM may offer prolonged duration off systemic therapy. Lower pre-RT CA 19-9 and CEA, absence of extrapancreatic disease, and stability/respons of CTX at time of liver RT may select for patients most likely to benefit.

A phase I/II study of RX-3117, an oral antimitabolite nucleoside, in combination with nab-paclitaxel (nab-PC) as first-line treatment of metastatic pancreatic cancer (met-PC): Preliminary results. First Author: Hani M. Babiker, University of Arizona Cancer Center, Tucson, AZ

Background: RX-3117 is an oral small molecule antimitabolite, cyclosporin pyrimidyl nucleoside that is activated by cancer-enriched uridine cytidine kinase 2. Single agent RX-3117 has demonstrated efficacy in a phase III single agent clinical study of RX-3117 in met-PC and bladder cancer. RX-3117 in combination with nab-PC is being evaluated as first line treatment of met-PC cancer. Methods: This is a multicenter, open label phase I/II study (NCT03189914). Eligible subjects (aged ≥ 18 years) have histologically or radiologically proven met-PC with no prior therapies for metastatic disease, ECOG PS 0-1, and normal lab values. Phase I identified the MTD dose that is being further evaluated in the phase II: RX-3117 (700 mg administered orally once-daily for 5 consecutive days with 2 days off per week) and nab-PC (125 mg/m² administered weekly for 4 cycles – 1 cycle). One subject experienced a complete response (CR) after 6 cycles of therapy with normalization of CA19.9 (>76%). Three subjects exhibited a partial response (PR): two after 2 cycles (39-47%) and one after 4 cycles of therapy (36%). Eight subjects had stable disease for at least 2 months, and 4 patients had PFS of at least 4 months. The disease control rate (CR+PR+SD) was 86% in evaluable subjects while the overall response rate (CR+PR) was 29%. Conclusions: RX-3117 in combination with nab-PC appears to be safe and tolerable in subjects with met-PC. Antitumor activity per RECIST v1.1, as of September 21, 2018, phase I subjects and 13 phase II subjects were enrolled and treated (9 males and 12 females, median age 67 years). The most common (≥15%) related adverse events were nausea, diarrhea, fatigue, alopecia, decreased appetite, rash, vomiting, fever, and anemia. Fourteen subjects had at least one on-study scan (after 2 cycles). One subject experienced a complete response (CR) after 6 cycles of therapy with normalization of CA19.9 (>76%). Three subjects exhibited an partial response (PR): two after 2 cycles (39-47%) and one after 4 cycles of therapy (36%). Eight subjects had stable disease for at least 2 months, and 4 patients had PFS of at least 4 months. The disease control rate (CR+PR+SD) was 86% in evaluable subjects while the overall response rate (CR+PR) was 29%. Conclusions: RX-3117 in combination with nab-PC appears to be safe and tolerable in subjects with met-PC. Antitumor activity per RECIST v1.1.
Pulsed high-dose erlotinib with gemcitabine as second-line therapy for pancreatic adenocarcinoma. First Author: Christopher Larson, University of California San Diego Moores Cancer Center San Diego School of Medicine, San Diego, CA

Background: The options for treatment of pancreatic cancer follow progression on first-line therapy. The limited data associated with significant toxicity. Erlotinib has been approved for treatment of pancreatic cancer in first-line therapy. We conducted a phase I dose-escalation trial of erlotinib in combination with gemcitabine for patients that had failed first-line therapy. Erlotinib was administered at a novel pulsed-dose schedule where the drug was given orally for 3 days every two weeks. Purpose: Assess the safety and determine a recommended phase II dose for pulsed high dose erlotinib in combination with gemcitabine for pancreatic cancer, and obtain preliminary data on activity. Methods: Patients with pancreatic cancer that progressed on or after first-line therapy were treated in a dose escalation study with erlotinib at 750 to 2,000 mg daily for three days every two weeks in combination with weekly gemcitabine at 1,000 mg/m2 for three weeks on and one week off. Results: No dose limiting toxicities were encountered and erlotinib-induced rash was mild and transient. Median overall survival was 6.7 months of 20 ng/mL; based on AFP response (>20% increase from baseline) at Week 8. This study evaluated which patients in the real world would be eligible for these new treatments using SEC and MEC, and their prognostic impact. Methods: HCC patients who received S between 01/2008-06/2017 in British Columbia, Alberta, Princess Margaret Cancer Centre, and Sunnybrook Cancer Centre in Canada were included. Clinical, pathologic, laboratory and outcome data were collected. Patients were classified as eligible or ineligible based on available CELESTIAL, RESORCE, and REACH-2 clinical trial SEC or MEC. Median overall survival (mOS) for these groups was assessed using the Kaplan-Meier method. Results: A total of 730 patients were identified. Using SEC, only 13.1% of patients would be eligible for C, Reg, or Ram (table). Expanding eligibility to include patients who meet MEC increased the proportion of eligible patients to 31.7%. Patients who met SEC had longer mOS compared to those who were ineligible. The most common reasons for not meeting SEC across all 3 trials were ECOG $>2$ (61.7%) and CP $>8$ (63.9%). Higher ineligibility for Reg or Ram was likely driven by strict trial-specific criteria, with 28.0% of patients ineligible for Reg due to $>$5 intolerance and 58.9% ineligible for Ram due to AFP $>400$. Conclusions: Only a small proportion of real-world patients would be eligible for C, Reg, or Ram based on SEC. More than twice as many patients would likely receive treatment if MEC were applied. If MEC are adopted, ongoing real-world evidence generation will be important to evaluate outcomes in these unstudied patient groups.

CANCERS OF THE Pancreas, Small Bowel, and Hepatobiliary Tract

Alpha fetoprotein (AFP) response and efficacy outcomes in the phase III CELESTIAL trial of cabozantinib (C) versus placebo (P) in advanced hepatocellular carcinoma (HCC). First Author: Robin Kate Kelley, University of California San Francisco, Helen Diller Family Comprehensive Cancer Center, San Francisco, CA

Background: AFP response, defined as a decrease in serum levels of the tumor marker AFP after therapy may be associated with improved survival of patients (pts) with HCC treated with locoregional or systemic therapy, and high baseline AFP levels may be associated with poor prognosis. In the phase III CELESTIAL trial (NCT01908426), C, an inhibitor of MET, VEGFR, and AXL, significantly improved overall survival (OS) and progression-free survival (PFS) versus P in pts with previously treated advanced HCC. Here we evaluate clinical outcomes with C in CELESTIAL based on AFP response or progression on treatment. Methods: 707 pts were randomized 2:1 to receive C (60 mg daily) or P. Eligible patients had a pathologic diagnosis of HCC, Child-Pugh score of $\leq$70, a serum AFP $\geq$20ng/mL at baseline (n=576), and $\leq$20% increase from baseline (n=52) at 12-month overall survival was 27%. Progression free survival was not significant and there was no difference in median survival among these pts, 236 (71%) and 111 (69%), respectively, were evaluable for response when analyzed using best response through week 24.

Conclusions: The recommended phase II dose for erlotinib was 2,000 mg daily for three consecutive days every two weeks in combination with gemcitabine. Tolerability was excellent, and outcomes were better than expected for second-line therapy in pancreatic cancer. Further studies are warranted, both as therapy after first-line and as first-line therapy for patients unable to tolerate more aggressive regimens.

Clinical trial information: NCT02154737.

Regional, racial/ethnic, and socioeconomic disparities and treatment outcomes in patients with hepatocellular carcinoma (HCC) in the United States. First Author: Nehaar Parikh, University of Michigan, Ann Arbor, MI

Background: Racial/ethnic (R/E) minorities and patients of low socioeconomic (SE) status are reported to have higher mortality related to HCC than their counterparts. However, prior studies are limited to administrative datasets without annotation of clinical covariates. Here we analyzed clinical data with limited generalizability. The aim of this analysis was to characterize geographic, R/E, and SE disparities in HCC presentation, treatment, and survival among a representative sample of HCC patients in the US. Methods: TARGET-HCC is an observational, retrospective/prospective study of patients with HCC from academic and community sites. Complete medical records from consented patients are abstracted into a secure database. Multivariable logistic regression with random intercepts for site and Cox proportional hazard models with frailty adjustment were fit with adjustment for age, sex, BMI, liver disease etiology (LDE) and history of alcohol abuse to identify factors associated with early HCC detection, receipt of curative-intent therapy (CIT) and overall survival. Results: 925 patients with HCC (63% non-Hispanic white, 21% black, and 8% Hispanic) were consented from 42 sites in the US (22% Northeast, 27% Southeast, 21% Midwest, 14% South, and 16% West). Median age was 64 years and 76% were men. The most common LDE was hepatitis C (72%), and 72% had Child Pugh A cirrhosis. Most patients were diagnosed with early-stage HCC (72% Barcelona Clinic Liver Cancer 0/A). CIT was the initial therapy in 249 (32%), including 32% of BCLC 0/A. Although early tumor detection and CIT did not differ by region or R/E, there were SE disparities in CIT. Among those with early stage HCC, patients with private insurance (OR = 0.51, 95% CI 0.29-0.91) or Medicare (OR = 0.50, 95% CI 0.25-0.97) were significantly less likely to undergo CIT. Overall survival was associated with BCLC stage and type of HCC treatment, with no significant association with region, R/E, or insurance. Conclusions: In this sample of HCC patients there were no geographic or R/E disparities in early detection, treatment, and survival although SE disparity in administrative CIT were identified and warrant further study.
**Lymphocyte-to-monocyte ratio and neutrophil-to-lymphocyte ratio independently predict survival in resected small bowel adenocarcinoma.**

**First Author:** Brandon M. Huffman, Mayo Clinic, Rochester, MN

**Background:** Small bowel adenocarcinoma is a rare malignancy affecting approximately 2,000 patients per year. There is a paucity of evidence prognosticating patients with small bowel adenocarcinoma. We aimed to evaluate multiple factors in patients with resected small bowel adenocarcinoma to determine any association with survival outcomes. **Methods:** Ninety-three patients who underwent resection for stage I-II small bowel adenocarcinoma were retrospectively identified utilizing the pathology database at a single tertiary referral institution. All patients had complete follow-up data and were included in the survival analysis. JMP software was used for statistical analysis. Overall survival was performed utilizing Kaplan-Meier method, and log-rank tests were used for statistical comparisons. Cox proportional hazards were performed to control for age, gender, location of tumor, tumor size, tumor stage, and adjuvant therapy. Sensitivity analysis was performed to establish best cutoff points for continuous variables. All tests were two-sided and a P value of < 0.05 was considered significant. **Results:** The median age at diagnosis was 65 years (range 32-90), 68% were male. Median tumor size was 4.5 cm. There were 20, 36, and 37 patients with stage I, stage II, and stage III disease, respectively. Median overall survival (OS) was 151 months, 104 months, and 44 months for stages I, II, and III disease. In a multivariate analysis, independent predictor factors included presurgical lymphocytosis (LRR > 4.0, with a Hazard Ratio (HR): 0.13 (95% CI 0.007-0.69, p = 0.03)), presurgical neutrophil to lymphocyte ratio (NLR < 8.0, HR 0.39 (95% CI 0.17-0.96, p = 0.03), and tumor size < 7.5 cm, HR 0.22 (95% CI 0.07-0.85, p = 0.03). Age, stage, T stage, and N stage influenced overall survival in univariate analysis, but were not statistically significant on multivariate analysis. **Conclusions:** LMR and NLR independently predict survival in patients with resected small bowel adenocarcinoma.

**Stereotactic body radiation therapy for hepatocellular carcinoma with macrovascular invasion.**

**First Author:** Pablo Munoz-Schuffenegger, Radiation Medicine Program, Princess Margaret Cancer Centre, Toronto, ON, Canada

**Background:** In patients with hepatocellular carcinoma (HCC), macrovascular invasion (MVI) is associated with a poor prognosis. This study describes long-term outcomes of patients with HCC and MVI treated with stereotactic body radiation therapy (SBRT). **Methods:** Patients with MVI (A7 or A8) who were treated with SBRT from January 2003 to December 2016 were eligible for analysis. Patients who had extrahepatic disease or who had prior liver transplant were excluded. Demographical, clinical, and treatment variables were collected, with SBRT approval. The degree of vascular invasion was quantified into two categories: main portal vein branch/IVC and distal portal/ hepatic vein. **Results:** 128 eligible pts with HCC and MVI were treated with SBRT (n ≥ 4.5 Gy/fraction). The median age was 61 yrs (range: 39 to 90 yrs). Underlying liver disease was hepatitis B in 23%, hepatitis C in 45%, other in 20%; no known liver disease in 12%. Baseline Child-Pugh (CP) score was A5 in 67%, A6 in 20%, B7 or higher in 13%. 35% received previous liver-directed therapies. Median HCC volume was 153.7 mL (range: 3.9 to 1,813.5 mL). Median AFP was 205 µg/L (range: 1 to 1,713.5 µg/L). Median SBRT dose was 33.3 Gy (range: 27 to 54 Gy) in 6 fractions. Local control at 1 year was 87.4% (95% CI 78.6 to 96.1%). SBRT dose or HCC volume were not significant on univariate analysis. Median overall survival was 18.3 months (95% CI 11.2 to 24.1 months). ECOG PS < 1 (HR: 1.73, p = 0.03), CP score (HR: 1.67, p = 0.04), and treatment between 2004 and 2010 (HR: 2.28, p = 0.0009) were significant on multivariate analysis, while SBRT dose, HCC volume, and degree of vascular invasion were not. In 35 pts who received sorafenib following SBRT, median survival was 38.5 months (95% CI 17.23 to 43.16 months). 4/128 pts developed GI bleeding and 3/122 pts with liver function evaluable at baseline and 3 months had a deterioration in CP class. **Conclusions:** SBRT was associated with excellent outcomes for patients with HCC and MVI. Randomized phase III trials of SBRT are warranted and ongoing.

**Evaluation of disease-specific and functional symptom items on carcinoid tumor patients treated with telotristat ethyl.**

**First Author:** Stacie Hudgens, Clinical Outcomes Solutions, Tucson, AZ

**Background:** Within the pivotal, phase III TELESTAR trial, telotristat ethyl significantly reduced bowel movement (BM) frequency compared to placebo (P=0.001). (NCT01677910). Assessing patient-related outcomes can help understand the impact of changes in BM frequency on patient lives. An analysis was done to determine whether individual items on patient-reported outcome measures show relevant patterns over the course of treatment for patients with carcinoid syndrome (CS). **Methods:** The TELESTAR study was a phase III, double-blind, parallel-group, randomized, placebo-controlled study comparing placebo (PBO) to telotristat ethyl (TE) in 135 patients with Carcinoid Syndrome (CS). Clinical quality of life (QoL) measurements included the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and European Organisation for Research and Treatment of Cancer (EORTC) GINET21 scales. Analyses on identified individual gastrointestinal (GI) symptom and role function items were conducted using longitudinal generalized estimation equations (GEE; reference=PBO) to characterize the likelihood of a 1-grade categorical improvement (e.g., improvement by one category on the verbal response scale). Forest plots of odds ratios (OR) and associated confidence intervals (CI) on individual items are presented. **Results:** At week 12, the likelihood of patients experiencing a 1-grade improvement on most GI symptoms were equivalent (OR approx.1.0). The highest odds ratios observed with TE were for improvement in diarrhea (OR=1.86, CI=0.848-4.090) and a reduction in weight bother (OR=2.95, CI=0.723-12.199), in parallel to TELESTAR results for bowel movement frequency reduction and weight gain. Interference with daily activities (IADL) and limitations in doing work demonstrated similar outcomes (IADL OR=1.63, CI=0.67,4.288; Work OR=1.97, CI=0.722,5.376). **Conclusions:** The overall pattern of item level change on telotristat suggested clinical relevance for bowel movement frequency reduction and weight gain, and it was consistent with symptomatic and functional benefit in CS. Clinical quality of life outcomes are provided in NCT01677910.

**The need for improvement in the management of fatigue, depression and pain in pancreatic cancer.**

**First Author:** Amy Westermann, Pancreatic Cancer Action Network, Manhattan Beach, CA

**Background:** Pancreatic cancer (PC) and its treatments result in symptom and side effect burden and can impact patient’s overall quality of life (QOL). **Methods:** Patient reported information on management of side effects and symptoms were collected using PanCure’s Pan-Info registry (01/2016 – 07/2018). **Results:** Patient reported information on side effects, pain and depression is detailed in the table. Side effects: 84% reported fatigue and 8% reported taking anti-nausea medication. 72% reported nausea or vomiting during treatment and 83% reported taking anti-nausea medication. Pain: Of the 90% of patients who reported pain related to PC, 27% did not take pain medication. 47% visited the ER and 32% were hospitalized due to pain. Depression: Of the 83% of users reported feeling depressed during PC, 46% were diagnosed with depression, 37% prescribed anti-depressant, and 48% did not see a therapist. **Conclusions:** Nausea was reported as the most concerning symptom. Fatigue, pain and depression were generally unmanaged. ER visits and hospitalizations due to pain were frequently reported. An improvement in the management of these side effects and symptoms is needed as it can affect patient’s ability to tolerate treatment, improve overall QOL, and may lower overall healthcare costs.

**Patient reported information on side effects, pain & depression management.**

<table>
<thead>
<tr>
<th>Drug Therapy Side Effects</th>
<th>Reported (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=770</td>
<td></td>
</tr>
<tr>
<td>reported fatigue</td>
<td>72% (94%)</td>
</tr>
<tr>
<td>taking anti-fatigue medicine</td>
<td>64% (88%)</td>
</tr>
<tr>
<td>reported nausea or vomiting</td>
<td>550% (76%)</td>
</tr>
<tr>
<td>taking anti-nausea medication</td>
<td>64% (89%)</td>
</tr>
<tr>
<td>reported low blood count</td>
<td>598% (78%)</td>
</tr>
<tr>
<td>received blood transfusions, Growth Factors, and/or iron infusions</td>
<td>310% (39%)</td>
</tr>
<tr>
<td>Pain</td>
<td>n=88</td>
</tr>
<tr>
<td>reported pain related to PC</td>
<td>74% (95%)</td>
</tr>
<tr>
<td>discussed pain with HCP</td>
<td>65% (88%)</td>
</tr>
<tr>
<td>HCP recommended or prescribed pain medication</td>
<td>62% (84%)</td>
</tr>
<tr>
<td>taking/have taken prescribed medication</td>
<td>54% (73%)</td>
</tr>
<tr>
<td>taking/have taken over the counter medication for pain</td>
<td>46% (62%)</td>
</tr>
<tr>
<td>did not take pain medication</td>
<td>20% (27%)</td>
</tr>
<tr>
<td>visited ER</td>
<td>35% (47%)</td>
</tr>
<tr>
<td>visited ER more than once</td>
<td>19% (26%)</td>
</tr>
<tr>
<td>hospitalized due to pain</td>
<td>19% (26%)</td>
</tr>
<tr>
<td>hospitalized due to pain more than once</td>
<td>14% (19%)</td>
</tr>
</tbody>
</table>

**Depression**

| n=63                      |              |
| felt depressed at some point during PC | 52% (83%) |
| diagnosed with depression due to PC | 24% (46%) |
| prescribed anti-depressant | 19% (37%)   |
| not seeing a therapist     | 25% (46%)   |
Carcinoids of the ampulla: Long-term follow-up after endoscopic resection.
First Author: George Nyasha Baison, Virginia Mason Medical Center, Seattle, WA

Background: Neuroendocrine tumors (NET) or carcinoids of the ampulla are exceedingly rare in comparison to duodenal NET. Surgical management is widely accepted as the treatment of choice for NETs in patients that refuse surgery or are poor operative candidates, endoscopic resection may be option. We present a consecutive case series at a tertiary care center describing our experience with endoscopic resection of ampullary NET. Methods: This is a retrospective review with a long-term follow-up of patients with endoscopic NET that were endoscopically resected. Outcomes were analyzed based on the histopathologic classification system proposed by the World Health Organization in 2000. Results: Twelve patients (9 male, 3 female), ranging in age from 41 to 86 (mean 59) underwent endoscopic ampullectomy for ampullary NET, with a mean follow-up time of 5 years. Patients had refused surgery or were poor surgical candidates. All, but one incidentally found case, were symptomatic on presentation, with gastrointestinal bleeding being the main symptom. No patients had a hormonal syndrome. The mean size of the lesions was 21 mm (6 mm to 35 cm). Six (50%) patients had a well-differentiated, benign lesion, 6 (50%) patients had a well-differentiated NET with unknown malignant potential (gangliocytic parangangioma). Eight (67%) were completely excised during the initial endoscopy with 4 requiring re-resection. Only 2 patients developed recurrence, after 2.5 and 10 years and this necessitated a pancreaticoduodenectomy. Five patients had complications (2 for bleeding and 3 for post-ERCP pancreatitis), with zero deaths. Conclusions: Unlike duodenal carcinoids, ampullary NET are rare. Pancreaticoduodenectomy can be offered to fit patients except for gangliocytic parangangiomas that do not require an aggressive operation. However, for those that refuse surgery or are poor candidates, endoscopic ampullectomy may be an option with acceptable short and long-term outcomes.

A retrospective study of hepatic arterial infusion (HAI) FUdR/Dex and mitomycin C (MMC) for chemotherapy refractory unresectable intrahepatic cholangiocarcinomas (ICC). First Author: Gustavo Dos Santos Fernandes, Memorial Sloan Kettering Cancer Center, New York, NY

Background: ICC are aggressive tumors with approximately 6,000 cases a year in US. The 5-year survival rate is less than 30% even for localized disease. There is only one approved line of systemic (SYS) treatment and further treatment options are necessary. HAI chemotherapy is an option to treat liver predominant cancers. Methods: After obtaining IRB approval, we retrospectively reviewed patients (pts) with ICC chemio refractory unresectable liver limited (LL) or liver dominant (LD) disease who received intrahepatic chemotherapy with HA-MMC. Baseline characteristics, previous lines of therapy, toxicity profile, combinations and radiographic responses were reviewed. Tumor genomic analyses were performed on samples using an on-site next generation sequencing (NGS) assay. Results: Between January 2011 and August 2019, 19 patients with ICC with LL or LD disease were treated with HAI FUdR/Dex/MMC at Memorial Sloan Kettering Cancer Center. Disease was confined to the liver in 58% of the pts. All pts had previous chemotherapy (1-4 lines) and 14 (74%) previously had HAI FUdR/Dex. Of the 19 pts, 56% had HAI with FUdR/Dex and MMC, 43% had FUdR/Dex/MMC, 43% had FUdR/Dex/MMC, MCC and SYS and 5% had HA-MMC and SYS. Seventeen patients were evaluable for response, two are being treated and will have response assessment for the meeting. Response was noted in 4 (23.5%), stable disease in 6 (35.5%) and progressive disease in 7 (41%) pts. Median overall survival from treatment was 6 months (0.36-26). Median progression free survival was 3.65 months (0.36-9.53). Four patients had dose reductions. Common toxicity attributed to MMC was grade (G) one fatigue (32%), thrombocytopenia G0/G1 (5%) and G2 (5%). Of the 12 tumors analyzed to date the most 92% of tumors harbored at least one (0-10) genomic alteration. Common genomic alterations were ARID1 (25%), RAS/A (25%), IDH1/2 (16.6%), NTRK (16.6%), TERT (16.6%), NRAS (16.6%), CDKN2 (16.6%). FGFR2-FOXP1 and GTL2MTN1 fusions were found in one patient each. Conclusions: HAI FUdR/Dex/MMC contains chemotherapies that are active for heavily pretreated refractory unresectable ICC. This strategy should be further investigated. Translational data will be presented.

A new clinically based staging system for gallbladder cancer. First Author: Siddhartha Yadav, Mayo Clinic, Rochester, MN

Background: Current staging systems for gallbladder cancer (GBC) are inadequate, as they are based on surgical pathology, and therefore are not relevant for unresectable patients and patients undergoing neoadjuvant chemotherapy. Methods: Patients with a confirmed diagnosis of GBC who were seen at Mayo Clinic between the years 2000 and 2016 were included in this study. Data on demographic and tumor characteristics and outcomes were collected by retrospective review of electronic medical records. A model predictive of overall survival was developed using Cox proportional hazard regression analysis. Harrell’s C statistic was calculated to evaluate the predictive accuracy of the model and compared with the TNM staging system. Results: A total of 523 patients were included in the final analysis, with a median age of diagnosis of 68 years. The median duration of follow up of the entire cohort was 12 months. In multivariate analysis, factors predictive of poorer overall survival were: ages 65-74 years (HR: 1.80, 95% CI: 1.33-2.43) and ages 75+ years (HR: 2.93, 95% CI: 2.12-4.06) compared to age <55 years; tumor size ≥ 5 cm by imaging (HR: 1.24, 95% CI: 1.01-1.55); nodal involvement by imaging (HR: 1.49, 95% CI: 1.21-1.84); involvement of distant organs by imaging (HR: 2.85, 95% CI: 2.16-3.75); ECOG performance score of 2 or higher (HR: 3.75); involvement of distant organs by imaging (HR: 2.85, 95% CI: 2.16-3.75); ECOG performance score of 2 or higher (HR: 1.78, 95% CI: 1.36-2.32) compared to ECOG 0; albumin level < 3.5 g/dL (HR: 1.40, 95% CI: 1.08-1.81); and alkaline Phosphatase level ≥ 200 IU/L (HR: 1.49, 95% CI: 1.21-1.84). Using these seven predictive factors of survival we created a four-tier staging system. The median survivals of Stages I, II, III and IV created in our novel system were 64, 34, 20 and 7 months with corresponding hazard ratios of 1.5, 2.5 and 8.5 respectively. The C-statistic for this novel staging system was 0.68 compared to C-statistic of 0.69 for the TNM staging system, indicating similar performance in predicting survival. Conclusions: We have created a novel clinically-based staging system for patients with GBC based on nonoperative information at the time of diagnosis. This staging system performs on par with the current surgical pathology based TNM staging system.
20 patients were enrolled on protocol from November 2015 with withdrawal of consent. Primary endpoint was objective response rate. Patients with advanced GI/lung NETs and pNETs who had evidence of progression within 12 months of study entry on at least one prior therapy. Patients received ibrutinib 560mg daily until unacceptable toxicity, progression of disease, or withdrawal of consent. Primary endpoint was objective response rate.

Results: 20 patients were enrolled on protocol from November 2015 - December 2017 (15 carcinoid and five pNETs). No patients experienced objective response. Median PFS was 3.1 months. A total of 43 drug related AEs were captured as probably or definitely associated with ibrutinib. Five patients experienced probably or definitely related grade 3 AEs and one patient experienced a probably related grade 4 AE. Five patients discontinued treatment prior to radiographic assessment.

Conclusions: ibrutinib does not show significant evidence of activity when compared to other agents (e.g. Everolimus) in well-differentiated gastroenteropancreatic and lung NETs.

Clinical trial information: 02575300.

Phase II study of ibrutinib in advanced carcinoid and pancreatic neuroendocrine tumors.

First Author: Taymyeh A. Al-Tobah, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL

**Background:** Ibrutinib is an orally administered, inhibitor of Bruton’s tyrosine kinase (Btk). Preclinical data suggest that mast cells are recruited with neuroendocrine tumors (NETs) where they remodel the stroma and stimulate angiogenesis, driving macroscopic tumor expansion. Ibrutinib inhibits mast cell degranulation, and has been associated with regression of a mouse insulinoma model.

**Methods:** A prospective, phase II trial evaluated patients with advanced GI/lung NETs and pNETs who had evidence of progression within 12 months of study entry on at least one prior therapy. Patients received ibrutinib 560mg daily until unacceptable toxicity, progression of disease, or withdrawal of consent. Primary endpoint was objective response rate.

**Results:** 20 patients were enrolled on protocol from November 2015 - December 2017 (15 carcinoid and five pNETs). No patients experienced objective response. Median PFS was 3.1 months. A total of 43 drug related AEs were captured as probably or definitely associated with ibrutinib. Five patients experienced probably or definitely related grade 3 AEs and one patient experienced a probably related grade 4 AE. Five patients discontinued treatment prior to radiographic assessment.

**Conclusions:** Ibrutinib does not show significant evidence of activity when compared to other agents (e.g. Everolimus) in well-differentiated gastroenteropancreatic and lung NETs.

Clinical trial information: 02575300.

**434** Poster Session (Board #N14), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

**Clinical outcomes of hepatocellular carcinoma variants compared to hepatocellular carcinoma.**

First Author: Katerina Mary Zaka, Winship Cancer Institute of Emory University, Atlanta, GA

**Background:** There is no consensus regarding treatment for HCC variants. Clinical outcomes of HCC variants differ from pure HCC. The aim of this study is to compare clinicopathological characteristics, treatment, outcome, overall and PFS of HCC variants with pure HCC.

**Methods:** Patients with HCC and variants with 81110-3/81153 and 8180/3 ICD-0-3 codes were identified from National Cancer Database between 2004 and 2013. Univariate and multivariate survival analyses were conducted to assess the associations between outcomes and variants. Overall survival (OS) and PFS were the outcomes analyzed. OS was calculated from the surgery date. While this unexpected results could reflect selection bias of therapy, further analysis will account for tumor stage when calculated from the surgery date. While this unexpected results could reflect selection bias of therapy, further analysis will account for tumor stage when calculated from the surgery date.

**Conclusions:** HCC variants underwent surgical resection more often than HCC. HCC had the best 5-year OS. Liver transplant is commonly performed in HCC variants.

**435** Poster Session (Board #N15), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

**Outcomes for patients with borderline resectable (BR) and locally advanced (LA) pancreatic cancer (PC) treated with induction FOLFIRINOX (FFX) +/- radiation (RT) followed by surgery compared to induction FFX followed by consolidative RT.**

First Author: Michael Cecchin, Yale University, New Haven, CT

**Background:** Induction FFX for PC deemed either BR or LA at diagnosis provides an opportunity to downstage pts with the aim of an R0 surgery. The addition of RT after induction FFX may further downstage. However, there is a paucity of data regarding long-term survival for BR and LA pts successfully downstaged and resected. We performed a retrospective review of BR and LA PC treated with induction FFX +/- RT followed by surgery or consolidative RT at the Yale Cancer Center (YCC) to assess survival in these two cohorts.

**Methods:** Clinical data was abstracted for pts with BR or LA PC who had surgery or received consolidative RT after surgery without induction FFX +/- RT at the YCC from 2010-2018. Surgical pts were re-reviewed by a radiologist to assess vascular involvement (BR vs. LA) using NCCN criteria. Univariate and multivariate analyses, fibrolamellar histology, female sex, diagnosis between 2009 and 2013, treatment at academic center, well/moderately differentiated histology, early stage, and chemotherapy was associated with better OS compared to pure HCC, male sex, diagnosis between 2004 and 2006, treatment at community cancer program, poorly differentiated, late stage, and no chemotherapy (p < 0.001). Conclusions: HCC variants underwent surgical resection more often than HCC. HCC had the best 5-year OS. Liver transplant is commonly performed in HCC variants.

**436** Poster Session (Board #N16), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

**Neoadjuvant therapy duration and outcome of patients with resectable and borderline resectable pancreatic ductal adenocarcinoma (PDAC).**

First Author: Safi Shaida, Indiana University Melvin and Bren Simon Cancer Center, Indianapolis, IN

**Background:** Neoadjuvant chemotherapy (NA CT) may improve surgical selection for resectable (R) PDAC, and margin negative resection in borderline resectable (BR) PDAC. Optimal duration of NA CT is unknown, as is the role of XRT with modern chemotherapy. We compared survival outcomes by duration of NA CT and XRT.

**Methods:** Patients with R or BR PDAC who underwent NA CT with or without XRT and followed by curative resection were included in this analysis. Data was extracted from an IRB approved pancreatic cancer database at Indiana University. Disease Free (DFS) and Overall (OS) survival were calculated from the surgery date and compared between: 1) < 3 v > 3 months NA CT and 2) NA CT with or without XRT.

**Results:** Between Summer 2006 and Summer 2018, 186 patients received NA CT with or without XRT and completed surgical resection. Median (range) age was 63 years (36, 84), stages were R=47%, BR=53%. Most patients received modified FOLFIRINOX or FOLFIRINOX (59%), or gemcitabine/nab- paclitaxel (13%) and 24% received XRT. There were four (3%) pathologic complete responders, all in the < 3 mo NA CT + XRT group. Percent node positive was lower in NA CT + XRT versus NA CT only (median 0% vs 7.4%, p < 0.001), but did not differ by duration of NA CT. With a median (range) follow-up time of 10.7 (0.7, 83.0) years, median OS was 21.5 mo (12.2, 21.9) with < 3 mo NA CT versus 16.3 (12.2, 19.9) with ≥ 3 mo NA CT (p = 0.02) and was 22.6 mo (17.0, 22.9) with NA CT + XRT versus 19.5 (13.1, 22.5) in NA CT only (p = 0.03). There was no difference in DFS by duration of NA CT or XRT.

**Conclusions:** In this study, patients who received a shorter course of chemotherapy and radiation had improved OS when calculated from the surgery date. While this unexpected results could reflect selection bias of therapy, further analysis will account for tumor stage at diagnosis, perioperative complications and use propensity score adjustment to examine/adjust for possible treatment selection bias.

**437** Poster Session (Board #N17), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

**Outcomes for patients with borderline resectable (BR) and locally advanced (LA) pancreatic cancer (PC) treated with induction FOLFIRINOX (FFX) +/- radiation (RT) followed by surgery compared to induction FFX followed by consolidative RT.**

First Author: Michael Cecchin, Yale University, New Haven, CT

**Background:** Induction FFX for PC deemed either BR or LA at diagnosis provides an opportunity to downstage pts with the aim of an R0 surgery. The addition of RT after induction FFX may further downstage. However, there is a paucity of data regarding long-term survival for BR and LA pts successfully downstaged and resected. We performed a retrospective review of BR and LA PC treated with induction FFX +/- RT followed by surgery or consolidative RT at the Yale Cancer Center (YCC) to assess survival in these two cohorts.

**Methods:** Clinical data was abstracted for pts with BR or LA PC who had surgery or received consolidative RT after surgery without induction FFX +/- RT at the YCC from 2010-2018. Surgical pts were re-reviewed by a radiologist to assess vascular involvement (BR vs. LA) using NCCN criteria. Univariate and multivariate analyses, fibrolamellar histology, female sex, diagnosis between 2009 and 2013, treatment at academic center, well/moderately differentiated histology, early stage, and chemotherapy was associated with better OS compared to pure HCC, male sex, diagnosis between 2004 and 2006, treatment at community cancer program, poorly differentiated, late stage, and no chemotherapy (p < 0.001). Conclusions: HCC variants underwent surgical resection more often than HCC. HCC had the best 5-year OS. Liver transplant is commonly performed in HCC variants.

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**107**

**CANCERS OF THE PANCREAS, SMALL BOWEL, AND HEPATOBLIARY TRACT**
**CANCERS OF THE PANCREAS, SMALL BOWEL, AND HEPATOBILIARY TRACT**

**438** Poster Session (Board #N18), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Treatment of hepatocellular carcinoma (HCC) after sorafenib (S) over the last 10 years.

**Background:** Until recently there were no standard treatments for HCC patients after S. This study characterizes subsequent treatments (STx) received by HCC patients over the past 10 years and assesses their impact on survival.

**Methods:** HCC patients treated with S between 01/2008 - 06/2017 in British Columbia, Alberta, and two cancer centers in Toronto, Ontario, Canada (Princess Margaret and Sunnybrook Cancer Centre) were included. Clinical, pathologic, laboratory, treatment, and outcome data were collected. The Kaplan-Meier method was used to assess overall survival (OS) based on STx, and stratified according to a better prognostic group (BPG), defined as ECOG 0-1 and CP-A, and a worse prognostic group (WPG), defined as ECOG ≥2 or CP-B/C.

**Results:** A total of 730 patients were identified. 177 (24.2%) received STx (table). Patients who received STx had longer median OS (mOS) than those who had no further treatment (12.1 vs. 3.3 months; p < 0.001). For patients treated with localized, systemic, or palliative radiation treatment, mOS was 16.8, 10.5, and 8.6 months, respectively (p < 0.001). After S, there were 206 (30.7%) patients in the BPG and 444 (69.3%) in the WPG. BPG patients more likely to receive STx compared to WPG patients (60.5% vs. 39.5%; p < 0.001). BPG patients who received STx had better mOS than those who did not (15.9 vs. 7.0 months; p < 0.001). WPG patients also had better mOS if they received STx compared to those who did not (6.0 vs. 2.6 months; p < 0.001).

**Conclusions:** Only a small proportion of HCC patients received subsequent treatment after sorafenib. This is likely due to poor performance status, liver dysfunction, or lack of treatment options. Patients who received subsequent treatment had improved mOS, regardless of whether they were in the better or worse prognostic group.

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>Number of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized</td>
<td>53 (7.3)</td>
</tr>
<tr>
<td>SBRT</td>
<td>21 (2.9)</td>
</tr>
<tr>
<td>TACE</td>
<td>21 (2.9)</td>
</tr>
<tr>
<td>RFA</td>
<td>12 (1.6)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>25 (3.4)</td>
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<tr>
<td>Clinical Trial</td>
<td>75 (10.3)</td>
</tr>
<tr>
<td>Ablation</td>
<td>15 (2.0)</td>
</tr>
<tr>
<td>Cabozantinib</td>
<td>15 (2.0)</td>
</tr>
<tr>
<td>Robituzumab</td>
<td>10 (1.3)</td>
</tr>
<tr>
<td>Immunotherapy</td>
<td>9 (1.2)</td>
</tr>
<tr>
<td>Other Trial dx</td>
<td>22 (3.0)</td>
</tr>
<tr>
<td>Palliative RT</td>
<td>27 (3.7)</td>
</tr>
</tbody>
</table>

*Does not add up to 100% since some patients received multiple treatments*

**439** Poster Session (Board #N19), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Undertreatment of noncurative pancreatic adenocarcinoma?: A population-based analysis of patterns of care. First Author: Michail Mavros, University of Toronto, Toronto, ON, Canada

**Background:** Noncurative pancreatic adenocarcinoma (PA) portends a guarded prognosis. Advancements in systemic therapy have improved this outlook. It is unknown whether patients get access to these therapies. We sought to define patterns of access to care and therapy for noncurative PA.

**Methods:** We conducted a population-based analysis of nonresected PA over 2005-2016 by linking administrative healthcare datasets. Primary outcome was nonreceipt of cancer-directed therapy (radiation/chemotherapy/NRCTD). The first contact and overall consultations with specialized care (surgery, medical, or radiation oncology) were examined. Multivariate models examined factors associated with NRCDT. **Results:** Of 10,881 patients surviving a median of 3.3 months (IQR: 12.8-5.5), 62% had NRCDT. More of patients of older age (65% of 71-80 years old, 89% of >81 years old), high comorbidity burden (68%), and low socioeconomic status (69%), had NRCDT. Distance from residence to nearest cancer center did not differ based on NRCDT. 35% of all patients did not see medical oncology, including 56% of NRCDT patients; 17% had no consultation with specialists. First contact with specialized care was surgery for 55% of all patients, and 50% with NRCDT. Most patients saw palliative care (81%) at median 27 days (IQR: 9-75) after diagnosis. Older age (OR 0.42 [0.37-0.48], and OR 0.14 [0.12-0.16] for 71-80 and >81 years respectively), lowest income quintile (OR 0.62 [0.54-0.71]) and rurality (OR 0.63 [0.56-0.71]) were independently associated with lower odds of seeing medical oncology. First contact with oncology was independently associated with higher odds of receiving therapy (OR 1.42, 1.32-1.53) compared to surgery. **Conclusions:** The majority of patients with noncurative PA did not receive cancer-directed therapy. Of those, more than half did not see medical oncology. While some patients may not be eligible to therapy, we identified disparities in receipt of cancer-directed therapy that need to be assessed and addressed. There is a need for additional assessment for therapy and undertreatment, especially for vulnerable populations. This information is important to optimize access to and delivery of evidence-based care, and improve PA outcomes.

**440** Poster Session (Board #N20), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Comparison of radiation treatment volumes for borderline resectable pancreatic cancer. First Author: Trevor Scott Blument, University of Cincinnati, Cincinnati, OH

**Background:** Optimal radiation target volumes for downsizing and local control in patients with borderline resectable pancreatic cancer (BRPca) are undefined. Most local recurrences are near the celiac axis (CA) and superior mesenteric artery (SMA), as demonstrated by pattern of failure mapping (Dholakia et al JROBP 2013). Methods for generating target volumes include simulating vascular regions at risk of recurrence. **Methods:** CT simulation scans of 14 patients with BRPca from an institutional prospective trial were used to create treatment volumes for comparison. Treatment volumes from three current prospective trials (PREOPANC, Alliance AO21101, and Alliance AO21501) were generated for each patient based upon their respective protocols. The trials’ volumes were compared to two reference volumes created for coverage evaluation. A customized vasculature (CustVasc) CTV was based on the CA, SMA, and vessels abutting the tumor. The Hopkins PTV reference volume was based upon the proximal 1 cm of the CA and 3 cm of the SMA, and expanded according to the study’s protocol. Boolean operators located regions the three prospective trials would not provide treatment when compared to reference volumes. **Results:** Table outlines the target volumes and the proportion of the CustVascPTV and Hopkins PTV covered by each trial definition. **Conclusions:** Symmetric expansion from the primary tumor to generate target volumes may not adequately cover the mesenteric vasculature which is at high risk of local recurrence and varies based on patient/tumor anatomy. An approach utilizing a customized target volume specifically includes the SMA and CA will improve coverage to this region at high risk of local recurrence.

<table>
<thead>
<tr>
<th>Alliance AO21101</th>
<th>Alliance AO21501</th>
<th>PREOPANC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose/Fractionation</td>
<td>50/4/Conventional</td>
<td>33 Gy/SBRT</td>
</tr>
<tr>
<td>Median volume (cc)</td>
<td>302.8 (262.8-385.4)</td>
<td>431 (18.2-66.3)</td>
</tr>
<tr>
<td>Mean % Coverage of CustVascPTV</td>
<td>70.8% (43.3-100%)</td>
<td>20.9% (12.1-50.8%)</td>
</tr>
<tr>
<td>Mean % Coverage of HopkinsPTV</td>
<td>48.6%</td>
<td>38.7%</td>
</tr>
</tbody>
</table>

**441** Poster Session (Board BPI), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Dosing modifications to increase tolerability of gemcitabine and nab-paclitaxel in treatment of pancreatic cancer in the elderly. First Author: Jasmine L Martin, Florida Atlantic University, Boca Raton, FL

**Background:** Gemcitabine and nab-paclitaxel has been reported to prolong survival in patients with metastatic pancreatic cancer. This drug combination was studied in such patients in the MPACT trial with an average age of enrolled patients being 63. Pancreatic cancer is a disease of the aging with a median age at diagnosis of 70. Reductions in dosing by 20% or more in one or both components and has been shown to improve the tolerability of this regimen, thereby increasing treatment exposure. Our study aims to examine dosing modifications in drug combination to increase tolerability and how this is affected by schedule and dosing modifications. **Methods:** A retrospective chart review was performed of 83 patients over the age of 70 with a median age of 79 who received this drug combination as first-line treatment for pancreatic adenocarcinoma at a single institution. Overall survival and progression-free survival were assessed as well as schedule modification, dose reduction, and rates of adverse events. **Results:** For patients with metastatic or non-metastatic disease, the mean overall survival and progression-free survival were found to be 10.57 months and 6.63 months, respectively. When only patients with metastatic disease are analyzed, these values were found to be 9.26 months and 6.05 months, respectively, which are similar to those observed in the MPACT trial. The most common adverse events of grade 3 or greater were fatigue in 34.9% of patients and hematologic adverse events including neutropenia in 27.7% and leukopenia in 25.3%. Adverse events of grade 1 or higher were 72.1% of patients. Dose reductions were commonly used to mitigate adverse events. Reductions in dosing by 20% or both drugs by at least 20% occurred in 84.3% of patients. **Conclusions:** Gemcitabine and nab-paclitaxel in treatment of pancreatic cancer is well tolerated in an elderly population with similar rates of adverse effects when compared with previous studies, though this population experienced a significantly higher rate of fatigue. Dose reductions were used frequently in this population to improve tolerability, which may have contributed to the observed increase in overall survival in this population.

Visit gicasy.org by search for abstract by full list of abstract authors and their disclosure information.
Neutrophil-to-lymphocyte ratio as a prognostic marker in patients with metastatic gallbladder cancer. First Author: Mohamed Mady, Mayo Clinic, Rochester, MN

Background: Neutrophil to lymphocyte ratio (NLR) has been used as an inflammatory-based prognostic marker for various malignancies. The aim of our study was to determine whether NLR can independently predict overall survival in patients with metastatic gallbladder cancer (GBC). Methods: We identified patients diagnosed with GBC who were treated at Mayo Clinic between the years 2000 and 2016. Patients who had nonmetastatic GBC were excluded along with the patients who did not have data for neutrophils and lymphocytes. Optimal cutoff point for NLR was identified by plotting martingale residuals against NLR and patients were divided into two groups, NLR ≥ 5 and NLR < 5. Demographic, follow-up data and outcomes were collected by retrospective review of electronic medical records. Fisher’s exact test was used to compare categorical variables, while The Mann-Whitney U test was used to compare continuous variables. Kaplan-Meier curves were plotted for NLR ≥ 5 and NLR < 5 and overall survival (OS) between the two groups were compared using log rank test. Multivariate survival analysis was performed using Cox-proportional hazard regression. Results: A total of 231 patients met our inclusion criteria, of which, 138 (60%) had NLR ≤ 5 and 93 (40%) had NLR ≥ 5. Patients with NLR ≥ 5 were more likely to be older and have poor performance score, lower albumin level, higher alkaline phosphatase level and higher platelet count. There were no significant differences noted in gender, race and administration of chemotherapy between the two groups. In univariate analysis, patients with NLR ≥ 5 at presentation had a significantly worse OS compared to those with NLR < 5 (Median survival: 3.6 vs. 8.8 months, p < 0.001). In multivariate analysis, adjusting for age, ECOG status, albumin, ALP, AST, ALT, bilirubin, platelet count and administration of chemotherapy, NLR of ≥ 5 was associated with a worse OS compared to NLR < 5 (HR: 1.70, 95% CI 1.20-2.39, p < 0.001). Median survival: 3.6 vs. 8.8 months, p < 0.001). Our study demonstrates that NLR ≥ 5 is an independent predictor of poor prognosis in patients with metastatic gallbladder cancer.

Impact of an inter-professional clinic on pancreatic cancer outcomes: The Princess Margaret Cancer Centre (PM) experience. First Author: Hamzeh Albaba, Princess Margaret Cancer Centre, Toronto, ON, Canada

Background: Patients with pancreatic ductal adenocarcinoma (PDAC) have limited treatment options. Management of complex symptoms and psychosocial social implications requires an interprofessional approach as prognosis is often poor. Patients with PDAC in Canada have been associated with improved clinical outcomes including survival. We aimed to evaluate the impact of an inter-professional approach for PDAC patients at the Wallace McCain Centre for Pancreatic Cancer (WMPC) at PM on their clinical outcomes and inclusion of these subtypes in AC clinical trials. Methods: The National Cancer Database (NCDB) was queried to identify patients with AC, AS, and SCC between 2004 and 2014. Overall survival was calculated using Kaplan-Meier methodology and multivariable (MVA) Cox regression models were fit to identify differences in survival outcomes between subtypes adjusted by baseline demographic and clinical variables. ClinicalTrials.gov was interrogated to identify inclusion of AS and/or SCC in contemporary PA clinical trials. Results: We identified 115,061 patients with pancreatic cancer. Median age was 69 (range 18 - 90) and median follow up was 54 months (95% CI 53 - 55). Age, sex, median income, education, comorbidities, race, and stage were significantly associated with overall survival (OS). OS by subtype compared to AC: AS HR of 0.99 (p = 0.59) and SCC HR 1.29 (p < 0.001). OS by subtype and stage compared to AC: stage I/II, AS HR of 0.98 (p = 0.59) and SCC HR 1.44 (p = 0.001); stage III, AS HR of 1.32 (p = 0.02) and SCC HR 1.48 (p = 0.03); stage IV, AS HR of 1.11 (p = 0.06), SCC HR 1.12 (p = 0.06). Data from 283 phase II or III interventional trials completed between 2008-2018 were exported from clinicaltrials.gov. The majority of trials listed did not specify inclusion or exclusion of AS or SCC subtypes. Conclusions: This is the largest report of clinical outcomes in rare subtypes of pancreatic cancer. SCC and to a lesser extent, AS, have worse OS compared to AC. It is unclear how rare pancreatic cancer subtypes are handled in the inclusion and analysis of clinical trial data and how this may impact enrollment and survival outcomes.
Resection of primary tumor in liver only metastatic midgut neuroendocrine tumors. First Author: Nicholas Manguso, Cedars-Sinai Medical Center, Los Angeles, CA

Background: Surgical management of metastatic midgut neuroendocrine tumors (NET) remains controversial. Resection of primary tumor only without liver resection is advocated only in select patients, frequently for palliation. Additionally, no standard algorithm exists, and the risk profile for these patients is not well documented in the literature. We evaluated these midgut NETs with liver metastasis in the National Cancer Data Base (NCDB) to determine if resection of the primary tumor only affected survival outcomes.

Methods: The NCDB was queried to identify patients with liver only metastatic midgut NET tumors between 2010 and 2015. Patients who underwent surgery of their liver metastases were excluded. The cohort was separated into two groups, those who underwent resection of the primary tumor and those who did not. Patient demographics, year of diagnosis, clinicopathologic tumor characteristics and Charlson/Deyo comorbidity index were compared among the two groups. The primary outcome was overall survival (OS). Kaplan-Meier estimates were used to predict OS. Results: One thousand nine hundred fifty-two patients with median age of 63 were identified. Median tumor size was 2.4 cm. Of these, 1,295 (66.0%) patients underwent resection of the primary tumor and 667 (34.0%) did not. Patients undergoing resection were younger (median age 63 vs. 65, \( p < 0.001 \)) and had smaller tumors (median 2.3 vs. 3.0 cm, \( p < 0.001 \)). There was no difference between the groups with respect to sex, year of diagnosis or Charlson/Deyo Comorbidity Score. Median follow up time was 42.8 months (IQR 29.7). A total of 483 deaths occurred in the entire cohort with a 5-year OS of 60.8%. The 5-year OS for patients undergoing resection of the primary tumor was 65.9% and 49.3% for those not undergoing resection (\( p < 0.001 \)). Conclusions: Patients with liver only metastatic midgut neuroendocrine tumors had an overall survival advantage when the primary tumor was resected. Patients with liver only metastatic midgut NET may benefit from surgical resection and should be evaluated for surgery at the time of diagnosis.

Comparison of neoadjuvant and adjuvant therapy for resectable pancreatic cancer using Markov decision modeling. First Author: MinSig Choi, Stony Brook University, Stony Brook, NY

Background: Meta-analysis of smaller studies have shown that neoadjuvant chemotherapy is more beneficial for patients with resectable pancreatic cancer than upfront surgery by comparing life expectancy (LE) and quality-adjusted life expectancy (QALE) for the entire patients (median age 63 vs. 65, \( p < 0.001 \)) and had smaller tumors (median 2.3 vs. 3.0 cm, \( p < 0.001 \)). The study results utilized literature data using several small clinical trials but no individual patient data was used and only gemzar based therapy was studied. Methods: Markov model was used to calculate the LE and QALE for adjuvant and neoadjuvant therapy models and individual patient parameters was used in the model to refine certain clinical outcome datapoints. We used 278 patients pancreatic cancer data from 2006 to 2017 from Stony Brook University and used the literature data from randomized clinical trials studying gemzar (GEM), gemzar and capecitabine (GEM+CAP) and modified FOLFIRINOX (mFOL). The median OS for each model was obtained by computer simulation. Results: Intensive adjuvant chemotherapy using mFOL had best simulation outcome with median OS (52.5 months), LE (81.5 months), and QALE (65.0 quality-adjusted life months) compared to using GEM (40.5, 66.5, and 52.9 months for median OS, LE, and QALE), GEM+CAP (16.5, 28.0 and, and 21.9 months for median OS, LE, and QALE), and 5-FU (16.5, 26.9, and 21.1 months for median OS, LE, and QALE). The neoadjuvant chemotherapy approach improved LE and QALE but not in median OS when compared to adjuvant therapy. Conclusions: Mathematical modeling confirms the improved clinical outcome for modified FOLFIRINOX in resectable pancreatic cancer. The benefit of neoadjuvant chemotherapy approach suggest further clinical trials are needed to determine the better treatment strategy for pancreatic cancer patients.

Local control following stereotactic body radiotherapy to adrenal oligometastases. First Author: Nicholas B Figura, Moffitt Cancer Center, Tampa, FL

Background: The role and associated risks of stereotactic body radiotherapy (SBRT) for adrenal metastases remain unclear. We report our single institution experience and report novel techniques to selectively deliver treatment while concurrently minimizing dose to nearby critical structures.

Methods: We retrospectively reviewed patients with evidence of metastatic adrenal disease originating from any primary histology treated with SBRT from 2013 to 2018. The primary endpoint was local control (LC). Secondary endpoints were disease-free survival (DFS), overall survival (OS), and treatment-related toxicity. LC, DFS, and OS were calculated with Kaplan-Meier analysis. Univariable and multivariable analysis were performed with long-rank and Cox proportional analysis. Results: A total of 45 adrenal metastases in 41 patients received SBRT. The median age was 67 years (range 40-80). The most common primary histologies were non-small cell lung cancer (51%), renal cell carcinoma (24%), and small cell lung cancer (10%). The median gross internal and planned target volumes were 21.23cc (range, 3.1-124.7cc) and 31.68cc (range, 5.2-175.9cc), respectively. The median dose administered was 50 Gy with 30 (67%) lesions receiving \( \geq 50 \) Gy and 14 (31%) receiving 60 Gy. Twenty-six (58%) lesions were selectively dose-painted. Of the 42 simulations, 26 (62%) were treated supine, 5 (12%) prone, and 11 (26%) in the left lateral decubitus position. At a median follow-up of 10.5 months, there were 3 local recurrences (LR). 12-month LC rate was 96% with a median LC of 35 months. All three LR were in the metachronous, oligometastatic patients. One patient developed a hypertensive crisis which required intravenous antihypertensives. Conclusions: Adrenal SBRT for oligometastatic disease is a reasonable, noninvasive option with excellent LC and minimal toxicity. Lesions in close proximity to radiosensitive organs may benefit from techniques, such as dynamic patient positioning and selective dose-painting, for further dose-escalation to optimize LC rates while simultaneously limiting associated toxicity risks.

Small bowel adenocarcinoma: A single center experience. First Author: Lindsay Marie Hannan, University of Washington/Fred Hutchinson Cancer Center, Seattle, WA

Background: Small bowel adenocarcinoma (SBA) represents only 2% of GI malignancies. There is limited data to guide clinical decisions, largely extrapolated from colorectal cancers (CRC). We evaluated treatment strategies and outcomes in patients with early (pts) with early and advanced SBA. Methods: We identified 56 pts with SBA diagnosed between 1/2005 - 1/2018 and treated at our institution. Demographics, pathological features, treatments, and molecular data were abstracted via medical record review. Data was analyzed with SAS statistical software. Results: Median age was 61, 57% male, site: duodenum (D 37.5%), duodenal ampulla (A 17.9%), jejunum (J 19 mos), ileum (12.5 %), unknown (12.5%). Predisposing conditions were: IBD (6), Lynch (2), and Peutz-Jeghers syndromes (1). Stage (stg) at diagnosis was (5%), II (20%), III (34%) and IV (41%). Primary tumor resection occurred in 33 pts: 21 received adjuvant chemotherapy, mostly FOLFOX; 17 developed metastatic disease. Treatment for metastatic SBA (n = 40) included 5FU-based chemotherapy without or with anti-VEGF (n = 18), or anti-EGFR therapies (n = 9). Median lines of therapy was 2 (range 1-7). For pts with stg III SBA, median DFS/OS was 21/38 mos. For stg IV pts, OS was 19.8 mos; 18/35/8/14 mos for D, A, J and I, respectively. Molecular biomarkers with targeted (28) or next generation sequencing (10) were available for 28 metastatic SBA pts: KRAS MUT (8), TP53 MUT (5), ERBB2 MUT (2), MSI-H (2), ERBB2, CCNE1 amplification (1 each), and NRAS, BRAF, CDKN2A, ERBB2, ATM, PIK3CA MUT (1 each). OS was 20 vs 19 mos for pts with KRAS MUT vs WT or stg IV SBA, respectively. Among 16 pts with KRAS WT SBA, OS for those treated (9) or not (7) with anti-EGFR antibodies was 25 mos vs 21 mos. One pt with KRAS WT SBA, ERBB2 amplification/ ERBB2 V777L activating mutation is alive 5yrs+ from stg IV diagnosis on anti-EGFR plus chemotherapy (best response was 4 mos SD with trastuzumab/ pertuzumab). Conclusions: This retrospective study demonstrates heterogeneity among SBA, overall inferior outcomes compared to CRC pts, but emphasizes genomic alterations which could be exploited therapeutically. Randomized studies for KRAS WT SBA pts should test the benefit from anti-EGFR targeted therapies in this rare tumor type.
Neoadjuvant therapy for body and tail pancreatic adenocarcinoma: Propensity score matched analysis using the National Cancer Database. First Author: Tommy Ivanics, Henry Ford Hospital, Department of Surgery, Detroit, MI

Background: The role of neoadjuvant systemic therapy in the management of body and tail pancreatic ductal adenocarcinoma (PDAC) is unknown. The aim of our study was to investigate the outcomes associated with neoadjuvant therapy for early stage body and tail PDAC. Methods: The National Cancer Database (NCDB) was queried for stage I and II body and tail PDAC between 2006-2014. Groups were defined according to treatment sequencing strategies into an upfront resection group (UR), resection followed by adjuvant therapy (R+AT), neoadjuvant therapy followed by resection (NAT+R), and neoadjuvant therapy followed by resection and adjuvant therapy (NAT+R+AT). Patients who underwent neoadjuvant therapy followed by resection were matched by propensity score with patients who underwent upfront resection. Overall survival was compared using Kaplan-Meier method and Cox proportional hazards regression model. Results: 441 patients received NAT+R+AT with or without AT compared to 1323 patients who underwent UR with or without AT. NAT+R had lower pathologic stage, lymph node positivity and a higher rate of margin negative resections compared to the matched UR cohort. In the propensity matched cohort, the median survival (MS) was higher in the neoadjuvant (NAT+R+NAT+R+AT) group compared to the upfront resection (UR+R+AT) group (26.6 vs. 22.9 mos; p < 0.001). When further stratified by treatment sequencing the MS was longer in a NAT+R+AT cohort compared to the R+AT group (36.0 vs. 25.3 mos; p = 0.005) (Table). However, there was no difference in MS between R+AT and NAT+R cohorts. On multivariable analysis, receipt of NAT represented an independent factor for survival (NAT+R+AT HR 0.41, 95% CI 0.32-0.54; NAT+R HR, 0.53, 95% CI 0.44-0.64; R+AT HR 0.61, 95% CI 0.53-0.70). Conclusions: There appears to be a survival benefit with neoadjuvant systemic therapy in patients with early stage body and tail PDAC. A systematic perioperative treatment sequencing approach (NAT+R+AT) appears to have the greatest survival benefit.

<table>
<thead>
<tr>
<th>Treatment sequence</th>
<th>Median Survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UR</td>
<td>15.4</td>
</tr>
<tr>
<td>R+AT</td>
<td>25.5</td>
</tr>
<tr>
<td>NAT+R</td>
<td>26.9</td>
</tr>
<tr>
<td>NAT+R+AT</td>
<td>36.0</td>
</tr>
</tbody>
</table>

Median survival of different treatment sequencing strategies for stage I and II body and tail PDAC

Combined radiotherapy and transarterial chemoembolization as a first-line treatment for hepatocellular carcinoma with macroscopic vascular invasion. First Author: Sang MIN Yoon, Department of Radiation Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Republic of (South)

Background: To evaluate the long-term clinical outcome of respiratory-gated conformal radiotherapy in combination with transarterial chemoembolization (TACE) as a first-line treatment for advanced hepatocellular carcinoma (HCC) with macroscopic vascular invasion (MVI). Methods: This was a retrospective analysis of patients who were diagnosed with HCC showing MVI who received TACE plus radiotherapy as their initial treatment between 2010 and 2015. Inclusion criteria were Child-Pugh A or B hepatic function and Eastern Cooperative Oncology Group performance score 0-2. None of the patients had a previous history of radiotherapy to the liver or extrahepatic metastasis. Results: A total of 467 patients were included in the study. Patients were between 34 and 87 years of age, and 89.3% were male. The median maximum tumor diameter was 9.8 cm and 297 patients (63.6%) had Child-Pugh A hepatic function. Two hundred and eighty (60%) patients had multiple tumors; 45% of tumors showed bilobar involvement. Unilateral portal vein invasion was observed in 206 (44.3%) patients and main/bifurcal portal vein multiple vascular invasion were observed in 261 (55.9%) patients. The median overall survival was 12.5 months, with one- and two-year survival rates of 52% and 28%, respectively. Larger tumor size, multiple tumors, infiltrative tumor type, Child-Pugh class B, and alpha-fetoprotein ≥ 200 ng/ml were independent predictors of overall survival. Grade ≥ 3 hepatic and gastrointestinal toxicities were observed in 3 (0.6%) and 5 (1.1%) patients, respectively. Conclusions: Radiotherapy combined with TACE as an initial treatment was a safe and effective modality for advanced HCC patients with MVI and could be considered as first-line therapy in patients with liver-confined HCC showing MVI.

Impact of neoadjuvant radiation on survival in patients with pancreatic cancer undergoing neoadjuvant chemotherapy followed by pancreatectomy. First Author: Francis Igor Macedo, Sylvester Comprehensive Cancer Center, University of Miami School of Medicine, Miami, FL

Background: Pancreatic adenocarcinoma (PDAC) carries a dismal prognosis. Neoadjuvant chemoradiation therapy (NACR) has been introduced to enhance the outcomes of patients with borderline resectable and locally advanced PDAC, however the role of radiation therapy remains largely unknown. Methods: The National Cancer Database (NCDB) was queried for patients with stage I-II PDAC who underwent surgical resection from 2004 to 2014. Patients undergoing NACR were compared to those undergoing neoadjuvant chemotherapy (NAC) alone. The association between clinical characteristics and overall survival (OS) was assessed using the Kaplan-Meier method and multivariable Cox regression model. Results: Of 3,133 patients, 2,351 (75%) patients underwent NACR and 782 (25%) NAC alone. Most patients were Caucasians (84%), treated at academic institutions (67%) and underwent chemotherapy (NAC) alone. The association between clinical characteristics and overall survival (OS) was similar between 2 groups (NACR vs. NAC: 15% vs. 17%, p = 0.545; 25.7 months (95% CI 24.4-26.7) vs. 25.1 months (95% CI: 23.9-27.5), and 20% vs. 22%, p = 0.616, respectively, Figure 1). Subgroup analysis of high-risk features (R1/R2 and N1) also showed no difference in survival outcomes. Neoadjuvant radiation was not an independent predictor associated with OS, whereas advanced age, R1/R2, T3/T4, NI, and poorly differentiated histology were independent negative prognostic factors. Conclusions: NACR is associated with lower rates of resection and OS compared to NAC alone. The role of radiotherapy in PDAC continues to evolve, however no convincing data is currently available to advocate the widespread use of neoadjuvant radiotherapy in the advanced setting. The few prospective clinical trials is still warranted to confirm these findings.
Neoadjuvant multimodal treatment of borderline resectable (BRPC) and locally advanced unresectable pancreatic cancer (LAPC) in Mexico. First Author: Vanessa Rosas Camargo, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico, DF, Mexico

Background: Pancreatic cancer remains a highly lethal disease. There is no consensus on treatment sequences and chemotherapeutic (CT) regimen in BRPC and LAPC. Our aim was to describe the multimodal treatment and outcomes in our population. Methods: We retrospectively reviewed medical records of patients (pts) with BRPC/LAPC and histological diagnosis of adenocarcinoma evaluated at Instituto Nacional de Ciencias Médicas y Nutrición from January 2011-December 2016. Clinical and pathological variables at diagnosis and treatment were recorded. Overall survival (OS) was estimated using Kaplan-Meier method and compared by Log-rank test. Results: 69 pts were evaluated, 39% (27) did not receive treatment. We analyze 42 treated pts. BRPC 33%/LAPC 67%. Median age was 58.8±7, 54.8% were female. Symptoms at diagnosis: 79% abdominal pain, 76% weight loss, 55% jaundice. ECOG performance status (PS): 0 (17%), 1 (69%) and 2 (14%). Main location was pancreatic head (76%). Median laboratory values: total bilirubin 1.04 mg/dL. (0.2-25), albumin 4.1 g/dL. (2.4-5.1), CA 19.9 182.8 U/mL. (0.8-4028). Local-rotomy at diagnosis was performed in 21%. All pts received induction CT (iCT). FOLFIRINOX was the most common regimen (37%), followed by FOLFOX4 (34%). The best overall response with iCT was stable disease (62%), progressive disease was observed in 24%, iCT followed by chemoradiation (CRT) could be delivered to 48% (20/42). Capectabine-based CRT was preferred (94%). Six pts (14%) underwent surgical resection after multimodal treatment (36% BRPC, 3.5% LAPC), 5 pts achieved R0 resection. The resection rate with single-agent iCT was 0% vs. 20% with combination iCT. Median OS was 15.6 months (m): 14.4 m for BRPC and 15.5 m for LAPC. Median OS according iCT: gemcitabine 7.8 m, fluorouracil 13.7 m, FOLFOX 15.5 m and FOLFIRINOX 24.6 m. Univariate analysis identified ECOG PS (0 vs 1, P = 0.014) and age (< 59 vs > 59, P = 0.0002) as strong predictors associated with OS. Conclusions: Early administration of combination CT followed by CRT and/or surgical resection in selected pts improves oncological outcomes in pts with BRPC/LAPC. In pts with good PS, iCT with FOLFIRINOX is the preferred regimen given best results.

Retrospective, cohort study evaluating empiric dose-reduced nab-paclitaxel with gemcitabine in metastatic pancreatic adenocarcinoma: A single institution experience. First Author: Olugbenga Olanrele Olowokure, University of Cincinnati, Cincinnati, OH

Background: The phase III MPACT trial was conducted to assess OS in patients with metastatic pancreatic adenocarcinoma (mPAC) receiving nab-paclitaxel (nab-P) 125 mg/m² + gemcitabine (G) 1000 mg/m² on days 1, 8, and 15 every 28 days. Due to reported increased incidence of adverse events (AEs) at this dose, practice at UC Health outside the setting of a clinical trial is to empirically dose reduce (EDR) nab-P to 100 mg/m². This study is a review of the EDR of EDR nab-P in G patients with mPAC compared to MPACT data. Methods: This prospective, single-center, cohort study included patients ≥18 years of age with mPAC (by biopsy) receiving first line therapy with EDR nab-P + G from January 1, 2012 to March 31, 2017. Primary outcome is OS. Secondary outcomes include PFS, CA19-9 percent reduction, incidence of grade ≥3 AEs. Results: See Table. Conclusions: In patients with mPAC, EDR nab-P + G demonstrated a median OS of 10 months and PFS of 5 months. 53% of patients had a 20% CA19-9 reduction from baseline with a 1 year OS rate of 45%. The incidence of grade ≥3 AEs appeared to be acceptable.

<table>
<thead>
<tr>
<th>Variable</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Closest margin distance</td>
<td>0.99 (0.96-1.01)</td>
</tr>
<tr>
<td>Preoperative biopsy</td>
<td>0.68 (0.44-1.06)</td>
</tr>
<tr>
<td>Male gender</td>
<td>1.40 (0.72-2.79)</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>1.32 (0.83-2.12)</td>
</tr>
<tr>
<td>Perineural invasion</td>
<td>0.78 (0.50-1.22)</td>
</tr>
<tr>
<td>Age</td>
<td>1.03 (1.01-1.05)</td>
</tr>
<tr>
<td>Tumor size</td>
<td>1.02 (1.00-1.03)</td>
</tr>
<tr>
<td>Lymph node positive</td>
<td>1.87 (1.21-2.90)</td>
</tr>
</tbody>
</table>

Resection margin distance in extrahepatic cholangiocarcinoma: How much is enough? First Author: Amir A. Rahmen-Azar, University of Wisconsin Hospital, Madison, WI

Background: Surgical resection is required for curative treatment of patients with extra-hepatic cholangiocarcinoma (EH-CCA). The objective of this study was to determine if the distance of the margin was associated with outcome. Methods: Patients who underwent curative-intent resection for EH-CCA between 2000 and 2015 at 10 hepatobiliary centers across the U.S. were evaluated using prospectively collected data. Cox proportional hazard model was utilized to evaluate the influence of the extent of the margin on outcome. Results: 538 patients with EH-CCA who underwent curative-intent resection were included: 383 (71%) undergoing RO resection, 153 (28%) undergoing RI resection, and 2 with R2 resection. A negative surgical margin (RO) was associated with improved recurrence-free (RFS) and overall survival (OS) (RFS: 10.5% vs. 3.6% (R1) and OS: 25.8% vs. 9.3% (R1)). Subsequently, further analysis on 161 patients with complete data on distance of resection margin, all undergoing RO resection, was performed to assess the impact of margin on outcome. On multi-variable analysis, the resection margin distance, analyzed as a continuous variable, was not associated with either improved RFS (RR 1.00, 95% CI 0.96-1.05; p 0.71) or OS (RR 0.99, 95% CI 0.96-1.01; p 0.49). Increasing age, increased tumor size, and LN metastasis were identified as independent predictors of OS; while RFS were mainly dependent on tumor size and LN metastasis (Table). Conclusions: Achieving RO resection is acceptable for EH-CCA tumors, and obtaining additional margin does not confer a benefit on overall survival. Increasing age, tumor size, and LN metastasis are independent predictors of RFS and OS, but increased margin width is not associated with improvement in either. Multivariable analysis of factors affecting OS of patients with extra-hepatic CCA who underwent surgical resection, with significant factors noted in bold.

Conclusions: The results of this study suggest that race/ethnicity influences the likelihood of receiving care at a low-volume center for any other tumor types. Racial/ethnic disparities in the use of high-volume centers for hepatobiliary and pancreatic cancer surgery. First Author: Susanna W de Geus, Boston Medical Center, Boston, MA

Background: The impact of hospital volume on the outcomes of cancer surgery has been well established. The present studies investigate how race/ethnicity influences the utilization of high-volume centers for hepatobiliary and pancreatic cancer surgery. Methods: Patients that underwent surgical resection for extrahepatic cholangiocarcinoma (HCCA), inoperable cholangiocarcinoma (ICC), extrahepatic cholangiocarcinoma (ECC), ampullary adenocarcinoma (AC), or pancreatic ductal adenocarcinoma (PDAC) between 2006 and 2015 were identified from the National Cancer Data Base. Hospitals were divided into low- and high-volume centers based on the number of cancer surgeries per year. Multivariable logistic regression analyses predicting receipt of care at a low-volume center based on age, sex, race/ethnicity, comorbidities, insurance, income, travel distance, geographic location, urban/metro location, and tumor stage were performed. All analyses were performed separately by tumor type. Results: 8,962 patients with HCC, 2,199 with ICC, 3,973 with ECC, 5,125 with AC, and 25,231 with PDAC were identified. Non-Hispanic black patients were more likely to undergo resection for AC (vs. non-Hispanic white: AOR, 1.326; p = 0.0001) at a low-volume centers. Hispanic patients more often underwent surgery for ECC (vs. non-Hispanic white: AOR, 1.731; p < 0.0001) or PDAC (vs. non-Hispanic white: 2.032; p < 0.0001) cancer at a low-volume center. Patients of Asian descent were significantly less often treated for HCC at a low-volume center (vs. non-Hispanic white: AOR, 0.664; p < 0.0001) compared to non-Hispanic whites. Non-Hispanic black, Hispanic, or Asian race/ethnicity did not impact the likelihood of receiving care at a low-volume center for any other tumor types. To determine if the likelihood of receiving care at a low-volume center for any other tumor types. Conclusions: The results of this study suggest that race/ethnicity influences the likelihood of receiving care at a high-volume cancer center, even after controlling for other barriers to access to care, including insurance status, income and travel distance.
TPS459

Trials in Progress Poster Session (Board #P18), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

GA CPI 613: A single arm, open-label phase I study of CPI-613 in combination with gemcitabine and nab-paclitaxel for patients with locally advanced or metastatic pancreatic cancer. First Author: Angela Tatiana Alistar, Atlantic Health System, Morristown, NJ

Background: Pancreatic cancer is the third leading cause of cancer death in the USA. There are no effective treatments for first line metastatic pancreatic cancer are FOLFIRINOX and gemcitabine plus nab-paclitaxel, which provide a median overall survival of 11-1months and 8-5 months with moderate toxicity. Safer and more effective treatments are needed. The glycolytic and mitochon- drial metabolism are aberrant in pancreatic cancer and contribute to cancer cell resistance to chemotherapy. Inhibition of glutamin metabolism can potentially syner- gize with therapies that increase intracellular reactive oxygen species such as Nab-Paclitaxel. CPI- 613 is a novel antimitochondrial developed by Rafael Pharmaceuticals that showed preclinical activity in pancreatic cancer cell lines as well as promising clinical activity in combination with modified FOLFIRINOX in patients with stage IV pancreatic cancer. Preclinical data suggests possible synergy of CPI-613 with nab-paclitaxel. Methods: This is a single arm, open-label, nonblinded phase I study of CPI-613 in combination with gemcitabine and nab-paclitaxel in patients with locally advanced or metastatic pancreatic cancer. Key eligibility criteria include: histologically or cytologically docu- mented and measurable locally advanced or metastatic pancreatic adenocarci-noma, ECOG performance status 0-2, first line treatment for both locally advanced or metastatic, CPI-613 will be infused intravenously with 10x24 dose of 500 mg/m2 followed by 1125 mg/m2 nab-paclitaxel and 1,000 mg/m2 gemcitabine on day 1, 8, 15 of a 28-day cycle. The study is comprised of a two-stage dose-escalation schema to evaluate the MTD of CPI-613. At least six months of treatment is planned for patients who have a response. Primary endpoints of the study are MTD of CPI 613 when combined with gemcitabine and nab-paclitaxel and secondary endpoints of the study are related adverse events, CR and PR. This study was initiated in February 2018 at Atlantic Health System and within first six months of that, 22 patients have been enrolled. Clinical trial information: NCT03435289.

TPS460

Trials in Progress Poster Session (Board #P19), Fri, 11:30 AM-10:00 PM and 5:30 PM-6:30 PM

Precision-Panc Master Protocol: Personalizing treatment for pancreatic cancer ISRCTN14879538—Part of Precision-Panc United Kingdom. First Author: Juan W. Vallee, The Christie NHS Foundation Trust, Manchester, United Kingdom

Background: A major challenge of lower incidence cancer types is that to make significant advances a network approach is required to coordinate research, generate greater clinical capacity and recruit sufficient patients. This is particularly the case for pancreatic cancer (PC). To address this, we established Precision-Panc, a synergistic and dynamic platform aiming “disease discovery”, “translational research” and “clinical development”. Methods: Central to the clinical development is the Precision-Panc Master Protocol, a multi-centre “portal” protocol recruiting patients with known or suspected PC, to enable enrolment into PRIMUS (Pancreatic cancerR Indivudalised Multi-arm Umbrella Study), examining different treatment regimens and/or biomarker development. Eligible patients are identified prior to the diagnostic biopsy to obtain Stage 1 (Screening) Consent for extra tissue to be taken in the same biopsy setting. Patients who already have a diagnosis are asked to provide additional research biopsy. Once the PC diagnosis is made, Stage 2 (Registration) Consent is obtained for molecular profiling at the central reference laboratory using Precision-Panc NGS Diagnostic (bespoke clinical grade assay), including germline testing of 12 PC predisposition genes. The results may inform eligibility for a PRIMUS study. There is no sample size calculation due to the nature of the Master Protocol. However, individual PRIMUS studies will be appropriately powered according to their study design and primary endpoint. Results: Adults aged >16 years with either a hypodense pancreatic mass highly suspicious of PC (+/- distant metastases) or histologically confirmed PC and its variants, willing and able to undergo tumour biopsy to obtain sufficient tissue for molecular profiling; deemed suitable to receive chemotherapy and/or radiotherapy and/or surgery pending stage of disease; must give both Stage 1 and 2 informed consent. Conclusion: The study opened on 28 Dec 2017; 78 patients have been screened for Precision-Panc, 43 of whom have gone on to be registered and 19 have then been randomised to the PRIMUS-001 study (first- line metastatic). Clinical trial information: ISRCTN14879538.

TPS461

Trials in Progress Poster Session (Board #P20), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Phase 2 trial of durvalumab and radiation revaccination in patients with metastatic adenocarcinoma of the pancreas who have progressed through first-line chemotherapy. First Author: Michael David Chuong, Miami Cancer Institute, Miami, FL

Background: Emerging data suggest that immunotherapy combined with radiation therapy (RT) can lead to robust anti-tumor immune responses within many tumor types. While not highly immunogenic, pancreatic cancer has been shown to respond to immunotherapy especially when combined with RT. Our research hypothesis is that the combination of RT and immunotherapy (durvalumab) is well tolerated and stimulates a clinically significant pancreas- cancer specific immune response. Methods: Metastatic pancreatic cancer patients who have progressed through first-line chemotherapy will receive durvalumab every 4 weeks and will concurrently receive 24 Gy in 3 daily fractions to one pancreatic cancer lesion during week 3 followed by 24 Gy in 3 daily fractions to a second lesion during week 5. Durvalumab will continue until disease progression. Secondary endpoints include overall response rate, overall survival, duration of response, safety and tolerability, and impact on quality of life. Current evidence of clinically significant corneal or retinal disorder; history of current evidence of calcium and phosphate homeostasis disorder or systemic mineral imbalance. Dysregulation of fibroblast growth factor receptor (FGFR) signaling by FGFR genetic alterations is implicated in many cancers, including cholangiocarcinoma (CCA). FGFR translocations with fusion partners occur in <10% to 20% of intrahepatic CCA tumors. Pemigatinib is a selective oral inhibitor of FGFR1, 2, 3. Preliminary data from the ongoing phase 2 study show efficacy and tolerable safety in patients (pts) with CCA with FGFR2 translocations. We present the design for a phase 3, open-label, randomized trial investigating pemigatinib (in combination or as a single agent) during chemotherapy in the first-line treatment of pts with advanced/metastatic or unresectable CCA with FGFR2 rearrangement. Methods: Eligible pts (target, N = 432) are ≥ 18 years (≥ 20 years for Japanese pts) and have ECOG performance status ≤ 1 and histologically confirmed advanced (locally advan- ced, metastatic, or recurrent) CCA with a documented FGFR2 rearrangement. Key exclusion criteria include prior systemic therapy, excluding adjuvant/neoadjuvant treatment completed ≥ 6 months before enrollment; current evidence of clinically significant corneal or retinal disorder; history of calcium and phosphate homeostasis disorder or systemic mineral imbalance with ectopic calcification of soft tissues; and known, untreated CNS metas- tases or history of uncontrolled seizures. Pts are randomized 1:1 and stratified by geographic region and tumor burden into 2 treatment groups: pemigatinib starting dose 13.5 mg once daily continuously on a 3-week cycle; or gemci- tabine (1000 mg/m2) and cisplatin (25 mg/m2) administered intravenously on days 1 and 8 of every 3-week cycle for up to 8 cycles until disease progression or unacceptable toxicity. Crossover to pemigatinib may be allowed once progressive disease is confirmed. The primary endpoint is progression-free survival (based on independent central review using RECIST v1.1). Secondary endpoints include overall response rate, overall survival, duration of response, disease control rate, safety and tolerability, and impact on quality of life. Clinical trial information: NCT03656536.

TPS462

Trials in Progress Poster Session (Board #Q01), Fri, 11:30 AM-10:00 PM and 5:30 PM-6:30 PM

Trial design for a phase 3 study evaluating pemigatinib (INCB054828) versus gemcitabine plus cisplatin chemotherapy in first-line treatment of patients with cholangiocarcinoma with FGFR2 rearrangement. First Author: Tanios S. Bekaii-Saab, Mayo Clinic, Phoenix, AZ

Background: Dysregulation of fibroblast growth factor receptor (FGFR) signaling by FGFR genetic alterations is implicated in many cancers, including cholangiocarcinoma (CCA). FGFR2 translocations with fusion partners occur in <10% to 20% of intrahepatic CCA tumors. Pemigatinib is a selective oral inhibitor of FGFR1-2, 3. Preliminary data from the ongoing phase 2 study show efficacy and tolerable safety in patients (pts) with CCA with FGFR2 translocations. We present the design for a phase 3, open-label, randomized trial investigating pemigatinib (in combination or as a single agent) during chemotherapy in the first-line treatment of pts with advanced/metastatic or unresectable CCA with FGFR2 rearrangement. Methods: Eligible pts (target, N = 432) are ≥ 18 years (≥ 20 years for Japanese pts) and have ECOG performance status ≤ 1 and histologically confirmed advanced (locally advan- ced, metastatic, or recurrent) CCA with a documented FGFR2 rearrangement. Key exclusion criteria include prior systemic therapy, excluding adjuvant/neoadjuvant treatment completed ≥ 6 months before enrollment; current evidence of clinically significant corneal or retinal disorder; history of calcium and phosphate homeostasis disorder or systemic mineral imbalance with ectopic calcification of soft tissues; and known, untreated CNS metas- tases or history of uncontrolled seizures. Pts are randomized 1:1 and stratified by geographic region and tumor burden into 2 treatment groups: pemigatinib starting dose 13.5 mg once daily continuously on a 3-week cycle; or gemci- tabine (1000 mg/m2) and cisplatin (25 mg/m2) administered intravenously on days 1 and 8 of every 3-week cycle for up to 8 cycles until disease progression or unacceptable toxicity. Crossover to pemigatinib may be allowed once progressive disease is confirmed. The primary endpoint is progression-free survival (based on independent central review using RECIST v1.1). Secondary endpoints include overall response rate, overall survival, duration of response, disease control rate, safety and tolerability, and impact on quality of life. Clinical trial information: NCT03656536.
Cancers of the Pancreas, Small Bowel, and Hepatobiliary Tract

**TPS463** Trials in Progress Poster Session (Board #02), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Nant cancer vaccine an orchestration of immunogenic cell death by overhauling immune suppression and activating NK and T cell therapy in patients with third line or greater metastatic pancreatic cancer. First Author: Tara Elisabeth Seery, Chan Soon Shiong Institute for Medicine, Laguna Hills, CA

**Background:** Pancreatic cancer has multiple mechanisms to prevent immune recognition that lead to the creation of an immunogenic tumor microenvironment. We hypothesize that effective and sustained response against tumors requires a coordinated approach that: 1) reverses the immunosuppressive tumor microenvironment, 2) induces immunogenic tumor cell death and 3) reengages NK and T-cell tumor response against a 4. cascade of tumor antigens. To test this hypothesis, we developed the NANT Cancer Vaccine (NCV), which combines metronomic low-dose chemotherapy, radiotherapy, and multifaceted immunotherapy. In proof-of-concept trials, the NCV was tested in 10 patients with 3rd-5th or greater pancreatic cancer. These trials showed that the NCV could safely be administered in an outpatient setting, with AE’s that were manageable by dose-reduction, and preliminary survival results that exceed the standard of care in this heavily-treated population. We believe these results warrant further research, and this abstract describes our newly-designed trial. Methods: A phase Ib, single-arm, open-label trial of the NANT Cancer Vaccine in patients with recurrent metastatic pancreatic cancer has been initiated. Treatment will occur in 3-week cycles of low-dose chemotherapy (aldorourubicin, cyclophosphamide, oxaliplatin, nab-paclitaxel, 5-FU/L), antiangiogenic therapy (bevacizumab), SBRT, engineered allogeneic high affinity CD6 NK-92 cells (nAHC), IL-15RαFc (N-803), adenoviral vector-based CEA vaccine (Ad-CEA), yeast vector-based RAS vaccine (Ye-RAS), and an IgG1 (bL1) inhibitor, avolumab. The primary endpoint is treatment-related adverse events. Secondary endpoints include ORR, DCR, PFS, and OS. A maximum of 24 patients will be enrolled. Clinical trial information: NCT03586869.

**TPS464** Trials in Progress Poster Session (Board #03), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Phase II multicenter pilot study of safety, efficacy, and immune cell profiling in advanced hepatocellular carcinoma (HCC) on combination of sorafenib (SOR) plus nivolumab (NIVO). First Author: Bridget Keenan, University of California San Francisco, San Francisco, CA

**Background:** The antiangiogenic tyrosine kinase inhibitor (TKI) SOR prolongs survival in advanced HCC, but responses occur in fewer than 5% of patients (pts) and median progression-free survival (PFS) is less than 6 months. Immune checkpoint inhibition (CPI) with the PD-1 inhibitor, NIVO, achieved an overall response rate (ORR) of approximately 20% in sorafenib-naive pts enrolled on CheckMate 040 trial. The most recent phase II study in a current clinical studies, TKI can inhibit regulatory T cells and myeloid derived suppressor cells, immune cell subsets which may contribute to CPI resistance. CD8+ T cells in sorafenib-resistant tumors are characterized by PD-1 expression, providing rationale for a combined approach. The combination of TKI or the anti-angiogenic bevacizumab with CPI improves anti-tumor activity in HCC mouse models and in preliminary clinical studies. This study will examine the safety, maximum tolerated dose (MTD), and ORR of the combination of SOR plus NIVO in advanced HCC pts, along with correlative analyses of tumor and circulating immune cells. Methods: Eligible pts must have Child-Pugh A liver function and advanced HCC, without prior systemic therapy and measurable by RECIST 1.1. In Part 1 (3+3 dose escalation), SOR dose will be 400 mg QD or BID plus NIVO 240 mg IV Q2 weeks. In Part 2, Arm 1, pts will start NIVO Cycle 1, Day 1 (Q2D), with addition of SOR at MTD on CIDIS; in Part 2, Arm 2, SOR is given at MTD at CID with addition of NIVO of CIDIS. Primary endpoints are MTD of SOR (Part 1) and ORR by RECIST 1.1 with H. 7.5% vs. H. 25% (Part 2). For expected sample size of 24 evaluable pts in Part 2, the power is 83% with 1-sided alpha > 5% to determine ORR > 25% by Chi-square tests. Secondary endpoints are safety, duration of response, PFS, and overall survival. Exploratory endpoints include peripheral and tumor immune cell profiling, PD-L1 expression, and alpha-fetoprotein (AFP) response. An interim safety analysis will be performed after 50% of planned patients in Part 2. Ongoing patients will continue and at the end of Part 2 will allow for investigation of the tumor microenvironment on SOR, NIVO, and combination. Clinical trial information: NCT03439891.

**TPS465** Trials in Progress Poster Session (Board #04), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

A randomized phase II study of cabiraluzumab (cabira) + nivolumab (nivo) ± chemotherapy (chemo) in advanced pancreatic ductal adenocarcinoma (PDAC). First Author: Andrea Wang-Gillam, Washington University Siteman Cancer Center, St. Louis, MO

**Background:** Treatment options for PDAC are limited; thus, new therapies that can improve outcomes and extend survival are needed. PDAC is associated with high infiltration by tumor-associated macrophages (TAMs) that inhibit antitumor T-cell activity. Blocking colony stimulating factor (CSF-1R) signaling—which supports the recruitment, differentiation, and maintenance of immunosuppressive macrophages in tumors—may lead to depletion of TAMs and upregulation of T-cell checkpoints. Cabira, a humanized IgG4 monoclonal antibody, binds to CSF-1R and blocks its signaling, a key determinant of TAM activation and survival. By reducing TAMs and promoting a proinflammatory microenvironment, cabira may stimulate T-cell responses, thereby sensitizing PDAC to therapy with nivo (anti-PD-1). In a phase Ib/2 study cabira + nivo was tolerable and showed evidence of on-target treatment modulation and durable clinical benefit in heavily pretreated patients (pts) with advanced PDAC (Wainberg et al. J Immunother Cancer. 2017 abst O42; Carleton et al. J Clin Oncol. 2018 abst 3020). Here we describe a randomized, open-label, phase 2 study evaluating the safety and efficacy of cabira + nivo ± chemo in advanced PDAC. Methods: Pts aged ≥18 y with locally advanced/metastatic PDAC that progressed on/after first-line chemo (gemcitabine [gem] or 5-Fu/biphasic gem [5-FU]) will be enrolled. Pts with active/suspected autoimmune disease, uncontrolled significant cardiovascular disease, or prior exposure to select immune cell-modulating antibodies are not eligible. Depending on prior chemo received, pts will be randomized to 1 of 4 arms (n=40 each): cabira + nivo; cabira + nivo + gem/nab-paclitaxel; cabira + nivo + oxaplatin/5-FU/luxovuricin; or investigator’s choice of standard-of-care chemo. Endpoints include median progression-free survival (primary), overall survival rate, objective response rate, median duration of response, pharmacokinetics, and safety. In a completed secondary safety cohort, 12 pts were treated with cabira + nivo + chemo monitored for 4 wk; competitive enrollment is open, with 32 pts enrolled. (NCT0333626, NCT02526007) Clinical trial information: NCT0333626.

**TPS466** Trials in Progress Poster Session (Board #05), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Celiac plexus radiosurgery for pain management in advanced cancer patients: An international phase II trial. First Author: Yaacov Richard Lawrence, Sheba Medical Center, Ramat Gan, Israel

**Background:** Many cancer patients, especially those with pancreatic cancer, suffer from severe back/epigastric pain. Contemporary approaches (opioids, celiac blocks, systemic chemotherapy) are often inadequate. This clinical trial investigates the benefits of a high-dose pain modulation (radiosurgery) which is focused on the retroperitoneal celiac plexus nerve bundle. Preliminary results from a single institution pilot trial NCT02356406 are promising: pain relief is substantial and side effects minimal. The main aim of the trial is to establish safety/efficacy in the setting of an international multicenter study. Exploratory analyses will examine the relationship between pain reduction and subjects’ quality-of-life, functionality, and caregiver burden.

**Methods:** Eligibility criteria include a diagnosis of metastatic/unresectable malignancy, uncontrolled pain defined as ≥ 5 on 10-point BPI-SF scale despite analgesic use, typical retroperitoneal pain syndrome, prognosis ≥ 8 weeks, ECOG 0-2, anatomical involvement of the celiac plexus (e.g. any pancreatic cancer, or any other cancer involving the celiac trunk). Exclusion criteria include previous upper abdo. radiation. The intervention consists of a single 25 Gy radiation fraction delivered to the celiac plexus, using anterolateral aspect of the aorta from the 12th thoracic to 2nd lumbar vertebral body as a surrogate structure. The primary tumour may be irradiated at physicians’ discretion. Dose-painting technique limits dose to organs at risk. Pain intensity will be measured using Brief Pain Inventory Short Form (BPI-SF), and quality of life with FACT-Hep. The primary endpoint is complete or partial pain response, defined as a decrease between the score immediately before treatment and 3 weeks post-treatment. A change of two or more on the BPI 10-point pain scale is defined as clinically significant. Secondary endpoints include other BPI pain endpoints, pain at 6 weeks, analgesic use, toxicity (CTCAE v4.03), quality of life and functional measures. Analgesia is not restricted. Expected accrual is 114 patients over three years. Supported by Gateway for Cancer Research, additional support from Israel Cancer Association. Clinical trial information: NCT03323489.
TPS467
Trials in Progress Poster Session (Board #06), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
MORPHEUS: A phase Ib/II study platform evaluating the safety and clinical efficacy of cancer immunotherapy (CIT)-based combinations in gastrointestinal (GI) cancers. First Author: Jayesh Desai, Peter MacCallum Cancer Centre and Royal Melbourne Hospital, Melbourne, Australia

Background: CIT has significant survival benefits across multiple tumor types, but durable response is experienced by a small subset of patients. To extend clinical benefit to more pts, efficacious CIT combinations (combos) targeting multiple cancer immune escape mechanisms need to be identified. The MORPHEUS platform includes multiple ph Ib/II trials designed to identify early signs of safety and efficacy of CIT combos. Using a randomized trial design, multiple treatment (tx) arms are compared with a single control arm in each pt cohort. We present three GI-specific MORPHEUS trials, each assessing CIT combos that could concurrently enhance multiple aspects of the cancer immune response. Methods: The MORPHEUS trials described here are global, open-label, randomized, Ph Ib/II trials enrolling pts with pancreatic ductal adenocarcinoma (PDAC), gastric or gastroesophageal junction cancers or colorectal cancer (CRC). New arms with novel CIT combos (table) are opened as new txs become available, and arms with minimal efficacy or unacceptable toxicity are closed. Studies include multiple cohorts for pts receiving different lines of tx (1L and 2L PDAC and gastric; 3L CRC). Pts with loss of clinical benefit to toxicity are closed. Studies include multiple cohorts for pts receiving different lines of tx. Primary endpoints include safety and investigator-assessed ORR (RECIST v1.1); secondary endpoints: PFS, OS, DCR and DOR. Clinical trial information: NCT03193190, NCT03281369, NCT03555149.

Molecule Target Proposed Mechanism of Action
Atezolizumab PD-L1 Reactivates antitumor immune response
Bevacizumab VEGF Recruits T cells to TME, DC maturation
BL-8040 CCR4 Recruits T cells to TME
Cobimetinib MEK1/2 Recruits T cells to TME, promotes T-cell survival and tumor immune recognition
Imprine PAMP Activates innate and adaptive immunity
Isatuximab CD38 Decreases Tregs; restores CD8+ T-cell function
Linaclotide DPP-4 Restores intra-tumoral chemotactic gradient and immune cells
PEGanist PEGylated anti-mitotic Restores intratumoral chemotactic gradient and immune cells
R06874281 FAP-Lv2 Activates immune effector function; promotes intratumoral immune responses
Selicreumab CD40 Drives T-cell responses; stimulates immune responses

List not exhaustive

TPS468
Trials in Progress Poster Session (Board #07), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
FOENIX-101: A phase II trial of TAS-120 in patients with intrahepatic cholangiocarcinoma harboring FGFR2 gene rearrangements. First Author: Lipika Goyal, Massachusetts General Hospital, Boston, MA

Background: Intrahepatic cholangiocarcinoma (ICCA) is a cancer arising from the intrahepatic bile duct. Standard treatment of unresectable, recurrent, or metastatic ICCA is with cytotoxic chemotherapy. Sample size calculations have been identified as oncogenic drivers in 10-20% of ICCA tumors, but no targeted agents have been established to date. TAS-120 is an investigational irreversible FGFR-4 inhibitor in development as a once-daily oral treatment for ICCA. Based on initial studies in multiple tumor types expressing FGFR abnormalities, ICCA was identified as a tumor type with potential susceptibility to FGFR inhibition and high unmet need. A phase I portion of the trial with an ICCA expansion cohort demonstrated tolerability and preliminary evidence of clinical efficacy with TAS-120 as a continuous, once-daily oral treatment in patients with ICCA. The most common AEs in the phase I portion of the trial were hyperphosphatemia, a mechanism-based on-target side effect, cutaneous AEs, and gastrointestinal AEs. The phase I portion of the study is continuing to enroll, and final results are anticipated in early 2019. Based on preliminary findings, a phase II portion of the study (FOENIX-101; clinicaltrials.gov registration NCT02052778) has been initiated. Methods: The phase II portion of the trial is a global, single-arm study of TAS-120 in patients with ICCA harboring FGFR2 gene rearrangements. The study will enroll approximately 100 adult patients with locally advanced or metastatic ICCA that progressed after ≥1 systemic therapies and with an ECOG PS of 0 or 1. Prior systemic therapy must include gemcitabine plus platinum-based chemotherapy. Screening for FGFR2 gene rearrangements will be performed at a central laboratory. The primary endpoint is objective response rate based on RECIST v1.1. Secondary endpoints include duration of response, disease control rate, overall survival, progression-free survival, safety, and health-related quality of life. Clinical trial information: NCT02052778.

TPS469
Trials in Progress Poster Session (Board #08), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
PANOVA-3: A phase III study of tumor treating fields with nabpaclitaxel and gemcitabine for front-line treatment of locally advanced pancreatic adenocarcinoma (LAPC). First Author: Uri Weinberg, Novocure Ltd., Haifa, Israel

Background: Tumor Treating Fields (TTFields) are a non-invasive, regional antimitotic treatment modality, which has been approved for the treatment of patients with glioblastoma by the FDA. 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 was the first trial testing TTFields in pancreatic cancer patients, and demonstrated the safety 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 of adding TTFields to nab-paclitaxel and gemcitabine combination in LAPC. Methods: Patients (N = 556) with unresectable, LAPC (per NCCN guidelines) will be enrolled in this prospective, randomized trial. Patients should have a measurable disease per RECIST Criteria. Patients with unresectable LAPC will be stratified based on their performance status and geographical region, and will be randomized 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 (150 kHz) will be delivered at least 18 hours/day until local disease progression per RECIST Criteria v1.1. Follow up will be performed q6w, including a CT scan of the chest and abdomen. Following local disease progression, patients will be followed 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 of 0.75 in overall survival. Type I error is set to 0.05 (two-sided) and power to 80%. Clinical trial information: NCT03377491.

TPS470
Trials in Progress Poster Session (Board #09), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM
Phase II HEPANOVA trial of tumor treating fields concomitant with sorafenib for advanced hepatocellular carcinoma. First Author: Anca Grosu, German Cancer Research Center (DKFZ), Heidelberg and German Cancer Consortium (DKTK), Freiburg, Germany

Background: Tumor Treating Fields (TTFields) are a non-invasive, regional antimitotic treatment modality, which has been approved for the treatment of glioblastoma by the FDA. TTFields predominantly act by disrupting the formation of the mitotic spindle during metaphase. TTFields were effective in multiple preclinical models of hepatocellular carcinoma (HCC), leading to a significant increase in cell death. The Phase 2 HEPANOVA study is the first trial testing TTFields in HCC patients, and is designed to test the safety and efficacy of adding TTFields to sorafenib in advanced HCC. Methods: Patients (N = 25) with unresectable HCC who are not amenable to any local treatment will be enrolled in this prospective, single-arm study. The study enrolls patients with ECOG score of 0-2 and Barcelona clinic liver cancer (BCLC) stage C. Patients must have a measurable disease per RECIST Criteria. Having implanted electronic devices in the torso is exclusionary. Sorafenib will be administered at standard dose (400 mg twice daily). TTFields (150 kHz) will be delivered for 18 hours/day until local disease progression per RECIST Criteria. Clinical follow up will be performed q4w, and a CT/MRI scan q6w. Following disease progression in the liver, patients will discontinue TTFields and be followed monthly for survival. Overall response rate will be the primary endpoint and in-field control rate, progression-free survival rate at 12 month (PFSS2), OS rate at 1 year and toxicity will all be secondary endpoints. Sample size was calculated using an exact test for proportions considering the weighted average of ORR of patients who had either complete or partial response per RECIST criteria in historical studies with sorafenib is 4.5%. A sample size of 25 patients was required to achieve a power of approximately 80% at a one-sided alpha level of 0.05 using a single sample Exact test for proportions. Clinical trial information: NCT03606590.
TPS471  
**Trials in Progress Poster Session (Board #Q10),**
Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Trybeca-1: A randomized, phase 3 study of erysayase in combination with chemotherapy versus chemotherapy alone as second-line treatment in patients with pancreatic adenocarcinoma (NCT03665441). **First Author:** Pascal Hammel, Hopital Beaujon, Clichy, France

**Background:** Second-line treatment options for advanced pancreatic adenocarcinoma are currently limited. Eryssayase, asparaginase (ASNase) encapsulated in red blood cells (RBCs) is an investigational product under development. Following infusion, asparaginase and glutamine are actively transported into RBCs where they are hydrolyzed by the encapsulated ASNase. We have recently reported the outcome of a randomized Phase 2b study inpatients with advanced pancreatic cancer whose disease progressed following first-line treatment(NCT02195180). Eryssayase in combination with gemcitabine monotherapy or FOLFOX combination therapy improved overall survival (OS) and progression free survival (PFS). The safety profile of eryssayase was acceptable. The results of this Phase 2b study provided a rationale for initiating this confirmatory Phase 3 pivotal trial (TRYbeCA-1).

**Methods:** TRYbeCA-1 is an international, randomized, open-label Phase 3 trial (N = ~500) of eryssayase 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 2:1 ratio to receive gemcitabine/abraxane or irinotecan-based therapy (FOLFIROFI [FLGmcl acid-fluorouracil/irinotecan regimen] or irinotecan/liposomal injection/5-fluorouracil/leucovorin) or without eryssayase, 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; available tumor tissue; and adequate organ function. The primary endpoint is OS. Key secondary endpoints include PFS and objective response rate, safety, quality of life, pharmacokinetics and pharmacodynamics, and biomarker research. An HR in OS of 0.725 is being targeted representing a conservative estimate based on the P2b data and is is of clinical relevance. A significant increase in OS or PFS will be established to review safety at regular intervals and to review efficacy data at the planned interim and final analyses. Clinical trial information: NCT03665441.

TPS472  
**Trials in Progress Poster Session (Board #Q11),**
Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

A phase Ib trial of anti-VEGFR/PDGFR vorolanib combined with immune checkpoint inhibitors (CPIs) in solid tumors. **First Author:** Nusayba Ali Bagegni, Washington University School of Medicine in St. Louis, St. Louis, MO

**Background:** Immune CPIs have become a standard treatment option for many advanced malignancies, including gastric (G)/GE junction (GEJ) and hepatocellular cancer (HCC). But resistance is inevitable. Data suggests angiogenesis plays a key role in tumor-mediated immune regulation. Vascular endothelial growth factor (VEGF) can inhibit intra-tumor T cell trafficking, while anti-VEGF therapy can improve T cell infiltration, potentially enhancing response to CPIs to overcome resistance. Vorolanib (V), a potent oral VEGFR/PDGFR inhibitor, has anti-angiogenic properties with a favorable toxicity profile. This phase Ib study is aimed to assess the safety and efficacy of V + CPIs, pembrolizumab (P) or nivolumab (N), in pts with advanced solid tumors.

**Methods:** The primary objective is to determine the recommended phase 2 dose (RP2D) of V + CPIs. Secondary objectives include safety, toxicity and objective response rate (ORR) and survival outcomes. Correlatives include analysis of angiogenic factors and tumor infiltrating lymphocytes as response biomarkers in archived tumor tissue and peripheral blood. Key eligibility for dose escalation cohort includes pts with solid tumors who can receive standard P or N, and for dose expansion cohort includes pts with PD-L1+ G/GEJ cancer who progressed on one or two lines of chemo, refused or are not candidates for chemo; or HCC Child-Pugh A treated with or refused sorafenib, ECOG PS 0-1 and adequate organ function. Key exclusions include prior CPI, significant bleeding, thrombosis, autoimmune disease or condition requiring corticosteroid use. A 3+3 design will be utilized to determine maximum tolerated dose and RP2D. V started at 300 mg PO daily in a 28-day cycle or P 200 mg IV Q 21-day cycle (max 36 pts). Dose level advancement occurs when all pts complete cycle 1 of assessed level, 20 additional pts (10 HCC, 10 PD-L1+ G/GEJ cancer) will be treated at RP2D. Response assessment by RECIST v1.1 or every 3 cycles of 3 or 2 cycles in N. ORR 20% or greater warrants further investigation. Enrollment is ongoing. Clinical trial information: NCT03311222.

TPS473  
**Trials in Progress Poster Session (Board #Q12),**
Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

A randomized clinical trial of chemotherapy with gemcitabine/cisplatin/nabpaclitaxel with or without the AXI inhibitor bemcentinib (BGB324) for patients with advanced pancreatic cancer. **First Author:** Muhammad Shaalan Beg, The University of Texas Southwestern Medical Center, Dallas, TX

**Background:** The Axl pathway coordinately mediates immune evasion and drug resistance in pancreatic cancer. Systemic AXI inhibition can enhance the efficacy of cancer therapy by blocking tumor cell proliferation, survival and drug resistance associated with epithelial-mesenchymal transition (EMT), and targeting innate immune suppression in the tumor microenvironment. Bemcentinib (BGB324) is a first in class, selective oral inhibitor of Axl. Our group has shown that bemcentinib therapy, in combination with gemcitabine, improved survival in multiple preclinical models of pancreatic cancer.

**Methods:** This is a multicenter, randomized, phase Ib/2 clinical trial of nab-paclitaxel/gemcitabine/cisplatin with or without bemcentinib. Patients with metastatic pancreatic cancer, good performance status and preserved liver, kidney and hematologic function are eligible. The treatment schedule is as follows: Bemcentinib 100 or 200 mg daily, nabpaclitaxel 125 mg/m2, gemcitabine 1000 mg/m2 and cisplatin 25 mg/m2 intravenously on D1, every 21 days. 3-12 patients will be recruited in part 1 following a modified 3+3 dose finding scheme. Part 2 of the study is a 1:1 randomized phase 2 design enrolling 62 patients. The primary objective is to determine complete response rate. Secondary endpoints are overall response rate, PFS and adverse events. A parallel biomarker study will accompany the trial analyzing blood and tissue samples to determine the effect of chemotherapy and bemcentinib on 1) Axl pathway activity in tumor tissue, 2) changes in immune landscape including upregulation of immune cytokines, and immune cell infiltration into the tumor, 3) apoptosis and decreased proliferation of tumor and 4) to identify predictive biomarkers of response. Clinical trial information: NCT03649321.

TPS474  
**Trials in Progress Poster Session (Board #Q13),**
Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Adjuvant chemotherapy of S-1 versus S-1 plus metformin for resected pancreatic cancer: A multicenter and randomized phase II trial. **First Author:** Masato Narita, Kyoto Medical Center, Kyoto, Japan

**Background:** Adjuvant chemotherapy with S-1 in patients with resected pancreatic ductal adenocarcinoma (PDAC) improved the 5-year survival rate to 44.1% and therefore has been a standard of care in Japan. Recent epidemiologic data has revealed possibility of metformin (a drug for type II diabetes) improving the prognosis of PDAC. In this context, we compare the efficacy and safety of S-1 plus metformin with S-1 alone as adjuvant chemotherapy in patients with resected PDAC. **Methods:** This multicenter randomized phase II study was conducted at 29 institutions in Japan (Registry Number; UMIN000020681). Key eligibility criteria are age 20 years or more with good performance status; histologically proven PDAC of stage I-II without macroscopic residual tumor. Patients receiving preoperative treatment for PDAC and previously treated with DPP-4 inhibitor, GLP-1, and metformin are excluded. After giving written consent to the study, patients are randomly assigned either study group (S-1 plus metformin) or control group (S-1 alone), balancing residual tumor status, nodal status, and institutions. S-1 is given orally for 2 weeks in a 3-week cycle. Cycles are lasted for 6 months. In the study group, metformin is administrated together with S-1 for 2 years. The treatment would be discontinued when the patient has either recurrence or unacceptable toxicity. The primary endpoint is 2-year OS, and the secondary endpoints are relapse-free survival and incidence rate of adverse events. Sample size was calculated based on the data in previous trials, with an expected 2-year survival rate in the control group of 65%. An improvement in 2-year survival rate from 65% in the control group to 78% in the study group, yielding a hazard ratio of 0.58, is considered clinically relevant in this population. A total of 3 events in each group were required for a power of 80% at a two-sided alpha 20% to detect a difference in OS using an unstratified log-rank test. A total of 160 patients (80 per group) were estimated to achieve the specified number of events in the scheduled follow-up duration of this study scheduled follow-up 2 years and it has been started from January 2018. Until September 2018, 17 patients have been enrolled. Clinical trial information: UMIN000020681.
**TPS475**

Trials in Progress Poster Session (Board #014), Fri, 11:30 AM-10:00 PM and 5:30 PM-6:30 PM

**Phase II randomized, double-blind, study of mFOLFIRINOX plus ramucirumab versus mFOLFIRINOX plus placebo in advanced pancreatic cancer patients**

**hcm GI14-19B. First Author: Walid Labad Shiba, Winship Cancer Institute of Emory University, Atlanta, GA**

**Background:** The prognosis of pancreas adenocarcinoma (PCA) remains poor. A chemotherapy backbone is the current standard of care in PCA. The choice of a chemotherapeutic backbone may impact the efficacy of antiangiogenic therapy in PCA. Ramucirumab has increased activity with fluoropyrimidines (5FU) because 5FU increases VEGF expression. **Methods:** This is a double-blind, placebo controlled Phase II study. Subjects with mild to severe Ramucirumab or a placebo followed by mFOLFIRINOX every two weeks of a 28 day cycle until progression or discontinuation for other reasons. The primary endpoint of this clinical trial is nine month PFS defined as the time from enrollment to the time of progression or death. Among the key inclusion criteria, subjects must have recurrent or metastatic pancreatic adenocarcinoma (PCA) with no prior first-line systemic treatment, ECOG PS 0-1, adequate organ function, no DVT, PE or other thromboembolism within three months of randomization. Total number of patient enrolled as of September 19, 2018 is 48 of 85 at eight sites; 27 male (56%), 42 Caucasians (87.5%), three African American (6.2%), one Asian (2%). Median age is 63 (40 - 76). Majority of patients (41) had de novo metastatic disease and six with recurrent disease after surgery. Regimen has been tolerated well with no unanticipated events.

**Clinical trial information:** NCT02528215

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**TPS476**

Trials in Progress Poster Session (Board #015), Fri, 11:30 AM-10:00 PM and 5:30 PM-6:30 PM

**A phase II, open-label pilot study evaluating the safety and activity of naltrexone in combination with 5-FU and oxaliplatin in preoperative treatment of pancreatic adenocarcinoma (NEA-NAIRI study). 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 (5-fluorouracil, leucovorin, oxaliplatin and irinotecan) regimen in the perioperative setting. However, FOLFIRINOX often requires a dose modification and growth factor support or higher dose toxicities which can complicate care delivery when given neoadjuvantly. Irinotecan liposomal injection (NAIRI) is FDA approved with a very tolerable safety profile in refractory metastatic PCa. The current study aims to substitute NAIRI for traditional irinotecan in the standard FOLFIRINOX regimen and demonstrate safe and effective delivery in the neoadjuvant setting. **Methods:** This phase II, open-label, single-arm study targets patients with borderline resectable PCa without metastatic disease. Other key eligibility criteria include age ≥ 18 years, measurable disease by RECIST v1.1, adequate organ function, and Eastern Cooperative Oncology Group performance status of 0-1. Patients receive FOLFIRINOX regimen as per table every two weeks for four months followed by disease reassessment. Patients who remain surgical candidates will undergo surgical resection within four to eight weeks following last dose of therapy. The primary endpoint is to assess safety and feasibility of regimen in perioperative setting. Secondary endpoints include R0 resection rate, clinical, biochemical and radiological response rate and patient-reported quality of life as measured by the HCl validated FACT-G scale. Enrollment of 28 evaluable patients is expected to patients to demonstrate a reduction in historical 30 day postoperative complication rate. FOLFIRINOX-NAIRI regimen. Clinical trial information: NCT03483038.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose</th>
<th>Route/Duration</th>
<th>Schedule</th>
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<tr>
<td>NAIRI</td>
<td>60 mg/m²</td>
<td>IV over 90 minutes</td>
<td>1 every 14 days</td>
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<tr>
<td>Oxaliplatin</td>
<td>100 mg/m²</td>
<td>IV over 120 minutes</td>
<td>1 every 14 days</td>
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<tr>
<td>Leucovorin</td>
<td>400 mg/m²</td>
<td>IV over 120 minutes</td>
<td>1 every 14 days</td>
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<tr>
<td>Sevoflurane infusion</td>
<td>2400 mg/m²</td>
<td>IV continuous infusion for 46 hours</td>
<td>1 every 14 days</td>
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**TPS477**

Trials in Progress Poster Session (Board #016), Fri, 11:30 AM-10:00 PM and 5:30 PM-6:30 PM

**A phase II study of ADI-PEG 20 and FOLFOrx in patients (pts) with advanced hepatocellular carcinoma (HCC). First Author: James J. Harding, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY**

**Background:** Arginine depletion interferes with pyrimidine metabolism as well as DNA damage repair pathways, and preclinical data indicate that pairing Arginine depletion interferes with pyrimidine metabolism as well as DNA damage repair pathways, and preclinical data indicate that pairing Arginine depletion interferes with pyrimidine metabolism as well as DNA damage repair pathways, and preclinical data indicate that pairing Arginine depletion interferes with pyrimidine metabolism as well as DNA damage repair pathways, and preclinical data indicate that pairing Arginine depletion interferes with pyrimidine metabolism as well as DNA damage repair pathways, and preclinical data indicate that pairing Arginine depletion interferes with pyrimidine metabolism as well as DNA damage repair pathways, and preclinical data indicate that pairing Arginine depletion interferes with pyrimidine metabolism as well as DNA damage repair pathways, and preclinical data indicate that pairing Arginine 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Trials in Progress Poster Session (Board #Q18), Fri, 11:30 AM-1:00 PM and 5:30 PM-6:30 PM

Avenger 500, a phase III open-label randomized trial of the combination of CPI-613 with modified FOLFIRINOX (mFFX) versus FOLFIRINOX (FFX) in patients with metastatic adenocarcinoma of the pancreas. First Author: Philip Agop Philip, Karmanos Cancer Institute, Wayne State University, Detroit, MI

**Background:** Metastatic pancreatic ductal adenocarcinoma (PDAC) is one of the deadliest cancers. Current treatments using FOLFIRINOX and gemcitabine plus nab-paclitaxel, provide median survivals of 11.1 and 8.5 months, respectively. PDAC cells have altered metabolism. CPI-613 is a novel TCA cycle inhibitor that targets cancer cells. In a phase I study mFFX plus CPI-613 resulted in a 61% objective response rate with 3 of 18 patients achieving a complete response. **Methods:** Avenger 500 (NCT03504423) is an open-label randomized trial of CPI-613 plus mFFX versus FFX in untreated patients with metastatic PDAC. 500 patients will be randomized 1:1 between arms. The experimental arm comprises CPI-613 500 mg/m² on day 1 and 3 of a 14-day cycle. The mFFX regimen is the standard dose and schedule of 5-Fluorouracil but reduced doses of oxaliplatin (65 mg/m²) and irinotecan (140 mg/m²). The control arm is standard dose FFX. There are two co-primary endpoints: Overall Response Rate (ORR, Complete Response + Partial Response). Best response within the first 12 cycles will be used for this determination, to be confirmed by independent, blinded, central review. Progression-Free Survival (PFS), is the second co-primary endpoint. Secondary endpoints are overall survival, duration of response and safety. Patient reported outcomes will be compared using the NCCN-FACT FHSI-18. An interim analysis will be done after 167 patients are evaluable for response. The difference in ORR will be tested using a Lan-DeMets Pocock type boundary for futility and efficacy. Futility will be declared if it is larger than 20%. The PFS hazard ratio will be tested using a Lan-DeMets O’Brien-Fleming type boundary. Efficacy will be declared if the hazard ratio is less than 0.48. The final analysis will be done with 500 patients randomized, when ~375 PFS events are available. Significance will be reached if the PFS hazard ratio is less than 0.80, or the difference in ORR is at least 11%. If the trial reaches significance for either primary endpoint, overall survival will be tested. Clinical trial information: NCT03504423.
A randomized, double-blinded, placebo-controlled multicenter phase II trial of adjuvant immunotherapy with tecemotide (L-BLP25) after R0/R1 hepatic colorectal cancer metastasectomy (LICC). Final results. First Author: Carl Christoph Schimanski, Klinikum Darmstadt GmbH and Universitätmedizin der Johannes Gutenberg-Universität Mainz, Darmstadt and Mainz, Germany

Background: Hepatic metastasectomy is the only potential curative treatment option for stage IV colorectal cancer (CRC) limited to liver metastases (LM). After R0 resection of LM the high recurrence rate remains a major challenge. L-BLP25 is an antigen-specific cancer vaccine targeting mucin 1 (MUC1). The LICC trial aimed to improve survival outcome in mCRC patients (pts) after R0/R1 LM resection. Methods: This LICC trial, a binational, multicenter, double-blinded, placebo controlled phase II trial, included pts with stage IV limited CRC after resection of primary tumor and LM (RO/R1) within the last 8 weeks, ECOG 0/1 and adequate organ function. Pts were 2:1 randomised to receive L-BLP25 or placebo. L-BLP25 930 μg was administered as 8 weekly subcutaneous doses followed by 6 week maintenance intervals until recurrence or a maximum of 2 years. Cyclophosphamide 300 mg/m2 (CP) or matching saline (NS) was given intravenously 3 days prior to first L-BLP25/placebo. Co-primary endpoints were recurrence-free survival (RFS) and 3-year overall survival (OS). Secondary endpoints were RFS and OS in subgroups with different MUC1 expression and safety. Differences in RFS and OS were analyzed with exploratory log rank tests on the intention-to-treat population. Results: Of 121 pts enrolled between Oct 2011 and Dec 2014, 79 pts received L-BLP25+CP, 42 placebo+NS. Baseline characteristics were well balanced. Median age was 60 years. Median RFS was 6.1 months (90% CI: 5.8-8.8 vs. 11.4 months (90% CI: 5.0-20.3) and estimated 3-year OS rate 69.1% vs. 79.1% for L-BLP25 and placebo, respectively. Two-factorial Cox regression models showed no impact of MUC1 expression or treatment on RFS or OS. The most common L-BLP25-related grade 3/4 adverse events were diarrhea, anemia and back pain. There was one death in the L-BLP25 arm due to Merker cell carcinoma assessed by the investigator as being potentially related to vaccination. Conclusions: The LICC trial failed to meet its primary endpoint of significantly improving RFS and OS with L-BLP25. MUC1 expression was not associated with outcome. Clinical trial information: NCT01462513. Clinical trial information: NCT01462513.
A randomized phase III trial of 5-fluorouracil (SOX) versus UFT/leucovorin as adjuvant chemotherapy for high-risk stage III colon cancer: The ACTS-CC 02 trial. First Author: Takao Takahashi, Department of Surgical Oncology, Gifu University Graduate School of Medicine, Gifu, Japan

Background: The ACTS-CC 02 trial was designed to verify the superiority of postoperative adjuvant chemotherapy with 5-fluorouracil (SOX) over UFT/leucovorin (LV), one of the standard oral fluoropyrimidine regimens in Japan, in terms of disease-free survival (DFS) in patients (pts) with high-risk stage III colon cancer (any T, N2, or positive nodes around the origin of the feeding arteries). The results of the safety analysis have been reported previously (Clin Colorectal Cancer, 2018). We now present the 3-year DFS results as the primary endpoint.

Methods: Pts who underwent curative resection for pathologically confirmed stage III colon cancer were randomly assigned to receive either UFT/LV (300-600 mg/day of LV according to body surface area [BSA]) and 75 mg/day of LV on days 1-28, every 35 days, 5 courses) or SOX (100 mg/m² of oxaliplatin on day 1 and 80-120 mg/day of 5-FU according to BSA on days 1-14, every 21 days, 8 courses). The primary endpoint was DFS. Results: From April 2010 through October 2014, a total of 966 pts were enrolled at 260 institutions. The full analysis set, excluding pts who withdrew informed consent before protocol treatment, comprised 478 and 477 pts in the UFT/LV group and SOX group, respectively. The median age was 65.0 years. The ECOG PS was 0 in 94.0%, and the disease stage was IIIA/IIIB/IIIC in 13%/50%/46.6%. The 3-year DFS rate was 60.6% in the UFT/LV group and 62.7% in the SOX group (HR: 0.90; 95% CI: 0.74-1.09; p = 0.28); the superiority of SOX was not demonstrated. In stage IIIb, the 3-year DFS rate was 69.3% and 68.5% in the UFT/LV group and SOX group, respectively (HR: 1.01; 95% CI: 0.74-1.37; p = 0.90). In stage IIIC, the 3-year DFS rate was 50.6% and 55.8% in the UFT/LV group and SOX group, respectively (HR: 0.82, 95% CI: 0.63-1.06; p = 0.21). Notably, in the N2b subgroup, the 3-year DFS rate was 46.3% and 54.7% in the UFT/LV group and SOX group, respectively (HR: 0.76, 95% CI: 0.55-1.05; p = 0.03).

Conclusions: SOX was not shown to be superior to UFT/LV in pts with high-risk stage III colon cancer. However, the oxaliplatin-based regimen was suggested to be more effective in advanced disease, such as stage IIIC and N2b. Clinical trial information: JapicCTI-101073.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.

CANCERS OF THE COLON, RECTUM, AND ANUS

Total neoadjuvant therapy with short course radiation compared to concurrent chemoradiation in rectal cancer. First Author: William Chapman, Washington University School of Medicine in St. Louis, Saint Louis, MO

Background: Total Neoadjuvant Therapy (TNT), or delivery of all radiation and chemotherapy prior to surgery, has improved complete response and downstaging rates compared to adjuvant therapy in patients with rectal cancer. Data regarding the use of short course radiation in the setting of TNT (SC-TNT) are limited. This study compares the pathologic complete response rate (PCR), Neoadjuvant Rectal (NAR) Score - a validated predictor of outcome based on tumor downstaging, and recurrence rates for patients receiving SC-TNT versus chemoradiation (CRT).

Methods: Patients who underwent neoadjuvant therapy followed by total mesorectal excision for Stage II or III rectal cancer from 2009 to 2018 were included in this retrospective cohort study. CRT recipients (50-55Gy/25-28 fx with concurrent 5-FU and leucovorin) comprised one cohort; the other included SC-TNT recipients (25-35Gy/5 fx followed by CAPOX or FOLFIRINOX chemotherapy). The primary outcome of PCR rate was assessed in univariate analysis; the secondary outcome of NAR score was calculated and categorized as “Low” (< 8), “Intermediate” (8-18), and “High” (> 18). Recurrence rates were measured and classified as local, distant, or both. Results: Of 388 eligible patients, 236 (60.8%) were treated with CRT and 152 (39.2%) underwent SC-TNT. On univariate analysis, the SC-TNT cohort had more advanced disease (77% Stage III disease vs. 67%, p = 0.04) and longer elapsed time between radiation completion and surgery (Median 131 vs. 63 days; p < 0.01). SC-TNT achieved a numerically higher PCR rate compared to CRT (25.0% vs. 19.1%, p = 0.16). Odds of achieving a “Low” NAR Score trended higher among the SC-TNT cohort (OR 1.45, 95% CI 0.9-2.3). Recurrence rates were also similar (14.2% vs. 14.9%, p = 0.87) over comparable follow-up (CRT = 30.5 months [IQR 11.1-49.0]; SC-TNT = 23.3 months [IQR 10.9-61.0]; p = 0.83).

Conclusions: SC-TNT yielded a PCR rate of 25% and overall recurrence rate of 14.9% among patients with locally advanced rectal cancer. Short course radiation with neoadjuvant multimodality chemotherapy is at least as effective as long-course CRT.

Cancer Recurrence Rates (%)

<table>
<thead>
<tr>
<th></th>
<th>CRT</th>
<th>SC-TNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>14.3</td>
<td>14.9</td>
</tr>
<tr>
<td>Local</td>
<td>2.7</td>
<td>2.8</td>
</tr>
<tr>
<td>Distant</td>
<td>10.3</td>
<td>11.4</td>
</tr>
<tr>
<td>Both</td>
<td>1.3</td>
<td>0.7</td>
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Immuneoncology clinical utility to identify good prognostic colon cancer stage II patients with high-risk clinico-pathological features for whom adjuvant treatment may be avoided. First Author: Jerome Golan, Laboratory of Integrative Cancer Immunology, INSERM, Paris, France

Background: Immuneoncology Colon is an IVD test predicting the risk of relapse in early-stage colon cancer (CC) patients, by measuring the host immune response at the tumor site. It is a risk-assessment tool providing independent and superior prognostic value than the usual tumor risk parameters and is intended to be used as an adjunct to the TNM classification. Risk assessment is particularly important to decide when to propose an adjuvant (adj) treatment for stage (St) II CC patients. High-risk stage II patients defined as those with high-risk features (HRRF) including T4, lymph nodes < 12, poor differentiation, VELIPI, bowel obstruction/perforation can be considered for adj. chemotherapy (CT). However, additional risk factors are needed to guide treatment decisions. Methods: A subgroup analysis was performed on the St II untreated patients (n = 1300) from the Immuneoncology international validation study (Paquery The Lancet 2018). The high-risk patients (with at least 1 clinico-pathological high-risk feature) were classified in 2 categories using predefined cutoffs: Low Immunooncology versus High Immunooncology and their five-year time to recurrence (5Y TTR) was compared to the TTR of the low-risk patients (without any clinico-pathological high-risk feature). Results: Among the patients with high-risk features (n = 630), 438 (69.5%) had a High Immunooncology score corresponding 5Y TTR of 87.4 (95% CI 83.9-91.0), statistically similar (logrank p value not stratified vs 0.42; Wald stratified by center vs 0.20) to the TTR 89.1 (95% CI 86.4-91.6) observed for the low-risk patients (with no clinico-pathological feature). Furthermore, 5Y TTR for these patients was statistically similar to those of St II patients with high-risk features and a High Immunooncology score (n = 438, who received adj; CT in n = 162) (5Y TTR of 83.4 (95% CI 77.6-89.9)). Conclusions: These data show that despite the presence of high-risk features that usually trigger adj. treatment, when not treated with CT, a significant part of these patients (42% of 59%) have a recurrence risk similar to the low-risk patients. Therefore, the Immunooncology test could be a good tool for adj. treatment decision in St II patients.
Metastatic patterns and prognostic significance of signet ring cell carcinoma of the colon: Retrospective analysis of SEER database. First Author: John Khoury, Beaumont Health, Department of Hematology and Oncology, Oakland University William Beaumont School of Medicine, Royal Oak, MI

**Background:** Signet ring cell carcinoma of the colon (SRCC) represents less than 1% of all colon carcinomas. We retrospectively examined the metastatic patterns and prognostic significance of SRCC in comparison to adenocarcinoma (AC) of the colon.

**Methods:** A total of 763 patients diagnosed with SRCC and 42,875 patients with AC of the colon from 2004 to 2012 were identified from the Surveillance, Epidemiology and End Results (SEER) database. Age, race, gender, primary site, grade, stage, metastatic site and survival data were collected. Results: Out of 43,638 patients, 78.7% were white, 12.5% black and 8.8% other races. Median age of diagnosis was 67.5 years for SRCC as compared to 69.1 years for AC. SRCC was more likely to be grade III or IV (92% vs 21.6%; p < 0.001), to be found in the right colon (63.7% vs 49.4%; p < 0.001) and to present as advanced stage (40.2% vs 29.4% for stage III and 37.1% vs 22.3% for stage IV; p < 0.001). SRCC was more likely to present with metastases to the brain (11.0% vs 13%; p < 0.001) and bone (6.4% vs 4.1%; p < 0.001), while AC subjects were more likely to present with metastases to the liver (77.0% vs 22.1%; p < 0.001) and lung (21.2% vs 5.8%; p < 0.001). The 5 year overall survival rate (5-YSR) was 28.2% (CI, 24.5% to 32.4%) for SRCC compared to 50.8% (CI, 50.1% to 51.6%) for AC (Hazard ratio for death, 1.38; CI 1.26 to 1.52; p < 0.001). The differences in survival rates were statistically significant for stage I and stage II. However, SRCC had a lower 5-YSR for stage III (34.5% vs 55.4%) and stage IV (3.3% vs 10.8%). Conclusions: SRCC has a worse survival rates for advanced stages when compared to AC. SRCC presents at an earlier age, with advanced tumor grade and stage at diagnosis. The metastatic behavior of SRCC is different than AC with a higher incidence of brain and bone metastases at diagnosis.

Impact of cardiac comorbidity on outcomes of adjuvant chemotherapy (ADJ) for colorectal cancer (CRC): A real-world population-based study. First Author: Shu Lucy Liu, BC Cancer, Vancouver, BC, Canada

**Background:** Cardiac comorbidities such as myocardial infarction (MI) and congestive heart failure (CHF) may pose challenges in the treatment of CRC. As the population ages, cancer patients (pts) will be increasingly affected by cardiac comorbidities. We performed a population-based analysis of CRC to evaluate the prevalence of MI and CHF, use of ADJ, and survival outcomes.

**Methods:** We evaluated 8601 pts diagnosed with rectal stage 2 or 3 CRC from 2004 to 2015 in Alberta, Canada. Baseline patient, tumor, and treatment characteristics were compared between those with and without MI or CHF. Survival analysis was conducted using Kaplan-Meier methods and Cox regression models. Results: In total, 506 (5.9%) patients (pts) had MI and 440 (5.1%) had CHF. CRC patients with prior MI or CHF were older (median 76 and 79 years, respectively) and had worse Charlson Comorbidity Index (median CCI 2 for both) than those without cardiac comorbidities (median age 67 and CCI 0) (p<0.001). Twenty-four and 15% of pts with a MI or CHF history, respectively, received ADJ when compared to their counterparts (52% and 53%, respectively, p<0.001). Among those who received ADJ (N=3409), an oxaliplatin-based regimen was used in 26% of MI pts versus 42% of those without MI (p=0.002), and in 31% of CHF pts versus 42% of those without CHF. Kaplan-Meier analysis revealed significantly worse overall survival (OS) in pts with prior MI (HR = 1.01, 95% confidence interval CI) 0.79-1.33, p<0.001) or CHF (HR = 1.13, 95% CI 1.01-1.27, p = 0.02). Neither MI nor CHF were predictors of CSS (p=0.24). Neither MI nor CHF were predictors of OS (HR = 1.09, 95% CI 0.89-1.33, and HR = 0.99, 95% CI 0.77-1.35, respectively). Conclusions: CRC pts with MI or CHF experienced lower use of ADJ and worse OS, but no difference in CSS was observed. ADJ-treated pts with prior MI appeared to benefit while worse outcomes persisted in pts with prior CHF to appear to be driven by non-cancer related causes.
Epidemiological trends of HPV-related anal cancers amongst males globally: A systematic literature review. First Author: Anuj Walia, Global Medical Affairs, Merck & Co., Inc., Kenilworth, NJ

**Background:** Anal cancer is associated with human papillomavirus (HPV), a sexually transmitted infection, which can be prevented by the HPV vaccine. Few countries do recommend vaccination for the male population, but all sexually transmitted infections, which can be prevented by the HPV vaccine, are recommended for the male population, but all high-risk males reported to the general population.

Methods: The incidence of anal pre-cancers increased the most among high-risk males from 1980 to 1989 in the general population. The burden of anal cancer and pre-cancers is highest among high-risk individuals in the US. For HIV-positive males, mean incidence of anal cancer increased from 10.5 during 1980-1989 to 42.3 in 1996-2004 per 100,000 PYs, and for HIV-negative males, mean incidence increased from 8.1 mm to 12.6 mm between 1984 and 2013. The mean pre-cancer incidence among HIV-positive males increased from 17.4 mm during 1980-1989 to 29.5 mm in 1996-2004 per 100,000 PYs. Conclusions: This systematic literature review demonstrates the increase in anal cancer and pre-cancer incidences over time in men, especially in high-risk male populations. The burden of anal cancers and pre-cancers is higher in all populations. The importance of preventative interventions such as HPV gender-neutral vaccines is emphasized. Few countries do recommend vaccination for the male population, but all high-risk males reported to the general population.

Relation between the size of nonmetastatic and metastatic lymph nodes and outcomes in patients with stage III colon cancer. First Author: Kazutake Okada, Tokai University, Isehara, Japan

**Background:** In colon cancer, retrieval of less than 12 lymph nodes is a risk factor for recurrence. We previously reported that the long-axis diameter of the largest LNs (maximum LNs) is associated with a higher number of retrieved LNs and better outcomes in stage II disease (Int J Colorectal Dis 2015). Furthermore, the postoperative survival without metastasis is a prognostic factor in stage III colon cancer.

Methods: The study group comprised 190 patients with stage III colon cancer from 2005 to 2014. For each patient, one negative LN and one positive LN with the longest long-axis diameter were selected, and the diameter was measured on HE stained specimens. The endpoint of survival analysis was relapse-free survival (RFS). The cut-off value (COV) was determined by using receiver operating characteristic curves. Results: The mean long-axis diameter of maximum negative and positive LNs were 8.5 ± 3.7 and 9.9 ± 4.9 mm, respectively. Factors related to the number of retrieved LNs were the tumor size (less than 4.3 cm: 13.5 ± 6.4; 4.3 cm or more: 16.6 ± 7.3; p = 0.004) and the long-axis diameter of maximum negative LNs (< 8.1 mm: p = 0.020). The diameter of maximum positive LNs was not a prognostic factor. Multivariate analysis, the tumor size (≥ 4.3 cm/ < 4.3 cm, HR 3.02; p < 0.001), venous invasion (absent/present, HR 0.41; p = 0.017), the number of LNs (≥ 12: 12, HR 0.56; p = 0.043), and the diameter of maximum negative LNs (≥ 8.1 mm: < 8.1 mm, HR 0.45; p = 0.008) were independent prognostic factors. Conclusions: In stage III colon cancer, the long-axis diameter of negative maximum LNs was a prognostic factor. Enlarged negative LNs are caused by hyperplasia of cell components in LNs. The size of negative maximum LNs might reflect the tumor immunity of the host.

Utility of restaging patients with stage II/III rectal cancer following neoadjuvant chemo/XRT: A systematic review. First Author: Leah E. Hendrick, University of Tennessee Health Science Center, Department of Surgery, Memphis, TN

**Background:** In the US, patients with clinical stage II/III rectal cancer typically receive neoadjuvant chemoradiation (chemo/XRT) over 5-6 weeks followed by a 6-10 week break before proctectomy. As this chemotheraphy is delivered at radio-sensitizing doses, there is essentially a 3-month window during which potential systemic disease is untreated. Evidence regarding the utility of restaging patients prior to proctectomy is limited. Methods: PubMed, Scopus, Web of Science, and the Cochrane Library were searched for studies evaluating the utility of restaging patients with locally advanced rectal cancer after completion of long course chemo/XRT, and reporting changes in management after restaging. Studies that were non-English, included < 50 patients, or examining the diagnostic accuracy of specific imaging modalities were excluded. Study quality was evaluated using the modified Newcastle Ottawa Scale. Results: Eight studies were identified including a total of 1251 patients restaged between completion of chemo/XRT and proctectomy. All studies were retrospective (6 single institution, 2 multi-institution). Restaging identified new metastatic disease in 72 (6.0%) patients, with 4 studies reporting specific sites: liver (n = 28), lung (n = 8), adrenal (n = 1), bone (n = 1), and multiple sites (n = 7). Overall, progression (distant or local) was detected in 85 (6.8%) patients and resulted in a reported change in management in 71 (5.7%) patients. One study identified an association of high-grade tumors with progression (p = 0.05); however, this was not reported in any other study. Moreover, tumor-related prognostic characteristics were inconsistently reported among studies, precluding meta-analysis. Conclusions: Although restaging between completion of neoadjuvant chemo/XRT and proctectomy detects > 8.1 mm in only a small percentage of patients, findings may alter the treatment plan. A multi-institutional collaboration with analysis of well-defined prognostic variables may better identify a group of patients most likely to benefit from restaging.
Population pharmacokinetics (popPK) of Sym004 to evaluate the effect of intrinsic and extrinsic factors on exposure in metastatic colorectal cancer (mCRC). First Author: Lene Alifrangis, Symphogen A/S, Ballerup, Denmark

Background: Sym004 consists of two anti-EGFR monoclonal antibodies (futuximab and modotuximab) directed against non-overlapping epitopes in the EGFR domain III. Sym004 induces rapid and efficient removal of the EGFR from the cancer cell surface by triggering EGFR internalization and degradation and has shown promising efficacy in mCRC patients. Based on a post-hoc analysis of a Phase 2 study, a Phase 3 trial in genomically selected mCRC patients is in preparation. Methods: The aim was to establish a popPK model for Sym004 in order to i) evaluate impact of covariates (intrinsic and extrinsic factors) on Sym004 exposure and ii) provide exposure metrics for a PK/PD analysis. Sym004 serum concentrations were obtained from 330 patients with mCRC (n = 247) or advanced solid tumors (studies Sym004-01, Sym004-02, Sym004-05 and Sym004-06). Sym004 (0.4-18 mg/kg) was dosed by i.v. infusion weekly or every 3rd week, or as a 9 mg/kg loading dose followed by 6 mg/kg weekly (9/6 mg/kg weekly). Non-linear mixed effects modelling was done in NONMEM v7.3.0. Covariates evaluated included body weight, age, sex, race, albumin, renal function, hepatic function, tumor type and size, ECOG and previous anti-EGFR treatments. Results: The base popPK model was a 2-compartment model with linear and non-linear Michaelis-Menten type elimination and a priori inclusion of body weight on CL, Vmew, V1 and V2. The model captured the non-linear PK well. The final covariate model retained covariates whose point estimates were outside the range of 0.8 to 1.25 and whose 90% confidence intervals did not overlap with the null value and included only body weight and albumin. Inter-individual variability was estimated for CL, Vmew and V1 and in the range of 18-30%. Simulations were used to assess the clinical relevance of the covariates as judged by the magnitude of change in the exposure of the Phase 3 dose regimen of 9 mg/kg weekly.

Conclusions: The popPK model described the Sym004 PK data well. No covariates were present that changed the Sym004 exposure in a clinically significant manner which would necessitate a dose modification.

Sidedness in metastatic colorectal carcinoma: Which are the factors which influence the prognosis? First Author: Maria Kopay, Centre Antoine Lacassagne, Nice, France

Background: Recent reports demonstrate prognostic and predictive impacts of the location of the primary tumor in metastatic colorectal cancer (mCRC). Our retrospective analysis aimed to determine the influence of primary site on metastatic distribution and disease evolution. Methods: From our database all patients (pts) with mCRC (except transverse carcinoma) treated from 1/12/2007 to 1/12/2016 in our institution were collected. Univariate and multivariate analyses were performed to identify predictors of overall survival (OS). Results: A total of 284 pts with available data were analyzed: 83 with Right-sided Colon Cancer (RCC) (29%), 123 with Left-sided Colon Cancer (LCC) (43%) and 78pts with Rectal Cancer (RC) (28%). Hepatic, lung lymph nodes and peritoneal metastases were respectively found in 63%, 36%, 23% and 20% of the population. The incidence or number of liver metastases were not influenced by sidedness (p = 0.06). RCC presented more bilobar involvement compared to RCC and RC (p = 0.017). Peritoneal carcinomatosis was significantly correlated to colon cancer (p = 0.002), whereas lung metastases were more common in RC (p = 0.001). Patients with RCC more often presented distal lymph node involvement (p = 0.018). RAS mutation status was known for 24/pts (80%), of those 117 (47%) were RAS mutated with no significant differences between RCC, LCC and RC (p = 0.4). BRAF mutation (p = 0.007) was more common in RCC. On a multi-variable analysis, primary tumor resection (PTR) and complete response after first line therapy were associated with a better OS but only a trend was observed for RCC and RC. Lung, lymph and peritoneal metastasis were associated with worse OS (Table). Conclusions: These results suggest that mCRC had different clinical presentation at diagnosis, the association with molecular features may explain the independent prognostic factor for OS of the sidedness.

Immunological nomograms predicting prognosis and guiding adjuvant chemotherapy in stage II colorectal cancer. First Author: Junjie Peng, Fudan University Shanghai Cancer Center, Shanghai, China

Background: The type, abundance, and location of tumor-infiltrating lymphocytes (TILs) have been associated with prognosis in colorectal cancer. The objective of this study was to assess the prognostic role of TILs and to develop a nomogram for accurate prognostication of stage II colorectal cancer. Methods: Immunohistochemistry was conducted on the tissues of the 6th intraepithelial CD3+ and stromal FOXP3+ TILs, and to estimate PD-L1 expression in tumor cells for 168 patients with stage II colorectal cancer. The prognostic roles of these features were evaluated using Cox regression model, and nomograms were established to stratify patients into low and high-risk groups and compare the benefit from adjuvant chemotherapy. Results: In univariate analysis, patients with high intraepithelial CD3+ and stromal FOXP3+ TILs were associated significantly with better relapse-free survival (RFS) and overall survival (OS), except for stromal CD45RO+ TILs whereas PD-L1 expression wasn’t associated with RFS or OS. In multivariate analysis, patients with high intraepithelial CD3+ and stromal FOXP3+ TILs were associated with better RFS (p < 0.001 and p = 0.032, respectively), while only stromal FOXP3+ TILs was an independent prognostic factor for OS (p = 0.031). The nomograms were well calibrated and showed a c-index of 0.751 and 0.757 for RFS and OS, respectively. After stratifying into low and high-risk groups, the high-risk group exhibited a better OS from adjuvant chemotherapy (3-year OS of 81.9% vs. 73.4%, p = 0.006). Conclusions: These results may help improve the prognostication of stage II colorectal cancer and identify a high-risk subset of patients who appeared to benefit from adjuvant chemotherapy.
Outcomes of younger patients diagnosed with locally advanced rectal cancer. First Author: Rosemary Habib, Westmead Hospital, Westmead, Australia

Background: The incidence of rectal cancer is higher in the older population. In developed nations there has been a rise in incidence in young onset rectal cancer (yRC). We evaluated and compared the presentation and survival outcomes of treatments for locally advanced rectal cancer in yRC patients to that of older patients. Methods: All cases of rectal cancers referred to a large tertiary referral cancer centre in Western Sydney between 2009-2016 were examined. Patient demographics, presenting symptoms, treatment, clinical pathological characteristics, progression free survival (PFS) and overall survival (OS) were obtained. Under 50 years old was used as the cut-off age for defining yRC. Results: One hundred sixty-two patients were identified, 33 in the yRC and 129 in the older patient group. The median age at diagnosis was 62 (24 - 92). Median follow-up was 40 months. There was no difference in presenting symptoms between the two groups, with per rectal bleeding being the most common symptom at presentation. 17.5% of yRC presented with stage IV disease, compared with 22.1% of older patients. yRC were more likely to complete neoadjuvant therapy (97% vs 89%; P=0.02) and were more likely to proceed to surgery (91% vs 72%; P=0.02). There were no significant differences in surgical outcomes, including complications and postoperative TNM staging. yRC were more likely to have microsatellite high tumours (18% vs 4%; P=0.01). No statistical differences were seen in survival outcomes, including OS and PFS, between yRC and older patients. Eight progressions (eight deaths) were observed in the yRC group and 40 progressions (36 deaths) were observed in the older patient group. Conclusions: 20% of rectal cancers were considered yRC. These patients were more likely to complete neoadjuvant therapy and proceed to surgery. In this cohort, median PFS and OS were longer compared to the older patient group, although this was not statistically significant. yRC were more likely to have MMR deficiency. Patients under 50 years with alarm symptoms including per rectal bleeding require vigilance in investigations to allow for earlier detection and appropriate management of rectal cancer.

CANCERS OF THE COLON, RECTUM, AND ANUS

Safety of compression therapy using newly developed gloves for oxaliplatin induced neuropathy prevention. First Author: Yukinori Koyama, Shimane Prefectural Central Hospital, Izumo, Japan

Background: Oxaliplatin (1-OHP) is a key drug commonly used in primary and metastatic colorectal cancer treatment. However, 1-OHP is associated with nonhematological adverse effects, including peripheral neuropathy (PN). About 90% of patients who received 1-OHP experience PN after single dose of 1-OHP and PN is likely to be negatively associated with quality of life. There is no established effective prophylactic management for chemotherapy induced PN according to the 2014 American Society of Clinical Oncology (ASCO) guideline. Recently, compression of hands during injection of drugs has been reported to be effective for chemotherapy induced PN. We developed new gloves for compression therapy which are reusable and low cost. We prospectively analyzed the safety of the gloves. Methods: Patients who received 1-OHP were eligible for this phase I study. Wrist and hand size were measured and appropriate size of gloves were selected. The pressure of hands is estimated to be 20-33 hPa. Patients start to wear the gloves on both hands, from 30 min before the injection of 1-OHP until 30 min after the injection. Peripheral neuropathy was evaluated at each treatment cycle using common terminology criteria for adverse events (CTCAE) version 4.0. Results: Between October 2017 and August 2018, fourteen patients (median age 66 years [range 39-79years], 7 male and 7 female) were enrolled and were evaluated. No patients withdrew from the study due to safety concerns. No safety events were identified for any safety variables assessed during the trial. CTCAE grade 2 or higher sensory PN was observed in four (28.6%) patients. The average time until grade 1 or more neuropathy appeared was 27.8 days and average dose of 1-OHP was 225mg. Conclusions: Compression therapy with the new gloves had no safety concerns, demonstrating a profile favorable for further development for prevention of oxaliplatin induced PN. Clinical trial information: 000029671.
**Background:** Microsatellite instability (MSI) testing has become critically important in clinical cancer care of patients with cancer given the recent pan-tumor FDA approval of pembrolizumab for use in patients with MSI-H (MSI-H) tumors. We previously demonstrated the robustness of a novel proprietary algorithm for determination of MSI status via NGS from solid tumor biopsy specimens (U Clinc Oncol 34, 2016 (suppl; abstr 1523)). Traditional MSI tests such as PCR or IHC are impractical for pan-tumor adoption, as MSI-H prevalence outside of gastrointestinal and endometrial cancers is usually <1%. NGS-based ctDNA profiling provides an opportunity for both MSI and actionable alteration testing in patients in whom tissue-based biopsy is not available. **Methods:** Genomic DNA (gDNA) from five previously characterized MSI-H cell lines: (DLD1, 22Rv1, LNCap, RL952, CL188), and one MSS cell line (SCC9) was enzymatically-fragmented to simulate ctDNA and titrated to various dilution levels with DNA from a healthy hmapap subject (NAI2878). Samples were screened with a 70-gene panel, FoundationOne Liquid, that includes 180 mononucleotide repeat sequences (8-26bp long in the human reference genome). Length variability in the 180 repeat loci was utilized to generate an overall MSI score via principal components analysis. The NGS based MSI algorithm was applied to all the samples. **Results:** Assessment of these six cell lines, targeting five dilution levels confirmed by SNP mixing ratios, show that our NGS based MSI test for liquid biopsies has 96% sensitivity at >2% tumor fraction with 100% PPV. The regression intercept of the MSI-H dilution samples with the pre-established MSI-H calling threshold shows our method has a LOD of 0.6% tumor fraction. MSI-H prevalence data from liquid biopsies of gastrointestinal tumors obtained during clinical care will also be presented. **Conclusions:** These data demonstrate the feasibility of using NGS-based liquid biopsy assays for MSI testing. This ctDNA-based approach may allow for increased access to checkpoint inhibitors in a pan-tumor setting, which would be especially relevant for cancers where routine MSI testing is impractical or when tissue is not available.
Review of updated colorectal cancer disease management data in the
Colombian National Administrative Cancer Registry. First Author: Robert
Hsu, University of Miami/Jackson Memorial Hospital, Miami, FL

Background: The Office of High Cost of the Colombian Health Ministry
created the National Administrative Cancer Registry (NACR) in 2015 to obtain
nationwide cancer data to find areas for improvement in cancer delivery. From
initial data, a collaboration of healthcare experts identified 15 disease man-
agement indicators in colorectal (CRC) cancer in Colombia. In this study, we
look at 2017 NACR data to investigate significant findings. Methods: We
obtained NACR data compiled from the Department of Health Ministry from
January 2, 2016-January 1, 2017 consisting of 32 departments and 112 nu-
meralities. The 2017 NACR data for CRC includes 11 of 15 updated disease
management indicators - time to diagnosis, proportion of patients with col-
orectal cancer in situ, proportion of new cases identified in early stages,
proportion of patients with TNM staging, proportion of patients with TNM
staging before treatment, time before treatment, time between neoadjuvant
therapy and surgery, time between surgery and adjuvant therapy, proportion
of stage I and II patients receiving curative surgery, proportion of patients with
nutritional support, mortality rate, and incidence. Results: The incidence of
CRC was 5.2 cases per 100,000 people and the mortality was 3.6 cases per
100,000 people. The time to diagnosis was on average 50.7 days. 3.6% of CRC
cases were in situ. 35.6% of cases were identified in early stages, and 51.3% of
cases had TNM staging with 45.1% staged prior to treatment. The time to initial
treatment was 63.7 days. The time between neoadjuvant therapy and surgery
was 116.1 days and the time between surgery and adjuvant therapy was
75.5 days. 24.2% of stage I and II patients received curative surgery. 9.8%
patients received nutritional support. Conclusions: The updated NACR data
show significant wait times for treatment and exaggerated wait times for
patients needing neoadjuvant or adjuvant therapies. The findings show sig-
ificant work is needed in providing supportive services. There needs to be
further investigation into follow-up after initial treatment. Further directions
should include more data collection of adjuvant and neoadjuvant wait times
and outcomes data of specific treatment modalities.

Early detection of lower GI tract tumors by dedicated assessment of the
colon on routine computed tomography (CT) imaging: An observational
study. First Author: John Chang, Banner MD Anderson Cancer Center, Gilbert,
AZ

Background: We have previously reported that up to 48% of the early
features of colorectal cancer (subtle wall thickening, pericolic stranding,
and small lymph nodes in the draining nodal station) were not identified on
the original report and pelvis (CTAP) reports. This resulted in a 36% de-
crease in five-year survival based on historical data. In this report, we assessed
whether dedicated assessment of the colon on routine CT scans could lead to
early detection of colorectal cancer. Methods: 210 CTAPs over a three-month
period were screened from the emergency room records at a tertiary care
care hospital. 194 scans met eligibility. Exclusion criteria included: cases known to
be malignancies involving the colon, mesentry and bowel and was recorded. A blinded
evaluation of the eligible case was then performed by a board-certified ra-
diologist with attention specifically to the colon and the mesentery for the
suspicious early features of CRC. The concordance and discordance was then
tabulated. Discordant findings were re-evaluated to determine if the discor-
dance was true. Results: 72/194 patients were male, median age 44.5 years
(range 20 - 89). 55/194 patients (29.1%) included in the study were noted to
have suspicious features. 26 had abnormal lymph nodes, 24 had abnormal
colic wall thickening and 16 had pericolic stranding and/or wall edema.
45/55 studies were truly discordant from the original interpretation. These
included one missed colorectal cancer (confirmed), one likely small bowel
neuroendocrine tumor (no follow up), and one likely transitional cell carci-
roma of the right renal pelvis (no follow up). Conclusions: Dedicated search of the
colon and mesentery on CTAP can identify subtle findings, although their
true relevance is being evaluated in a larger future study. Our observ-
ations do indicate that there may be a potential role of focused evalua-
tion of the colon and mesentery on routine CTAP in an attempt to
potentially increase the rate of cancer detection especially in younger low-
average risk patients.

S110 Poster Session (Board #D11), Sat, 7:00 AM-7:55 AM and
12:15 PM-1:45 PM

S111 Poster Session (Board #D14), Sat, 7:00 AM-7:55 AM and
12:15 PM-1:45 PM

Visit qicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
DNA damage response pathway mutations contribute to a high proportion of hereditary colorectal cancer in patients from the Republic of Macedonia. First Author: Marija Stanišević, Center for Biomolecular Pharmaceutical Analyses, UKM-Faculty of Pharmacy, Skopje, Republic of Macedonia

Background: Hereditary factors are assumed to play a role in 35-45% of all colorectal cancers with 5%-10% associated with high penetrant disease-causing mutations in genes correlating to hereditary polyposis (HP) or hereditary nonpolyposis syndromes (HNPPC). Although inherited germine mismatch repair and APC gene mutations contribute significantly to CRC, still a genetic diagnosis cannot be obtained in > 50% of familial cases.

Methods: We performed a targeted NGS sequencing of 103 probands with clinically diagnosed HP (39) or HNPPC (64) using a multigene panel on two different platforms (Illumina Cancer Panel and Ion Torrent custom panel), covering coding and exon/intron sequences of 100 genes implicated in hereditary cancers. Results: Overall, the molecular defect was identified in 60 (58%) index patients. As expected, a large percentage (82%) of these patients exhibited the presence of clearly pathogenic mutations in well-known genes associated with hCRC (APC, MUTYH, BMPRIA, NTHLI1 in HP, MLH1, MSH2, PM56, MSH6 in HNPPC). Surprisingly, all except one (FLCN c.1285dupC, detected in a patient with Bannayan-Riley-Ruvalcaba syndrome (BRRS)) did not result in mutations in the involved genes in the damage response pathway, of which 3 in CHEK2 (c.1038delT; c.1229delC; c.579T=G) in 2 in BRCA1 (c.2932C>T) and 1 in each of BLM (c.1642C>T), BRCA2 (c.4446_4446+5dupAACAGA), FANCM (c.2953delC, FH (c.1431_1433dupAAA) and ERCC2 (c.1403C>G). Clinically, six of these cases exhibited the HNPPC type X phenotype (mutations in BRCA2, BRIP1, FANCM and CHEK2) while the other four were classified as oligopolyposis (mutations in BLM, FH and CHEK2). Conclusions: Our data indicate a significant association of DNA damage response pathway deficiencies and carcinogenesis in patients with hCRC syndromes exhibiting either the HNPPC type X or oligopolyposis phenotype. No genetic defects were detected within the analyzed genel panel in 44 (42%) families, indicating the need of extended exome/whole genome analyses in a substantial portion of patients with this disease.

Microsatellite instability detection from plasma of colorectal cancer patients. First Author: Jing Sun, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Background: MSI, detected in 15% of colorectal cancer (CRC) patients, is a hermimutable phenotype caused by deficiency in DNA repair system. Currently, MSI detection is limited to tissue samples. Detection of MSI from blood samples has been explored but confounded by low sensitivity due to the trace amount of ctDNA present. In this study, we developed a NGS read count-based algorithm-BMSISEA (blood MSI signature enriched analysis) to detect MSI from blood samples. Methods: Matched tumor and adjacent normal tissues were obtained from 50 MSI-H CRC patients to establish a microsatellite pattern for MSI-H tumors. Whole blood cell (WBCs) from 100 CRC patients were used to establish a microsatellite pattern for MSS. Plasma samples were obtained from 75 CRC patients with known MSI status assessed by IHC (138 MSI-H and 37 MSS) to validate the algorithm. Results: To establish features for MSI-H and MSS tumors, 51 microsatellite loci covered by ColonCore panel with mononucleotide repeats longer than 10bp were scanned using paired tumor and adjacent normal tissues and 8 loci with significant differential read count distribution were identified. MSI signature enrichment analysis was performed using WBCs to establish a microsatellite signature for MSS tumors. For each locus, the number of total reads supporting either MSI-H (denoted as K in the equation) or MSS (N-K, where N refers to the total number of reads supporting either MSI-H or MSS at a specific locus) were counted. The MSI signature enrichment analysis was performed using hypergeometric test. The log-transformed p values were used to calculate 2 scores. The final microsatellite status was reflected by log-transformed p values. For each locus, the number of total reads supporting either MSI-H or MSS at a specific locus were counted. The MSI signature enrichment analysis was performed using hypergeometric test. The log-transformed p values were used to calculate 2 scores. The final microsatellite status was reflected by MS score, which was the sum of z scores of all loci. A MS score of 15 was derived to differentiate MSS and MSI-H tumors. Both simulation data and data generated using clinical samples revealed more than 98% sensitivity and 100% specificity with ctDNA percentage greater than 1%. This method is still reliable if the ctDNA percentage drops to 0.4%, yielding sensitivity of 93.3% and specificity of 100%. Conclusions: We developed a sensitive algorithm which can reliably detect MSI status with ctDNA fraction greater than 0.4% with sensitivity of 93.3% and specificity of 100%.
S16 Poster Session (Board #D19), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM
Prospective clinical study using expressed sequencing variants on stool-derived eukaryotic RNA transcripts (seRNA) for colorectal cancer screening. First Author: Erica Kay Barnett, Washington University School of Medicine, St. Louis, MO

Background: Colorectal cancer (CRC) is the second leading cause of cancer related deaths in the United States. The high mortality rate is largely attributable to the high frequency of late-stage diagnoses, caused by low patient compliance with screening guidelines. A reliable and noninvasive screening alternative is needed for the 40 million noncompliant patients. The development of a novel nucleic acid extraction method to isolate stool-derived eukaryotic RNA (seRNA) permits reliable and noninvasive evaluation of biomarkers derived from the gastrointestinal (GI) epithelium. This method enables sequencing-based tools for the detection of patients with CRC and adenomas. Methods: Stool samples were obtained from 96 individuals prior to undergoing a screening colonoscopy. Fecal immunochemical tests (FITs) were obtained for each sample. RNA isolates underwent custom library preparation, next-generation sequencing, and somatic variant identification. An seRNA assay assessed the probability of CRC risk using results from the FIT, mutational burden of transcripts implicated in precancerous change (APC), and mutational burden of transcripts associated with malignant transformation (KRAS / TP53). Results: When compared to results from a colonoscopy and subsequent biopsy, the seRNA risk assessment attained a 100% sensitivity for CRC, a 71.4% sensitivity for advanced adenoma, and an 88.5% specificity for no neoplastic findings. Conclusions: A single-center, IRB-approved, prospective and blinded clinical study is being conducted in 450 patients to further develop this seRNA assay. Supplemental data will include expression from 408 seRNA transcripts. Preliminary analysis described herein indicates this assay could be the most sensitive noninvasive screening test for the detection of CRC and adenomas.

S17 Poster Session (Board #D20), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM
Financial distress amongst older adults with gastrointestinal (GI) malignancies. First Author: William Varnado, UAB Hematology/Oncology, Birmingham, AL

Background: Many patients with cancer report financial distress (FD); however, the magnitude of FD in the growing number of older adults with cancer remains less clear, particularly in those with GI malignancies. The purpose of this study was to evaluate the proportion of older adults with GI malignancies reporting FD and to characterize geriatric assessment (GA) and cancer-related factors associated with FD. Methods: Older adults (≥ 60yrs) seen in the GI oncology clinic at the University of Alabama Birmingham (UAB) were asked to fill out a patient-reported GA, entitled the Cancer & Aging Resilience Evaluation (CARE), at their visit. The CARE includes questions pertaining to patient's independence in Activities of Daily Living (ADLs), Instrumental Activities of Daily Living (IADLs), falls, physical function, polypharmacy, and comorbidity. A single item question regarding FD from the patient satisfaction questionnaire (PSQ-18) was included. FD was defined as agreement with the phrase "Do you have to pay for more medical care than you can afford." Demographic and GA characteristics were compared between those with and without FD using Chi-square and t-tests. Results: 233 patients completed the CARE, a median of 71-days after diagnosis. Median age 68y (60-96); 54.5% male and 76.0% non-Hispanic white. Most common cancer types included colorectal (39.1%) and pancreatic cancers (20.6%). A total of 62 patients (26.6%) had FD. Patients with FD were more likely to be younger (61.1 vs. 70.7y, p < 0.001), of black race (17.1% vs. 15.8%, p = 0.07), to have more than three comorbid conditions (37.1% vs. 15.8%, p = 0.007), to have more than one comorbid condition (93.1% vs. 82.6%, p = 0.052), to report impaired IADLs (61.3% vs. 43.9%, p = 0.055), and impaired mobility (27.4% vs. 14.6%, p = 0.069). No associations were found with GI cancer type or stage, marital status, time from diagnosis, or hearing/vision impairments. Conclusions: Over a quarter of the older adult population with GI malignancies report FD. Several GA and demographic factors were associated with FD that may help identify older patients at risk for FD.

S18 Poster Session (Board #E1), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM
Association between primary tumor site, perioperative CEA ratio, and overall survival in patients with colorectal cancer. First Author: Thomas A Odeny, University of Missouri-Kansas City, Kansas City, MO

Background: There are differences in the incidence, clinical presentation, molecular pathogenesis and outcome of colorectal cancer (CRC) based on the tumor location. Emerging research suggests that the perioperative carcinoembryonic antigen (CEA) ratio is a prognostic factor for CRC patients. We aimed to determine the relationship between perioperative CEA ratio, age, tumor stage, and overall survival among patients with CRC. Methods: We analyzed 111 patients who underwent resection for CRC at KUMC. After excluding patients without pre- or post-operative CEA data, 62 patients for whom we had sufficient data were included. FFPE biopsies from CRC patients in stage I (N = 34) and stage II (N = 63) were analyzed. Next-generation sequencing and somatic variant identification were performed. Results: The median age was 61 years, 54% male, 31% smokers, 74% left-sided tumors, median preoperative CEA ratio, and 5-year survival among patients with CRC. Conclusions: Our findings demonstrate that perioperative CEA ratio, and overall survival in patients with colorectal cancer is influenced by tumor location.
Validation of the NCI Colorectal Cancer Risk Assessment Tool for baseline advanced neoplasia in a veterans cohort. First Author: Laura W. Musselwhite, Duke Cancer Institute, Duke University Medical Center, Durham, NC.

Background: Tailoring screening strategy to colorectal cancer (CRC) risk may improve efficiency for all stakeholders. We applied the National Cancer Institute (NCI) CRC Risk Assessment Tool, which calculates 5-10-year, and 20-year absolute risk of colorectal cancer to determine whether it could be used to predict baseline risk of colorectal cancer precursors in a Veterans cohort undergoing first screening colonoscopy. Methods: This was a prospective evaluation of whether the NCI CRC Risk Assessment Tool which offers an absolute risk over time, could be used to estimate baseline cancerous precursors (advanced neoplasia) in Veterans undergoing first screening colonoscopy. Family, medical, dietary and physical activity histories were collected at the time of screening colonoscopy and used to calculate absolute 5, 10, and 20-year CRC risk, and to compare estimated CRC risk to observed AN. Sensitivity analyses were performed. Results: Of 3,212 Veterans undergoing screening colonoscopy, 94% had complete data available to calculate risk (N = 2,934, median age 63 years, 100% men, and 15% minorities). 11% (N = 313) were diagnosed with AN on baseline screening colonoscopy, The area under the curve for predicting AN was 0.60 (95% CI: 0.57-0.63, p < 0.0001) at 5 years, 0.60 (95% CI: 0.57-0.63, p < 0.0001) at 10 years and 0.58 (95% CI: 0.54-0.61, p < 0.0001) at 20 years. At 5 years, we calculated the sensitivity (0.18, 95% CI: 0.14-0.22), specificity (0.91, 95% CI: 0.90-0.92) positive predictive value (0.19, 95% CI: 0.15-0.24) and negative predictive value (0.90, 95% CI: 0.89-0.91) considering the top 10th percentile of risk tool scores as a positive result. Conclusions: The NCI CRC Risk Assessment Tool had modest discriminatory function for predicting AN risk at 5, 10 and 20 years. The Tool’s specificity and negative predictive value were quite good, highlighting its usefulness in risk prediction. This tool may be useful to inform the benefit-risk assessment of screening colonoscopy for patients with competing comorbidities.

Characteristics and survival among early onset and standard onset colorectal cancer by race. First Author: Ana Araujo Vilelaarduna, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY.

Background: The incidence of early-onset colorectal cancer (EO) is increasing. Guidelines recommend to start screening colonoscopy at 45 yr in Non-Hispanic Black (NHB). We compare the clinical features and outcomes between EO and standard-onset (SO) colorectal cancer (CRC) among racial groups. Methods: Patients with CRC adenocarcinoma, available race/ethnicity and stage were identified using the SEER registry. Clinical features and 5-year overall survival (OS) is described by race and age groups. Results: 190,670 patients were identified; EO rates were higher for minorities than NHB. Median age at diagnosis in EO was 44 and was similar among racial groups; while it was 71 in SO, being lower among minorities compared to NHB (67 vs. 72 years, p < 0.01). Left-sided tumors accounted for 77.4% of tumors in EO while it was 60.8% in SO for minorities versus NHB. The most common CRC location for EO was the rectum and sigmoid colon for SO. EO was most commonly diagnosed as stage III. Surgery and radiation hazards were higher for EO at all stages. OS was higher in all stages of EO compared to SO. Conclusions: EO frequency is higher in all minority groups and most commonly located in the rectum. Despite higher stage and OS, SO is higher for EO which might be due to higher treatment rates. Early screening should be extended to all minority groups.

Prevalence of KRAS, NRAS, and BRAF gene mutations in metastatic colorectal cancer patients: A systematic literature review and meta-analysis. First Author: Kimberly Lowe, Amgen, Seattle, WA.

Background: A systematic literature review and meta-analysis was conducted to summarize the prevalence of KRAS, NRAS, and BRAF mutations in mCRC patients. These mutations have substantial implications for treatment decisions among mCRC patients. Methods: Multiple databases were searched to identify observational studies and clinical trials (standard of care arms only) to identify potential sources of heterogeneity in mutation prevalence. Results: The meta-analyses included 275 studies comprising over 77,000 mCRC patients. The summary prevalence estimate was 35.9% for KRAS mutations, 7.1% for BRAF mutations, and 4.1% for NRAS mutations. Female patients had significantly more KRAS and BRAF mutations than males (KRAS: 42.2% vs. 37.3%, p = 0.016; BRAF: 1.0% vs. 0.7%, p = 0.016), and significant variation by study location was observed for both KRAS (p = 0.025) and BRAF (p = 0.002) mutation prevalence. Conclusions: The prevalence of KRAS, BRAF, or NRAS mutations in mCRC patients varies significantly by gender and study location, compared to patients with wild-type tumors. The results of these analyses are informative for clinicians, patients, and researchers.

Characteristics and survival among early onset and standard onset colorectal cancer by race. First Author: Ana Araujo Vilelaarduna, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY.

Background: The incidence of early-onset colorectal cancer (EO) is increasing. Guidelines recommend to start screening colonoscopy at 45 yr in Non-Hispanic Black (NHB). We compare the clinical features and outcomes between EO and standard-onset (SO) colorectal cancer (CRC) among racial groups. Methods: Patients with CRC adenocarcinoma, available race/ethnicity and stage were identified using the SEER registry. Clinical features and 5-year overall survival (OS) is described by race and age groups. Results: 190,670 patients were identified; EO rates were higher for minorities than NHB. Median age at diagnosis in EO was 44 and was similar among racial groups; while it was 71 in SO, being lower among minorities compared to NHB (67 vs. 72 years, p < 0.01). Left-sided tumors accounted for 77.4% of tumors in EO while it was 60.8% in SO for minorities versus NHB. The most common CRC location for EO was the rectum and sigmoid colon for SO. EO was most commonly diagnosed as stage III. Surgery and radiation hazards were higher for EO at all stages. OS was higher in all stages of EO compared to SO. Conclusions: EO frequency is higher in all minority groups and most commonly located in the rectum. Despite higher stage and OS, SO is higher for EO which might be due to higher treatment rates. Early screening should be extended to all minority groups.

Evaluation of routine image follow-up in nonmetastatic colorectal cancer after curative surgical resection. First Author: Lara Azevedo Diniz, A.C. Camargo Cancer Center, São Paulo, Brazil.

Background: Follow-up surveillance is performed after primary treatment in colorectal cancer (CRC), but it is controversial in the literature the cost benefit of an intensive examination in terms of outcomes and resources. Intensive follow-up after surgery for colorectal cancer has been challenged by new first published data (CEA watch trial and FACS trial). These new data suggest that a less intensive follow-up program based on carcinoembryonic antigen (CEA) measurements or CEA-triggered imaging would be enough to detect most of the recurrences. We believe that there is a high percentage of patients with curable recurrence disease and normal CEA value, for whom image screening would be necessary to detect early disease recurrence and malignant CEA value, for whom image screening would be necessary to detect early disease recurrence. Survival is not a surrogate of disease cure and normal CEA value, for whom image screening would be necessary to detect early disease recurrence. Results: Of the 372 patients analyzed, 110 (29.5%) had recurrent disease with a median follow-up time of 34 months. Of the 110 recurrences detected, 75 (68.1%) were detected by CEA elevation in combination with CT image, 33 (30%) were detected only by CT image and 2 (1.8%) neither by CT nor by CEA alteration. There was no clinic feature that would predict pattern of recurrence when analyzed by chi square test. Metastasiscmy rate from this analysis 53.6% and it was similar among both groups. Recurrence rate after metastasiscmy was 59.3%. There is a 5-year overall survival difference between patients that underwent or not metastatic surgery (79.4% vs. 54%, p = 0.01). Conclusions: CEA-based follow-up program and CEA-triggered imaging failed to detect early recurrence in almost 30% of cases. We believe that this number is high enough to allow us to continue to perform image test during CRC follow-up.

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Circulating tumor DNA testing and research in patients with gastrointestinal malignancies.
First Author: Faisal Shahjahan, Mayo Clinic, Jacksonville, FL

**Background:** The hallmark of circulating tumor DNA (ctDNA) is its rapid turnaround and non-invasive nature. According to American Society of Clinical Oncology (ASCO) and College of American Pathologists joint ctDNA review published in March 2018, there is no sufficient evidence to support the use of ctDNA in practice for GI cancers. However, there were numerous studies presented at ASCO Annual Meeting supporting its value. We aimed to summarize on its role in the management of gastrointestinal cancers based on the studies presented recently. **Methods:** We limited our search to key-words 'ctDNA', 'circulating tumor DNA', 'cell-free DNA (ctDNA)' and/or 'liquid biopsy', at the 2018 ASCO Annual Meeting library abstracts and presentations. **Results:** There were 35 studies that revolved around ctDNA as a diagnostic tool, prognostic marker and a measure of tumor heterogeneity in gastrointestinal cancers. Depending on the assay used, the results of several studies showed that ctDNA was able to identify relevant mutations including RAS, HER2/Neu, BRAF, MET, BRCA2, APC, TP53, ROS1, PTEN and NFI. The prognosis in terms of tumor mutation burden, objective response rate, metastasis and survival was also estimated based on ctDNA. The findings showed that higher baseline ctDNA levels and/or increased number of mutations detected in ctDNA were associated with poor survival and multi-site metastasis. Right-sided colon cancer was associated with higher number of mutations in ctDNA than left-sided colon and rectal cancer. Similarly, tubular adenocarcinoma subtype of gastric cancer was more likely to have higher ctDNA levels than signet-ring cell subtype. The response to therapy and the residual metastatic disease which was otherwise not detected on imaging could be detected by ctDNA as well. **Conclusions:** The research at ASCO 2018 report an increasingly promising role of ctDNA in many forms in patients with gastrointestinal malignancies. Experts at the meeting argued that the ctDNA should indeed be ready for prime time for certain GI malignancies including colorectal cancers. Prospective studies and studies showing its feasibility into practice can potentially help revise the current guidelines.
529 Poster Session (Board E102), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Racial disparities and treatment outcomes among patients admitted with a diagnosis of colorectal cancer: Analysis of the 2014 national inpatient sample database. First Author: Ipkonmwoosa Enofe, Michigan State University, East Lansing, MI

Background: Colorectal cancer is the fourth most common cancer in the United States and the second most common cause of death. Despite universal advocacy for screening colonoscopies and early diagnosis, racial disparities in screening and diagnosis of colorectal cancer exist and affect patients outcomes. In this analysis we determine racial disparities and treatment outcomes for colorectal cancer treatment in the United States. Methods: We performed a retrospective analysis of the National Inpatient Sample 2014 Database (HCUP, NIS) which contains records of all hospital discharges in the United States Patients 18 years and older with a diagnosis of colorectal cancer were identified by their ICD 9 codes along with treatment they had for colorectal cancer. We then used multivariable regression to identify the effect of race on receiving a therapeutic procedure (open surgical, laparoscopic or robotic) during hospitalization and outcomes as it relates to inpatient mortality. We adjusted for patients age, sex, number of comorbidities (elixhauser comorbidity score), insurance type, and hospital level characteristics (i.e. size, teaching status) and location (urban and rural location). Results: There were 25,749 discharge diagnosis of colorectal cancer in the United States in 2014 of which 19,300 were associated with undergoing a procedure for colorectal cancer treatment. Whites accounted for the majority of colorectal cancer admissions (65%) while blacks 11.4%, Hispanics 8.0%, Asian/Pacific Islanders 3.2%, and Native Americans 0.4%. Blacks had the lowest frequency of procedure related admissions and were less likely to undergo a therapeutic procedure relating to colorectal cancer treatment (67.5% vs. 76.6%, p < 0.01), compared to white patients. For specific procedures, black patients had lower levels of chemotherapy compared to white patients (55% vs. 63%, p < 0.01), compared to white patients. Hispanics (77% vs. 82%, p < 0.01), compared to white patients. Procedures related colorectal cancer admission. However, there was no significant variation between races. Conclusion: Asian/Pacific Islanders had a significantly higher mortality for non-procedure related colorectal cancer admissions. Further studies are warranted to understand the above findings.

530 Poster Session (Board E103), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

On the road again: Travel patterns and outcomes in rectal cancer. First Author: Mary Kledzik, John Wayne Cancer Institute, Santa Monica, CA

Background: Associations between high volume centers and outcomes have many advocating for centralization of cancer care, which can lead to increased travel, patient burden, and cost. There is, however, some conflicting data regarding outcomes for patients with more advanced disease. This study aims to explore factors associated with travel and the impact on survival for patients receiving surgery for rectal adenocarcinoma. Methods: All patients ≥18 years of age with rectal adenocarcinoma that had a surgical resection were identified using the National Cancer Database from 2004-2014. Univariate and multivariate (MV) regression analyses determined factors associated with travel distance (=<50 miles, 50-100 miles, >100 miles) as well as the impact of travel on overall survival (OS). Results: Of 83,933 patients, those that traveled the furthest were more commonly younger, while non-Hispanic, insured, and with less comorbidities (all p < 0.05 on MV analysis). Cancer stage, surgical approach, and type of surgery were not associated with travel distance (=<50). Increased travel distance improved 5-year OS for stage IV disease (10%, p < 0.002), and trended toward significance for stage II (4.0%, p=0.06) and stage I (4.3%, p=0.09) disease. After controlling for other factors, travel distance did not impact OS for stage II/III disease. However, patients traveling 50-100 miles had an increased risk of death (stage I HR 1.16, CI 1.04-1.30; stage IV HR 1.19, CI 1.07-1.32). This was similar in the entire cohort where traveling 50-100 miles had an increased risk of death (HR 1.09; CI 1.03-1.14). Patients treated at low volume centers did have improved outcomes across all stages (p < 0.01). Patients treated in academic hospitals had improved outcomes in stages I and IV (p < 0.02). Conclusions: Younger, white, non-Hispanic patients are most likely to travel longer distances for rectal cancer treatment, regardless of stage. Increased hospital volume improves OS while travel and use of academic centers may impact patients with stage IV disease. Educating patients and healthcare providers regarding the influence of travel and hospital volume could help reallocate some resources, decrease financial toxicity, and ease the travel burden for patients.

531 Poster Session (Board E104), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

The role of Parvimonas micra in intestinal tumorigenesis in germ-free and conventional APC<sup>min/+</sup> mice. First Author: Jun Yu, Department of Medicine and Therapeutics, State Key Laboratory of Digestive Disease, Institute of Digestive Disease, Li Ka Shing Institute of Health Sciences, CUHK Shatin Research Institute, The Chinese University of Hong Kong, Shatin, Hong Kong

Background: Our in-house meta-analysis of fecal shotgun metagenomic sequences from colorectal cancer (CRC) and control subjects from four cohorts of various ethnicities identified a higher abundance of Parvimonas micra in CRC patients. Aimed to investigate the effect of P. micra in colon tumor formation, growth and development. Methods: We collected 309 fecal samples and 259 colon biopsies from patients with CRC, advanced adenoma and healthy subjects. P. micra was selected from the above patient groups. Then, CRC patient, APC<sup>min/+</sup> germ-free (GF) mice were orally gavaged with P. micra, or Esherichia coli. Colon epithelial cell line NCM460 and cancer cell lines HT-29 and Caco-2 were exposed to P. micra or E. coli conditional medium. Results: P. micra was significantly enriched both in the feces (n = 207, p < 0.01) and tissue biopsies (n = 99, p < 0.01) of CRC patients compared with controls (n = 102 for fecal samples, n = 160 for tissues biopsies). APC<sup>min/+</sup> mice gavaged with P. micra exhibited significantly higher tumor burden (p < 0.01) and tumor load (p < 0.01), compared to mice gavaged with either E. coli or non-bacterial control. Consistently, cell proliferation was significantly higher in the colon tissues of P. micra gavaged GF mice relative to control mice evidenced by increased Ki-67 positive cells (p < 0.05) and PCNA protein expression (p < 0.01) at weeks 20 and 32. In line with this, colon cell lines NCM460, HT-29 and Caco-2 exposed to P. micra conditional medium significantly increased proliferation, compared to control group (all p < 0.05). Flow cytometry analyses showed that Th2 and Th17 cells were markedly increased, while Th1 were reduced in the lamina propria of the colon tissues of P. micra gavaged mice compared to control mice (all p < 0.01). Consistently, P. micra colonization in GF mice was associated with increased expression of pro-inflammatory cytokines, including TNF-α, IL-6 and IL-12 (all p < 0.01). Conclusions: The abundance of P. micra was significantly increased in the feces and tissue biopsies of CRC patients. P. micra promotes intestinal carcinogenesis in APC<sup>min/+</sup> mice and increase cell proliferation in GF mice. The tumor promoting effect of P. micra is associated with altered immune responses and enhanced inflammation in the gut.

532 Poster Session (Board E105), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

High-serum blood sugar level significantly enhances oxaliplatin resistance in stage III colorectal cancer patients. First Author: Jaw-Yuan Wang, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

Background: FOLFOX4 chemotherapy is one of the most widely used adjuvant therapies in patients with stage III colon cancer after surgical resection. However, chemoresistance is associated with a poor prognosis. The prognostic impact of high blood sugar levels on oxaliplatin resistance in CRC patients is an unexplored topic. Methods: A total of 157 patients with stage III CRC were classified according to their serum blood sugar level (=126 or ≥126 mg/dL). Clinicopathological features and clinical outcomes (oxaliplatin resistance) of the two groups were analyzed. Results: The univariate analysis, both disease-free and overall survival of CRC patients was found to be significantly associated with serum blood glucose levels (both P < 0.05) but not DM history. In vitro cell proliferation assay was performed through D (+)glucose administration. After metformin administration, enhanced proliferation of CRC cells with D (+)glucose administration could be reversed and oxaliplatin sensitivity considerably increased (P < 0.05). Furthermore, phosphorylation of two glycolysis related target proteins, SMAD3 and MYC, notably increased with high glucose concentration. Conclusions: In summary, hyperglycemia could affect clinical outcomes in CRC patients receiving adjuvant chemotherapy, with the underlying oxaliplatin resistance mechanism possibly associated with increasing phosphorylation of SMAD3 and MYC and upregulation of G9A expression.
Mismatch repair/microsatellite instability (MMR/MSI) testing practices among United States physicians treating patients (pts) with advanced/metastatic colorectal cancer (mCRC). First Author: Jennifer Eriksson, Commercialisation & Outcomes, ICON plc, Stockholm, Sweden

Background: Approximately 12-15% of all CRCs are associated with defects in the DNA mismatch repair pathway, NCCN 2017 guidelines emphasized universal MMR/MSI testing for all pts with a personal history of CRC. The study objective was to assess US physicians’ MMR/MSI genetic testing practices for mCRC pts. Methods: A non-interventional, cross-sectional online survey was conducted among 151 physicians (91 oncologists, 15 surgeons and 45 pathologists) treating mCRC pts in the US. A draft survey was first developed based on a targeted literature review and exploratory interviews with 15 physicians, and then pilot tested with a new series of 10 physicians. Physicians were eligible if they were US based with at least 5 years of experience treating CRC pts, had at least one mCRC pt in their routine care in the past 6 months of practice, and experienced with MMR/MSI testing including having ordered at least 1 MMR/MSI test for CRC in the past 6 months. Physicians were invited to participate through a market research panel. Descriptive and logistic regression analyses were performed. Results: Awareness of specific MMR/MSI testing guidelines was lower in the US compared to Europe (81%, 127/151) vs 98% (152/157) of physicians who had specific published guidelines with majority 67.2% (80/119) being aware of NCCN guidelines. Universal testing for all CRC pts was performed by 68.9% (104/151) physicians, while 29.8% (45/151) selectively orders the test for some CRC pts. Key barriers for testing included insufficient tissue sample to enable running the test (48.3%, 73/151), patient refusal to have the test done (35.8%, 54/151) and insurance cost concerns for the pts (31.1%, 47/151), while 27.2% (41/151) reported no barriers. There were no statistically significant differences based on physician specialty, practice type and years of practice. Conclusions: The survey demonstrated high awareness and compliance with MMR/MSI testing guidelines although universal testing rates seem to be suboptimal. Addressing the key physician barriers to testing along with increased communication and education on the benefits of testing may help to enhance testing rates.

KRAS mutation status to predict response in first-line capox and bevacizumab therapy for metastatic colorectal cancer. First Author: You Yone, Charing Cross Hospital, London, Imperial College Healthcare NHS Trust, London, United Kingdom

Background: Capecetabin and Oxaliplatin (CAPOX) combined with the humanized anti-vascular endothelial growth factor Bevacizumab represents a standard first-line treatment for metastatic colorectal cancer (mCRC). However, the response rate is only approximately 50% and currently there is no biomarker available to predict treatment response. This study aims to correlate KRAS status with response to CAPOX and Bevacizumab (CAPOX-Bev). Methods: Forty-five patients with mCRC were retrospectively screened between January 2012 and December 2015 at Broomfield Hospital, UK. DNA was extracted from formalin-fixed paraffin-embedded (FFPE) tissue samples (Qiagen FFPE tissue kit). Twelve mutations in Exons 2, 3 and 4 of the KRAS gene were analysed using a real-time quantitative polymerase chain reaction (qPCR) assay (EnTrogen). Treatment response was assessed according to RECIST criteria version 11 by comparing pre-treatment and post-treatment radiological CT scans. The KRAS status was correlated with CT tumour response (responders: partial response and complete response; non-responders: progressive disease and stable disease). A Chi-square test was used to determine the correlation between KRAS status and tumour response. Results: 19/45 patients were KRAS wild type (WT, 42%) and 26 were KRAS mutant (MT, 58%). 8/19 (42%) KRAS WT patients were responders, compared to 3/26 (12%) KRAS MT patients. Conversely 11/19 (58%) KRAS WT patients were non-responders, compared to 23/26 (88%) MT patients. The correlation of treatment response and KRAS status was statistically significant (p = 0.018), with a 31% difference in response rate between KRAS WT (42%) and KRAS MT (12%) groups. Conclusions: Within this pilot retrospective analysis, KRAS mutations demonstrated clinical value in identifying patients who are more likely to respond to first-line CAPOX-Bev in advanced colorectal cancer. This finding requires prospective evaluation within a large patient population to further detect potential differences in overall and progression free survival.

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Expanded RAS and BRAF V600 testing as predictive biomarkers for single agent cetuximab in the randomized phase III CO.17 trial. First Author: Jonathan M. Gore, BC Cancer, Vancouver, BC, Canada

Background: KRAS/NRAS (RAS) testing of exons 2, 3, and 4 is standard prior to anti-EGFR treatment in metastatic colorectal cancer and many consider BRAF V600 (BRAF) mutations predictive. CO.17 was a randomized phase III trial comparing cetuximab vs best supportive care (BSC) in unselected patients (pts). Re-analysis tested only KRAS exon 2, thus the benefit of cetuximab in RAS/BRAF wild type (WT) pts is unclear. Methods: We retrospectively performed expanded RAS/BRAF testing using a highly sensitive digital PCR method (Beamlign; 1% allele frequency detection limit) on micro-dissected archival tissue from 248 CO.17 pts. Additional pts without available archival tissue, with prior Sanger sequencing or therscreen results were included in analyses if mutations were previously identified (n = 77). Overall survival (OS), progression-free survival (PFS), and response rates (RR) were compared by molecular profile. Results: CO.17 was previously published and results presented above. RAS WT, with 72 (45%) exon 2, 21 (4%) exon 3 and 6 (4%) exon 4 KRAS mutant, and 20 (4%) NRAS mutant pts. Seven (3%) BRAF WT, and 97 (30%) confirmed RAS/BRAF WT pts were identified. Results are summarized as a test of interaction indicated RAS status was predictive for PFS (p = 0.0001) and OS (p = 0.037) and BRAF status reached significance as a predictive marker for PFS (p = 0.089) but not OS (p = 0.24). Conclusions: These updated results demonstrate an improved PFS (HR 0.25 vs 0.40 previously) and OS (HR 0.51 vs 0.56 previously) for cetuximab in RAS/BRAF WT pts compared to prior analyses that included only KRAS exon 2 mutation status. We provide an estimate of single agent cetuximab efficacy for future anti-EGFR re-challenge studies and demonstrate further support that BRAF mutations may predict lack of benefit from anti-EGFR therapy. Clinical trial information: NCT00079066.
Background: In comparative clinical trials with time-to-event outcomes, the long-term efficacy of the treatment is of greater importance than short-term effect. Long-term outcome is considered to be crucial. The conventional methods to predict outcomes earlier are warranted.

Methods: We considered both the primary and updated results for the PRIME to assess the validity of the procedure, and then estimated the long-term efficacy in the two trials. We used the reconstructed overall survival (OS) data obtained by scanning the Kaplan-Meier curves in the literature. Fitting the data to the Weibull distribution, we estimated the parametric group contrast measures including the difference in the 3- and 5-year restricted mean survival times and mean survival times. Results: The extrapolated parametric OS curves from the primary PRIME results fitted well with the observed Kaplan-Meier curves for OS in the updated results. The parametric estimations demonstrated that, in the PRIME trial, panitumumab plus FOLFOX arm increased 2.6 (0.5-13.7, 7.9 (2.1-13.7), and 12.8 (5.0-25.1) months in survival on average over 3-, 5- and 7-years, respectively, compared to FOLFOX arm. In PEAK trial, compared to bevacizumab plus FOLFOX arm, panitumumab plus FOLFOX arm increased 3.6 (0.7-6.5), 7.9 (2.1-13.7), and 12.8 (5.0-25.1) months in survival on average, respectively. Conclusions: The estimators for parametric survival curve would provide the informative summaries for long-term survival profile to the clinicians and patients.

Poster Session (Board #F5), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

The correlation between DPYD*9A (c.857 > C) genotype and dihydrooriprimidine dehydrogenase deficiency phenotype in patients with gastrointestinal malignancies treated with fluoropyrimidines: Updated analysis. First Author: Anu Singh Maharjan, ARUP Laboratories, The University of Utah, Salt Lake City, UT

Background: The correlation between DPYD*9A (c.857 > C) genotype and dihydrooriprimidine dehydrogenase (DPD) deficiency phenotype is controversial. In our cohort of 28 patients with gastrointestinal malignancies (GI) treated with fluoropyrimidines, DPYD*9A was the most commonly diagnosed variant (46%) and there was a noticeable genotype-phenotype correlation (Kushman et al). In this updated analysis, a larger cohort of a mixed racial background was genotyped for DPYD*9A variant to confirm the incidence and genotype-phenotype correlation. Methods: Between 2011 and 2018, in addition to genotyping for high risk DPYD variants (DPYD*2A, DPYD*13 and DPYD*9B), genotyping for DPYD*9A variant was performed on 72 patients. Results: DPYD variants were identified in 61 patients. DPYD*2A was identified in 3 patients and DPYD*9B was identified in 2 patients (one patient had double heterozygous *9A and *9B). Heterozygous DPYD*9A was identified in 46 patients (46%) and homozygous DPYD*9A was identified in 11 patients (16%). Among patients with DPYD*9A variant, Caucasians represented 59% and African Americans represented 46%, 27 patients (47%) were females. In our updated analysis, 29 patients with limited stage disease, 19 (65.5%) had an induction of ERCC1. In these patients change in expression did not correlate with RFS. We did not find any significant correlation of DFS with baseline expression of ERCC1 in either group. Conclusions: We confirm our hypothesis that the ERCC1 gene is induced in vivo in a sub-population of patients on treatment with Oxaliplatin. This induction can serve as a potential marker of resistance to oxaliplatin based chemotherapy in mCRC as evidenced by the significant difference in DFS. Further analyses of the influence of ERCC1 polymorphisms on outcomes is underway.
Germline pharmacogenomics of thymidylate synthase gene in patients with gastrointestinal malignancies treated with fluoropyrimidines-based chemotherapy regimens. First Author: Saad Awan, The University of South Alabama, Mobile, AL

Background: fluoropyrimidines are antimetabolites that target the S phase of the cell cycle. The active metabolite, 5-fluorodeoxyuridine monophosphate inhibits thymidylate synthase (TS) enzyme, thus preventing DNA synthesis and ultimately cell death. While controversy exists in the literature, polymorphism in the promoter region of thymidylate synthase gene (TYMS) that decrease TS expression has been associated with increased fluoropyrimidines-associated toxicities. This study explored the association between polymorphism in the promoter region of TYMS gene and fluoropyrimidines-associated toxicities in patients with gastrointestinal malignancies with mixed racial background. Methods: Between 2011 and 2018, 126 patients were genotyped for TYMS. Patients with known high risk thymidylate dehydrogenase gene variants were excluded. Fluoropyrimidines-associated toxicity was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (v 5.0). Fisher’s exact test was used for statistical analysis. Results: TYMS genotypes that predict increased TS expression (3R/3R, 3R/3R, 3R/2R, 2R/2R, 2R/4R, 3R/4R) were identified in 55 patients (44%). TYMS genotypes that predict decreased TS expression (2R/2R, 2R/2R) were seen in 71 patients (56%). Among patients with genotypes that predict increased TS expression (3R/3R, 3R/3R, 3R/2R, 2R/2R), patients had increased TS expression (22%) while among patients with genotypes that predict decreased TS expression, 30 patients had grade 3-4 toxicities (42%) (P = 0.0219). Compared to patients with genotypes predicting increased TS expression (17 out of 31 patients (55%) with 2R/2R TYMS genotype had grade 3-4 toxicity (P = 0.0039) and 15 out 40 patients (38%) with 2R/3RC and 3RC/3RC TYMS genotype had grade 3-4 toxicity (P = 0.0108). Among patients with 2R/2R TYMS, Caucasians represented 61% and African Americans represented 39%. Females represented 65% of the patients. Conclusions: Polymorphism in the promoter region of TYMS gene that predict decreased TS expression due to 2R/2R variant was associated with grade 3-4 fluoropyrimidines-associated toxicities.

Poster Session (Board #F8), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

RAS amplified colorectal cancers are enriched in RAS-WT, BRAF-WT, MSS tumors and may predict for anti-EGFR resistance. First Author: Marwan Fakhri, City of Hope, Duarte, CA

Background: Pre-clinical models implicate RAS amplifications (RAS) as a mechanism of resistance to anti-Epidermal Growth Factor Receptor (EGFR) therapies. Yet, there is little guidance on the impact of RAS on colorectal cancer (CRC) patient characteristics and response to anti-EGFR. Methods: Between 2011 and 2018, 126 patients were genotyped for RAS. All but 2 COH pts with RAS were predominantly left-sided (11/12). 7/12 patients were treated with anti-EGFR therapy. All 7 pts were RAS/BRAF wild-type: 6 with RAS-a and 1 with RAS-b. The median CN was 27 (7-72); 8/12 pts had amplification than the overall population (29% vs. 5% had ≥ 2R). The incidence of MSI-H, RAS and BRAF short variant mutations in the overall, RAS, and RAS-b populations were (MSI-H: 5%, 0%, 0%), (RAS: 54%, 32%, 2%), and (BRAF: 6%, 1%, 0%), respectively. RAS-a tumors had higher level of genomic amplification than the overall population (29% vs. 5% had ≥ 5 genes amplified). Cohort included 338 mCRC, 12 pts (3.6%) had RAS-a. The median RAS CN was 27 (7-72); 8/12 pts had RAS-b (100%). All 2 COH pts with RAS-a had RAS/BRAF-WT tumors. Both pts with concurrent RAS mutations had relatively low RAS CN (7.53). Tumors with RAS were predominantly left-sided (11/12); 7/12 pts were treated with anti-EGFR therapy. All 7 pts were RAS/BRAF wild-type: 6 left-sided 3 pts PTF, 1 right-sided and 2 pts irinotecan-based. All 4 pts chemo-refractory (all irinotecan-based). All 4 chemo-refractory pts had concurrent genomic alterations. We subsequently investigated City of Hope characterized this population based on patient characteristics and other RAS/BRAF status in tissue and/or liquid biopsies and tumour location (sidedness) are predictive markers of patients’ response to anti-EGFR mABs. MI-R3-3p expression has been correlated with clinical benefit from anti-EGFR mABs with chemotherapy. We aimed to validate the predictive power of miR-31-3p in a prospective cohort of chemo-refractory mCRC patients treated with single agent anti-EGFR mABs in the PROSPECT-C trial (NCT02994888). Methods: MI-R3-3p was tested in i-situ hybridization in 91 pre-treatment (PT) core biopsies from 45 mCRC patients. Sequential tissue biopsies obtained PT, at time of best response and at disease progression were tested to monitor changes in miR-31-3p expression over treatment. In 34 patients miR-31-3p, expression, 30 patients had grade 3-4 toxicities (42%) (P = 0.0219). Compared to patients with genotypes predicting increased TS expression, 17 out of 31 patients (55%) with 2R/2R TYMS genotype had grade 3-4 toxicity (P = 0.0108). Among patients with 2R/2R TYMS, Caucasians represented 61% and African Americans represented 39%. Females represented 65% of the patients. Conclusions: Polymorphism in the promoter region of TYMS gene that predict decreased TS expression due to 2R/2R variant was associated with grade 3-4 fluoropyrimidines-associated toxicities.
Gender and survival benefit from initial irinotecan in metastatic colorectal cancer: Analysis of the XELAVIRI (AIOKRK0101) study. First Author: Dominik Paul Modest, Department of Hematology and Oncology, Klinikum Grosshadern, University of Munich, Munich, Germany

Background: XELAVIRI compared initial versus sequential irinotecan (ir) in combination with fluoropyrimidine (FP) plus bevacizumab (bev) in patients (pts) with mCRC, trial identification NCT0249636. In the full analysis set of the study, non inferiority of time to failure of strategy (TFS) of the sequential use could not be demonstrated (primary endpoint). Methods: The secondary endpoints overall response rate (ORR), progression-free survival (PFS) as well as overall survival (OS) were evaluated in female versus male pts as well as molecular subgroups (RAS mutational status). Interaction of treatment and gender was tested by likelihood ratio tests. Results: Of 412 patients, 281/410 were male/female. In female pts, ORR was 43% in both arms, PFS was 8.9 (95% CI 6.8-11.1) versus 10.1 (95% CI 8.5-11.8) months (HR: 1.09 (95% CI 0.76-1.55), P = 0.65) in pts with initial ir versus pts without initial ir, respectively. In females, a trend for inferior OS with initial ir was seen: 21.8 (95% CI 14.8-28.8) months with initial ir versus 28.4 (95% CI 21.9-34.9) months without initial ir (HR: 1.46 (95% CI 0.95-2.24), P = 0.08). This difference was significant in the multivariate analysis (HR: 1.73 (95% CI 1.04-2.86, P = 0.034). Male pts benefitted across all analysed endpoints from initial ir: ORR was 58.3% with initial ir and 33.6% without ir (P < 0.001), PFS was 10.1 (95% CI 9.2-11.0) versus 7.4 (95% CI 6.3-8.5) months (HR: 0.54 (95% CI 0.42-0.69), P < 0.001) and OS 23.9 (95% CI 19-28.6) versus 20.5 (95% CI 18.1-22.9) months (HR: 0.63 (95% CI 0.47-0.85), P = 0.002), with initial ir versus without initial ir, respectively. Interaction of treatment and gender was seen for ORR (P = 0.018), PFS (P = 0.002) and OS (P = 0.001). Additional data including treatment and toxicities will be presented at the meeting. Conclusions: This unplanned exploratory analysis suggests that gender might interact with efficacy of ir in the context of FP and bev. While male patients derived a significant and clinically meaningful benefit from initial use of ir, this was not observed in female patients. Clinical trial information: NCT0249636.

CANCERS OF THE COLON, RECTUM, AND ANUS

Poster Session (Board #F12), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Circulating tumor derived cell-free DNA (ctDNA) to predict recurrence of metastatic colorectal cancer (mCRC) following curative intent surgery or radiation: Interim results. First Author: Mikaela Esquivel, University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA

Background: Over half of patients (pts) with oligometastatic CRC treated with definitive surgery or radiotherapy experience cancer recurrence. Early detection of ctDNA could identify high risk pts for additional intervention to eliminate micrometastatic disease. Here we report interim results of a prospective study aiming to determine ctDNA detection rates using a sensitive multiplex assay and to correlate post-procedure ctDNA detection with radiographic mCRC recurrence. Methods: Pts with mCRC intending to undergo a curative intent procedure were prospectively recruited at a single site. ctDNA was collected pre-procedure, 3 weeks (wks) post-procedure, and at multiple follow-up timepoints. ctDNA detection utilizing a multi-gene sequencing panel (Guardant Health) included somatic variant and epigenetic assessments. A novel variant classifier was applied to differentiate tumor derived versus non-tumor derived alterations. A SNP’s two-stage design in planned interim analysis to assess 36K post-procedure ctDNA detection rate was employed. Results: Of 25 pts enrolled, 21 (84%) had evaluable paired pre- and post-procedure samples. In these 21 pts, the 3 wks post-procedure sample was collected after surgery (N = 20) or radiation (N = 10) to address liver (N = 17), lung (N = 3), or ovarian (N = 1) metastases (colon resection (N = 6), ctDNA was detected (+) in 15/21 (71%) pre- and 12/21 (57%) post-procedure samples. ctDNA was (+) in 17/21 (81%) post-procedure samples with carcinoembryonic antigen (< 5 ng/ml). Conclusions: In this interim analysis of pts with mCRC undergoing curative intent procedures, the post-procedure ctDNA detection rate was 52%. The similarity between the observed post-procedure ctDNA detection and expected recurrence rate suggests promise for recurrence prediction using this approach. Given post-procedure ctDNA detection rate was higher than the expected recurrence rate, future correlative studies focusing on severe oligometastatic CRC are warranted.

cDNA detection in 21 evaluable pre- and post-procedure sample pairs.

Poster Session (Board #F13), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Role of enterocyte-specific gene polymorphisms in adjuvant treatment for Stage III colorectal cancer. First Author: Mitsuaki Sunagawa, Department of Gastroenterology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan

Background: Enterocyte subtype of the Colorectal Cancer (CRC) Assigner classifier is known as favorable to oxaliplatin-based adjuvant treatment for Stage III CRC. We previously reported potential predictive value of single nucleotide polymorphisms (SNPs) in enterocyte-related genes in metastatic CRC (Sunagawa, ASCO2018). In this study, we examined clinical significance of MS4A4A and CDX2 SNPs in adjuvant treatment (AT) for Stage III CRC. Methods: 350 patients with Stage III CRC were included in this study: 274 received AT (discovery cohort: median age = 62, median follow-up = 59.9 months) and 76 received surgery alone (control: median age = 75, median follow-up = 58.0 months). 68 and 206 patients received FOLF and oral fluoropyrimidine, respectively. SNPs were analyzed by PCR-based direct sequencing. Disease-free survival and overall survival (OS) were analyzed using Kaplan-Meier curves, logrank test, and Cox proportional hazards regression. Results: In discovery cohort, the G/A variant in MS4A4A rs4939378 was associated with lower 5y survival rate than any A allele in uni- and multivariable analyses (70% vs 90%, univariate: HR 2.29, 95% CI 1.03-5.06, P = 0.035; multivariable: HR 2.58, 95% CI: 1.15-5.76, P = 0.021). Patients with the G/G variant in CDX2 rs3812663 had better OS than those with any A, though not significant in univariable analysis (15y survival rate: 95% vs 82%, univariable: HR 0.34, 95% CI: 0.13-1.1, P = 0.078). There was no significance in the control, and significant associations were observed between MS4A4A genotypes and groups (interaction P = 0.007). In addition, there was no interaction between MS4A4A rs4939378 and FOLF vs oral fluoropyrimidine. Conclusions: Our findings suggest that MS4A4A and CDX2 gene polymorphisms may predict outcome in patients with Stage III CRC. However, the clinical significance of the SNPs for oxaliplatin seems to differ depending on tumor stage. Further research and validation study is warranted to explore the association of the SNPs with carcinogenesis or cancer progression.
Classification of BRAF mutated colorectal cancer based on microsatellite stability. First Author: Michitaka Nakano, Department of Gastrointestinal and Medical Oncology, National Kyushu Cancer Center, Fukuoka, Japan

Background: BRAF mutated metastatic colorectal cancer (CRC) shows poor outcome in spite of development of the treatment. Thus, classification of BRAF mutated CRC based on therapeutic target is warranted. Particularly, about half of the BRAF mutated CRC reveals high microsatellite instability (MSI-H) that is characterized by high mutation burden and frequent infiltration of lymphocytes. Hence, the patients with BRAF mutation carrying MSI-H would potentially benefit from immune-check point inhibitor. However, the precise evaluation of immune status of these patients has not been clarified. Furthermore, the character of BRAF mutation with microsatellite stability (MSS) is not fully investigated. Methods: Tumor genomic information of BRAF mutated CRC with MSS/MSI-H was downloaded from open database, Gene Expression Omnibus (GEO); GSE75316 (n = 59), GSE35896 (n = 62), GSE39582 (n = 585). Gene expression of BRAF mutation with MSI-H/MSS (GSE75316; n = 5/3, GSE35896; n = 1/5, GSE39582; n = 31/4) were normalized and differentially expressed genes were identified by using GeneSpring (Agilent technologies). Pathway analysis was performed by GSEA. Results: Pathway analysis revealed subsets regarding cytotoxic T cell (FDR q value: 0.09), helper T cell (FDR q value: 0.05), natural killer T cell (FDR q value: 0.1), and activated inflammatory response (FDR q value: 0.16) were significantly enriched in BRAF mutation with MSI-H (FDR q value < 0.25 means significant). The differentially expressed genes were identified in both of 2 groups. Significantly high expression of Granzyme A, Granzyme B, and Perforin were observed in BRAF mutated MSI-H. At the same time, highly expressed genes included MLH1 were identified in BRAF mutated MSS. Conclusions: High infiltration of cytotoxic T cells was suggested by the pathway analysis and expression of Granzyme A, B, and Perforin among BRAF mutated MSI-H. The activated immune status within these patients suggested the potential response of immune-checkpoint inhibitors. Furthermore, our data would give us a clue in considering the therapeutic strategy against BRAF mutated MSS, that will be the remained population among BRAF mutated CRC to which effective treatment have not been established.

The prognostic role of PD-L1 expression according to MSI status in stage III colon cancer after curative resection. First Author: Sang-Hee Cho, Department of Hemato-Oncology, Chonnam National University Hwasun Hospital, Hwasun, Republic of Korea

Background: Tumors expressing PD-L1 can render immune inactivated via triggering of PD-L1 receptor on T cells with various pathways. Based on this mechanism, the blockade PD-L1/PD-1 pathway has been used as a therapeutic strategy for metastatic CRC. In the present study, we evaluate the prognostic role of PD-L1 expression associated with microsatellite status in surgically resected stage III colon cancer patients. Methods: PD-L1 expression was performed by immunohistochemistry from 182 stage III colon cancer patients after curative resection. Using the immunohistochemical stain, percentages of PD-L1 positive tumor cells and staining intensity were evaluated and categorized as ‘strong’ and ‘weak’ positive group. Clinical and histopathologic parameters including of MSI status and survival outcomes were analyzed with IOD expression which stands for the suppressive immune environment. Results: Strong PD-L1 expression was observed in 29% of all patients, PNI and lymphocyte response response were more frequently shown in strong PD-L1 patients. Among these patients, MSI was shown in 23 patients (12%). Although there was no significant difference between MSI and PD-L1 status, strong PD-L1 tended to better OS in MSI colon cancer (P = 0.056). In contrast, strong PD-L1 expression significantly correlated with significantly worse prognosis in disease free survival (P = 0.001) and overall survival (P < 0.001) than weak PD-L1 expression in MSI patients regardless of adjudvant chemotherapy. In MSI patients, the strong PD-L1 expression was tended to be more frequently shown in strong PD-L1 expression patients (36.4%) than weak PD-L1 expression patients (43.3%). Conclusions: The expression of PD-L1 is differently affected on the survival according to the status of microsatellite. There is no significant relationship between the expression of PD-L1 and prognosis in MSI stage III colon cancer patients. However, in MSI colon cancer which showed worse prognosis as a highly immunogenic property, strong PD-L1 expression is significantly associated with poor prognosis on survival outcomes reflecting of immunosuppressive microenvironment in curative resected stage III colon cancer patient.
Nr12 methylene as a prognostic biomarker across all stages of colorectal cancer (CRC). First Author: Sean Michael O’Cathail, CRUK/MRC Institute for Radiation Oncology, Oxford, United Kingdom

Background: Keap1/Nr12 is an important intracellular canonical stress response pathway, with Nr12 acting as a potent transcription factor. Lung cancer is known to acquire constitutive activation of the pathway thus promoting survival, resisting chemOTHERAPY and dysregulating metabolism. Mechanisms of pathway activation include methylation of KeAP1, somatic mutation and direct activation by KRAS, BRAF and MYC, its role in CRC is unknown. Due to its role as a transcription factor, activated in many ways, we hypothesise a methylene of Nr12 regulated genes would act as a prognostic biomarker in CRC.

Methods: Using a candidate gene approach and publicly available data (GSE17536), we derived and trained a 36-gene methylene to aggregate Nr12 pathway expression, using principal component analysis and co proportional hazard models. GSE4333 was used for validation in stage II/III CRC. The first line metastatic FOCUS trial was used for validation in Stage IV disease. Results: 601 patients were included in the validation analysis. Nr12 methylene expression is associated with worse DFS outcomes in stage II/III disease in Cox PH models comparison (LRT, p = 0.0075) and worse OS in stage IV disease (LRT, p = 0.0057). On multivariate analysis, Nr12 expression remained significant when adjusted for known prognostic factors of adjuvant chemotherapy and Duke’s stage in stage II/III disease (ANOVa, p = 0.03), BRAF V600E and sildesness in stage IV disease (ANOVA, p = 0.0025). Using the median cut point, high expression has a HR 2.36 (CI 1.27-4.38) in stage II/III disease and HR 1.39 (CI 1.12-1.72) in metastatic disease. Conclusions: Nr12 expression is a novel, robust prognostic biomarker. Its potential mechanism of poor prognosis across all stages of colorectal cancer. Greater understanding of its mechanistic role could lead to targeted strategies to improve outcomes in CRC.

Poster Session (Board #F20), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Somatic POLE proofreading domain mutations by next generation sequencing to predict outcomes in stage II colorectal cancer. First Author: Shaobo Mo, Fudan University Shanghai Cancer Center, Shanghai, China

Background: Stage II colorectal cancers (CRC) exhibit unique molecular heterogeneity due to patients with somatic POLE mutations are defined as a distinct tumor subgroup. The aim of this study was to clarify the characteristics and prognostic effect of somatic POLE proofreading domain mutations by next generation sequencing (NGS-POLE EDM-mutations) and wild-type POLE, the difference was not statistically significant (p = 0.037). Though there is DFS difference between patients with non-NGS-POLE EDM-mutations and wild-type POLE, the difference was not statistically significant (p = 0.42).

Conclusions: Stage II CRC patients with NGS-POLE EDM-mutation identify a special cancer subset with better immune environment predicting excellent outcomes.
A phase II study of GVAX colon vaccine with cyclophosphamide and pembrolizumab in patients with mismatch repair-proficient (MMR-p) advanced colorectal cancer. First Author: Mark Yarchoan, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD

Background: Mismatch repair proficient (MMR-p) colorectal cancer (CRC) is refractory to single-agent programmed cell death protein 1 (PD1) inhibitors. Cancer vaccines may prime the tumor microenvironment for anti-PD1 therapy. Colon cancer clinical trials of allogeneic, whole-cell, GM-CSF-secreting vaccine that induces T-cell immunity against tumor-associated antigens. GVAX has previously been studied in combination with low-dose cyclophosphamide (Cy) to inhibit regulatory T cells. Methods: We conducted an open label, single-arm, phase 2 study of GVAX/Cy in combination with the PD1 inhibitor pembrolizumab in patients with MMR-p CRC who had received at least two prior lines of therapy in the metastatic setting. Patients received pembrolizumab plus Cy on day 1, GVAX on day 2, of a 21 day cycle through 4 cycles, and were then continued on a maintenance regimen of pembrolizumab every 3 weeks with Cy/GVAX given every 12 weeks. Results: Seventeen patients were enrolled. There were no objective responses, and the disease control rate was 18% by RECIST and 29% by irRC. The median progression free survival was 12.2 months (95% CI 6.6, 17.6). We found that patient baseline and pre-treatment characteristics that were significantly different between the MMR-p (n = 10) and non-MMR-p (n = 7) cohorts included age, gender, and disease status at baseline.

Conclusions: The GVAX C+ and GVAX C- regimens were manageable with minimal toxicity. The disease control rate was higher than expected in the MMR-p cohort. Clinically meaningful outcomes were observed for patients enrolled on the GVAX C+ regimen. Further studies should be performed to determine if GVAX C+ is superior to GVAX C+ and if further clinical benefit can be achieved with the addition of pembrolizumab.
Analysis of UGT1A polymorphisms and RAS: RAF mutations based on phase II study of biweekly XELIRI plus bevacizumab as a second-line therapy in patients with metastatic colorectal cancer. First Author: Hiroaki Tanioka, Department of Clinical Oncology, Kawasaki Medical School Hospital, Kurashiki, Japan

Background: We have previously reported biweekly XELIRI + bevacizumab 10 mg/kg as second-line chemotherapy in metastatic colorectal cancer (mCRC). In this study, we investigated relationships between efficacy/toxicity and biomarkers (polymorphisms of UGT1A, somatic mutations of RAS, BRAF and PIK3CA). Methods: Patients with mCRC who had received prior chemotherapy including oxaliplatin based regimens were eligible for this study. Treatment protocol administered cetirabine 1.000 mg/m2 twice daily from the evening of day 1 to the morning of day 8, intravenous irinotecan 150mg/m2 on day 1, and bevacizumab 10 mg/kg on day 1 every 2 weeks. Results: Between January 2013 and July 2015, 51 patients were enrolled in this study. The patients' characteristics were as follows (N=51): median age, 66 years (range 41-82); male/female, 29/22; the median PFS was 5.47 months (95% CI, 4.23-7.40 months), the median OS was 13.5 months (95%CI, 11.57-20.23months), and the median TTF was 4.5 months (95%CI, 3.97-6.93 months). The response rate was 16% (95%CI, 7.2-29.1), and the disease control rate was 76% (95%CI, 61.8-86.9). Grade 3 or higher adverse events were mainly febrile neutropenia in two patients and hypertension in 14 patients (28.6%). The patients with UGT1A (387G>T) genotype had a trend to suffer from diarrhea (p=0.089 by Fisher's exact test). The summary of somatic mutations of cancer was RAS (wild/mutant = 21/23), BRAF (wild/mutant = 39/5), PIK3CA (wild/mutant = 42/0), and MSI (MSS/MSI-H = 42/2). There was no statistical association between efficacy and somatic mutations. The sample size might influenced such the results. Conclusions: In mCRC patients, biweekly XELIRI + bevacizumab 10 mg/kg is effective and feasible as second-line chemotherapy. We found several biomarkers that predict toxicities in this study. Further study is required for predicting the efficacy based on biomarkers using somatic mutations of cancer and germline polymorphisms. Clinical trial information: UMIN000009260.
Patient-derived colorectal cancer spheroids for single cell characterization of intratumor heterogeneity in response to EGFR inhibition. First Author: Jeremy D. Kratz, University of Wisconsin Carbone Cancer Center, Madison, WI

Background: Epidermal growth factor receptor inhibitors (EGFRi) have improved clinical outcomes in patients (pts) with metastatic colorectal cancer (mCRC). Molecular profiling and primary tumor (tumor) sidedness are used to predict population benefit. Our group has recently demonstrated that patient-derived organotypic cancer spheroids (PDOCS) and optical metabolic imaging (OMI) can predict in vivo chemotherapy response. Translational tools are needed to characterize targeted therapeutic response to predict clinical outcomes.

Methods: PDOCS were generated from patients with mCRC at time of molecular profiling. Following culture maturation, PDOCS were treated with physiologic doses of EGFRi panitumumab in combination or alone. Response was evaluated in sphere diameter and OMI to exploit intrinsic autophuorescence of NAD(P)H and FAD at sphere and single-cell level. Effect size was calculated using Glass’s delta (d) defined as differences in means between treatment groups normalized to control standard deviation with comparison to predetermined sensitivity thresholds.

Results: PDOCS from pts with mCRC were generated from tissue biopsies, surgical specimens, and malignant effusions (n = 38). Mutational profiles of stably transfected RAS status from normal to control standard deviation with comparison to predetermined sensitivity thresholds. PDOCS were evaluable for experimental and clinical response. KRas mutation predicted primary resistance to EGFRi with no difference in diameter (Ga = 0.01) or single cell response by OMI (Ga = 0.02). Widely type PDOCS had significant response with decreased diameter with EGFRi (P < 0.001). Gaussian fit of single-cell analyses revealed heterogeneity in EGFRi sensitivity. Differential sensitivity to EGFRi in RAS wild type population correlated with clinical response. Conclusions: PDOCS predict response to panitumumab in these preliminary investigations. Diameter and OMI analyses provide complementary information of line specific sensitivity. Further studies are warranted to characterize the molecular profiles underlying intratumor heterogeneity. Prospective investigations are needed to understand the predictive role of this technique in targeted therapeutic response.

CANCERS OF THE COLORECTAL AND ANUS
integrated profiling of the patterns of pathologic response to neoadjuvant chemoradiation and the genomic-based radiation sensitivity in rectal cancer. First Author: Zhiguan Yuan, Moffitt Cancer Center, Tampa, FL

Background: Given the lack of biomarkers to predict a pathologic complete response (pCR) after neoadjuvant chemoradiation (NACRT) for rectal cancer, selection for non-operative management (NOM) mandates complete clinical response. We have previously developed/validated a model to assess genomic-based tumor radiosensitivity: the radiosensitivity index (RSI), which formulates a clinically actionable model to calculate genomic-adjusted radiation dose (GARD). We determined the profiles of RSI and GARD for rectal cancer and correlated these findings with the pathologic response patterns.

Methods: One hundred seventeen rectal cancer patients treated from 2009 to 2018 at NACRT were assessed for the tumor regression grade (tumor regression grade (TRG); 1 = moderate response; 2 = partial response; 3 = poor response). RSI was analyzed in an independent tissue cohort of 113 resected rectal cancer samples. GARD was derived as described before, which shows a high GARD value indicated a superior therapeutic effect of radiation. Results: Median follow-up from completion of NACRT was 26 months. The primary tumor stages were 71% T2, 84% T3, and 9% T4. The majority of patients (92%) received concurrent 5-FU or Capecitabine and (83%) received RT dose of 50.4 Gy (range 45-56 Gy). Median time from end of NACRT to surgery was 61 days (range 36-105 days). The patterns of pathologic response were TRG 0 (n = 24, 21%), 1 (n = 52, 53%), 2 (n = 29, 27%), and 3 (n = 12, 13%), suggesting heterogeneity of tumor radiosensitivity to treatment with similar tumor stage and treatment regimens.

The median RSI for the tissue cohort was 0.46 (range 0.09-8.81) with 37% of the samples considered radiosensitive based on prior data. GARD value ranges varied from 2.7 to 7.3 (median 2.9), suggesting heterogeneous RT therapeutic effects. Conclusions: The findings from the clinical cohort were consistent with the tissue cohort showing significant heterogeneity in the individual tumor radiosensitivity and GARD-based RT therapeutic effects. With the development of GARD-based prospective trials, we anticipate more biology-based customized RT dosing which could optimize patient selection for NOM and individualize the most appropriate dose for each patient.

Oncogenic alterations detected by droplet digital PCR in patients with metastatic colorectal cancer resistant to cetuximab. First Author: Ruijiao Liu, Fudan University Shanghai Cancer Center, Shanghai, China

Background: Anti-EGFR therapy is the standard of care for metastatic colorectal cancer (mCRC) patients with RAS and BRAF wild-type (wt). Secondary alterations of several genes have been identified as possibly resistant mechanisms to EGFR blockade, including mutations of KRAS, NRAS, BRAF, and EGFR-ectodomain, as well as amplifications of HER2 and c-MET. In this study, we investigated alterations of these targeted genes for mCRC patients with acquired resistance to cetuximab treatment by using non-invasive droplet digital PCR (ddPCR) to detect circulating tumor DNA (ctDNA).

Methods: We enrolled 38 RAS and BRAF wt patients, who progressed after failure of cetuximab contained regimens between Jul 2015 and Jan 2018. A total of 23 secondary alterations were found in 17 (77/36, 44.7%) cetuximab-resistant patients. The targeted gene alterations were detected as follows: 9 (9/23, 39%) RAS mutations, 5 (22%) HER2 amplifications, 5 (22%) EGFR mutations, 2 (9%) c-MET amplifications, 1 (4%) BRAF and 1 MEK mutation. Among 17 patients, 6 patients had multiple alterations, including 2 patients with KRAS+EGFR mutations, 2 patients with HER2+c-MET co-amplifications and 2 patients with KRAS+HER2+MET exon 2 and 3 multiple mutations. Primary sites were left-sided in 15 cases and right-sided in 2 cases, descending colon (12 cases) was the most common primary. Eleven patients were synchronous disease. Twelve patients received cetuximab as first line therapy, whereas 5 patients in the ≥2nd-line setting. All of these 17 patients, plasma levels of oncogenic alterations detected by ddPCR were showed dynamic changing and good agreement with tumor responding status.

Conclusions: Oncogenic alterations detected by ddPCR were found in almost half mCRC patients resistant to cetuximab. Dynamic changes of specific alteration may facilitate making decisions for selection of anti-EGFR mAb during the treatment course. Further studies in a larger population are needed to confirm these findings.
Identification of site-specific genome alterations in metastatic colorectal cancer: Sub-study 003 of the SCRUN-Japan GI-Screen. First Author: Takuro Mizukami, Department of Clinical Oncology, St. Marianna University School of Medicine, Kawasaki, Japan
Background: Primary tumor sidedness is known to be an independent prognostic factor and a predictor for the efficacy of anti-EGFR antibody. However, limited information is available regarding the role of primary tumor sidedness as a predictive factor for the treatment of metastatic colorectal cancer (mCRC) patients (pts), including gene mutation profiles, prognosis, and prediction for treatment. This study was conducted as a sub-study of the SCRUN-Japan Gi-Screen, the Nationwide Cancer Genome Screening Project in Japan. Methods: Among participants of the Gi-Screen 2003-01-CRC, untreated pts with mCRC which samples were collected from primary site were eligible. DNA and RNA were extracted from FFPE tumor samples and then were analyzed by the Oncomine Cancer Research Panel detecting gene mutations, copy number variants (CNV), and fusions across 143 genes in a CLIA certified CAP accredited laboratory. The detected genomic variant data were classified according to genetic drivers of cancer including gain- and loss-of-function or single nucleotide variant based on the Oncomine Knowledgebase. Results: Among 1011 enrolled pts from Feb, 2015 to Mar 2017, a total of 561 samples were analyzed (median age, 66.0 years; 232 [41.4 %] female). Frequency of female, undifferentiated, mucinous or signet ring cell subtype were mutually increased in EO compared with LO pts. Cox proportional hazards models were used to estimate cause-specific survival (CSS) and examine factors associated with CSS. Conclusions: This study revealed the site-specific survival and gene alterations in Japanese mCRC pts. These novel knowledge provide an intriguing background to investigate new targeted approaches in these pts and represent the progress toward precision medicine. We will analyze the site-specific therapeutic effect of molecular targeting agents, including anti-EGFR antibody. Clinical trial information: UN0000031242.

RS LS Rectum RS LS Rectum
KRAS mutation as a predictor for cause-specific survival in early- versus late-onset colorectal cancer: A United States population-based study. First Author: Albert Y. Lin, VA Palo Alto Health Care System, Palo Alto, CA
Background: While the overall incidence rates for colorectal cancer (CRC)–the third leading cancer diagnosis in the US–have been decreasing over the last several decades, incidence rates for early-onset (EO, age 20-49 years) CRC have shown an upward trend. Multiple studies have documented mutations in KRAS proto-oncoprotein (KRAS) as a poor prognostic factor for colorectal cancer survival.[1] However, limited information is available regarding the role of primary tumor sidedness as a predictive factor for the treatment of metastatic colorectal cancer (mCRC) patients (pts). Data from the Nationwide Cancer Genome Screening Project in Japan (SCRUN-Japan) of 2003-01-CRC was analyzed. Methods: Survival, Epidemiology, and End Results (SEER) Program data were queried to identify pathologically-confirmed CRC cases diagnosed between 2010 and 2015 among residents of the 13 SEER regions. Results were compared between EO and LO using Chi-square tests. Kaplan-Meier and Cox proportional hazards models were used to estimate cause-specific survival (CSS) and examine factors associated with CSS. Results: Of 202,173 CRC cases, 3,842 EO and 17,819 LO CRC cases had KRAS testing with a KRAS mutation found in 5% of patients (5%). EO tumors harboring mutated KRAS, EO tumors with KRAS mutations were more frequently found in females (52%) vs. 45%, P < 0.001), left-sided (LS) or rectal cancers (62% vs. 48%, P < 0.001), stage II/IV (89% vs. 81%, P < 0.001), and grade III/IV (28% vs. 18%, P = 0.038). Compared to CSS in EO with KRAS mutation, LO with KRAS mutation was associated with worse prognosis–with an overall hazard ratio of 1.09 (95% CI, 1.03-1.15, P < 0.001). Results [HR (95% CI)] from Cox analyses on a subset of patients with KRAS mutations are shown below. Conclusions: Despite EO CRC carrying worse prognostic factors than LO CRC, it confers better CSS than LO CRC. EO CRC is distinct from LO CRC in clinical and pathological features, in addition to its response to mutation KRAS. Mutated KRAS is an independent prognostic factor in LS colon and rectal cancers among the EO, but not in the EO population.

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<th>KRAS: mutated vs. wild-type</th>
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<tr>
<td>Mutated (95% CI)</td>
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<tr>
<td>Female</td>
<td>0.96 (0.99)</td>
<td>1.19 (1.29)</td>
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<tr>
<td>Male</td>
<td>1.03 (1.08)</td>
<td>1.29 (1.34)</td>
</tr>
<tr>
<td>Left-sided (LS)</td>
<td>0.96 (0.99)</td>
<td>1.19 (1.29)</td>
</tr>
<tr>
<td>Right-sided (RS)</td>
<td>1.02 (1.06)</td>
<td>1.24 (1.34)</td>
</tr>
</tbody>
</table>

(Adjusted for sex, T, N, M stage, histology, and tumor grade; risk side-

CANCERS OF THE COLON, RECTUM, AND ANUS

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The relationship between tumor budding, tumor microenvironment, and survival in patients with primary operable colorectal cancer. First Author: Hester Catharina Van Wyk, Academic Unit of Surgery, University of Glasgow, Glasgow, United Kingdom

Background: Tumor budding is an independent prognostic factor in colorectal cancer and has recently been defined by the International Consensus Conference on Tumor Budding. The aim was to use the ITBCC budding evaluation method to examine relationships between tumor budding, tumour factors, tumour microenvironment, gene expression profiles and survival in patients with primary operable CRC. Methods: Hematoxylin and Eosin (H&E) stained slides of 953 CRC patients, diagnosed between 1997 and 2007 were evaluated for tumor budding according to the ITBCC-criteria. The tumour microenvironment was evaluated using tumour stroma percentage (TSP) and Klintrup-Makinen (KM) grade to assess the tumour inflammatory cell infiltrate. Differential gene expression was assessed using TempO-Seq gene expression profiling (BioSpyder Technologies Inc., CA, USA) using the Surrogate-Plus targeted panel (2,733 genes selected for biological diversity, maximal information content, and widespread pathway coverage). Results: High budding (n = 269/28%) was significantly associated with TNM stage (P < 0.001), venous invasion (P < 0.001), weak KM grade (P < 0.001), high TSP (P < 0.001) and reduced cancer specific survival (CSS) (HR = 5.04; 95% confidence interval [CI], 3.50-9.53; P < 0.001) and was independent of venous invasion, KM grade, and Ki67 proliferation index. RNA expression analysis was employed using TempO-Seq to determine differential gene expression between tumours with and without budding (n = 18). Three genes were identified as significantly differentially expressed: S100A2 (S100 calcium binding protein A2) was upregulated by 2.9 fold (padj < 0.0001); REG1A (regenerating family member 1 alpha) was downregulated by 4.7 fold (padj < 0.01); and LCN2 (lipocalin 2) was downregulated by 2.2 fold (padj < 0.01). Conclusions: Tumor budding stratifies patients survival in primary operable colorectal cancer and associates with differing gene expression profiles and factors of the tumour. Therefore, the ITBCC budding evaluation method should be used to assess tumour budding as supplement the TNM staging system and can help to further subdivide colorectal cancer into new prognostic groups.

Predicting the pathologic complete regression with hematologic markers during neoadjuvant chemoradiotherapy in the locally advanced rectal cancer. First Author: Jae-Sung Kim, Department of Radiation Oncology, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea

Background: The present study aimed to evaluate the hematologic markers for predicting the pathologic complete regression during and after neoadjuvant chemoradiotherapy (CRT) in patients with locally advanced rectal cancer. Methods: Total 297 patients with rectal cancer underwent neoadjuvant CRT followed by surgical resection and performed complete blood counts (CBC) serially during and after CRT. The timepoints of CBC were before CRT (pre-), three weeks after the day of starting CRT (intra-); and four weeks after CRT (post-). We calculated the platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte (NLR), derived neutrophil-to-lymphocyte (dNLR) using the serial CBC test. The ratio of change in PLR (cPLR), NLR (cNLR), and dNLR (cdNLR) was calculated as the change of value/pre-value. Chi-square and T-test for univariate analysis and multivariate logistic regression were performed to identify the significant predictor for pCR. Receiver operating characteristics (ROC) analysis was used to compare the predictive values.

Results: The overall rate of pCR was 15.9%. The Pre-Hb, pre-NLR, intra-PLR, intra-NLR, intra-cPLR, intra-cNLR, post-WBC, post-Hb, and post-cPLR were significantly different between patients with pCR and no pCR. In the multivariate logistic regression, pre-Hb (OR 1.456 p-value .026), intra-cPLR (OR 4.949, p-value < .001), and post-WBC (OR 0.664, p-value .048) were significant predictors for pCR. In the comparison of ROCs, intra-cPLR was the most accurate predictor for pCR among the hematologic variables (AUC = 0.74, p = .001). Conclusions: Change of PLR during neoadjuvant CRT is the clinically applicable and significant predictor for pCR with high negative predictive value in the patients with LRC.
Background: Several previous reports indicated that cetuximab (Cmab) rechallenge may be efficacious in some patients for whom Cmab was previously effective. Liquid biopsy can detect some emerging mutations for resistance with Cmab. Considering the plasticity and elasticity of sensitive clones, we assumed we could identify the patients with benefit from Cmab rechallenge by liquid biopsy in the E-Rechallenge Trial.

Methods: The E-Rechallenge Trial is a multicenter phase II study in mCRC patients who have become refractory to fluoropyrimidines. L-CHIP, Cmab, and bevacizumab, and in whom previous treatment with Cmab was effective in any earlier line (achieving CR, PR, or SD that persisted for ≥6 months). The other main eligibility criteria are: RAS wild type, measurable disease, aE7 ≥16 weeks between the last dose of Cmab during previous treatment and the start of Cmab rechallenge. Protocol treatment is the combination of weekly Cmab with biweekly CPT-11. Additional research of ctDNA was conducted optionally. Baseline plasma samples were analyzed for biomarkers when analyzing the potential predictive association with PFS, levels of these markers were associated with worse survival. Biomarker changes were quantified as fold change [log2(C1D21/baseline)] and differences between arms were evaluated using the Mann-Whitney test.

Results: Between Dec. 2014 and Oct. 2017, 33 patients were strong. The primary endpoint; the rates of PR/SD/PD were PR 15.6%/SD 40.6%/PD 58.8%. Twenty-four of 33 patients participated in the additional research.

Conclusions: Cmab rechallenge showed some activity in the salvage setting, in patients for whom Cmab was previously effective. KRAS, BRAF, and EGFR S492R mutations using digital PCR (Lbix probe, RIKEN GENESIS). A cut-off of the mutation allele frequency was >0.1%

Poster Session (Board #H10), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

**Characterization of chemoradiation-induced changes in immune cells and targets for personalized therapy in locally advanced rectal cancer (LARC).**

First Author: Elisa Fontana, The Institute of Cancer Research and The Royal Marsden Hospital, London, United Kingdom

Background: Neoadjuvant radio/chemoradiotherapy (CRT) is a treatment milestone for LARC. The importance of immune response in CRT efficacy is increasingly realised. However immune cell changes associated with poor and good response are not completely understood.

Methods: Matched archival pre-CRT biopsies and post-CRT resection specimens from patients (pts) treated with neoadjuvant CRT were retrieved. Delta-TCD (tumor cell density, estimated using quantitative point counting on virtual tissue H&E) and k-means clustering method were used to classify pts into groups of pts with significant increase in innate immunity and decrease in adaptive immunity across all pts (CIBERSORT and SSGSEA analyses). Between good and poor responders there were 6% (39/636) and 2% (15/636) of genes significantly affected by CRT (Bonferroni t-test, q-value <0.05). All being markedly up-regulated in the Rego arm compared to the placebo after treatment. Conclusions: In this hypothesis generating report, VCAM-1, PDGF-AA were the top biomarkers of interest and the potential predictive association with PFS, where a lower hazard was observed for pts receiving Rego. Candidate prognostic markers were identified, including PIGF and VEGF-R1, key factors in VEGF biology. Biomarker changes observed here may offer insights into potential combinatorial strategies with Rego for future studies.
ABSTRACT WITHDRAWN
Th17 cell pathway-related genetic variants in metastatic colorectal cancer: A meta-analysis using TRIBE, MAVERIC, and FIRE-3

Poster Session (Board IH7), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Regorafenib in Patients with Treatment-Resistant Metastatic Colorectal Cancer: RAS, BRAF, and MEK Status-Subtype Analysis

Poster Session (Board IH8), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Association of consensus molecular subtypes (CMS) with time to progression (TTP), progression free survival (PFS), and overall survival (OS) with second-line FOLFIRI ± regorafenib in metastatic colorectal cancer (mCRC).

Post hoc analysis of clinical trial data in patients with metastatic colorectal cancer treated with standard chemotherapy and uncontrolled disease progression

Poster Session (Board IH9), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Activity of EGFR inhibition in atypical (non-V600E) BRAF-mutated metastatic colorectal cancer.

Poster Session (Board IH10), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Association of consensus molecular subtypes (CMS) with time to progression (TTP), progression free survival (PFS), and overall survival (OS) with second-line FOLFIRI ± regorafenib in metastatic colorectal cancer (mCRC).

Poster Session (Board IH11), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Guanylate cyclase C (GUCY2C) as a prognostic and therapeutic target in colorectal cancers (CRCs) arising through divergent genomic mechanisms

Poster Session (Board IH12), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Guanylate cyclase C (GUCY2C) as a prognostic and therapeutic target in colorectal cancers (CRCs) arising through divergent genomic mechanisms

Poster Session (Board IH13), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Association of consensus molecular subtypes (CMS) with time to progression (TTP), progression free survival (PFS), and overall survival (OS) with second-line FOLFIRI ± regorafenib in metastatic colorectal cancer (mCRC).

Poster Session (Board IH14), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Association of consensus molecular subtypes (CMS) with time to progression (TTP), progression free survival (PFS), and overall survival (OS) with second-line FOLFIRI ± regorafenib in metastatic colorectal cancer (mCRC).

Poster Session (Board IH15), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Association of consensus molecular subtypes (CMS) with time to progression (TTP), progression free survival (PFS), and overall survival (OS) with second-line FOLFIRI ± regorafenib in metastatic colorectal cancer (mCRC).

Poster Session (Board IH16), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Association of consensus molecular subtypes (CMS) with time to progression (TTP), progression free survival (PFS), and overall survival (OS) with second-line FOLFIRI ± regorafenib in metastatic colorectal cancer (mCRC).

Poster Session (Board IH17), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Association of consensus molecular subtypes (CMS) with time to progression (TTP), progression free survival (PFS), and overall survival (OS) with second-line FOLFIRI ± regorafenib in metastatic colorectal cancer (mCRC).

Poster Session (Board IH18), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM
Quantifying the evolution of tumor architecture using serial circulating tumor DNA. First Author: Jason Henry, MD Anderson Hematology/Oncology Fellowship, Houston, TX

Background: There is limited data regarding changes in the genomic landscape in individual patients over time as serial tissue biopsy has risk and is of uncertain clinical benefit. The advent of circulating tumor DNA (ctDNA) allows for safe and repeated molecular sampling with the potential to investigate tumor architecture in individual patients over time as serial tissue biopsy has risk and is of uncertain clinical benefit. The advent of circulating tumor DNA (ctDNA) allows for safe and repeated molecular sampling with the potential to investigate tumor architecture. From 5/15 to 12/17, 116 patients with metastatic CRC had between three to 12 blood specimens taken over the treatment course. Plasma was tested using targeted NGS assay (Guardant Health Inc., Redwood City, CA). Tumor mAF was established for each patient as the fold change between the mutant mAF of 1% and limit of detection for serial samples with the lowest mAF. Mutations not failing within this window were excluded from analysis. Substantial treatment induced selective pressure (SP) was defined as a decrease in the mutant mAF of > 50% in patients with at least an initial mAF of 1%. Results: 116 patients with a total of 317 serial blood samples were evaluable after accounting for ctDNA variations over time. Specimens were collected a median of 12 months apart, with a median of three specimens per patient. Thirteen percent (11%) did not have any changes in mutations on serial sampling, however the remainder of patients gained an average of 1.1 mutations per time point (mut/tp), and lost 1.0 mut/tp. 31% of patients demonstrated evidence of substantial treatment-induced SP. These patients were more likely to demonstrate a change in clonal architecture of the tumor (46% greater rate than those without SP, P = 0.04), predominantly through gain. In contrast, clonal hematopoiesis alterations that may be induced by chemotherapy, such as JAK2V617F, were neither gained or lost.

Conclusions: After correction for variations over time in the total amount of ctDNA in circulation, we identify numerous changes in tumor architecture with serial sampling. For the first time in colorectal cancer we demonstrate that when treatment-induced SP is applied the rate of tumor evolution is increased, demonstrating potential value of monitoring changes in tumor architecture over the disease course.
Detection of methylated BCAT1 and IKZF1 in stage II/III rectal cancer receiving chemoradiation. First Author: Chin-Tung Chen, Memorial Sloan Kettering Cancer Center, New York, NY

**Background:** In liquid biopsy, analyses of circulating tumor DNA (ctDNA) in blood have been used as a tool in cancer screening, identifying tumor mutations and monitoring treatment responses/recurrences. Aberrant methylation of some genes have been associated with cancer. T wo genes, BCAT1 and IKZF1, are highly methylated and specific to colorectal cancer (CRC) in blood. Detection of these two methylated genes in post-surgery samples also correlates with higher chance of recurrence. Here we investigated the presence of methylated BCAT1 and IKZF1 at multiple time-points for each patient.

**Methods:** Plasma was extracted from blood within 4 hours of the blood collection. ctDNA was extracted from plasma and bisulfite converted using commercially available kits. Real-time qPCR was used to analyze the converted DNA in three replicates and deemed positive if at least one replicate detected either methylated BCAT1 or IKZF1. Quantification of both genes was determined using separate gene-specific standard curves. **Results:** Nine Stage II/III rectal cancer (RC) patients were enrolled into the study, with one pre-treatment blood draw and several subsequent draws collected throughout the treatment cycles. Five patients tested positive for at least one of the methylated genes prior to treatment. Four of these five patients showed an immediate drop in detection for the assayed genes after one cycle of chemotherapy and either remains at low concentration or is undetectable through the rest of the treatment cycles. These patients either have partial or complete response to the treatment regimen. One patient with continuous high levels of methylated BCAT1 and IKZF1 post-treatment have received two months surgery. **Conclusions:** Methylated BCAT1 and/or IKZF1 were detected in over 50% of the Stage II/III RC patients pre-treatment. This assay is sensitive to the effect of chemotherapy regimen. A significant number of these patients showed a partial/complete response to their treatment regimen and/or reduction in tumor burden, which is reflected in the loss of detection of these two genes. This study shows that this assay may be a viable tool to pair with Imaging for assessment of patient response to treatment regimen.

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**603** Poster Session (Board #J6), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM


**Background:** Lymphotoxin alpha (LTA) is a proinflammatory cytokine expressed by inflammatory cells with a role in the regulation of tumor microenvironment (TM). A putatively functional genetic polymorphism in LTA, at locus +80 (Thr26Ala, rs1049818), has been associated with altered expression of LTA. Here, we sought to evaluate whether this polymorphism associates with two main endpoints (progression-free survival (PFS) and overall survival(OS)) in colorectal cancer (CRC). **Methods:** TNs retrospective cohort study was conducted in 166 CRC patients from a single tertiary hospital. Whole blood was used to isolate genomic DNA. Genotyping of LTA +80 C > A was performed through real-time qPCR allelic discrimination using specific Taqman probes, and confirmed by sequencing. Retrospective data and long-term outcomes were reviewed. Age and gender-adjusted logistic regression analyses were undertaken. Analyses were conducted after stratification by baseline lymphocyte count (LC < 1x10^3/µL vs. > 1x10^3/µL). Kaplan-Meier curves with Log-rank Test were used. Subsequent multivariate Cox regression proportional hazards models were calculated (P for retention > 0.1). **Results:** Participants' median age was 65.9 (IR, 57.5-74.3) years, the majority were males (63%), and 58% with colon cancer. At diagnosis, 45.2% were stage III and 18.1% stage IV. The median follow up time was approximately four years (IQR, 25.5-67.0 months). We found a significant association in carriers of the A allele to have lower LC on linear trend analysis (P for trend = 0.013). Multivariate comparisons between LTA genotypes of additive model showed an independent protective effect for heterozygous and homozygous mutant compared to C-homozygous in the association with disease progression (HR = 0.5, 95 CI = 0.3-0.97, P = 0.041), only in subjects with baseline LC > 1x10^3/µL. In this group, a significant independent protective effect for all-cause mortality was observed in A-carriers (HR = 0.4, 95 CI = 0.10-0.97, P = 0.042). **Conclusions:** This LTA genetic variant in subjects with baseline LC > 1x10^3/µL is associated with DFS and OS in CRC. The understanding of the impact of this polymorphisms on the evolution of the disease can bring us new information on TM regulation.
CANCERS OF THE COLON, RECTUM, AND ANUS

Poster Session (Board #J11), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

608 Risk score and prognosis modeling based on mRNA expressivity in the tumor microenvironment of GI cancers. First Author: Sunyoung S. Lee, Roswell Park Comprehensive Cancer Center, Buffalo, NY

Background: Stromal elements in the tumor microenvironment (TME) impact prognosis and response to therapy. Advances in mRNA-seq improved understanding of gene expressivity, but few models exist to model prognosis in association with mRNA expression. Methods: Clinical data and mRNA-seq of 1,715 patients (pancreatic adenocarcinoma (PAAD), colorectal adenocarcinoma (CRC), hepatocellular carcinoma (HCC), gastric adenocarcinoma (GAAD), esophageal adenocarcinoma (EsoAd), and esophageal squamous cell carcinoma (EsoSCC)) were obtained from TCGA and the Cancer Genome Atlas (CGA) databases. mRNA expression was enriched in cellular and structural components of the TME and clinical data were analyzed using machine learning, multivariable Cox model, and Kaplan-Meier (KM) analysis to model risk score (RS) to predict prognosis.

Results: Genes associated with good and poor prognosis were identified via machine learning and statistical methods. Higher RS represents worse prognosis with max RS = 1 (Table). In all 6 cancers, high PG (the expression ratio of genes associated with poor to good prognosis) and old age are related to worst survival except EsoAd with younger pts having worse prognosis. The location of tumors in CRC and sex in HCC impact RS. When pts are grouped into 3 pt groups in each cancer, KM curves in pts with low, intermediate, and high RS are statistically different (p < 0.0001) with high hazard ratio (HR > 2).

Conclusions: Analysis of large data was assisted by machine learning and statistical methods, identifying genes associated with survival and creating RS as a tool to predict prognosis. This provides valuable information about prognosis for pts encountered in the clinic when genomic profiles are given. Computational modeling to predict response to chemotherapy and immunotherapy is underway.

Poster Session (Board #J12), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

609 A KRAS mutation is associated with an immunosuppressive tumor microenvironment in mismatch-repair proficient colorectal cancer. First Author: Michael Marco, MSKCC, New York, NY

Background: KRAS-mutant (KRAS\textsuperscript{mut}) colorectal cancers (CRCs) are associated with worse prognosis and resistance to therapy. We have previously shown that KRAS\textsuperscript{mut} CRCs have different transcriptomic signature of stromal and immune-related genes compared to KRAS-wild type (KRAS\textsuperscript{wt}) tumors. Here, we validated the immune-related changes in the tumor microenvironment associated with the KRAS mutation in CRC to guide the design of novel immunotherapy strategies.

Methods: The expression of different immune marker molecules (ligands) were assessed using multiplex immunofluorescence (M-IF) technique in both tumor core (TC) and invasive margin (IM). Sequential slides were cut from paraffin blocks of CRC resected at our institute. Each slide was stained with 4 immune markers using M-IF technique. The stained slides were scanned, and quantification of immune cells was done using ImageJ software. Student’s t test was used for statistical analyses. DNA was extracted from each tumor and profiled for 420 cancer genes using targeted exome-capture sequencing (MSK-IMPACT assay). DNA mismatch repair (MMR) proteins deficiency were analyzed by immunohistochemistry. Only MMR-proficient (pMMR) tumors were included. Results: A total of 39 patients with pMMR CRC were included. AJCC stages (I-III) were not different between KRAS\textsuperscript{mut} (n = 15) and KRAS\textsuperscript{wt} (n = 25) tumors. M2-macrophages (CD68+CD163+ cells) and IL-7 producing cells (IL7+) cells were significantly higher in MRR CRC (p = 0.002, and 2.9e-6 respectively), while T-helper cells (CD3+CD4+) were significantly lower (p = 3.9e-4) in TC of KRAS\textsuperscript{mut} tumors compared to KRAS\textsuperscript{wt}. Treg (CD3+CD4+FOXP3+) cells were significantly higher in IM of KRAS\textsuperscript{mut} tumors (p = 0.01). KRAS\textsuperscript{mut} tumors had significantly higher ratios of Treg:T-helper cells, and Treg:T cytotoxic cell (p = 0.008, and p = 0.04; respectively).

Conclusions: KRAS oncogene is associated with more pro-tumorigenic (M2 macrophages, IL7+ and Treg) and less anti-tumorigenic (CD4+ helper) immune cells in CRC. These results can be used to guide further research to design novel immunotherapy strategies against KRAS\textsuperscript{mut} CRC.
The impact of socioeconomic factors on outcomes of patients with locally advanced rectal cancer (LARC). First Author: Joanna Golfti, Ottawa Hospital, Ottawa, ON, Canada

Background: Patients with rectal cancer may experience disparities in outcomes due to various socioeconomic (SES) factors. We assessed the impact of SES factors on outcomes in patients with LARC who received neoadjuvant chemoradiation (nCRT) and surgery (Sx) in three Canadian provinces.

Methods: Associations between clinical variables, demographics, SES characteristics (2015 Canadian Census data), distance and time to the nearest cancer center (mapping software), and outcomes were evaluated.

Results: 1098 patients were included. Table 1. Median follow-up time was 67.8 months. The 5-year survival rate was 0.80 (95% CI 0.77-0.82). Factors predictive of disease-free survival in univariate analysis (UVA) included age, worse performance status (PS), driving time > 1 hour, median community income, and driving distance > 100 km. Factors that remained significant in multivariate analysis (MVA) included age (HR 1.01; 95% CI 1.00-1.02; p = 0.01), worse PS (HR 1.30; 95% CI 1.01-1.68; p = 0.04) and driving time > 1 hour (HR 1.31; 95% CI 1.01-1.71; p = 0.04).

Conclusions: Outcomes of patients with LARC undergoing nCRT are significantly associated with driving time to the nearest cancer centre, median community income, and community proportion with post-secondary education. Factors that remained significant in MVA included advanced age, worse PS, and distance > 1 hour to the cancer centre. Further efforts to understand and reduce these socioeconomic disparities are warranted.

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The combination of TASC-102 and bevacizumab as the third-line chemotherapy for metastatic colorectal cancer (TAS-CC3 Study). First Author: Chihiro Kosugi, Teikyo University Chiba Medical Center, Ichihara, Chiba, Japan

Background: TASC-102 improved overall survival of metastatic colorectal cancer (mCRC) patients with median progression free survival (PFS) of 2.0 months (RECURSE trial). Subsequently, the combination of TASC-102 and bevacizumab has been shown to extend median PFS with 3.7 months (C-TASK FORCE). However, this study included patients with 2nd line and 3rd line chemotherapy. Our study was planned exclusively for patients receiving this combination as a 3rd line chemotherapy to investigate clinical impact of this combination beyond cytotoxic doublet. Methods: This phase II study was conducted in investigator-initiated, open-label, single-arm, multicentered manner in Japan. Eligible patients were 20-80 years old, and had advanced cancer that had progressed after two lines of previous chemotherapy (ECOG performance status of 0 or 1). Primary endpoint was progression free survival (PFS), and the secondary endpoints were time to treatment failure (TTF), response rate (RR), overall survival (OS), and safety. Results: Between June 2016 and August 2017, 32 pts were enrolled. The median PFS was 4.5 months, and the median OS was 9.3 months. Partial response was observed in 2 patients. The most common adverse events above grade 3 were neutropenia (15 patients) followed by thrombocytopenia (4 patients). Treatment-related serious adverse events were reported in 1 patient. There were no non-hematologic adverse events above grade 3. No treatment-related deaths occurred. Conclusions: This is the first study which involves the combination TASC-102 and bevacizumab as the 3rd line chemotherapy in the setting beyond cytotoxic doublet for the patients with mCRC. This study met its primary endpoint PFS, which is comparable to the results of C-TASK FORCE study. This combination has a potential to be one of therapeutic options of the 3rd line chemotherapy for mCRC. Clinical trial registration: NCT022438.

Microsatellite instability (MSI) as an independent predictor of pathologic complete response (pCR) in locally advanced rectal cancer: A National Cancer Database (NCDB) analysis. First Author: Shaakir Hasan, Department of Radiation Oncology, Allegheny Health Network Cancer Institute, Pittsburgh, PA

Background: The relationship between microsatellite instability (MSI) and response to neoadjuvant chemoradiotherapy in rectal cancer is not well understood. We therefore utilized the national cancer database (NCDB) to investigate the association between MSI and pathologic complete response (pCR) in this patient population. Methods: We analyzed 5,086 patients between 2010-2015 with locally advanced rectal cancer who were tested for MSI and treated definitively with chemoradiation followed by surgery. Primary comparison groups were between 4,450 MSI-negative(-) and 636 MSI-positive(+) patients. Multivariable regression analysis was conducted to identify demographic, therapeutic, and clinical characteristics predictive of pCR. Cox proportional hazard ratios were used for survival. Results: All patients were treated with definitive chemoradiation (median dose 50.4 Gy) followed by resection within 4 months. MSI+ patients were associated with earlier year of diagnosis and higher grade tumors (P < 0.05). The overall pCR rate was 8.6%, including 8.9% for MSI- and 5.9% for MSI+ tumors (P = 0.00). Among those with lower T stage, pCR+ cases were significantly associated with a reduced pCR rate (OR = 0.65, 95% CI 0.43 - 0.96) with multivariable analysis. The 5-year survival for patients with pCR was 93% compared to 73% without it (P < 0.001). Conclusions: Microsatellite instability was independently associated with a reduction in pathologic complete response for locally advanced rectal cancer following neoadjuvant chemoradiation in this NCDB-based analysis.

The efficacy of neoadjuvant treatment in locally advanced rectal cancer with dMMR. First Author: Yanhong Deng, Sun Yat-sen University, Guangzhou, China

Background: The incidence of Mismatch repair gene deficiency (dMMR) was about 15% in colorectal cancer, but mostly in right side colon cancer, while in locally advanced rectal cancer, it is very rare. As is known, adjuvant chemotherapy with FU alone was not recommended in stage II colon cancer with dMMR or MSI. However, in locally advanced rectal cancer with dMMR or MSI, the efficacy of neoadjuvant treatment with SFU was not yet known. Methods: We enrolled patients with locally advanced rectal cancer from three prospective clinical trials, including the FOWARC study (N = 309), the mFOLFOXIRI neoadjuvant chemotherapy trial (N = 106) and the total neo-adjuvant treatment with FOLFOX and radiotherapy (N = 129). From the 544 patients, 35 (6.4%) patients were dMMR, 133 patients with unknown status of MMR. Among the 35 patients, 10 patients received SFU concurrent with radiotherapy (group A), nine patients underwent FOLFOX concurrent with radiotherapy (group B), and 12 patients received FOLFOX neoadjuvant chemotherapy alone (group C). Another four patients underwent mFOLFOXIRI neoadjuvant chemotherapy alone (group D), including one patient with nivolumab as neoadjuvant treatment after chemotherapy. Results: Totally, 4 (11.4%) patients achieved pathologic complete response, and 13 (37%) patients had tumor downstaging to ypT0-2N0M0 stage (0). In group A, the pCR rate was 10% (1/10), the tumor downstaging rate was 10% (1/10); In group B, the pCR rate was 33.3% (4/12), the tumor downstaging rate was 55.6% (5/9); In group C, the tumor downstaging rate was 41.7% (5/12). In group D, only one patient achieved pCR, and it is the one who received nivolumab as neoadjuvant treatment. Conclusions: The efficacy of neoadjuvant in locally advanced rectal cancer seemed not affected by the MMR status. But further study was needed.

Distribution of neuroendocrine marker-positive cells in colorectal cancer tissue and adjacent mucosa. First Author: Takaki Osimi, Tokai University, Isehara, Japan

Background: Neuroendocrine carcinoma (NEC) is a rare disease and has been reported to most frequently arise in the right side of the colon. In the 2010 WHO classification, mixed adeno-neuroendocrine carcinoma (MANEC) was defined as a neoplasm consisting of NEC and adenocarcinoma components. To clarify the histogenesis of NEC, we attempted to detect neuroendocrine marker-positive cells in cancer tissue and in the adjacent mucosa in patients with adenocarcinoma. Methods: The study group comprised 390 patients with stage II or III colorectal adenocarcinoma between 2007 and 2012. Immunostaining was performed with anti chromogranin A, synaptophysin, and CD56 antibodies. Cases with positively stained cells in cancer tissue were defined as positive. In the adjacent mucosa, at least 5 cm from the tumor, the numbers of positive cells per 15 HPF were measured. Results: Tumor location was right side in 181 patients, left side in 173, and the rectum in 36 patients. Positive rates of Chromogranin A in cancer tissues were 23.7% in the right colon, 13.2% in the left colon, and 19.4% in the rectum. Those of synaptophysin were 35.3%, 21.9%, and 30.6%, respectively. Those of CD56 were 22.6%, 8.0%, and 16.7%, respectively. Positive rates of these three markers in right colon were significantly higher than those in left colon and rectum. (p = 0.015, p = 0.0054, p = 0.0062). In the adjacent mucosa, the mean numbers of positive cells for chromogranin A were 62.2 ± 20.5 in the right colon, 131.9 ± 44.7 in the left colon, and 243.7 ± 60.2 in the rectum (p = 0.001). Those for synaptophysin were 47.7 ± 23.9, 195.3 ± 35.1, and 156.9 ± 56.8, respectively (p < 0.001). There were no significant differences in the number of positive cells for CD56 among the sites (p = 0.295). Conclusions: In cancer tissue, the rate of positive staining for neuroendocrine marker-positive cells was higher in the right side of the colon, whereas in normal mucosa the rates of positive staining for these cells were higher in the sigmoid colon and the rectum. These results suggest that neuroendocrine marker-positive cells are an acquired characteristic of cancer tissue.
Timing of first surveillance colonoscopy in stage I colon cancer patients is controversial. This study was conducted to assess the relationship between timing of first surveillance colonoscopy and 5-year colon cancer-specific survival. Methods: This was a retrospective cohort study of the Surveillance, Epidemiology, and End Results database combined with Medicare claims. Stage I colon cancer patients (66-84 years of age) were categorized according to receipt of first colonoscopy following cancer-directed surgery as: Year 1, Year 2, Year 3, and No Colonoscopy within 3 years of surgery. Propensity score weighting was used to balance covariates. Cox regression was used to obtain hazard ratios for the relative risk of 5-year colon cancer-specific death, adjusted survival estimates, and the number needed to treat (NNT) with colonoscopy in Year 1 to prevent a colon cancer-specific death in the other groups. Results: There were 8,494 stage I colon cancer patients available for analysis. Regarding 5-year colon cancer-specific mortality, compared to Year 1 patients, the No Colonoscopy group experienced 2.2 times the risk of colon cancer-specific death (HR, 2.23; 95% CI, 1.38 to 3.61). 

Background: Surveillance colonoscopy following curative surgery in stage I colon cancer patients is controversial. This study was conducted to assess the relationship between timing of first surveillance colonoscopy and 5-year colon cancer-specific survival. Methods: This was a retrospective cohort study of the Surveillance, Epidemiology, and End Results database combined with Medicare claims. Stage I colon cancer patients (66-84 years of age) were categorized according to receipt of first colonoscopy following cancer-directed surgery as: Year 1, Year 2, Year 3, and No Colonoscopy within 3 years of surgery. Propensity score weighting was used to balance covariates. Cox regression was used to obtain hazard ratios for the relative risk of 5-year colon cancer-specific death, adjusted survival estimates, and the number needed to treat (NNT) with colonoscopy in Year 1 to prevent a colon cancer-specific death in the other groups. Results: There were 8,494 stage I colon cancer patients available for analysis. Regarding 5-year colon cancer-specific mortality, compared to Year 1 patients, the No Colonoscopy group experienced 2.2 times the risk of colon cancer-specific death (HR, 2.23; 95% CI, 1.38 to 3.61). 

Conclusions: Although stage I colon cancer patients have a good prognosis, patients who received colonoscopy within one year of cancer-directed surgery experienced significantly better survival than patients who did not receive colonoscopy within 3 years of surgery. The results of this study justify efforts to ensure that stage I colon cancer patients receive colonoscopy surveillance testing approximately 1 year following cancer-directed surgery.
The prognostic value of systemic inflammatory factors in BRAF (V600E) mutant metastatic colorectal cancer (mCRC). First Author: Nieves Martinez Lago, Hospital Clinico de Santiago de Compostela, Santiago De Compostela, Spain

Background: Multiple studies have reported prognostic association of neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLT) and albumin levels with survival among patients with early and advanced metastatic colorectal cancer. However, it is unknown the prognostic impact in patients with BRAF (V600E) mutant metastatic colorectal cancer (mCRC). Methods: We conducted an observational, retrospective, multicentric study of patients with BRAF V600E-mt mCRC treated at nine university Spanish hospitals belonging to GITuD (Galician Research Group on Digestive Tumors). Demographic, clinical, pathological characteristics, overall survival (OS) and progression-free survival (PFS) data were retrospectively analyzed. Results: Data from 65 pts treated between November 2010 to June 2018 were recorded. Median age was 62.8 years (range 30–83), 55.4% female, 75.4% ECOG PS0–1, 49.2% right-sided colorectal cancer and median metastatic locations was 2 (range 1-5). With a median follow up of 64.6 months, median OS was 12.9 months (95% CI, 9.8–16.0) and first line PFS was 4.1 months (95% CI, 2.7–5.5). NLR (HR 2.294; p = 0.004), PLR (HR 6.329; p = 0.028) and albumin levels (HR 2.575; p = 0.001) were independent prognostic factors for OS. With higher NLR (> 3 vs. < 3) had a significantly lower OS 6.6 versus 17.5 months (HR 2.94; 95% CI 1.3-4.1, p = 0.004), which was also true for patients with higher PLR (> 200 vs. < 200); with OS 6.3 versus 14.5 months (HR 1.879; 95% CI 1.3-3.3, p = 0.002). With patients with low albumin level < 34.5 months (HR 2.575; 95% CI 1.2-5.5, p = 0.011), NLR was positively associated with PLR (p < 0.001). Neither NLR (p = 0.190) or PLR (p = 0.327) were associated with low albumin levels. A Systemic Inflammation Score (assigning one point to each factor), the predictive of worse 17.7 versus 8.7 versus 9.7 versus 5.0 months (p < 0.001), Patients with Systemic Inflammation Score 0 had significantly higher OS: 17.7 versus 8.2 months (HR 0.357; 95% CI 0.2-0.7, p = 0.001). Conclusions: NLR, PLR and albumin levels are significant prognostic factors in patients with BRAF V600E-mt mCRC.

CANCERS OF THE COLON, RECTUM, AND ANUS

Poster Session (Board #K7), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Phase I/II study of panitumumab (PANI) combined with trifluoridine/ tipiracil (FTD/TPI) in patients (pts) with previously treated RAS wild-type (wt) metastatic colorectal cancer (mCRC): Final results of APOLLON study. First Author: Yoshito Komatsu, Division of Cancer Chemotherapy, Hokkaido University Hospital, Sapporo, Japan

Background: Preclinical study reported that a combination of PANI with FTD/TPI demonstrated synergistic antitumor activity (Baba, 2017); however, no clinical study has been reported in this combination yet. Therefore, we conducted a phase I/II study to evaluate the efficacy and safety of this combination in pts with RAS wt mCRC. Here, we report the results of final analysis, including follow-up. Methods: Eligible pts had RAS wt mCRC refractory or intolerant to fluoropyrimidines, irinotecan, oxaliplatin, or anti-angiogenesis inhibitors, and had never been treated with anti-EGFR antibodies, FTD/TPI, or regorafenib (REG).Pts received four-week cycles of PANI (every two weeks) and FTD/TPI (twice daily, days 1 to 5 and 8 to 12). The primary endpoint was frequency of dose-limiting toxicity (DLT) in phase I and progression-free survival (PFS) rate at 6 months (M) in phase II, With a PFS rate at 6 M of 48% deemed promising and 29% judged unacceptable, and assuming a one-sided significance level of 5%, the necessary sample size to achieve a power of 80% was estimated to be 47 pts (target sample size, 52 pts). Results: Since no DLT occurred in phase I, the recommended dose was determined to be 6 mg/kg for PANI and 35 mg/m² for FTD/TPI. In phase II with a median follow-up of 16.5 M, the PFS rate at 6 M (n = 54) was 33.3% (90% CI 28.8–45.3; p = 0.24), and median PFS and overall survival were 5.6 M (95% CI 4.5-6.5) and 14.1 M (95% CI 12.7–19.3), respectively. The response rate and disease control rate were 37.0% and 81.4%, respectively. The most common grade 3 or higher adverse events (n = 55) were neutropenia (9.1%), febrile neutropenia (3.6%), anemia (2.2%), stomatitis (9.1%), and dermatitis acneiform (9.1%). Subsequent therapy was given to 39 pts (46.3%) treated with REG. Subgroup analyses stratified by age, PS, and primary lesion will be reported at the time of conference presentation. Conclusions: PANI combined with FTD/TPI showed favorable antitumor activity with an acceptable safety profile for previously treated RAS wt mCRC, although the primary endpoint of PFS rate at 6 M did not meet the prespecified threshold. Clinical trial information: NCT02613222.
Background: First line of RAS wild-type (WT) unresectable metastatic colorectal cancer (mCRC) can be doublet chemotherapy with an anti-VEGF (Vascular Endothelial Growth Factor), or an anti-EGFR (Epidermal Growth Factor Receptor). Waiting for RAS status, many oncologists initiate chemotherapy and add the anti-EGFR secondly. The objective was to compare the delayed introduction of the anti-VEGF to the immediate introduction of the anti-VEGF in first-line treatment of RAS WT mCRC. Methods: This was a retrospective cohort analysis from 2013 to 2016, multicentric with 28 health care centers. We included patients with RAS WT unresectable mCRC treated between 2013 and 2016 by a doublet chemotherapy with the anti-VEGF introduced immediately or with the anti-EGFR introduced at C2 or C3. Progression free survival (PFS), overall survival (OS) and response rate (RR) for the two cohorts were compared. Hazard ratios (HR) with 95% confidence interval (95%CI) were estimated with cox regression models weighted on propensity score to deal with potential confounders. Results: A total of 262 patients were included, 129 in the immediate anti-VEGF group and 133 in the delayed anti-EGFR group. Median follow-up was 37.9 months. Ninety-two patients had the anti-VEGF introduced at C2, 40 at C3. The median delay of RAS analysis was 19 days (IQR: 13-26). Patients treated with anti-VEGF's were more likely men (68% versus 56%), with more metastatic sites (≥ 5; 15% versus 9%). A propensity score including the number of metastatic sites and a possible previous treatment was built. Delayed anti-VEGFs were associated with longer PFS compared to immediate anti-VEGFs; 13.8 versus 10.0 months, p = 0.0244. After weighting, delayed anti-VEGFs were still associated with better PFS; HR 0.74, 95%CI (0.61 - 0.90), p = 0.0024. OS was not different between the two arms (30.5 vs 49.2 months, p = 0.3934), even after weighting (HR 0.86, 95%CI (0.69 - 1.08), p = 0.2024). There was a better RR with delayed anti-VEGFs: 66.7% versus 45.6%, p = 0.0007. Conclusions: Our findings suggest that, while waiting for RAS status, the delayed introduction of the anti-VEGF is a valid option, compared to the immediate introduction of the anti-VEGF.
A phase I study of TAS-102 in combination with oxaliplatin (TAS-OX) for refractory metastatic colorectal cancer (mCRC). First Author: Michael Cecchini, Yale University, New Haven, CT

Background: TAS-102 is an oral combination of the anti-metabolite 5-trifluorothymidine (FTD) and a thymidine phosphorylase inhibitor (TPi), preventing the degradation of FTD. It is approved as mCRC monotherapy with improved survival. Oxaliplatin is often reintroduced in mCRC after progressive disease (PD) on maintenance 5-FU although response is poor. The decreased efficacy may be related to acquired 5-FU resistance. We therefore explored the safety and efficacy of oxaliplatin in combination with an alternative and non-cross-resistant anti-metabolite, TAS-102.

Methods: Phase 1 of TAS-OX is a 3+3 dose-escalating study at a starting dose of TAS-102 25 mg/m² and oxaliplatin 85 mg/m² with three dose levels (table). TAS-102 is administered days 1-5 and oxaliplatin days 1-3, every 2 weeks. Eligible patients previously received 5FU, oxaliplatin, irinotecan, appropriate biologics, had measurable disease, usual laboratory parameters, and ECOG PS 0-1. The primary objective was to determine the recommended phase II dose (RP2D).

Results: Twelve patients were evaluable for dose limiting toxicity (DLT). No DLTs were observed. Treatment related grade ≥ 3 AEs were neutropenia (n = 4) and thrombocytopenia (n = 1). No AEs resulted in treatment discontinuation. Two patients (dose levels 2 and 3) required dose reductions for prolonged neutropenia. Median number of cycles for all treated patients was 6.4. The disease control rate (DCR) at 8 weeks was 67%. Best response in all evaluable patients was PR (8%) 7 (59%) SD and 4 (33%) PD.

Conclusions: The RP2D of TAS-102 is 35 mg/m² in combination with oxaliplatin 85 mg/m². No DLTs were observed and no unexpected AEs were seen. These data from this phase I study treated patients with advanced colorectal cancer.

Poster Session (Board 9K15), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

A retrospective study of a dexamethasone-sparing strategy of preventing acute and delayed emesis caused by CapeOx regimen with aprepitant for colorectal cancer. First Author: Miko Nakatsuka, Department of Pharmacy, Osaka University Medical Hospital, Suita, Japan

Background: CapeOx therapy which is combination with oxaliplatin (L-OHP) and capcitabine is one of the standard treatments for first line chemotherapy for unresectable colorectal cancer, or for postoperative adjuvant chemo-therapy for stage III colon cancer. L-OHP-based regimen is classified as moderately emetogenic chemotherapy. In the SENRI trial which we previously conducted as phase III trial, aprepitant, an NK-1 antagonist, showed the efficacy for prevention of emesis against L-OHP. On the other hand, even when in highly emetogenic chemotherapy & day 1, it is reported that dexamethasone after day 2 could be spared.

Methods: We retrospectively reviewed chemotherapy-naive 94 patients with colorectal cancer who underwent CapeOx therapy at our institution from April 2012 to March 2017. We assessed the relationship between emesis during the first cycle of CapeOx (day 1-5) and the use of dexamethasone on day 2-3.

Results: 10 patients underwent CapeOx plus bevacizumab, and 84 under went CapeOx. All patients received 5-HT3 receptor antagonist (palonosetron), B7; granisetron). 70 patients received aprepitant on days 1-3 and dexamethasone on day 1 (APR-D1 group). 22 patients received aprepitant on days 1-3 and dexamethasone on days 1-3 (APR-D3 group). 15 were dexamethasone only on days 1-3 without aprepitant (D3 group), and 7 were dexamethasone only on day 1 without aprepitant (D1 group). Acute complete response (CR; no vomiting and no rescue anti-emetics) rates were 100% in any groups. Delayed CR rate was 56% in APR-D1 group, 86% in APR-D3 group, 53% in D3 group, and 29% in D1 group, respectively. In multivariate linear regression with aprepitant, there was a significant difference in presence of dexamethasone (p = 0.028).

Conclusions: Acute emesis could be prevented by even only 1-day administration of dexamethasone when combined with the triplet prophylactics. However, in order to sufficiently prevent delayed emesis induced by L-OHP, it was suggested that addition of DEX on days 2 and 3 might be better.

Poster Session (Board 9K18), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

“Should we be generous in peritonectomy?": First prospective comparative analysis of total versus involved field periaeral peritonectomy in CRS-HIPEC for peritoneal surface malignancies from COLOrectal cancer–ISPSM collaboration study. First Author: S.P. Somashekhar, Manipal Comprehensive Cancer Center, Bangalore, India

Background: Peritonectomy is the important components in management of peritoneal surface malignancies (PSM). Immunofluoresesce study done after involved field peritonectomy (IFP) has showed disease in areas not suspected on gross examination stressing the need for total parietal peritonectomy (TPP) for complete cytoreduction. The aim of this study was to assess the morbidity & mortality, recurrence pattern & oncological outcomes of extent of parietal peritonectomy with CRS & HIPEC for colorectal carcinoma.

Methods: Patients with PSM from CRC underwent TPP or IFP with CRS-HIPEC. Pre & intraoperative data were analyzed with main focus on post-operative morbidity, mortality, recurrence pattern and oncological outcomes. Results: 40 cases of CRC of which four upfront, 17 interval and 19 recurrent cases. 19 & 21 patients underwent TPP & IFP respectively. Base line characteristics were comparable except median PCI (IT versus I2). TPP group had longer duration of surgery (11 vs 9), more blood loss (1300 vs 700 ml) increased diarrheamic reactions (46.2% vs 14.2%), multivisceral resection (46.2% vs 28.5%) Number of bowel resections, anastomosis and stomas were comparable. Overall TPP group had more G3-G5 morbidity (46.1% vs 35.7%) & surgical morbidity (30.7% vs 21.5%). TPP group had increased pleural & intra-abdominal collections which needed intervention. With a median follow up of 30 months, DFS was significantly higher in TPP group (25 months vs 16 months, p < 0.001) and median overall survival was 21 months in IFP group (yet to be achieved in TPP group). TPP group had more of the recurrences in visceral liver & lung (50.0%) followed by peritoneal (37.5%) & nodal (25.0%) whereas in IFP it was peritoneal (42.8%), visceral (38.4%) & nodal (15.3%).

Conclusions: It is the first prospective comparative study done on total parietal peritonectomy in PSM of colorectal cancer origin. TPP group had significantly higher DFS, with comparable postoperative morbidity. However, longer follow up and a prospective multi-institutional randomized study needs to be designed for more evidence of the same.
Evaluation of the re-introducing FOLFIRI or XELOX + bevacizumab in relapsed colorectal cancer patients treated with oxaliplatin as adjuvant chemotherapy (REACT study). First Author: Shigeyoshi Iwamoto, Cancer Center, Aichi Medical University, Nagakute, Japan

Background: Chemotherapy in relapsed colon cancer patients (pts) treated with oxaliplatin as adjuvant chemotherapy is under debate. REACT study aimed to investigate the efficacy of reintroducing FOLFIRI or XELOX + bevacizumab therapy for recurrent colorectal cancer pts after adjuvant chemotherapy including oxaliplatin. Methods: Pts with past history of adjuvant chemotherapy including oxaliplatin (FOLFIRI, XELOX or 5/5X) with a cumulative dose of more than 400 mg/m², and recurrence observed by imaging after more than 6 months post adjuvant chemotherapy participated in this trial. Primary endpoints were response rate (RR) and disease control rate (DCR). Key secondary endpoints were progression-free survival (PFS), time to first treatment failure (TFF), overall survival (OS) and safety. Results: A total of 31 pts were enrolled between Oct 2012 and Oct 2016. Of 29 eligible pts, 9 received FOLFIRI = bevacizumab, and 22 received XELOX = bevacizumab. 28 of the pts received bevacizumab. The RR was 66.7% (95% CI, 46.0-83.5) and the DCR was 88.9% (95% CI, 70.8-97.6). The RR for oxaliplatin-free interval was 100.0% (n = 4, 95% CI, 39.0-100.0) in 6 to 12 months, 60.9% (n = 25, 95% CI, 38.5-80.3%) over 12 month, respectively. Median PFS, TTF and OS were 10.9 months (95% CI, 7.0-14.9), 6.3 months (95% CI, 2.8-8.0) and 29.1 months (95% CI, 20.3-33.3). The most common grade 3 or 4 adverse event was hypertension (19.4%). Grade 3 or worse peripheral sensory neuropathy developed only two pts (6.5%). Allergic reactions occurred in 12.9% of the pts, with one fourth (25%) grade 3 or 4 adverse treatment-related adverse events. Conclusions: Re-introduction of oxaliplatin was feasible and achieved high RR or DCR in after more than 6 months post adjuvant chemotherapy including oxaliplatin. Clinical trial information: UMIN000006523.

Conclusions: Single site metastasis to the lungs is associated with better survival in metastatic colorectal cancer, (HR = 0.69, 0.54-0.88), regardless of primary tumor location or CEA levels. Previous studies have shown that prognosis in metastatic colorectal cancer with mutated KRAS. Individuals with lung metastasis had the best prognosis (HR = 0.80, 0.77-0.83), followed by those with liver metastasis (HR = 1.1, 1.07-1.15), while those with bone or brain metastasis had the worse prognosis. In a subgroup analysis, we assessed prognosis among individuals who received multi-agent chemotherapy and had not undergone surgery or received radiotherapy. Individuals with lung metastasis and KRAS mutant KRAS had better prognosis compared with those with liver metastasis, (HR = 0.69, 0.54-0.88), regardless of primary tumor location or CEA levels. Conclusions: Single site metastasis to the lungs is associated with better prognosis in mCRC, specifically among KRAS mutant tumors. This survival advantage should be taken into consideration in clinical decision-making.

**Nivolumab (NIVO) + low-dose ipilimumab (IPI) in previously treated patients (pts) with microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): Long-term follow-up. First Author: Michael J. Overman, MD Anderson Cancer Center, Houston, TX

Background: In the phase II CheckMate 141 trial, NIVO + low-dose IPI (10 mg/kg) provided meaningful clinical benefit in previously treated MSI-H/dMMR mCRC pts after a median follow-up of 13.4 mos. Here, we present long-term follow-up (median 25.4 mos) of these pts. Methods: Pts received NIVO 3 mg/kg + low-dose IPI (24 mos) followed by NIVO 3 mg/kg Q2W until disease progression. Primary endpoint was investigator (INV)-assessed objective response rate (ORR, RECIST v1.1). Results: Of 119 treated pts, 76% had ≥ 2 prior lines of therapy. ORR and disease control rates (DCR) were 58 and 89%, respectively (Table). Complete response (CR) rate increased with long-term follow-up: from 3 (13.4 mos) to 6% (25.4 mos). Median duration of response (DOR) was not reached, with 68% of responses ongoing at data cutoff. At 24 mos, progression-free survival (PFS) and overall survival (OS) rates were 60 and 74%, respectively. OS rates were 96, 56, and 29% in pts with CR or partial response (PR); stable disease (SD), and progressive disease (PD), respectively. Grade 3-4 treatment-related adverse events (TRAEs) occurred in 36% of pts; 10% (grade 3-4) and 13% (any grade) of pts had TRAEs leading to discontinuation. Conclusions: Long-term follow-up with NIVO + low-dose IPI provides durable clinical benefit with deepening of response and a manageable safety profile with no new safety signals, demonstrating long-term benefit of NIVO + low-dose IPI for previously treated pts with MSI-H/dMMR mCRC. Clinical trial information: NCT02060188.
Health-related quality of life in the early-access phase IIb study of trifluridine/tipiracil in pretreated metastatic colorectal cancer (mCRC): Results from PRECONNECT study. First Author: Julien Taieb, Hôpital Européen Georges-Pompidou, Sarbonne Paris Cité/Paris Descartes University, Paris, France

Background: Pivotal RECOURSE trial assessed efficacy and safety of trifluridine/tipiracil (FTD/TPI) in mCRC patients (pts) without collecting QoL data. Here we describe a preliminary analysis of QoL of mCRC pts treated with FTD/TPI in the ongoing phase 3b PRECONNECT study (NCT03306394).

Methods: Eligible pts who historically mCRC previously treated with available therapies and an ECOG-PS of 0/1, Pts received FTD/TPI (35 mg/m² twice daily) orally on days 1–5 and 8–12 of each 28-day cycle. ECOG-PS and QoL were assessed at baseline, every 4 weeks on FTD/TPI and at discontinuation. QoL was measured with EORTC QLQ-C30, EQ-5D index and VAS questionnaires. Utility score was based on EQ-5D index and values from Germany, UK and Spain. For QLQ-C30, clinical relevance was assessed using a 10 point threshold. Changes in utility score and VAS were deemed clinically relevant if ≥ 9 and ≥ 7, respectively. Only results where ≥ 10% of the initial cohort completed the questionnaires were assessed, corresponding to 7 cycles of treatment. Results: 464 pts were included at cutoff (1 November 2017). Median FTD/TPI treatment duration was 2.96 months (range 0.4–14.7). Median time to ECOG-PS ≤ 2 was 8.7 months with 74.3% of pts remaining at ECOG-PS 0/1 at discontinuation. At baseline mean QLQ-C30 global health status was 62.75 (SD = 20.50; median 66.67) with values for all scales in line with the EuroQol reference for mCRC (variation –10 points on function and ≤ 5 on symptom scales). Baseline EQ-5D VAS was 65.55 (SD = 20.11; median 70.00) and utility score 73.11 (SD = 20.71; median 75.27). There was no clinically relevant difference in mean change from baseline at any time point on global health status score nor any of functional or symptom scales. Similar results were obtained for utility score and VAS. Qol was maintained on FTD/TPI in all subgroups based on age and ECOG-PS for all scales except for appetite loss increase at cycle 5 in pts ≥ 65 and in ECOG-PS 0/1 in whom the score increased by ≥2.2 and 0.4, respectively. Conclusions: The first prospective data on QoL suggest that mCRC pts can maintain their QoL while on FTD/TPI treatment. Clinical trial information: NCT03306394.

Outcomes following stereotactic body radiotherapy (SBRT) in locally recurrent rectal cancer (LRRC) in a previously irradiated pelvis. First Author: Thomas Smith, Mount Vernon Cancer Centre, Northwood, United Kingdom

Background: Management of LRRC is challenging. There is no consensus regarding the best approach for patients not suitable for exenteration. Hyperfractionated re-irradiation is associated with > 10% grade 3 toxicity and 4–10% local control in patients and department. Here we report initial outcomes of an inocent cohort treated with SBRT. Methods: A prospective nationally maintained database for SBRT re-irradiation was interrogated. Eligibility criteria were pelvic recurrence in a previously irradiated colorectal cancer, not eligible for exenteration, > 60 days free of survival, > 60% from previous RT, ≤ 3 metastases, PS 0–1, SBRT dose of 30Gy in 5 fractions in ≤ 10 days was specified. Every 3 mo toxicity was assessed using the CTCAE v4.0, QoL using the EQ52, respectively and imaging was undertaken. Median pre-surgery free survival (PFS) and overall survival (OS) were calculated using the Kaplan-Meier method. Results: 28 patients with 33 separate pelvic lesions were treated between Oct 2015–June 2018. The median age was 64 years (range 36–84). 27/28 had received 45–50.4Gy in 25–28F with concurrent Capcitabine, 1/28 received 25Gy/5F, all followed by surgery. Combining SBRT, the cumulative effective dose received was >100Gy. The median GTV volume was 14.9cc (range 0.47–121.73cc). All completed the SBRT. There were minimal symptoms at baseline pain = 7, urinary = 3, GI = 3, nerve = 1. 48% grade 1 or grade 2 acute toxicity was reported at 6 weeks, with 25% grade 1 or grade 2 late toxicity, but no grade 3 toxicity reported with a median follow up of 10 months (range ≤ 30). There was an 8% local control rate with a median PFS of 12.2 months (95% CI 4.0–20.5) and a 2-year OS of 70.4% (95% CI 49.0–100)). 28% (8/28) solely progressed out of field. Conclusions: Acute toxicity is minimal in this cohort of patients with initial excellent local control. Follow-up is continued. SBRT appears effective and convenient for patients who are non-surgical candidates with pelvic recurrence and offers the opportunity for local and symptom control whilst deferring systemic treatment.

Improving clinician confidence and practice behavior on the therapeutic management of microsatellite-instability high (MSI-H) gastrointestinal (GI) cancers. First Author: Hansa Jaganathan, PlatformQ Health, LLC, Needham, MA, United States

Background: With recent advances of immunotherapy and updates to practice guidelines, clinicians may be challenged in applying and managing the outcomes of new treatment standards for their patients with MSI-H GI cancers. To address this need, a one-hour education session was provided to clinicians and learner responses were evaluated to determine the areas of improvement in the therapeutic management of MSI-H GI cancers. Methods: PlatformQ Health developed and executed a 1-hour online CME program on MSI-H GI cancers, which was broadcast live in March 2018 and offered online for 6 months. The program attracted a total of 439* learners. Survey-based evaluations before (n = 338) and after education (n = 147) targeted self-reported clinician data on confidence, practice behaviors, knowledge, and competence. Results: A self-reported survey (n = 56) conducted 8–12 weeks after education reported that 50% of learners were more confident in managing patients with MSI-H GI cancers, 41% in following NCCN practice guidelines for MMR/MSI testing, and 34% in utilizing checkpoint inhibitors for MSI-H GI tumors. Competence on selecting an appropriate treatment for a patient with MSI-H colon cancer significantly improved between pre- and post-education (52% and 63%, respectively; p = 0.001). Significant improvements in knowledge regarding the latest immunotherapy data (33% at baseline to 54% post-education; p = 0.001) and available methods for determining MMR/MSI status (18% at baseline to 48% post-education; p < 0.0001) were also observed. Conclusions: Outcomes results from education demonstrate learner improvements on facets of management of MSI-H GI cancers. Based on the analysis, further education is needed, particularly in areas of management of immune-related side effects in line with recent ASCO and NCCN guidelines, tools for determining dMMR/MSI-H status, and deciding on optimal treatment based on tumor status. *As of September 10, 2018, data collection is ongoing.
Temporal trends and disease characteristics associated with total neoadjuvant therapy (TNT) usage, First Author: Laila Babar, The Esophageal and Lung Institute, Allegheny Health Network, Pittsburgh, PA

Background: Neoadjuvant chemoradiotherapy (nCRT) followed by resection and postoperative multi-agent chemotherapy (mCRT) is the standard of care for locally advanced rectal cancer (LARC). Using this approach, mCRT administration is delayed several months, leading to concern for high rates of distant failure. To reduce the rate of systemic failure, a novel treatment approach known as total neoadjuvant therapy (TNT) has been increasingly employed, in which patients receive both mCRT and nCRT prior to resection. We utilized the National Cancer Database (NCDB) to examine temporal trends in TNT usage, as well as, any potential effect on survival. Methods: We queried the NCDB for patients diagnosed with LARC (Stage II/III) from 2004-2015 treated with nCRT or TNT. TNT was defined as mCRT initiated 90 days prior to the start of nCRT. Overall survival (OS) was calculated from the date of diagnosis to the date of last contact or death using Kaplan Meier curves to present the cumulative probability of survival, with log-rank statistics used to assess statistical significance between groups. Multivariable cox regression was used to identify predictors of survival and propensity score analysis was used to account for indication bias. Results: We identified 9,066 eligible patients, with 8,812 and 254 patients receiving nCRT and TNT, respectively. Nodal involvement and Stage III disease were predictive of TNT use, as well as, treatment in more recent year. TNT and nCRT had similar 5-year survival rates of 76% and 78%, respectively. MVA identified age >58, increased income, urban location, academic treatment facility, and lower comorbidity score as predictors of worse OS. Multivariable analysis with propensity score demonstrated increased age, higher comorbidity score, higher grade, African American race, and gender as predictive of worse OS. Conclusions: Our data demonstrates a trend toward increasing TNT use, particularly in patients with greater nodal involvement or clinical stage. Despite worse disease characteristics, patients treated with TNT had similar survival to those receiving standard nCRT. Randomized trials are underway to further define the clinical benefit of TNT.

Cost and effectiveness of genetic testing in metastatic colorectal cancer (mCRC) at Montefiore Medical Center (MMC), First Author: Nadeem Athai, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY

Background: Upfront testing for MSI, and mutations in KRAS, NRAS, and BRAF is recommended. The most cost-effective way of obtaining this information remains unclear. We examined cost of broad next generation sequencing (NGS), in comparison to hotspot (HT) and individual target (IT) testing in patients with mCRC with Medicare (MC) and commercial insurance (CI) at MMC. As a surrogate of effectiveness, we hypothesize that patients with NGS are more likely to enroll in clinical trials. Methods: Cost of individual and hotspot tests were derived from known reimbursement rates with insurances affiliated with MMC. Due to ongoing changes in current procedural terminology for NGS, we used known reimbursement amounts from our patients. We applied these costs to a model population of 1,000,000 people. We then evaluated clinical trial enrollment of patients who had either NGS or hotspot/individual testing. Results: MC costs for IT, HT, NGS testing were $1,504, $752, and $4,680 respectively. CI costs were $1,910, $814, $2,366 for IT, HT, and NGS testing respectively. When applied to our model population, NGS cost $941,604 and $1,131,016 more than individual and hotspot testing respectively for MC patients, and $2,432 and $72,924 more for CI patients. Analysis of effectiveness included 136 patients, wherein 8% of those with NGS (n = 5/61) were enrolled in clinical trials as a result of testing compared to 1% of those with HT/IT (n = 175). Conclusions: Broad spectrum NGS costs more than individual or hotspot testing in mCRC. However, patients with NGS testing were more likely to be enrolled in clinical trials, suggesting the need for studies to further evaluate ideal testing modality.

Predicting imminent disease progression in advanced colorectal cancer by a machine-learning algorithm, First Author: Yuri Kogan, Optima Ltd, Bene Atraoth, Israel

Background: In advanced cancers, predicting disease progression just before its clinical manifestation enables an earlier switch to the next treatment line, preventing deterioration in the patient’s state and potentially improving survival. Yet, given the ambiguity of current tumor markers in alerting to its clinical manifestation enables an earlier switch to the next treatment line, predicting disease progression with 57% sensitivity (100/175 tested) and 76% and 78%, respectively. MVA identified age >58, increased income, urban location, academic treatment facility, and lower comorbidity score as predictors of worse OS. Multivariable analysis with propensity score demonstrated increased age, higher comorbidity score, higher grade, African American race, and gender as predictive of worse OS. Conclusions: Our data demonstrates a trend toward increasing TNT use, particularly in patients with greater nodal involvement or clinical stage. Despite worse disease characteristics, patients treated with TNT had similar survival to those receiving standard nCRT. Randomized trials are underway to further define the clinical benefit of TNT.

Comparing cost of genetic testing between insurance types.

<table>
<thead>
<tr>
<th>Hypothetical Population</th>
<th>CMS Medicare (&lt;65 years)</th>
<th>Commercial Payor (&gt;65 and &lt;65 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Enrollees</td>
<td>83%</td>
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<tr>
<td>CRC patients</td>
<td>0.1%</td>
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<tr>
<td>CRC with</td>
<td>96%</td>
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<td>Adenocarcinoma</td>
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<tr>
<td>% testing</td>
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<tr>
<td>Cost of individual</td>
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<tr>
<td>Cost of hotspot testing</td>
<td>$752</td>
<td>$326,680</td>
</tr>
<tr>
<td>Cost of broad NGS</td>
<td>$4,680</td>
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</tr>
</tbody>
</table>

Hypothetical Population = 1,000,000

A phase I/II study of pexa-vec oncolytic virus in combination with immune checkpoint inhibition in refractory colorectal cancer: Safety report, First Author: Maria Pia Morelli, National Cancer Institute, Bethesda, MD

Background: The efficacy of immune checkpoint inhibitor has been limited to small portion of colorectal cancer (CRC) patients whose tumors with mismatch repair (MMR) gene abnormalities. There is an urgent need for patients with MMR proficient (pMMR) tumors. Oncolytic immunotherapy represents a novel therapeutic platform for the treatment of cancer with unique activity compared to conventional chemotherapy. The trial is to evaluate if the combination of Pexa-Vec oncolytic virus (PV) with immune checkpoint inhibition enhance antitumor immunity. Methods: Patients with microsatellite-stable and MSI-H mCRC refractory to PD-1 monotherapy were enrolled. Patients received either Arm A treated with PV + Durvalumab or Arm B with PV + Durvalumab and Tremelimumab. Each arm had two dose levels (DL) of PV, 3 x 10^9 pfu in DL1 and at 10^8 pfu in DL2, every 2 weeks for total 4 doses. The first dose of PV was administered on Day -12, followed by three more dose administration on Days 2, 16 and 30 in combination with the immune checkpoint inhibition. The primary endpoint is response rate, safety, tolerability and feasibility of these combination therapy in refractory metastatic CRC.

Results: Here we report the safety data of Arm A. A total of 9 patients was enrolled so far. The longest follow-up time is 8 months. Four patients received DL1 PV and subsequent five patients received DL2 PV. No DLT was observed at the time of this abstract. No grade 4-5 adverse event (AE) were observed. All patients experienced lymphopenia. All patients with DL2 developed fever, hypotension and papulopapular rashes and were successfully managed with antipyretics, fluid support and skin protection, respectively. The most frequent treatment-related AEs were lymphopenia (100%), fever (7 [87.5%]), chills (6 [75.0%]), hypotension (5 [62.5%]), papulopapular rashes (5 [62.5%]), flu-like symptoms (2 [25.0%]), Nausea/vomiting (2 [25.0%]). Conclusions: Pexa-Vec in combination with Durvalumab showed a favorable safety profile. Clinical trial information: NCT03260673.
Multicenter phase II/II study of biweekly trifluridine/tipiracil with bevacizumab combination for patients with metastatic colorectal cancer refractory to standard therapies (BITS study). First Author: Masahito Kotaka, Gastrointestinal Cancer Center, Sano Hospital, Kobe, Japan

Background: Trifluridine/tipiracil (FTD/TPI) plus bevacizumab (Bmab) combination therapy has shown a promising activity with manageable safety profile in patients (pts) with heavily pretreated metastatic colorectal cancer (mCRC). The aim of this multicenter, phase II/II study was to assess the activity and safety of biweekly FTD/TPI with Bmab combination for pts with mCRC who were refractory or intolerant to standard therapies. Methods: Inclusion criteria were ≥ 20 years; histologically confirmed unresectable mCRC; refractory or intolerant to fluoropyrimidine, irinotecan, oxaliplatin, anti-VEGF therapy, and anti-EGFR therapy (for tumors with wild-type RAS); ECOG PS 0 or 1; evaluable lesion according to the RECIST version 1.1. Phase IIb part is designed to recommend the phase IIa dose (RP2D), and pts received the RP2D in phase Ib part included in efficacy and safety populations. The primary endpoint in phase IIa part was an investigator-assessed progression-free survival (PFS) at 16 weeks (16w-PFS) with a hypothesis of 15% considered unacceptable and 38.7% deemed promising. Given a one-sided 16w-PFS with a hypothesis of 15% considered unacceptable and 38.7% deemed promising. Given a one-sided hypothesis of 15% was rejected (p # 0.0001). Response rate and disease control rate were 0% (95% CI 0.0 to 6.6%) and 59.1% (95%CI 43.3 to 73.7%), respectively. With a median follow up of 5.57 months (range, 153-797), median PFS was 4.25 months (95% CI 2.54 to 5.75). Grade 3 or higher adverse events were hypertension (40.9%), neutropenia (8.4%), leucopenia (14.6%), anemia (9.1%), anorexia (9.1%), nausea (6.8%), hyperbilirubinemia (6.8%) and proteinuria (6.8%). Conclusions: Biweekly FTD/TPI plus Bmab showed promising anti-tumor effect with acceptable toxicities. Clinical trial information: UMIN00002990.

Methods: First Author: Zachary D. Horne, Division of Radiation Oncology, Université de Montréal (CHUM), Montreal, QC, Canada

Background: Fluoropyrimidines (FU) are part of chemotherapy combinations for multiple gastrointestinal cancers. Deficient dihydropyrimidine dehydrogenase (DPD) activity can lead to severe life-threatening toxicities in 3-5% of populations tested. The DPD*2A polymorphism leading to deficient DPD activity is one of the most studied variants. Methods: We retrospectively performed chart reviews of all patients that tested positive for a heterozygous or homozygous DPD*2A mutation in samples obtained from patients treated at our institution. Conclusions: Our study documents the impact of implementing this test in routine clinical practice, including the effects on treatment types, delays and toxicities. Results: 2,617 patients were tested by PCR for the presence of DPD*2A in a period of 17 months: 25 patients tested positive. All were Caucasian. 24 of the 25 patients were heterozygous (0.92%) and one was homozygous (0.038%). A chart review was available for 20 patients: 15 were tested upfront while five were performed following severe toxicities on the first cycle of FU-based chemotherapy. Of the five patients identified following toxicities, all had grade 4 cytopenias, 80% grade ≥ 3 mucositis, 20% grade 3 rash and 20% grade 3 diarrhea, with an average of 15 days of hospitalisations due to febrile neutropenia. Seven of the 13 patients identified upfront received FU-based chemotherapy at reduced initial doses ranging from 25 to 50%. The average dose during the course of chemotherapy was 50% and ten patients reached 100% dosage. No grade ≥ 3 toxicities were observed. DPD*2A test results were available in an average of 6 days, causing no significant delays in treatment initiation according to 99% of queried physicians. Conclusions: Upfront genotyping before FU-based treatment is feasible in clinical practice. It may prevent severe toxicities and hospitalisations without delaying treatment initiation. The administration of chemotherapy at reduced doses appears to be safe in patients heterozygous for DPD*2A.
**Poster Session (Board #L16), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM**

Potentially avoidable acute care use among patients receiving oxaliplatin.

First Author: Eric Roeland, Massachusetts General Hospital, Boston, MA

**Background:** Oxaliplatin (OX), used primarily in gastrointestinal cancers, is considered moderately emetogenic while multiple guidelines classify carboplatin and cisplatin as highly emetogenic chemotherapy (HEC). The new oncology outcome measure (OP-35) from the US Centers for Medicare and Medicaid Services (CMS) deems 30-day post-chemotherapy inpatient (IP) and emergency room (ED) events “potentially avoidable” if involving nausea or emesis (NV) or any of eight other toxicities. We lack data comparing avoidable IP/ED and NV events for OX relative to platinum analogs as HEC.

**Methods:** We assessed OX, cisplatin, and carboplatin courses of therapy from 4Q 2012 to 1Q 2018 using the IBM Watson Explorys database. We identified IP/ED and OP-35 toxicities (anemia, dehydration, diarrhea, fever, hypotension, pain, pneumonia, or sepsis) by diagnosis and procedure codes, and stratified results by sex and age ≤70 (median age at diagnosis for colorectal cancer). An IP/ED event could involve ≥1 OP-35 toxicity. We also evaluated a FOLFINRINOX subgroup (receiving irinotecan ≤3 days after OX). Results: In sum, we identified 4,231 OX courses (382 FOLFINRINOX) (Table). OP-35 toxicities occurred in 75% of IP/ED events of these, 34% OX and 42% FOLFIRINOX involved NV. Rates of IP/ED, IP/ED OP-35-defined toxicity, and NV after OX were consistent with cisplatin and carboplatin. Among patients receiving OX, women age ≤70 (n = 1388) had 2.5× higher NV rates than (p < 0.001).

**Conclusions:** Roughly one-third of patients receiving OX experienced IP/ED events ≥30 days post chemotherapy. Most involved ≥1 of 10 OP-35 toxicities, meeting CMS’ criteria as potentially avoidable acute care. OX IP/ED rates were similar to other platinum analogs and were worse among younger women age ≤70, suggesting more aggressive antiemetic prophylaxis should be evaluated.

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**Poster Session (Board #L19B), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM**

Clinical impact of D3 lymph node dissection preserving left colic artery (LCA) compared to D3 without preserving LCA: Exploratory subgroup analysis of data from randomized controlled trial of laparoscopic versus open surgery for colon cancer from Japan Clinical Oncology Group study JCGO4044.

First Author: Tomonari Akagi, Oita University, Oita, Japan

**Background:** In curative resection of sigmoid colon and rectal cancer, it is unclear whether D3 lymph node dissection preserving left colic artery (LCA) (Group A) is beneficial compared to D3 without preserving LCA (Group B) in terms of clinical outcomes. Preservation of LCA is expected to maintain blood supply which results in preventing anastomotic leakage, intestinal paralysis, and so on.

**Methods:** The data of JCGO4044 (which is a randomized controlled trial comparing laparoscopic surgery for stage III/IIIC colon cancer) were used. Eligibility criteria in JCGO4044 included histologically proven colon cancer; T3 or deeper lesion without involvement of other organs; and so on. Hence, the patients were divided into two groups: Group A, and Group B.

**Results:** Among all randomized 1057 patients in JCGO4044, 631 patients who had received assigned sigmoid colectomy and anterior resection were included in the subgroup analysis. The number of patients was 135 in Group A and 496 in Group B. The patient backgrounds did not differ between groups. The median operative time, median blood loss, and so on were similar in both groups. The median operative time was 135 minutes in Group A and 295 minutes in Group B.

**Conclusions:** Short and long-term outcomes were better in Group A than Group B. It was considered that D3 lymph node dissection preserving LCA could be an alternative treatment for D3 lymph node dissection. Clinical trial information: C00000105.

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**Poster Session (Board #L19), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM**

The impact of psychosocial distress on survival in patients diagnosed with gastrointestinal (GI) malignancies. First Author: Zamzam Salam Al-Hashami, BC Cancer, University of British Columbia, Vancouver, BC, Canada

**Background:** A cancer diagnosis can cause psychological distress that adversely affects patients’ emotional, social, spiritual and physical capabilities. The aim of this study is to identify factors associated with increased risk for psychosocial distress and to evaluate the influence of anxiety and depression on survival of GI cancer patients.

**Methods:** All patients with GI malignancies referred to BC Cancer from 2011-2015 who completed a prospective Psychosocial Screen for Cancer were included in this study. Baseline characteristics were collected at diagnosis and from the BC Cancer registry. Patient groups were compared using the Chi-squared Fisher’s exact test. OS was calculated using the Kaplan Meier method, compared using the log rank test and Cox proportional hazards model.

**Results:** 8722 patients were included in the analysis. Baseline characteristic: median age 67, male 60%, metastatic disease 29%. Colorectal/anal cancers (60%) were the most common followed by pancreatic cancer (11%). Patients with anxiety and depression were more likely to be younger (aged 64 and less), female and have metastatic disease. Patients with anxiety were more likely to get chemotherapy. Depression was associated with less chemotherapy use. Anxiety and depression were associated with increased psychosocial needs including emotional, informational, physical, spiritual, social/family needs (p < 0.001). Psychosocial distress was not influenced by the patient’s geographic or socioeconomic status.

**Conclusions:** Patients with GI malignancies who are female, younger than 64 and have metastatic disease are at risk for psychosocial distress. Anxiety and depression were associated with poorer survival outcomes even when controlling for age, sex, metastatic status, social, spiritual and physical capabilities. Mobility resources to meet patients’ needs is important and should be implemented as part of patients’ comprehensive care.
CANCERS OF THE COLON, RECTUM, AND ANUS

655 Poster Session (Board BL20), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Long-term outcomes of surgical resection of lung metastases from colorectal cancer. First Author: Ryota Mori, Kansai Rosai Hospital, Amagasaki, Japan

Background: The lungs are one of the most frequent sites of metastases from colorectal cancer (CRC). Surgical resection has been widely performed on patients with pulmonary metastases from CRC with favorable outcomes. Surgical treatment is considered an effective option, but the surgical indication of lung resection has institutional bias. In our hospital, we aggressively perform surgery for lung metastases when the primary tumor and other metastases are controlled and all lung metastases are resectable. In this study, the aim is to investigate the long-term outcomes of resections of lung metastases from CRC in our institute. Methods: Between April 2009 and November 2020, patients who underwent lung resection from CRC with curative intent in our hospital were investigated retrospectively. Kaplan-Meier survival curves, log-rank tests, chi-squared test and T-test were used to analyze the survival rates and the factors predicting recurrence.

Results: Sixty-seven patients underwent lung resection of metastases from CRC. The median follow-up period was 25.3 (6-60) months. Five-year disease-free survival was 33.6% and 5-year overall survival was 63.9%. Because of pulmonary recurrence, second surgery was performed in 16 patients and a third surgery in three patients. 5-year overall survival rate after first lung resection in patients who underwent repeated lung resection was 49.2%. There was no significant difference between the number of patients with pulmonary recurrence and those with no recurrence after lung resection (p = 0.38). Twenty-one patients had experienced prior liver resection; the 5-year overall survival rate after lung resection in these patients was 57.9%. Factors predicting recurrence were vascular invasion (v ≥ 2) of primary tumor (p = 0.02), pre-operative serum CEA (p = 0.03) and CA-19-9 (p = 0.04).

Conclusions: The outcome of lung resection of metastases from CRC in our hospital was satisfactory. Aggressive lung resection for cases even after liver resection and repeated pulmonary recurrence may improve long-term outcomes. Vascular invasion of primary tumor and the pre-operative serum CEA and CA-19-9 level can be predictive markers for recurrence.

656 Poster Session (Board BL11), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Systematic review of three decades of clinical trials in metastatic colorectal cancer: Making lemonade out of lemons? First Author: Daniel Tannenbaum, University of Texas Medical Center at Houston, Houston, TX

Background: Despite multiple trials of new agents in metastatic colorectal cancer (mCRC), long-term outcomes remain poor. This study explores the changing trends in the design, interpretation and outcomes of phase III randomized controlled trials (RCT) in mCRC over time. Methods: Phase III RCTs of systemic therapy for mCRC with enrollment between 1986 and 2016 were identified through 4 electronic databases and grouped into 3 time periods (1986-1996; 1997-2006; 2007-2016). Study selection, quality appraisal and data collection were performed by 2 independent investigators. Study characteristics, primary and secondary endpoints, and authors' interpretation of results and conclusions were analyzed. Improvement in overall survival (OS) was the difference between experimental and control arms. A study was deemed positive if it met its end point, was recommended for further study or for adoption for clinical use (p ≤ 0.05 significant for all analyses). Results: One hundred fifty trials (T1=36, T2=62, T3=52) with 77494 patients (T1=12406, T2=39158, T3=25930) were included. Although 1st line therapy trials continued to be the most common across all T, the percentage (%) of trials evaluating 3rd line and beyond (T1=0, T2=3, T3=27) increased significantly over time as have trials with targeted agents (T1=11, T2=34, T3=79). Although OS remains the most common primary end point, more trials in T2 & T3 have used PFS as a primary endpoint (T1=54 vs. 47 & 44). The % of trials with negative results but interpreted as positive increased over time (T1=18; T2=42; T3=35). Across all T, the median improvement in OS of these trials significantly lower compared to the trials that met primary end point across all T (T1 = 0 vs 1.8 months, T2 = 0.1 vs 3.25, T3 = 0.25 vs 2.55). Conclusions: A significant shift has occurred over the past three decades in the design and interpretation of phase III trials in advanced CRC. Any interpretations of potential survival benefits from trials that have not met primary end point must be made with significant caution.

657 Poster Session (Board BZ2), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Clinical implications of microsatellite instability in mucinous colorectal cancer. First Author: Fergus Keane, University Hospital Galway, Galway, Ireland

Background: Colorectal Cancer (CRC) is becoming increasingly recognised as a heterogeneous tumor type. Mucinous histological subtype is identified in 10-15% of CRCs, most commonly those with microsatellite instability (MSI), and has traditionally been associated with unfavorable outcomes and poor response to chemotherapy. In contrast, MSI is associated with relatively favourable pathological features and better outcomes, compared with CRCs with microsatellite stability (MSS), such that the 2010 WHO classification considered mucinous CRC as a heterogeneous tumor type. Mucinous histological subtype is identified in 3-5% of CRCs. MSI mucinous CRC is considered low grade, while MSS mucinous CRC is considered high grade. The aim of this study is to establish the significance of MSI status in this group and highlights the clinical and prognostic significance of MSI status in this patient cohort.

Conclusions: In patients with mucinous colorectal cancer, MSI status is a useful marker of favourable histological and clinical features, and is associated with better outcomes. Our study supports the current 2010 WHO classification and highlights the clinical and prognostic significance of MSI status in this patient cohort.

658 Poster Session (Board BM3), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Genomic alterations in appendiceal carcinoma using circulating DNA. First Author: Walid Labib Shaib, Winship Cancer Institute of Emory University, Atlanta, GA

Background: Appendiceal cancers (AC) comprise around 0.5% of all gastrointestinal neoplasms. The genomic landscape of AC has not been well studied. The yield of circulating tumor DNA (ctDNA) from the plasma of patients with AC has not been reported. The aim of this study is to confirm the feasibility of using ctDNA and characterize common alterations in the genomic profile of AC. Methods: The molecular alterations in 372 plasma samples from 303 patients with AC using clinical-grade NGS of ctDNA conducted across multiple institutions, was evaluated. All samples were further analyzed for single nucleotide variants in 54-73 genes, copy number amplifications, fusions, and indels in selected genes. Results: A total of 303 AC patients were evaluated; 169 female (56%). Median age was 56.8 (range: 25-83); ctDNA NGS testing was done on 372 plasma samples; 48 patients had testing performed twice, 9 three times, and I was tested four times. Genomic alterations were defined in 207 (55.6%) samples with a total of 288 alterations identified after excluding variants of uncertain significance (VUSs) and synonymous mutations. TP53 associated genes were most commonly altered (n = 96, 33.3%), followed by KRAS (n = 41, 14.2%), APC (n = 19, 6.6%), EGFR (n = 15, 5.2%), BRAF (n = 13, 4.5%), NFI (n = 13, 4.5%), MYC (n = 9, 3.1%), FGFR (n = 8, 2.7%), PI3CA (n = 7, 2.4%), MET (n = 6, 2.08%), ATM in (n = 6, 2.08%). Other genomic alterations of low frequency, but clinically relevant: AR (n = 4, 1.39%), TERT (n = 4, 1.39%), CDK6 in 4 (1.39%), CDKN2A, B (n = 4, 1.39%), IDH2 (n = 3, 1.04%), CDK4 (n = 2, 0.69%), NTRK1 (n = 2, 0.69%), FGFR2 (n = 2, 0.69%), PIK3CA (n = 2, 0.69%), CDK4 in 2 (0.69%), and CDK6, CDKN2A, BRCA1, BRCA2, JAK2, IDH2, MAPK, NTRK1, CDH1, ARID1A, and PIK3CA were all reported once. Conclusions: Evaluation of ctDNA was feasible among individuals with AC. The frequency of genomic alterations in ctDNA testing is similar to those previously reported in tissue NGS. Liquid biopsies are non-invasive methods that can provide personalized options for targeted therapies in patients with AC.
Clinicopathological features, efficacy of anti-EGFR therapy, and survival outcomes in patients with BRAF non-V600 mutated metastatic colorectal cancer. First Author: Daisuke Kotani, Department of Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa, Japan

Background: BRAF non-V600 mutations occur in 2-3% of colorectal cancer. These mutations can be classified as RAS independent (class 2) or RAS dependent (class 3). We reported BRAF non-V600 mutations could be a negative predictive factor for anti-EGFR therapy in patients (pts) with pretreated metastatic colorectal cancer (mCRC), while mCRC pts with class 3 BRAF mutations could respond to anti-EGFR therapy because of its dependency on receptors and RAS. Methods: This study evaluates the efficacy to anti-EGFR therapy in a large cohort of pts with BRAF non-V600 mutated mCRC. Pts with mCRC referred to the participating centers from 2010 to 2017 were included. Clinicopathological features, efficacy of anti-EGFR therapy, and survival outcomes were stratified by BRAF mutational class. Results: One hundred seventeen pts with BRAF non-V600 mutated mCRC were identified. Median age was 58 years (range, 27-83), 68 pts (58%) were male, and 38 pts (33%) had right-sided tumors. Mucinous histology was seen in 11 cases (9%); concurrent RAS mutations occurred in 31 cases (27%), and 3 cases (3%) were MSI-H. Also, TP53 mutations were detected in 74 pts among 90 analyzed cases (82%). Regarding BRAF mutation subtype, 25/63/29 pts were classified as class 2/3/not reported (NR), respectively. Median OS in RAS wild-type/mutant were 44.8/34.6 months, respectively (p=0.082). The median OS in RAS wild-type pts with BRAF non-V600 mutations for class 2, 3, and NR were 25.7, 44.2, and 79.1 months, respectively (class 2 vs. 3, p=0.219). Among 40 pts treated with anti-EGFR therapy, response rates were 14%, 44%, and 40% for class 2, 3, and NR, respectively. Median PFS was 4.4, 8.3, 4.0 months for class 2, 3, and NR, respectively. Moreover, in 25 pts receiving anti-EGFR therapy as third or later line, response rate was 0%, 27%, and 50% in class 2, 3, and NR, respectively. Median PFS was 2.8, 3.7, and 4.0 months (p=0.762), respectively.

Conclusions: Pts with class 2 BRAF mutations tend to have a poor prognosis compared to those with class 3 mutations. While almost half of pts with class 3 BRAF mutations responded to anti-EGFR therapy, response was rare for pts with class 2 BRAF mutations, and none achieved objective response in the third or later line.

Simultaneous resection of colorectal cancer with synchronous liver metastases: A survey-based analysis. First Author: Christopher Griffiths, McMaster University, Hamilton, ON, Canada

Background: Decision to proceed with simultaneous or staged resection in synchronous colorectal cancer liver metastases (CRLM) varies and is usually left to the individual surgeon. We examined practice intentions and barriers to performing simultaneous resection. Methods: We developed and pilot-tested a tailored questionnaire to assess the practice intentions of general and hepatobiliary surgeons. Both were supportive of simultaneous resection for complex colorectal cancer were surveyed electronically. Four clinical scenarios of synchronous CRLM determined practice intentions. Both groups were less supportive of simultaneous resection for complex liver with low complexity (Likert =7-7; 83% vs. 98% p=0.001) or complex colorectal resections (57% vs. 73% p=0.042). Both groups were less supportive of simultaneous resection for complex liver with low complexity (Likert =7-7; 26% vs. 24% respectively, p=0.859) or high complexity colorectal resections (11% vs. 7.0% respectively, p=0.436). All perceived that simultaneous resection increases post-operative morbidity (63%), but not mortality (69%). Among hepatobiliary surgeons, the most common reason for simultaneous resections were comorbidities and extrahepatic disease, whereas general surgeons were more concerned about transfer to another facility. Conclusions: While general and hepatobiliary surgeons are supportive of one of the largest single institution with simultaneous resections, support is significantly lower among general surgeons. In addition to complexity of procedures and perceived morbidity, the need for transfer of care appears to be a barrier to simultaneous resections. The practice intentions and barriers described are important to identify knowledge gaps, guide future trials, and establish disease care pathways.

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Did the infuser alter your work habits? 51 (70.8)
Did you feel that your medical team appropriately prepared you? 54 (75)
Did the infuser affect your travel plans? 15 (20.8)
Did the infuser disturb your sleep? 27 (37.5)
Did the idea of an infuser deter you from chemotherapy? 25 (34.4)

Issues with bathing (73.6%), sleep (37.5%), exercising (30.6%), intimacy (26.4%), social interactions (25%) and anxiety (25%). These insights will be used to improve the education of future patients and a second assessment will follow. 72/73 patients approached over 6 months completed the survey with results below:

**Table:**

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
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<tbody>
<tr>
<td>Did the idea of an infuser deter you from chemotherapy?</td>
<td>3 (4.2)</td>
<td>67 (93.9)</td>
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<tr>
<td>Did the infuser affect your social interactions?</td>
<td>18 (25%)</td>
<td>54 (75)</td>
</tr>
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<td>Did the infuser disturb your sleep?</td>
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<td>Did you have anxiety associated with your travel plans?</td>
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<tr>
<td>Did wearing the infuser deter you from intimacy with your partner?</td>
<td>19 (26.4)</td>
<td>39 (54.2)</td>
</tr>
<tr>
<td>Did you feel that your medical team appropriately prepared you?</td>
<td>47 (64.5)</td>
<td>67 (93.9)</td>
</tr>
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<td>Did you have anxiety associated with wearing the infuser?</td>
<td>12 (16.4)</td>
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<tr>
<td>Did the infuser alter your work habits?</td>
<td>5 (6.9)</td>
<td>60 (83.3)</td>
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<td>Did the infuser affect bathing?</td>
<td>53 (73.6)</td>
<td>44 (60.1)</td>
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<tr>
<td>Did the infuser affect driving?</td>
<td>2 (2.8)</td>
<td>68 (94.4)</td>
</tr>
<tr>
<td>Did the infuser affect exercising?</td>
<td>22 (30.6)</td>
<td>44 (60.1)</td>
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Poster Session (Board #M8), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

**Ambulatory SFU Infusion pumps: Patient perceptions and quality of life.**

**First Author:** Manaf Al-Kadhimi, University of Chicago/North Shore, Evanston, IL

**Background:** Infusional-5-fluorouracil (inf-SFU), administered over 48 hours every 2 weeks, is frequently prescribed for the treatment of gastrointestinal cancers. A portable infusion device (ID) may be used for this purpose to enable treatment at home. At our institution, patients are educated by an oncology nurse as to what to expect, and how to function once they leave the infusion center. However, there is no formal process in place to report their experience and to record and analyze the results. The intended goal of this study was to accomplish this, such that the data could improve the education and experience of future patients. **Methods:** After verbal consent, a sequential cohort of patients, who had received 2 or more treatments with SFU for gastrointestinal cancer, was invited to complete a de-identified paper questionnaire concerning their experience. Eleven specific questions suggested by the ID group were included, with an opportunity to add comments. The surveys were then collated and reviewed. **Results:** See table. **Conclusions:** While most patients felt well prepared by their medical team as to what to expect from the ID (93.9%), >25% had issues with bathing (73.6%), sleep (37.5%), exercising (30.6%), intimacy (26.4%), social interactions (25%) and anxiety (25%). These insights will be used to improve the education of future patients and a second assessment will follow. 72/73 patients approached over 6 months completed the survey with results below:

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Poster Session (Board #M10), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

**Safety of bevacizumab in cancer patients with inflammatory bowel disease.** First Author, Ruth Gabriela Herrera Gomez, CHUV: Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

**Background:** Digestive and non-digestive cancers in patients with inflammatory bowel disease (IBD) are potentially sensitive to bevacizumab-based chemotherapy. Previous reports have suggested an increased toxicity in IBD patients receiving anti-VEGF agents. The safety of bevacizumab in this population is poorly documented. **Methods:** A retrospective review of records of patients with IBD treated with bevacizumab-containing chemotherapy for metastatic solid tumors in Gustave Roussy hospital between 2007 and 2016. **Results:** Twenty-eight patients (median age 43, range: 23-73) with a past history of IBD (6 ulcerative colitis, 22 Crohn’s disease) were identified. IBD was considered severe in four patients (14%). Patients presented a good control of IBD symptoms with a median number of 0 (range: 0-2) disease flares during the two years before bevacizumab initiation. Three patients were receiving corticosteroids, and another four were receiving mesalazine for IBD. No patient had abscess, fistula or hemorrhage at the time of bevacizumab initiation. The treated cancer was: colon (n = 8), rectum (n = 5), small bowel (n = 5), NSCLC (n = 4), ovary (n = 1), breast (n = 3) and other (n = 2). Patients received chemotherapy (SFU-based (LV5FU2, FOLFOX or FOLFIRI) in 17, oxaliplatin in 7, irinotecan in 8, taxanes in 7) with bevacizumab given at the approved dose-intensities of 2.5 mg/kg/week (19 pts) or 5 mg/kg/week (7 pts). Records of chemotherapy from 2 patients were missing. A median number of 8 cycles of bevacizumab (range: 2-39) was given concomitantly to chemotherapy and then as maintenance therapy, with the following grade >2 toxicities: hyper-tension in 6 cases (20%) and proteinuria in 3 (10%). No dose-limiting toxicity was observed. No change in IBD treatment was required. One patient developed grade 2 rectorrageia (identified as Crohn’s disease flare-up) after 6 months of bevacizumab FOLFIRI. After withdrawal of irinotecan, the patient was re-challenged with bevacizumab for another 6 cycles without recurrence of bleeding. **Conclusions:** In our experience, bevacizumab can be given to cancer patients with quiescent IBD at conventional doses with good clinical tolerance.

Poster Session (Board #M110), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

**Nintedanib versus placebo in patients receiving mFOLFOX6 metastatic chemorefractory colorectal cancer: TRICC-C trial—Final results from the randomized phase II trial of the AIO.** First Author: Thomas Jens Etrich, Ulm University, Ulm, Germany

**Background:** Anti-VEGF agents plus chemotherapy improve PFS of patients with mCRC in the first- and second-line-setting. During this treatment tumour angiogenesis is driven by other factors but VEGF. Nintedanib, a triple-tyrosine kinase inhibitor of VEGFR-1, -2, and -3, in addition to targeting VEGF as well as angiopoietin 2 and TIE2, additionally targets angiogenic escape mechanisms upon resistance to anti-VEGF treatment. The TRICC-C trial evaluates the combination of mFOLFOX6 plus Nintedanib. Final results of the randomized phase II trial are presented. **Methods:** Patients with mCRC having received one line of non-oxaliplatin containing palliative chemotherapy, with an ECOG-PS of 0/1 were randomized 1:1 in a double-blind design to receive: mFOLFOX6 plus Nintedanib (x 200 mg p.o./d, d2/4) or placebo, respectively, repeated every 14 days. Primary endpoint was PFS. Secondary endpoints were ORR, OS and safety. Patients who received at least one dose of trial medication were included in the efficacy and safety analyses. **Results:** From 2012 to 2015 53 patients (scheduled n = 180) were randomized. The trial was terminated prematurely due to slow accrual. Compared to mFOLFOX6 plus placebo (P=0.9), the combination of mFOLFOX6 plus Nintedanib (F+P) improved mPFS (F+P: 9.6 vs. F: 7.0 months, HR: 0.65; 95% CI 0.32-1.30; p = 0.2156), mOS (F+P: 26.9 vs. F: 18 months, HR: 0.73; 95% CI 0.50-1.06; p = 0.0720). ORR was comparable in both arms (F+P: 34% vs. F: 30%; p = 0.5333). Toxicity was low to moderate without major differences between both arms except G 3/4 neutropenia (F+N: 21%, F+P: 15%) and G2/3 anemia (F+N: 23%, F+P: 18%). **Conclusions:** Future results suggest a PFS, OS and DCR benefit for mFOLFOX6 + Nintedanib in the second-line therapy of mCRC. Due to the premature termination of the trial there was no statistical significance demonstrable. Showing no clinically significant PFS-benefit in the first-line situation (mFOLFOX6 versus Nintedanib), Nintedanib plus mFOLFOX6 could be an interesting therapeutic option for the second-line situation. Clinical trial information: NCT01362361.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Integrating geriatric assessment into routine gastrointestinal (GI) consultation: The Cancer and Aging Resilience Evaluation (CARE). First Author: Grant Richard Williams, University of Alabama at Birmingham, Birmingham, AL.

Background: Integrating Geriatric Assessment (GA) in the management of older adults with cancer is recommended, yet rarely practiced in routine oncologic care. In this report, we describe the feasibility of integrating the routine incorporation of GA in the management of older adults with GI malignancies and characterize GA impairments. Methods: CARE was adapted from the Cancer and Aging Research Group GA with modifications to create a completely patient-reported version. The CARE assesses self-reported functional status, physical function, nutrition, social support, anxiety/depression, cognitive function, comorbidities, and social activities. Patients ≥ 60yo referred for consultation to the GI Oncology clinic were asked to complete the CARE (paper/pencil) on their first visit. The completed CARE was collected during nurse triage and submitted to the clinical team prior to the physician encounter. Feasibility was defined as completion of the CARE by ≥ 80% of eligible patients during the initial consultation. Results: Between September 2017 and August 2018, 199 eligible new patients attended the GI Oncology Clinic, 192 (96.5%) approached, and 189 (95%) completed the CARE. Most patients (79.6%) felt the length of time to complete was appropriate (median time of 10 minutes [IQR 10-15 minutes]). The mean age was 70y (range 60-96), 54.3% were male, and 75.1% were non-Hispanic white. Common tumor types included colon (27.8%), pancreatic (21.2%), and rectal (10.2%) cancer; predominately advanced stage diseases (stage III: 26.9%; stage IV: 40.0%). GA impairments were prevalent: 48.6% reported dependence in Instrumental Activities of Daily Living, 18.0% reported dependence in Activities of Daily Living, 22.5% reported ≤ 1 fall, 29.4% reported a performance status ≥ 2, 33% were limited in walking one block, 75.7% reported polypharmacy (≥ 4 medications), and 84.3% had ≥ 1 comorbidity. Conclusions: Performing GA as a routine care of older adults with GI malignancies is feasible, and GA impairments are common among older adults with GI malignancies. A fully patient-reported GA such as the CARE may facilitate broader incorporation of GA in the routine clinic work flow.

FOLFOX rechallenge versus regorafenib in patients with metastatic colorectal cancer refractory to standard chemotherapy: A retrospective analysis. First Author: Maria Alessandra Cagienz, Fondazione Policlinico Universitario "A. Gemelli" - IRCCS - UC Oncologia Medica, Roma, Italy.

Background: Nowadays the optimal treatment for mCRC beyond second line is still questioned. During last years, regorafenib and TAS-102 showed to improve survival compared to best supportive care in pts with refractory mCRC. Some retrospective analyses compared the efficacy and safety of regorafenib and TAS-102 reporting no significant differences in survival and response outcomes. In real-world clinical practice, chemotherapy (CT) rechallenge is often considered for refractory mCRC. However, evidences regarding CT rechallenge is limited and no study has previously compared such approach with the recently approved antiangiogenic agent in late lines. The aim of this study was to compare the efficacy between CT rechallenge and regorafenib in pts with refractory mCRC. Methods: This is a monocentric retrospective study. We compared the efficacy of FOLFOX rechallenge and regorafenib in pts with mCRC refractory to at least 2 lines of standard CT, treated at Fondazione Policlinico Universitario "A. Gemelli" - IRCCS between Jan-10 and Jan-18. The primary endpoint was OS. Secondary endpoints were RR and PFS. Results: One hundred thirty-one pts received regorafenib and 43 FOLFOX rechallenge. OS was significantly higher with FOLFOX rechallenge than it was with regorafenib (13 vs. 6 months; HR 0.67, 95% CI 0.33-0.66; p = 0.0002). PFS was significantly higher in the FOLFOX rechallenge group compared to the regorafenib group (5 vs. 3 months; HR 0.64, 95% CI 0.46-0.89; p = 0.0073). Accordingly, RR was better in pts receiving FOLFOX rechallenge compared to regorafenib (25 vs. 3%; Chi-square p < 0.0001). Conclusions: Our study, although retrospective and small-sized, compared for the first time to our knowledge the efficacy of CT rechallenge to regorafenib in refractory mCRC. In our analysis, CT rechallenge with FOLFOX proved to be superior compared to regorafenib, with a survival and response benefit in pretreated mCRC. The survival benefit observed for rechallenge might be explained by the significantly higher tumor shrinkage achieved with CT rechallenge compared to regorafenib. Our results warrant further confirmation in wider and/or prospective analyses.

Safety and clinical activity of durvalumab monotherapy in patients with microsatellite instability-high (MSI-H) tumors. First Author: Neil Howard Segal, Memorial Sloan Kettering Cancer Center, New York, NY.

Background: MSI-H tumors have shown to be responsive to PD-1 inhibitor therapy. We evaluated the anti-PD-L1 mab durvalumab in patients with MSI-H tumors, in two ongoing studies: a phase 1/2, multicenter, open-label study in patients with advanced solid tumors; and a phase 2 single-center study in patients with advanced colorectal cancer (CRC). Methods: Patients with MSI-H tumors (determined locally by immunohistochemistry or sequencing) received durvalumab 10 mg/kg IV every 2 weeks for 12 months or until confirmed progressive disease, whichever was first. Objectives were to evaluate safety and antitumor activity (per investigator-assessed RECIST v1.1). Results: As of Oct 16, 2017, 62 MSI-H patients (97% with prior anti-cancer therapy) received treatment in the multicenter study; median duration of follow-up was 29 months. Treatment-related adverse events (TRAEs) occurred in 37 patients (60%), most commonly diarrhoea (15%), asthma (11%), fatigue (11%), nausea (10%), and hypertension (9%). Grade 3 TRAEs occurred in 2 patients (3%). There were no deaths or treatment discontinuations due to TRAEs. Objective response rates (ORRs) were 23% for the total population and 22% for patients with CRC; 9 of 14 responders were ongoing at data cutoff. As of Sep 13, 2018, 11 patients with MSI-H CRC were treated in the single-center study; median duration of follow-up was 30 months. One patient discontinued treatment due to treatment-related asymptomatic mononucleosis (resolved with steroids); response rate and survival were similar to the multicenter study. (Table: NCT02277667/NCT01935662; Clinical trial information: NCT01935662 and NCT02277667). Conclusions: Durvalumab had a tolerable safety profile, and showed promising antitumor activity and overall survival in patients with MSI-H tumors.
Methods:

Cancers of the Colon, Rectum, and Anus

671 Poster Session (Board BM16), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

The impact of multidisciplinary team (MDT) management on outcome of hepatic resection in liver-limited colorectal metastases. First Author: Salvatore Corallo, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy

Background: Hepatic resection is the gold standard treatment for pts with liver-limited mCRC with 5- and 10-yr survival rates reaching up to 60% and 20%. Although multidisciplinary team (MDT) management might ensure a more accurate assessment of pts and a faster referral to surgeons, reports discussing the impact of MDTs on survival are controversial and to date there are no strong evidences supporting routinely MDT discussion. The aim of this study was to evaluate the benefit of MDT management in pts with liver-limited mCRC in our single institution experience.

Methods: Clinical records of pts with liver-limited mCRC who underwent radical surgery at Fondazione Poli-clinic “A. Gemelli” - IRCCS from Jan-2006 to Dec-2016 were retrospectively analyzed. The objective of the analysis was to compare survivals of pts managed within our MDT (MDT cohort) to those of pts referred to surgery from other hospitals without MDT discussion (non-MDT cohort). Primary endpoints were DFS and OS. Differences in baseline characteristics and in post-morbid survival were evaluated. Results: Of the 619 pts analyzed, 230 were included in the MDT cohort and 389 in the non-MDT cohort. No significant difference between the two groups was found in terms of DFS (5vs21 m; p 0.09) and OS (55vs51 m; p 0.68). Concerning baseline characteristics, in the MDT cohort compared to non-MDT cohort there was a statistically higher number of median metastases (4.5vs2.6; p < 0.0001) and a higher rate of synchronous metastases (61.7vs39.3%; p < 0.001). Pre-operative CT rate was higher in the MDT group (75.8vs70.7%); the median duration of CT before surgery was significantly lower in MDT pts (7 vs 8 cycle; p < 0.001). Moreover, post-operative morbidity was significantly lower in the MDT cohort (6.2vs9.2%; p < 0.00001). Conclusions: Our study does not demonstrate a survival benefit from MDT management of pts with liver-limited mCRC. However, the analysis shows that MDT assessment allows to consider eligible for surgery pts with a more advanced disease. Moreover, MDT discussion seems to reduce the median duration of pre-operative CT with a consequent lower rate of post-operative morbidities. Our data warrant prospective validation.

673 Poster Session (Board BM18), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Surgery versus surgery with adjuvant radiotherapy for T4 colon cancer. First Author: Nikhil Sebastian, Ohio State University James Cancer Hospital Department of Radiation Oncology, Columbus, OH

Background: There is no randomized prospective evidence to clarify the role of adjuvant radiotherapy in localized colon cancer. Despite this, national consensus guidelines recommend that adjuvant radiotherapy be considered for patients with T4 disease. Given the lack of prospective data, the aim of this study was to evaluate the role of adjuvant radiotherapy in T4 colon cancer using two large national databases to help to guide treatment decisions.

Methods: We evaluated the association of receipt of adjuvant RT over time using the National Cancer Database (NCDB) and the Surveillance, Epidemiology, and End Results Program (SEER), as well as a disease-specific survival (DSS) using SEER. We analyzed cohorts of patients with historically confirmed locally advanced T4 adenocarcinoma of the colon, who underwent oncologic surgery with or without adjuvant radiation and had at least 5 years of follow up. For the NCDB cohort, we restricted RT patients to those who received a dose of 45-60 Gy and those who received treatment within 3 months after surgery. We used nearest-neighbor propensity score matching on the basis of age, race, sex, year of diagnosis, grade, N-stage, receipt of chemotherapy, anatomical sub-site, margin status, and comorbidity score. To validate our findings, using SEER, we used propensity matching using the same covariates (except comorbidity). Results: After matching of the NCDB cohort, cox regression showed no statistically significant association of adjuvant radiotherapy with OS (HR=1.08; 95% CI 0.99-1.30; p=0.448). Using SEER, cox regression showed no statistically significant association of adjuvant radiotherapy with OS (HR=1.08; 95% CI 0.50-1.63; p=0.731) or DSS (HR=0.84; 0.54 - 1.33; p=0.46). Conclusions: In summary, after comprehensively adjusting for covariates using two independent national databases, we found no statistically significant association of adjuvant RT with overall- or disease-specific survival for T4 colon cancer. These findings add to the retrospective nature of the data and should be tested in a prospective fashion.

672 Poster Session (Board BM17), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Predictors of survival in rectal squamous cell carcinoma: An analysis from the National Cancer Database (NCDB). First Author: Sri Harsha Tejia, University of South Carolina, Columbia, SC

Background: Rectal squamous cell carcinoma (RSCC) is a rare form of gastrointestinal malignancy. Using the NCDB, we determined the prognostic factors and survival outcomes of RSCC in the United States. Methods: We identified histologically confirmed cases of RSCC from the National Cancer Data Base (2004-2014). Univariate and multivariable methods were used to assess factors associated with survival. Kaplan-Meier method and log-rank test were used to perform overall survival (OS) analysis. Results: Of the 5,527 cases included in our analysis, 67% were female. Median age at diagnosis was 61 years and did not differ by sex. The proportion of patients with stages I, 2, 3 and 4 diseases were 22%, 26%, 20%, and 11%, respectively (30% unknown stage). Among the ones who received surgical resection of primary tumor, 41%, 30%, 20% and 8% are of stages I, 2, 3 and 4 respectively. The rate of R0 resection was 54%, 63%, 55% and 38% in stage I, 2, 3 and 4, respectively. The R0 resection rate was much higher in patients who received neoadjuvant chemo or radiation therapy or both (87%, 78%, 74%, and 57% in stages I, 2, 3 and 4, respectively) as compared to that of their counterparts. On stage wise sub-group OS analysis, stage 3 patients had OS benefit from surgery (as compared to no-surgery) (145 vs 90 months, p<0.001) as opposed to 4 disease (16 vs 11 months, p=0.06). Adjuvant radiation therapy improved the median OS in stage 3 patients (as compared to no-adjuvant radiation) in patients with positive surgical margins (not reached vs 40 months, p<0.001). Patients with stage 4 disease treated with radiation therapy had a better median OS (6 months) than those without (16 vs 6 months, p<0.001). On therapy wise sub-group analysis, the patients who received surgery only had a median OS of 145 months; surgery + chemoradiation (adjuvant and neoadjuvant) + RT had OS of 192 months. Results: This is the largest registry-based study on RSCC to date. RSCC had a diverse OS varied significantly according to stage of the disease at presentation and therapy received. Surgical resection of primary tumor was associated with improved OS as compared to that of patients who received chemoradiation.

674 Poster Session (Board BM19), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Phase III randomized, placebo-controlled, double-blind study of monosialotetrahexosylganglioside in prevention of oxaliplatin-induced neurotoxicity in stage III/II colorectal cancer patients. First Author: Yu-hong Li, Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China

Background: Monosialotetrahexosylganglioside (GM1) is a glycosphingolipid, which has antioxidant and neuroprotective properties. Cumulative neurotoxicity is a prominent toxicity of oxaliplatin-based therapy. This study was designed to assess the efficacy of GM1 for preventing oxaliplatin-induced neurotoxicity in colorectal cancer (CRC) patients. Methods: A total of 186 patients with stage II/III CRC undergoing adjuvant chemotherapy with modified FOLFOX6 (fluorouracil, leucovorin, and oxaliplatin) were randomly assigned to intravenous GM1 80mg per day or placebo from day 0 to day 4 during chemotherapy. The primary end point was the rate of grade 2 or worse cumulative neurotoxicity, measured by investigator using the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. The secondary end point were the chronic cumulative neurotoxicity measured by the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Chemotherapy-Induced Peripheral Neuropathy 20 (EORTC QOL-CIPN20), time to grade 2 neurotoxicity by using the NCI-CTCAE or the oxaliplatin-specific neuropathy scale, the rates of acute neurotoxicity measured by a numerical analog scale ranging from 0 to 10, and the rates of dose reduction or withdrawal of both arms. Results: There were no statistically significant differences in the rate of NCI-CTCAE grade 2 or worse neurotoxicity between the study arms (GM: 33.7% vs placebo: 31.6%; P=0.76). Similarly, there were no significant differences measured by EORTC QOL-CIPN20 neuropathy scale (P=0.89) or additional measures of neuropathy, including measurement of the time to grade 2 neurotoxicity by using the NCI-CTCAE (P=0.99) or an oxaliplatin-specific neuropathy scale (P=0.98). In addition, GM did not substantially decrease oxaliplatin-induced acute neuropathy. The rates of dose reduction or withdrawal of both arms were not significantly different (GM: 64.6% vs placebo: 54.6%; P=0.15). Conclusions: This study does not support using GM1 to prevent oxaliplatin-induced neurotoxicity. (NCT02251977) Clinical trial information: NCT02251977.

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Patterns of adjuvant therapy use and survival outcomes in patients with rectal cancer not receiving neoadjuvant therapy in an Australian cohort. 

First Author: Kate Jessica Wilkinson, Liverpool Cancer Therapy Centre, Liverpool, Australia

Background: Consensus international guidelines recommend the use of neoadjuvant chemoradiotherapy in patients with stage II-III rectal cancer. Despite this, due to factors including inaccurate/under-staging, patient comorbidities and acute presentations, a proportion will undergo upfront surgical resection. The survival benefit of adjuvant therapy is unclear in this real world, non-trial population. Methods: A retrospective analysis of patients presenting with stage II-III rectal adenocarcinoma in South Western Sydney and Illawarra Shoalhaven Health Districts, Australia, between 2006 to 2015 was performed. Data was extracted from electronic health records, with institutional ethics approval. Treatment modalities, clinical-pathological, recurrence and survival data were analyzed. The primary endpoint was overall survival (OS) by treatment modality. Results: 549 patients were identified, of which 295 (54%) underwent upfront surgical resection without neoadjuvant therapy. Of this cohort, 137 (46%) had no adjuvant therapy (Group A), 103 (35%) had adjuvant chemotherapy alone (Group B), and 55 (19%) had adjuvant radiotherapy +/- chemotherapy (Group C). Receipt of any adjuvant treatment was significantly associated with improved OS (5 year OS 56 vs. 79%, HR 0.44, 95% CI 0.3-0.6, p < 0.001) and recurrence free survival (5 yr RFS 25% vs. 47%, HR 0.66, 95% CI 0.5-0.9, p = 0.01), but not cancer specific survival (5yr CSS 75 vs. 80%, HR 0.78, 95% CI 0.5-1.3, p = 0.30). Group B had improved OS compared to Group A (5 yr OS 56% vs. 80%, HR 0.35, 95% CI 0.22 - 0.55, p < 0.001). There was a trend for improved OS in Group C vs. Group A (5 yr OS 56.0% vs. 69.2%, HR 0.79, 95% CI 0.61 - 1.01, p = 0.052). The improved OS in Group B versus Group A remained significant in multivariate analysis (HR 0.45, 95% CI 0.22 - 0.77, p = 0.005). Conclusions: Adjuvant chemotherapy improved OS in this real world cohort, and there was a trend to a benefit with adjuvant chemo-radiotherapy. However, the lack of difference in cancer specific survival suggests that this benefit may be partly driven by patient selection bias. Further exploratory analyses to identify sub-groups deriving a cancer specific survival benefit are required.
Conclusions:

p

95% CI 0.71-1.04; HR 0.78, 95% CI 0.51-1.20; 2L vs. 3L; with 3L and 2L anti-EGFR therapies ((3L and 2L: n = 2 studies each; HR 0.86. 95% CI 0.72- 17.85; P

Poster Session (Board #N6), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

A phase lb study of pembrolizumab (Pem) in combination with stereotactic body radiotherapy (SBRT) for resectable liver metastatic colorectal cancer (CRC). First Author: Anita Ahmed Turk, Indiana University School of Medicine, Indiana University Simon Cancer Center, Indianapolis, IN

Background: Adjunctive therapies are essential to enhance the effect of anti-PD1 therapies for the treatment of microsatellite stable (MSS) colorectal cancer. SBRT is utilized to treat liver metastatic CRC, causing an increase in immunogenic intratumoral and a rapid influx of responding immune cells. We hypothesize that radiation enhances immunogenicity of MSS CRC and potentiates effectiveness of PD-1 blockade. This phase lb study examines the safety and efficacy of the sequential combination of SBRT and Pem in patients for whom the goal is to resect all sites of known disease. Methods: Key eligibility criteria include MSS CRC and liver-confined metastatic disease with the therapeutic goal of resection of all radiographic disease with one operation. Subjects must be a candidate for SBRT to 1-3 liver metastases. Prior surgery and systemic chemotherapy are allowed. Subjects receive sequential SBRT and cycle 1 of Pem prior to operative management. Postoperatively, patients complete cycles 2-9 of Pem followed by scheduled surveillance with imaging every 12 weeks. The primary objectives are to determine the safety of this regimen and the recurrence rate at one year following clearance of metastatic disease. Secondary objectives include time to recurrence, DFS, and OS. Results: Nine patients (median age 61.5 (range 39-69)) have completed the intended neoadjuvant therapy, operative management, and at least one adenocarcinoma of CRC. All patients received prior FOLFOX. Any-grade AE (≥ 20%) through cycle 2 of Pem attributable to SBRT include fatigue (44%) and nausea (22%). Any-grade AEs related to Pem include lymphopenia (25%). Postoperative AEs included one case of biliary tract injury and biliary, not related to immunotherapy. One patient developed a rash following SBRT and Pem which may be an immunotherapy-related toxicity. No grade 3/4 immunotherapy AEs have occurred. Conclusions: The combination of SBRT, Pem, and surgical resection is well tolerated with no signal of increased immunotherapy-related toxicity. Clinical trial information: NCT02837263.

680 Poster Session (Board #N5S), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Retrospective analysis of clinical characteristics of mCRC patients receiving three or more lines of chemotherapy. First Author: Pilar Garcia Alfonso, Hospital General Universitario Gregorio Marañon, Madrid, Spain

Background: Prognostic and predictive factors are becoming more important in mCRC patients, and may have an impact on overall survival and in the number of lines of chemotherapy that a patient can receive. Methods: We conducted a retrospective analysis of 334 patients with mCRC. We analyzed the clinical characteristics of 133 patients diagnosed between the years 2015 and 2016 (n = 113) in order to identify significant association. Results: Several characteristics were significantly associated with receiving > 3 lines of chemotherapy: (n = 103): age ≥ 80 years (n = 93, OR = 3.07, p = 0.001), ECOG 0-1 (n = 98, OR = 3.21, p = 0.001), metastatic disease (n = 56, OR = 2.07, p = 0.002). Partial or complete response rate in the first line of chemotherapy was also significantly associated with receiving ≥ 3 lines of treatment (n = 65, OR = 0.31, p = 0.001). Tumor mutational status was analyzed in 333 patients: KRAS mutation was detected in 163 over 333 patients (48.9%), NRAS in 26 (7.8%), BRAF in 110 (33.3%), PIK3CA in 126 (37.8%), PIK3CB in 110 (33.3%) and PIK3CD in 68 (20.3%). KRAS mutation was found in 60/103 patients (53.3%), NRAS in 7/77 (9.5%), BRAF in 5/84 (5.9%) and PIK3CA in 8/80 (10%). Tumor mutations were not significantly associated with ≥ 3 lines of chemotherapy. No significant association was found between sex, tumor location (right versus left, p = 0.22) and left (p = 0.75, p = 0.75), liver or lung isolated metastases and ≥ 3 lines of chemotherapy. We also performed in our database a survival analysis in the 334 patients: those who received ≥ 3 lines of chemotherapy had significantly higher survival rates than those who received 3 lines of treatment (32.7% vs. 11.6% in the group of patients receiving < 3 lines of chemotherapy, HR = 5.6, CI 95% 1.2-21; p < 0.001). Conclusions: Retrospective analysis showed that mCRC patients with < 80 years, ECOG 0-1, primary tumor and/or metastases resected and those with complete or partial response in the first line of treatment have a higher probability of receiving ≥ 3 lines of chemotherapy.

CANCERS OF THE COLON, RECTUM, AND ANUS

668 Poster Session (Board #N7), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
Background: Anti-EGFR plus chemotherapy (CT) promotes high response rates (RR) and median overall survival (OS) surpasses 30 months in RASwt/BRCAwt mCRC. After disease progression (PD), resistance mechanisms have been described. The aim of our study was to evaluate efficacy of anti-EGFR re-challenge (TRECC). Methods: We retrospectively analyzed a cohort of patients (pts) with mCRC. All pts had received anti-EGFR plus CT and were discontinued for different reasons. During the treatment, there was re-challenge with an anti-EGFR + CT. We aimed to evaluate progression-free survival (PFS) and OS after re-challenge and prognostic factors associated with PFS. Results: Sixty eight pts met the study criteria. Median follow-up after re-challenge was 39.3m. Discontinuation after first exposure was 25% due to PD; 75% for other reasons. Median anti-EGFR free interval was 10.5m. At re-challenge, main CT regimen was: FOLFIRI 58.8%, Cetuximab and Panitumumab were used in 59 and 9 pts respectively, mPFS after re-challenge was 6.6m; mOS was 24.4m. Objective response rate (CR + PR) at re-challenge was 42.6%. In an univariate analysis, adverse prognostic factors related to PFS were: absence of objective response at first EGFR exposure (HR 2.12, CI 1.34 - 3.34; p = 0.01), disease progression at first EGFR discontinuation (HR 2.41, CI 1.38-3.94; p = 0.03), no prior PD as reason for first discontinuation statistically significant (HR 1.99, CI 1.39-3.09; p = 0.01), and mPFS was 3.3m and 8.4m and mOS was 7.5m and 33.4m in patients with PD as reason for PD discontinuation and other reasons respectively. Conclusions: Re-challenge therapy is commonly used due to paucity of effective lines of treatment for mCRC. In our analysis, pts that stopped first anti-EGFR therapy due to PD have shorter survival, suggesting these pts do not benefit from TRECC. However, interruption due to treatment holiday after PR/CR resulted in longer PFS. In conclusion, for a selected group of pts, TRECC could be considered a strategy of treatment. Due to the limited number of pts, our data should be evaluated in a prospective cohort of patients.

Conclusions: The dataset included 93,070 patients with stage II and 66,701 patients with stage III CA. Of the stage II patients with LVI, 20% received adjuvant chemotherapy (CT) and median OS was 6.91 years for those who did versus 6.07 years for those who did not receive adjuvant CT. Conclusions: Our data suggest that LVI is an important predictor of OS in stage II and III CA. There is evidence that adjuvant chemotherapy improves OS in advanced CA but there remains uncertainty as to the benefit in stage II. Despite this uncertainty, guidelines suggest consideration of adjuvant CT in patients with high-risk stage II disease. Our study supports the recommendation that LVI be considered a high-risk feature in stage II disease. Further studies are necessary to examine whether the type or duration of CT should differ for patients with CA and LVI.

Background: Presence of lymphovascular invasion (LVI) is known to be a predictor of lymph node involvement in colon adenocarcinoma (CA). Lymph node involvement is associated with poorer prognosis necessitating adjuvant therapy. While some studies have suggested that LVI is a predictor of worse overall survival (OS) and cancer-specific survival (CSS) in stage II CA, the significance of LVI in the prediction of survival is not well established. In a comprehensive North American data set, patients with stage II CA with LVI had median OS of 11.2 years as compared to 13.1 years for patients without LVI. Our aim was to evaluate the effect of LVI on median OS for stage II CA patients with and without LVI. Methods: Patients with stage II and III CA with LVI data available and those who had CT with disease progression (PD) were included in the study. The primary endpoint of PII was proportion of 3-year event-free survival (EFS). The expected 3-year EFS was determined as 80% and the threshold was 60%. The power of 80%, threshold and expected 3-year EFS as 60% and 75%, respectively. Conclusions: When the primary endpoint in PII part is proven to be satisfactory, we can regard this combined endpoint in PII part (P I) as satisfactory. In conclusion, the results suggest that LVI is an independent predictor of OS and EFS. LVI should be considered a high-risk feature in stage II disease. Further studies are necessary to examine whether the type or duration of CT should differ for patients with CA and LVI.
impact of sarcopenia on outcomes in patients with rectal carcinoma treated with trimodality therapy. First Author: Maria Sandoval, New York Medical College, Valhalla, NY

Background: Sarcopenia has been identified as a negative prognostic factor in several gastrointestinal malignancies. We sought to evaluate whether total psoas area (TPA) was predictive of grade ≥ 3 toxicity, recurrence and overall survival in patients with rectal carcinoma who received trimodality therapy.

Methods: After IRB approval, a retrospective analysis of 112 patients with biopsy-proven rectal cancer treated with neoadjuvant chemoradiation followed by surgery and adjuvant chemotherapy was performed. The L4 vertebra was identified on pre-treatment axial CT and the bilateral psoas muscles were manually contoured to determine the skeletal muscle index, which was normalized to total TPA. Sarcopenia was defined as TPA less than the median of the cohort. (< 1463 mm3/m2). Acute toxicity was defined as within 3 months of radiation based on Common Terminology Criteria for Adverse Events version 4. Chi-square was used to assess differences between groups. Time to event analysis was estimated by Kaplan-Meier methods followed by log rank comparison. Predictor variables for outcomes were assessed with Cox regression.

Results: Median follow-up was 31 months. Female gender was strongly associated with being sarcopenic (P < 0.001) otherwise no other differences in clinical or treatment characteristics were found. 20 patients (17.8%) developed recurrence (95% CI: 13.7 to 22.3), 20 (17.8%) had a grade ≥ 3 toxicity, and 14 (12.5%) died. Survival and time to recurrence was similar between patients with sarcopenia and those without. Median age and follow up is 58 years ± 27 months, respectively. Patients were staged based on AJCC 8th edition. 80 pts (70%) received chemotherapy, 11 (10%) received surgery, and 13 (12%) received radiation. 56 pts (50%) did not tolerate therapy. 28 pts received 5FU-based therapy, 13 PR in (46%), stable disease (SD) in 4 (14%), and progressive disease (PD) in 31 (55%); 3 (5%) did not tolerate therapy. 28 pts received 5FU-based treatment, 13 PR in (46%), SD in 6 (21%), and PD in 7 (25%); 2 (7%) did not tolerate therapy. Median overall survival was 11.4 months. 21/66 (32%) pts underwent molecular sequencing of tumor; the most common alterations were KRAS 11 (52%), TP53 13 (11%) and the remaining were other KRAS/BRAF/APC and TP53/RB1. There was no significant difference in response to cis/cisplatin and SUFT-based chemotherapy. To date, choice of systemic therapy and sequencing of these drugs remains poorly understood. We examined clinical and molecular characteristics to better define predictors of response to cis/cisplatin and SUFT-based treatment. Methods: Patients (pts) with colorectal HGNEC treated at MSKCC from 1990-2018 were identified. MANEC mixed adeno-neuroendocrine carcinoma) were excluded. Demographics, clinical parameters, and molecular data (next-generation sequencing of tumor tissue), were collected. Results: 65 pts (mean age 58, 52% male) were identified, 13 (20%) with small cell carcinomas, 52 (79%) metastatic, 13 (20%) locally advanced. 27 (42%) received surgery and 11 (17%) received radiation. 56 pts received cis/cisplatin-based therapy, partial response (PR) in 18 (32%), stable disease (SD) in 4 (7%), and progressive disease (PD) in 31 (55%); 3 (5%) did not tolerate therapy. 28 pts received SUFT-based treatment, 13 PR in (46%), SD in 6 (21%), and PD in 7 (25%); 2 (7%) did not tolerate therapy. Median overall survival was 11.4 months. 21/66 (32%) pts underwent molecular sequencing of tumor; the most common alterations were KRAS II (52%), TP53 13 (62%), BRAF 7 (33%), APC 8 (38%), R17 (33%). Most tumors (13/21, 62%) harbored alterations in genes traditionally altered in colorectal adenocarcinoma (KRAS/BRAF/APC) and in HGNEC (TP53/RB1). There was no significant difference in response to cis/cisplatin or SUFT-based chemotherapy based on location of the primary tumor (right vs. left) (p = 0.69), histologic features of the primary (p = 0.14), and for response to cis/cisplatin or SUFT-based chemotherapy by molecular alterations in KRAS (p = 0.94), BRAF (p = 0.24), APC (p = 0.28), TP53 (p = 0.58), or RB1 (p = 0.28). In HGNEC of the colon, the importance of the primary tumor is not clear.

Conclusions: Colorectal HGNEC are highly aggressive tumors; treatment options consist of cis/cisplatin and SUFT-based chemotherapy. To date, choice of systemic therapy and sequencing of these drugs remains poorly understood. We examined clinical and molecular characteristics to better define predictors of response to cis/cisplatin and SUFT-based treatment. Methods: Patients (pts) with colorectal HGNEC treated at MSKCC from 1990-2018 were identified. MANEC mixed adeno-neuroendocrine carcinoma) were excluded. Demographics, clinical parameters, and molecular data (next-generation sequencing of tumor tissue), were collected. Results: 65 pts (mean age 58, 52% male) were identified, 13 (20%) with small cell carcinomas, 52 (79%) metastatic, 13 (20%) locally advanced. 27 (42%) received surgery and 11 (17%) received radiation. 56 pts received cis/cisplatin-based therapy, partial response (PR) in 18 (32%), stable disease (SD) in 4 (7%), and progressive disease (PD) in 31 (55%); 3 (5%) did not tolerate therapy. 28 pts received SUFT-based treatment, 13 PR in (46%), SD in 6 (21%), and PD in 7 (25%); 2 (7%) did not tolerate therapy. Median overall survival was 11.4 months. 21/66 (32%) pts underwent molecular sequencing of tumor; the most common alterations were KRAS II (52%), TP53 13 (62%), BRAF 7 (33%), APC 8 (38%), R17 (33%). Most tumors (13/21, 62%) harbored alterations in genes traditionally altered in colorectal adenocarcinoma (KRAS/BRAF/APC) and in HGNEC (TP53/RB1). There was no significant difference in response to cis/cisplatin or SUFT-based chemotherapy based on location of the primary tumor (right vs. left) (p = 0.69), histologic features of the primary (p = 0.14), and for response to cis/cisplatin or SUFT-based chemotherapy by molecular alterations in KRAS (p = 0.94), BRAF (p = 0.24), APC (p = 0.28), TP53 (p = 0.58), or RB1 (p = 0.28).
**691 Poster Session (Board RN6), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM**

**Disease characteristics and treatment outcomes of young colorectal cancer patients. First Author: Hiral D. Parekh, University of Florida Health Cancer Center, Gainesville, FL**

**Background:** The incidence of colorectal cancer (CRC) in young patients (<50 years) is increasing but little is known about disease characteristics and treatment outcomes in this patient population.

**Methods:** CRC patients diagnosed at < 50 years of age (NI institutional registry 2000-2017) constituted the IRB approved study cohort. Statistical methods included descriptive statistics, univariable Cox proportional hazard regression model, Pearson chi-square exact and Wisconsin rank sum test. Results: The median age at diagnosis was 45 years (range 17-70, n = 286) with 232 (74%) diagnosed between age 40-60. One third (33.7%) of patients had rectal primary and most common histology was adenocarcinoma (ACa, 84.6%) and 20% of those had poorly differentiated tumor. More than half of patients had an advanced primary (T3/T4, 65%) and 44% had lymph node positive disease. A trend towards increased delivery of perioperative therapy was seen in early staged disease. (See Table) Patients who underwent curative resections had better hemoglobin (p = 0.005) and albumin levels (A8p, p < 0.000) and lower CA19.9 levels (p = 0.000). Factors associated with downstaging were low aBI levels: 34 g/l, advanced primary tumor (T3/T4), nodal disease (N1/N2) and presence of diffuse metastasis. For stage 4 disease, the cancer-specific survival (CSS) at 1 year was 77.2%, 3-year CSS was 46.7% and 5-year CSS was 29%; survival was better (HR = 0.4, 95% CI 0.2-0.6, p = 0.000) among patients who underwent metastectomy.

**Conclusions:** Our data suggests that younger CRC patients were more likely to be managed in an aggressive manner with a higher proportion of early stage patients receiving perioperative therapy. A suggestion of an improved CSS was seen in advanced stage disease even with similar prognostic factors. Review of larger datasets are warranted.

**Characteristics and OS (n=286)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OS (%)</th>
</tr>
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<tbody>
<tr>
<td>Resection of primary tumor</td>
<td>168/277 (89%)</td>
</tr>
<tr>
<td>Pathology</td>
<td></td>
</tr>
<tr>
<td>Acinar 147 (51%)</td>
<td></td>
</tr>
<tr>
<td>Squamous cell 39 (14%)</td>
<td></td>
</tr>
<tr>
<td>Mixed 3 (1%)</td>
<td></td>
</tr>
<tr>
<td>Perioperative therapy to stage</td>
<td>5 (2.6%)</td>
</tr>
<tr>
<td>1</td>
<td>38 (13.2%)</td>
</tr>
<tr>
<td>2A</td>
<td>20 (7.0%)</td>
</tr>
<tr>
<td>3A</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>3C</td>
<td>23 (8.0%)</td>
</tr>
<tr>
<td>3</td>
<td>67 (23.6%)</td>
</tr>
<tr>
<td>4</td>
<td>1 (0.7%)</td>
</tr>
<tr>
<td>5</td>
<td>1 (0.7%)</td>
</tr>
<tr>
<td>6</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Metastatic for stage 4 (n=99)</td>
<td>5 (2.6%)</td>
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</tbody>
</table>

**Phase I study of prooperative capcitabine and levantinib with external radiation therapy in locally advanced rectal adenocarcinoma. First Author: Jessica Frakes, Moffitt Cancer Center, Tampa, FL**

**Background:** Despite routine use of neoadjuvant chemoradiation, patients with advanced rectal tumors experience significant rates of treatment failure and recurrence. Radiation resistance is a particular problem. Dual targeting of PDG and VEGFR (Vascular endothelial cell growth factor receptor) in combination with radiation can enhance tumor response. Vextent of kinase activities of VEGF-1-3, FGR-1-4, PDGRa, KIT, and RET and in vivo results show that it effectively delays the growth of human colorectal xenografts. Methods: This is a phase I clinical trial of levantinib and capcitabine administered with radiation. Patients with stage II or III rectal cancer confirmed by endoscopic ultrasound or MRI were eligible for the study. In this 3+3 phase I study with 3 cohorts, patients were treated with escalating doses of levantinib administered in combination with standard doses of capcitabine (850 mg/m² PO BID D1-5 weekly for 5.1 to 6 weeks) and external beam radiation therapy (I00 mg CD 0.5 weekly for 5.1 to 6 weeks). Patients underwent surgery 6-10 weeks after neoadjuvant therapy. Results: Nine patients have been enrolled in the 3 cohorts with the median age of 51 years. Lenvatinib dosing started at 14 mg PO daily ( cohort 1) and was safely escalated to 20 mg PO daily ( cohort 2) followed by 24 mg PO daily ( cohort 3). There were no DLTs at the maximum tested dose of levantinib (24 mg). 5 patients have undergone low anterior resection and 4 have had abdominoperineal resection. The pathological complete response (pCR) rate was 33.33%, and downstaging was observed in 100% of patients. Median neoadjuvant rectal cancer score (NAR) was 8.7. Three pts had grade 3 events (2 hypertension (HTN), 1 lymphopenia) without any grade 4 events. Most common AEs were HTN and fatigue. No perioperative complications were observed. Tissues for all pts have been collected for planned correlative studies. Conclusions: This study shows that the combination of levantinib with capcitabine, and EBR is well tolerated. NAR score and downstaging rates are encouraging. Currently we are enrolling 10 additional pts at the maximum tested dose of levantinib to further evaluate efficacy and safety. Clinical trial information: NCT02935309.

**692 Poster Session (Board RN7), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM**

**Organ preservation in rectal cancer patients treated with total neoadjuvant therapy. First Author: Rosa Maria Jimenez-Rodriguez, Colorectal Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY**

**Background:** Retrospective case series suggest that watch-and-wait (WW) is a safe alternative to total mesorectal excision (TME) in selected patients with a clinical complete response (CCR) after chemoradiotherapy (CRT). Because treatment strategies vary and the total number of patients treated at different institutions have not been reported, the proportion of rectal cancer patients who can potentially benefit from WW is not known. Here, we report the results of a treatment strategy incorporating WW in a cohort of rectal cancer patients treated with total neoadjuvant therapy (TNT).

**Methods:** Consecutive patients with stage II/III (MRI staging) rectal adenocarcinoma treated with TNT from 2012 to 2017 by a single surgeon were included. TNT consisted of mFOLFOX6 (8 cycles) and CapeOx (5 cycles) either before or after CRT (5600 Gy in 28 fractions with sensitizing fluorouracil or capcitabine). Tumor response was assessed with a digital rectal exam, endoscopy, and MRI according to predefined criteria. Patients with a CCR were offered WW, and patients with residual tumor were offered TME. WW and TME patients were compared based on intention to treat, using the chi-square or rank sum test. Relapse-free survival (RFS) was evaluated by Kaplan-Meier analysis.

**Results:** A total of 109 patients were identified. One patient died during CRT. Of the 108 patients, 64 (59%) had an incomplete clinical response, 4 of the 64 patients declined surgery or had local excision, and 60 underwent TME. The remaining 44 patients (41%) had a CCR and underwent WW. On average, patients in the WW group were older and had smaller, more distant tumors. Median radiation dose, number of chemotherapy cycles, number of adverse events, or length of follow-up (28 months) did not differ between the TME and WW groups. Five (11%) of the 44 WW patients had local tumor regrowth, at a median of 14 (4-25) months after TNT; 2 of these patients had a synchronous metastasis. Six (10%) of the 60 TME patients had a pathological complete response. RFS did not differ between the TME and WW groups (log rank P = 0.09). Conclusions: Approximately 40% of patients with stage II/III rectal cancer treated with TNT achieve a clinical complete response and can benefit from a WW approach with the aim of preserving the rectum.

**693 Poster Session (Board BN9), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM**

**HIPEC scoring system: A prooperative model including clinical and radiographic parameters to improve patient selection. First Author: Gabrielle Gauvin, Fox Chase Cancer Center, Philadelphia, PA**

**Background:** Most studies looking at long-term outcomes in patients undergoing cytoreductive surgery/hyperthermic intraperitoneal chemotherapy (CS/HiPEC) are based on scoring systems performed at the time of the operation. With a morbidity as high as 67%, it is crucial to carefully choose the patients who will benefit from this procedure. In this study, we evaluated prooperative factors that could impact patient outcomes. Results were used to create a predictive model for patients considered for CS/HiPEC.

**Methods:** Patients assessed for CS/HiPEC at our tertiary cancer center between 2012 and 2017 were considered for this study. Postoperative complications, recurrence free survival (RFS) and overall survival (OS) were used as endpoints, and multivariable analysis accounting for demographics, clinical, bloodwork, radiologic and pathologic findings was performed. **Results:** Sixty-eight patients were considered for CS/HiPEC. Preoperative elements found to have an impact on OS were lymph node involvement (p = 0.000) and high extent of carcinomatosis (p < 0.000) on computed tomography (CT) scan. Findings that impacted RFS were lymphovascular invasion (p = 0.042), lymph node involvement (p = 0.061) and omental caking (p = 0.030) on CT. Our prooperative predictive model is presented in table. An increased rate of complications was seen in smokers (p = 0.031), obese patients (p = 0.005) and carcinomatosis diagnosed < 12 months from the primary diagnosis (p = 0.069).

**Conclusions:** In our experience, performing CS/HiPEC did improve OS (p = 0.036) after adjustment for age, race, smoking, and BMI. Conclusions: Preoperative findings could help physicians in their discussions with patients prior to pursue CS/HiPEC. These interesting findings will be used to inform the next step of our study: a prospective clinical trial.

**CS/HiPEC: Prooperative predictive model.**

<table>
<thead>
<tr>
<th>OS</th>
<th>HR</th>
<th>(95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RFS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>3.49</td>
<td>104.0/85</td>
<td></td>
</tr>
<tr>
<td>Imaging</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinomatosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>3.12</td>
<td>10.6-87.3</td>
<td>0.031</td>
</tr>
<tr>
<td>High</td>
<td>14.03</td>
<td>3.4-58.0</td>
<td>0.018</td>
</tr>
<tr>
<td>Lymph Node Involvement</td>
<td>0.72</td>
<td>0.82-4.06</td>
<td>0.91</td>
</tr>
<tr>
<td>Imaging Caking</td>
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<td></td>
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</tr>
<tr>
<td>Present</td>
<td>0.34</td>
<td>0.1-4.0</td>
<td>0.30</td>
</tr>
<tr>
<td>Absence</td>
<td>4.21</td>
<td>1.4-12.6</td>
<td>0.020</td>
</tr>
</tbody>
</table>

*HR: Hazard Ratio, **CI: Confidence Interval

Visit gicasym.org to search by abstract for the full list of abstract authors and their disclosure information.
A multivariate model to define risk groups among patients with curatively resected stage I and II colon carcinoma: Final report of a retrospective cohort study. First Author: Luis F. Onate-Ocana, Instituto Nacional de Cancerologia, Mexico City, Mexico

Background: Patients with stage I or II colon carcinoma (CC) have a 10 or 20% risk, respectively, of presenting recurrent disease after a potentially curative surgical resection and adjuvant chemotherapy have not improved survival in this setting. In this study, we present a multivariate model to define risk groups. Methods: Consecutive cases with stage I and II CC treated at a single cancer center in Mexico City, from January 1992 to December 2016, were included in this 25-year cohort. Clinical history and biochemical data were registered, and colon resection was performed with curative intention with standard lymphadenectomy. Standard hematoxylin-eosin slides and CDX2 immunohistochemistry (IHC) slides were analyzed by two independent pathologists. The Kaplan-Meier method and Cox model were used to analyze the association of prognostic factors and overall survival (OS). Results: 3,301 cases of colorectal cancer were treated during this study, but only 556 patients with stage I and II CC were included in the database; 266 women (47.8%) and 290 males (52.2%) (mean age 57.9 years); 52 (9.4%), 431 (77.5%), 36 (6.5%) and 37 (6.7%) were pT1M0 stages I, Ila, Iib, and Iic, respectively. RO resection was performed in 548 patients (98.6%) and R1 in 8 (1.4%). Location in the left colon (HR 1.63), hemoglobin (HR 0.93), serum albumin (HR 2.45), prognostic nutritional index (D28) (HR 2.29), mean platelet count (HR 0.998), time to recurrence (HR 0.94), basal carcinoembryonic antigen (HR 1.0), TNM stage (stage I reference category, Ila (HR 5.64), Iib (HR 4.42), Iic (HR 9.281), R1 residual disease (HR 2.8), negative CDX2 IHC (HR 2.1), and use of adjuvant chemotherapy (HR 0.629) were included in the final model as independent predictors of OS (model p < 0.0001). Predicted survival functions using this model defined three distinct risk groups. Conclusions: This multivariate model has significant prognostic value to the pTNM classification. This model can be useful for stratifying prognosis in patients with CC and will aid in the design of randomized clinical trials evaluating the usefulness of adjuvant chemotherapy in this subgroup of patients with CC.

Stage II and III rectal adenocarcinoma outcomes related to lymphovascular invasion. First Author: Shalana BL O’Brien, Fox Chase Cancer Center, Philadelphia, PA

Background: Lymphovascular invasion (LVI) has been shown to be associated with nodal involvement and higher rates of local recurrence in rectal cancer. In some studies, the presence of LVI has also been associated with worse overall survival; however, these have been mostly smaller, single-institutional studies with lower power. Our goal was to examine the effect of LVI on prognosis in a large and inclusive database. Methods: Outcomes of patients with clinical stage II and stage III rectal adenocarcinoma in the National Cancer Data Base (NCDB) from 2010 to 2015, in whom LVI data were available, were included. Exclusion criteria included patients who did not receive neoadjuvant radiation and chemotherapy, neoadjuvant or adjuvant. Overall survival was compared in patients with and without LVI, controlling for age, sex, race, comorbidities, socioeconomic factors, and T and N stages using Kaplan-Meier survival curves and Cox proportional hazards regression analysis. Median overall survival and hazard ratios with 95% confidence intervals are reported where available. Results: The dataset included 9206 patients with stage II and 12640 patients with stage III rectal adenocarcinoma for which LVI data were available and who received the study’s previously defined standard of care. The proportion of patients with LVI was 11% in stage II and 16% in stage III rectal cancer. After adjusting for age, sex, race, T or N stage, and other clinical and demographic variables, LVI was associated with worse overall survival (stage II HR 1.87, 95% CI 1.62-2.16, p < 0.0001) and in stage III HR 1.61(2.02, p < 0.001) rectal cancer. The median overall survival was not reached in stage II rectal cancer patients without LVI versus 5.73 years with LVI. In stage III rectal cancer, the median overall survival was 6.91 years without LVI versus 6.21 years with LVI. Conclusions: Lymphovascular invasion is an independent risk factor of mortality in stage II and III rectal cancer. Stage II rectal cancer patients without LVI have comparable overall survival to those defined, potentially identifying a group of patients that may benefit from de-escalated therapy. Further studies will be guided at identifying if benefits with chemotherapy are associated with LVI status.

Assessing hematologic ratios as biomarkers for psychosocial distress. First Author: Abigail Fang, City of Hope Cancer Center, Duarte, CA

Background: Psychosocial distress is common among cancer patients and has been shown to have deleterious effects on a patient’s quality of life, treatment, and outcomes. Neutrophil-lymphocyte ratio (NLR), lymphocyte-monocyte ratio (LMR), and platelet-monocyte ratio (PMR) have been associated with poor outcomes in some cancers. Therefore we hypothesized that these ratios may be correlated to distress. This study looked at request for social work follow up as a surrogate marker for distress and investigated relationships between these ratios and markers of patient distress. The CV increased from 2004 to 2014 in colorectal cancer (AAPC +3.85%) and from 86 in 2004 to 128 in 2014 in colon cancer (AAPC +5.04%). Conclusions: Total WTs for CRC in Manitoba have increased from 2004 and 2014. This may reflect the growing challenges in providing increasingly complex cancer care to geographically dispersed populations in a universal healthcare system.
Gastrectomy tube for nutrition and bowel obstruction in patients with advanced malignancy: Less is more.

**First Author:** Gabrielle Guavin, Fox Chase Cancer Center, Philadelphia, PA

**Background:** Malnutrition and malignant bowel obstruction (MBO) are common consequences of advanced malignancy. Both lead to a poor prognosis, frequent hospitalizations, and have a negative impact on quality of life. The aim of this study is to explore patients' experience with g-tube placement practices to better define the role of g-tube role in advanced malignancy.

**Methods:** Patients who underwent g-tube placement at our tertiary cancer center between 2013 and 2017 were included in this study. Patients' demographics, diagnosis, procedures, postoperative course, and clinical data were collected. Complications and survival were used as endpoints.

**Results:** Two hundred forty-two cancer patients with an average age at diagnosis of 61 years (range 21-94) underwent g-tube placement for nutrition (76.4%), decompression (MBO) (22.7%), or both (0.8%). Active treatment within 3 months of g-tube insertion was seen in 37.8% of the nutrition group versus 29.1% in the MBO group (p = 0.208). Successful insertion was achieved in 96.8% of patients, but nine patients required more than one method of insertion attempt. In the nutrition group, successful method of insertion was 88.1% in interventional radiology, 8.8% in operating room, and 3.8% in endoscopy suite, compared to 81.8%, 14.5%, and 3.6% for the MBO group, respectively (p = 0.426). Post-placement complications were significantly less frequent in the nutrition group (24.1% vs. 54.3%, p < 0.001). Consultation pattern in the MBO group revealed that 45.5% had a palliative consult, 56.4% were seen by social work, and 47.3% went to hospice. Survival in the MBO group was significantly shorter than in the nutrition group at 30 days (52.7% vs. 90.3%, p < 0.001), 1-year (54.6% vs. 5.9%, p<0.001), and three years (24.1 vs. 1.8%, p < 0.001) after g-tube placement.

Conclusions: In our experience, most patients who undergo g-tube insertion who are not receiving active treatment and a large proportion of patients who receive a decompressive g-tube have a life expectancy of less than a month. These findings will inform the next step of our study: creating a discussion tool to help the patient and family to better define the role of g-tube role in advanced malignancy.

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**Poster Session (Board #IP5), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM**

**Title:** Pharmacogenomics-guided chemotherapy and supportive care for patients with metastatic colorectal cancer.

**First Author:** Pashtoon Murtaza Kazi, Mayo Clinic, Jacksonville, FL

**Background:** In metastatic colorectal cancer (CRC), pharmacogenomics (PGx) testing presents a unique opportunity to improve outcomes since the genes CYP, UGT1A1, and DPYD encoding the enzymes metabolizing the chemotherapy drugs, 5-fluorouracil and irinotecan, are already well known. In the TRIBE clinical trial, proportion of patients with serious adverse events (SAEs) was higher in those with DPYD*UT1A1 aberrations and were dose dependent. Critical barrier has been integration into clinical practice. We aimed to report the feasibility and results of incorporating PGx testing into clinical practice.

**Methods:** As a quality improvement initiative, we integrated the use of OneOmne RightMed comprehensive test through funding from our center's institutional medicine which reports on 28 genes and over 350 medications of interest. Pharmacists provided dosage recommendations based on test results real-time. Results: 126 patients have had the PGx testing since November 2017. Results have been available within 3-5 days. The table outlines the analyzed results thus far of variants in UGT1A1 and the DPYD-genes alongside the CYP450 genes. Of these, 59% had a DPYD*UT1A1 aberration and 100% had at least one actionable aberration related to supportive care medications from all possible PGx testing.

Conclusions: Preemptive comprehensive PGx testing can be integrated into clinical practice in real-time for cancer patients. This sets the stage for a prospective randomized clinical trial to demonstrate the amount of benefit this can result in these patients.

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**Poster Session (Board #IP6), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM**

**Title:** Outcomes and utilization of adjuvant chemotherapy (AT) for stage II colon cancer (CC-II) in elderly population.

**First Author:** Afshaneh Barzi, University of Southern California/Norris Cancer Center, Los Angeles, CA

**Background:** The use of AT in elderly patients (pts) with CC-II is controversial. We used Surveillance Epidemiology End Results (SEER) linkage with Medicare claims to explore the patterns of AT and chemotherapeutic (CT) in pts with CC-II diagnosed between 2004-2009. Colon cancer was identified using ICD-9-Codes. Triage staging information was used to classify pts as stage II and its subgroups. We restricted our cohort to pts who had surgery within 4 months (mos) of the diagnosis using ICD-9-Codes: 45.7x and 45.8x and excluded pts who died within 3 mos after the surgery as well as those who were enrolled in a health maintenance organization. We searched Medicare, outpatient facility, or carrier claims in the 4 mos after surgery to identify pts who received AT using ICD-9-diagnoses and procedure codes, HCPCS, and revenue center codes. Logistic regression was used to assess the relationship between demographics and clinical characteristics of pts in each group and receipt of AT. KaplanMeier method was used for survival analysis. We performed a flexible parametric survival analysis to estimate the 3-year survival benefit for each group, controlling for demographics and clinical characteristics.

**Results:** A total of 15,310 pts were included in our study. Among these, 14% (n=2,168) received AT of which 7% (232) received escalation containing regimens. Pts and tumor characteristics are reported in the table. After adjusting for pts and tumor characteristics, probability of survival at 3 years was 72.9% for pts who received AT and 74.2% for those who did not, p=0.06 (95% CI, 0.96-1.17), with a HR= 0.9. The AT used was declining over time.

**Conclusions:** Although AT is used in healthier and higher risk elderly pts with colon cancer, it was not associated with significantly improved overall survival.
Neoadjuvant treatment in a Mexican cohort of patients with locally advanced rectal cancer: Oncologic outcomes and prognostic factors.  
First Author: Zuleyma Nieto Garcia, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico, Mexico  
Background: Preoperative chemoradiotherapy (CRT) followed by total mesorectal excision (TME) and adjuvant chemotherapy (CT) is the standard of care for locally advanced rectal cancer (LARC). Total neoadjuvant therapy (TNT) consists of induction CT followed by CRT prior to surgery. This is an alternative strategy recommended in guidelines. Objective: To describe neoadjuvant strategies, oncologic outcomes and prognostic factors in a cohort of patients (pts) with LARC treated at a referral center in Mexico City. Methods: We retrospectively reviewed medical records from pts with LARC (T3/T4N0-3) treated with any neoadjuvant strategy at Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán" from January 2010 to December 2015. Clinical and pathological information was registered. Survival was estimated by Kaplan-Meier method. Univariate analysis for prognostic factors was performed and survival was compared by the log rank test. 
Results: 43 pts were included. Median age was 62 y/o (19-83), 51% were female. Median stage (CS) II(19%) and CS III (99%), 36% pts were T3 and 4(N=68%). Local recurrence (LR) was local in 19 (45%), mid at 30%, middle third 56% and upper third 12%. 63% were moderately differentiated adenocarcinoma. 84% had TNT. Induction CT with FOLFOX-4 regimen for 3 months followed by CRT (SOA G in 28 fractions concurrently with fluoropyrimidines) and TME. Surgery; ultra-low anterior resection (AR) 48%, low AR 28% and abdominoperineal resection 24%. One patient did not accept surgery. Of the 32 pts with ultra-low and low AR, 94% had protective ileostomy. The pathologic complete response (pCR) ypToypN0 rate was 45% (19/42). Median follow-up was 48 months. There were 8/42 recurrences (19%); local only 23%, systemic only 12% and both 5%. None of the pts with pCR recurred. All pts with residual nodal disease recurred (5/5). The 5-year relapse-free survival rate was 73%. There were 7 deaths, one pt died without disease. The 5-year overall survival rate was 83%. 
Conclusions: In pts with LARC the TNT is associated with high rates of pCR and favorable oncological outcomes. JCR and residual nodal disease after neoadjuvant therapy were strongly associated with recurrence and survival.

Comorbidity and Systemic Inflammation Are Independent Prognostic Factors in Patients With Colorectal Cancer: A ScotScan Collaborative Study.  
First Author: James Hugh Park, University of Glasgow, Glasgow, United Kingdom  
Background: Although inextricably linked, both comorbidity and systemic inflammatory responses have been shown to determine survival in patients undergoing surgery for colorectal cancer (CRC). The present study examines the interrelationships between comorbidity (ASA grade) and systemic inflammation (modified Glasgow Prognostic Score (mGPS)) in patients from a prospectively collected dataset. Methods: Clinico-pathological characteristics and outcome of consecutive patients undergoing potentially curative resection of TNM III/II (Glasgow Royal Infirmary, Scotland) and Sarبان (France) were prospectively collected. ASA grade and mGPS (mGPS = 0-2, 0 = CRP < 10mg/L, 2-CRP > 10mg/L, 2-CRP > 10mg/L and albumin < 35g/L) prior to surgery was recorded and relationship with overall survival (OS) examined. Results: 2,295 patients (Scotland: n = 1,234, Norway: n = 1,061) were included. Patients from Norway were more likely to be older, female and have higher ASA grade (all P < 0.001), and more likely to have colon cancer (78% vs. 46%, P < 0.001), even after propensity score matching (P = 0.027). Patients from Scotland were more likely to be older, female and have higher ASA grade (all P < 0.001), and more likely to have colon cancer (76% vs. 67%, P = 0.001). From the whole cohort, patients with significant AC (P = 0.001), even after propensity score matching (n = 736, OR 0.36 95% CI 0.25-0.51, P < 0.001), ASA grade and mGPS were significantly associated; 21% of ASA 1 patients had mGPS = 1 compared to 41% of ASA 4 patients (P < 0.001). In the propensity-matched cohort, both increasing ASA (HR 1.98 95% CI 1.57-2.49, P < 0.001) and mGPS (HR 1.20 95% CI 1.02-1.41, P = 0.027) were associated with OS independent of age and gender. However, mGPS = 1 was an independent predictor of overall survival (HR 0.55 95% CI 0.37-0.82, P = 0.003). On univariate analysis, significant AC (P = 0.011) was the only independent predictor of overall survival. Conclusions: The burden of aortoiliac calcification appears to play an important role in influencing long-term outcome following colorectal cancer resection, independent of traditional determinants such as TNM stage and ASA grade. While validation is required, further investigation of the mechanism underlying this relationship is warranted.
Racial effect of early stage colorectal cancer outcomes in a comprehensive cancer center.

**Background:** Oncologic treatment at National Cancer Institute (NCI) designated comprehensive cancer centers improves outcomes in a variety of malignancies, understanding the drivers behind this is vital to help bring the world-class care being administered at comprehensive cancer centers to underserved populations across the U.S. One component of colorectal cancer care that has a paucity of data afforded to it is the effect of increased time from diagnosis to surgery on survival.

**Methods:** Patients diagnosed with AJCC stage II or stage III colorectal cancer between 4/2001 and 12/2015 and either underwent surgery or adjuvant chemotherapy within the University of Texas Southwestern system were selected. Several pertinent data points were abstracted via the EMR including date of diagnosis, surgery, adjuvant chemotherapy, progression, and death. A retrospective analysis was performed on the abstracted data to determine if the number of days between diagnosis and surgery was correlated with increased survival. Spearman coefficients were calculated to determine correlations between the data. All tests were two-sided.

**Results:** Out of 203 patients identified, 113 patients had complete data available and were included in the study. The average age at diagnosis was 62.6 and average follow-up time was 41 months. Median time to surgery was 21 days (25th percentile-75th percentile: 4 - 53 days). There was a significant negative correlation between days from diagnosis to surgery and mortality (Spearman’s r = −.392, p < .001). Survivors had a mean of 42.7 days from diagnosis to surgery (SD = 56.4) and nonsurvivors had a mean of 61.7 days (SD = 46.9).

**Conclusions:** There was a significant negative correlation seen in days between diagnosis and surgery and survival during the study period, which indicates that early surgical intervention may be an underappreciated indicator of quality colorectal cancer care.

Further research should be conducted to better understand the relationship between early surgical intervention and prognosis in limited-stage colorectal cancer.

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Impact of the prior chemotherapy with two different fluoropyrimidines on the efficacy of CapeIRI or FOLFIRI in metastatic colorectal cancer: An exploratory analysis of the phase III AEEXPT trial.

**Background:** Modified CapeIRI (irinotecan 200 mg/m² on day 1, capecitabine 1600 mg/m² on days 1-14 every 3 weeks) with or without bevacizumab (± BV) has shown non-inferiority of overall survival compared with FOLFIRI ± BV based on the phase III study, AEEXPT, as second-line chemotherapy for patients with mCRC. In this exploratory analysis of the AEEXPT trial, the impact of the prior chemotherapy with two different fluoropyrimidine backbones ( fluorouracil and leucovorin (± BV) or infusional 5-FU) on the efficacy of CapeIRI or FOLFIRI was evaluated. Patients were randomized to receive standard FOLFIRI ± bevacizumab or modified CapeIRI ± bevacizumab after failure to fluoropyrimidine-based chemotherapy in the AEEXPT study. Prior fluoropyrimidine backbones were categorized into oral fluoropyrimidine-based (eg, capecitabine or S 1) regimen (oral 5-FU group) and fluorouracil and leucovorin-based regimen (infusional 5-FU group). Assessed endpoints included overall survival, progression-free survival, response rate, and safety.

**Results:** Prior fluoropyrimidine backbone was available for 642 patients among all 650 randomized patients (oral 5-FU group in 291, and infusional 5-FU group in 351). Median overall survival was 17.0 and 16.7 months for FOLFIRI ± BV and CapeIRI ± BV in the prior oral 5-FU group, and 14.9 and 16.7 months for FOLFIRI ± BV and CapeIRI ± BV in the prior infusional 5-FU group. Median progression-free survival was 7.9 and 8.6 months for FOLFIRI ± BV and CapeIRI ± BV in the prior oral 5-FU group, and 6.8 and 7.3 months for CapeIRI ± BV in the prior infusional 5-FU group. Significant differences were not observed in the efficacy of CapeIRI or FOLFIRI regardless of prior fluoropyrimidine backbones. Therefore, CapeIRI ± BV could also be effective for patients after failure of oral fluoropyrimidine-based chemotherapy (eg, CapeOX ± BV).
712 Poster Session (Board #P17), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Synchronous brain metastasis and impact of primary tumor side in colorectal cancers. First Author: Mahvish Muzaffar, East Carolina University, Greenville, NC

Background: 25% of patients with colorectal cancer (CRC) present with synchronous metastatic disease. The incidence of brain metastasis (BM) in CRC is very low (1.2-3.2%) and tend to occur later in the disease course. Synchronous BM/SMB in CRC is very rare. We sought to explore the impact of primary tumor characteristics on BM. Methods: Surveillance Epidemiology and End Results Program (SEER) 18 registries research data on primary colorectal cancer cases diagnosed during 2010-2015 with brain metastasis at diagnosis were identified. Patients with unembalmed primary site and autopsy alone cases were excluded. Demographic and colorectal cancer characteristics including age, gender, race, tumor grade and primary tumor side were analyzed. Logistic regression models were used to test the association between survival and synchronous metastatic cancer. Results: A total of 475 cases met the inclusion criteria. The mean age was 64.04 yrs. (range 26-95). Majority of the patients (80%) were white, 12% black and others (8%). Male: Female ratio was 11.58%. Patients had primary tumor on left side (spleenic flexure, sigmoid, rectosigmoid and rectal) and 42% had right sided (ascending colon, hepatic flexure, cecum, transverse colon) primary tumor. The median overall survival was 5 months with 1 year survival of 26% in the whole cohort. The 1-year overall survival was 21% for patients with right sided primary tumor versus 30% for patients with SBM and left sided primary tumor (p = 0.033). The median disease specific survival was 5 months for right side and 7 months for Left sided tumor with SBM. The regression model showed that higher grade (RR 1.4, p = 0.003) and right sided primary tumor (RR 4.2, p = 0.004) were associated with worse outcome among patients with SBM in colorectal cancer. Conclusions: Synchronous brain metastasis is very rare in colorectal cancer. Tumor side seems to be prognostic even in this aggressive disease subset. This differential outcome further indicates that sidedness should be considered in goals of care and treatment decisions.

714 Poster Session (Board #P19), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Pelvic radiotherapy in combination with radical resection of the primary tumor improves survival in patients with metastatic rectal adenocarcinoma: A national cancer database analysis (NCDB). First Author: Paul B. Renz, West Virginia University Cancer Institute, Morgantown, WV

Background: With recent advances in systemic therapies and increased survival of patients with metastatic rectal cancer, the role of primary tumor resection may be of increased importance and is often debated. However, the role of combining radiotherapy to surgical resection in the metastatic setting is unknown. Accordingly, we utilized the NCDB to quantify survival in metastatic rectal adenocarcinoma patients with primary tumor resection with and without pelvic radiotherapy. Methods: Of the 15,643 Stage IV rectal adenocarcinoma patients receiving chemotherapy from 2004 to 2015, 4,021 patients had primary tumor resection with sufficient follow up for analysis. Patients were stratified by receipt of pelvic radiotherapy (n = 1,862) or no pelvic radiotherapy (n = 2,159). Univariable/multivariable analyses and propensity-adjusted Cox proportional hazard ratios for survival were performed. Results: Median age was 63 years (IQR 56-71). Of the patients included in this study, from which 21,587 (97.1%) were AC and 640 (2.9%) were SCC. There were more patients with T3/T4 disease (69.6% vs 46.5%) or N disease (41.5% vs 27.3%) in the surgery plus radiotherapy arm. Median survival was 46.3 months vs. 35.3 months in favor of adding radiotherapy (p = 0.001). The 2, 5 and 10 year overall survival were 68.4%, 24.8%, and 9.5% for surgical resection alone compared to 77.2%, 39.6%, and 22.3% for surgery + radiotherapy. On multivariable analysis radiotherapy was associated with a statistically significant reduction in the risk of death (HR 0.718; 95% CI 0.566-0.905). Conclusions: Our study indicates that adding radiotherapy to surgical management of the primary tumor in patients receiving systemic chemotherapy for metastatic rectal adenocarcinoma improves survival. Prospective investigation of the management of the rectal primary tumor with chemotherapy, pelvic radiotherapy, and surgical resection is warranted.

Visit pgiacs.org to search by abstract for the full list of abstract authors and their disclosure information.
NSABP FC-1t: A phase II study of neratinib (N) plus trastuzumab (H) or plus cetuximab (C) in patients (pts) with "quadruple wild-type" (WT) metastatic colorectal cancer (mCRC) based on HER2 status—Amplified (amp), non-amplified (non-amp), WT, or mutated (mt). First Author: Samuel A. Jacobs, NSABP Foundation, and The University of Pittsburgh Cancer Institute, Pittsburgh, PA.

Background: HER2 has been shown to be a validated therapeutic target for the treatment of mCRC. Preclinical and clinical evidence supports the use of HER2-targeted agents in each of these mCRC cohorts. In HERACLES, treatment-refractory, KRAS ex2 (codons 12 and 13) WT, HER2 amp mCRC pts were treated with T and lapatinib (L). Objective response rate (CR or PR) was 8/27 and disease control rate (CR, PR, and SD > 16 wks) was 16/27. Duration of response ranged from 24-94+ wks. Anecdotal reports have shown activity of N in HER2 mts from several cancer types. In mCRC PDX models with qualifying HER2 mts, T plus N was more active than either drug alone. In quad WT, HER2 non-amp PDX models, C plus TKI resulted in major tumor regressions not seen with C monotherapy. In NSABP FC-7, a trial of C + N in cetuximab refractory pts, HER2 amp was observed in 2/23 primary tissue samples; after C exposure, HER2 amp was seen in 5/17 samples, presumably selecting pressure of C. HER2 amp was concordant in tissue (CISH) and blood using cTNA. Methods: This multi-center 3-cohort phase II trial is currently enrolling pts (total planned N = 35). Pts with quad WT, HER2 amp (n = 15) with prior anti-EGFR therapy will receive C 400 mg/m2 iv loading dose followed by 250 mg/m2 po daily (Arm 1). Pts with quad WT, HER2 non-amp (n = 15) with no prior anti-EGFR therapy will receive C 400 mg/m2 iv loading dose followed by 250 mg/m2 po daily (Arm 2). Pts with quad WT, HER2 non-amp (n = 15) with no prior anti-EGFR therapy will receive C 400 mg/m2 iv loading dose followed by 250 mg/m2 po daily (Arm 3). Pts with quad WT and HER2 status are defined below: Arm #1: HER2 amp confirmed in blood by Guardant360 assay, and prior treatment with C or panitumumab (P). Arm #2: HER2 mt with qualifying mt or without prior treatment with C or P. Arm #2: HER2 non-amp or HER2 amp and no prior therapy with C or P. The primary aim is 6+mos progression-free survival for each cohort. Secondary aims: response rates and toxicity. Exploratory aims: genetic and molecular analyses. Specific drug combinations will be evaluated in PDX models. NCT03457896. Support: Puma Biotechnology, Inc.; NSABP Foundation, Inc. Clinical trial information: NCT03457896.
TPS720 Trials in Progress Poster Session (Board #05), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

ABT-165 plus FOLFIRI versus bevacizumab plus FOLFIRI in patients with metastatic colorectal cancer (mCRC) previously treated with fluoropyrimidine/oxaliplatin and bevacizumab. First Author: Zev A. Wainberg, University of California Los Angeles School of Medicine, Los Angeles, CA

Background: Dual variable domain immunoglobulin ABT-165 targets human vascular endothelial growth factor (VEGF) and delta-like ligand 4 (DLL4). Combined VEGF and DLL4 blockade increased inhibition of subtumoral xenograft growth of human colon cancer-derived cell lines versus blockade of either axis alone. In vivo, ABT-165 plus chemotherapy (CT) induced tumor regression with improved efficacy, vs anti-VEGF monoclonal antibody plus CT. In a phase 1 study, tolerable recommended phase 2 dose was identified for ABT-165 plus FOLFIRI and showed promising efficacy. This phase 2 trial in progress assesses efficacy/safety of ABT-165 plus FOLFIRI vs bevacizumab (bev) plus FOLFIRI in patients with second-line mCRC. Methods: This is an open-label, multicenter, phase 2 randomized (1:1) trial (NCT0336859) in patients (≥ 18 years; Eastern Cooperative performance status: 0-1) with histologically and cytologically confirmed mCRC who progressed after fluoropyrimidine/oxaliplatin and bev. ABT-165 (25 mg/kg) plus FOLFIRI (irinotecan: 180 mg/m2; leucovorin: 400 mg/m2; fluorouracil bolus: 400 mg/m2; infusion: 2400 mg/m2) or bev (5 mg/kg) plus FOLFIRI are given intravenously on day 1 of each 14-day cycle, until disease progression/untolerable toxicity. Primary endpoint is progression-free survival (PFS). Secondary endpoints include overall survival (OS), objective response rate (ORR), and safety. Exploratory endpoints include biomarkers predictive for efficacy/safety, correlation of PDL4 levels with PFS, OS, and ORR, pharmacodynamic effects, efficacy/safety-exposure relationships in ABT-165 arm. Hazard ratios of PFS and OS comparing the 2 groups are estimated using Cox proportional hazard model. Kaplan-Meier methodology is used to estimate PFS and OS curves, median PFS and OS, and their 95% confidence intervals. Safety is assessed by ABT-165 exposure, adverse events (AES), serious AES, all deaths, and changes in laboratory data and vital signs. Archival tissue is collected and evaluated for DLL4 expression and angiogenesis signature. Approximately 100 patients are planned to be enrolled, with recruitment initiated January 2018. Clinical trial information: NCT0336859.

TPS721 Trials in Progress Poster Session (Board #06), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

A phase II clinical trial platform for sensitization testing using total neoadjuvant therapy (TNT) in rectal cancer: NRG-G002. First Author: Thomas J. George, NRG Oncology, and The University of Florida Health Cancer Center, Gainesville, FL

Background: Locally advanced rectal cancer (LARC) improvements have plateaued due to an inability to consistently deliver adjuvant therapy and effective novel therapies. Systematic testing of new chemotherapy and radiation sensitizers is needed to advance treatment outcomes. This NCTN multi-arm randomized phase II modular clinical trial platform utilizes TNT with parallel experimental arms (EA) in LARC. The EAs are not intended for direct comparison, but rather to test a variety of sensitizers or hypotheses in a consistent and homogenous high-risk patient (pt) population with correlative biomarkers. Success of any EA will be determined by achievement of pathologic endpoints compared to a control arm. Methods: The NRG-G002 trial serves as a modular platform to assess novel sensitizers to neoadjuvant chemotherapy and/or chemoradiotherapy (chemoRT) in LARC. Eligibility includes LARC with any one of the following: distal location (CT3-4; ≤5 cm from anal verge, any N); bulky (any cT4 or tumor within 3 mm of the mesorectal fascia); high-risk for metastatic disease (cN2); or not a candidate for sphincter-sparing surgical resection. After randomization, pts receive neoadjuvant FOLFOX 4 x mo—chemoRT (capcitabine with 50.4 Gy)—surgical resection 8-12 wks later. The first EA will assess activity of veliparib with standard chemoRT. Enrollment to this EA is complete (results anticipated late 2019). The second EA, testing pembrolizumab concurrently with and following chemoRT, is currently active, with several other EAs in development. Primary endpoint is demonstrated improvement in Neoadjuvant Rectal Cancer score for the EA v control representing a 20% relative risk reduction in DFS HR and 3-4% absolute OS improvement. Secondary endpoints include comparisons of OS, DFS, toxicity, pCR, cCR, therapy completion, negative surgical margins, sphincter preservation, sphincter function, and quality of life—assessments of molecular and radiographic predictors of response and distant failure. Target accrual is 79 evaluable pts/arm with additional EAs added through protocol amendments. NCT02923256. Support: U10CA180868, 180822, UG189687, U24196067; AbbVie, Merck. Clinical trial information: NCT02921256.

TPS722 Trials in Progress Poster Session (Board #07), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

The Global POLAR program: Calmangafodipir used on top of modified FOLFOX6 (5-FU/FA and oxaliplatin) to prevent chemotherapy induced peripheral neuropathy (CIPN). First Author: Per Pfeiffer, Department of Oncology, Odense University Hospital, Odense, Denmark

Background: Oxaliplatin (OXA), is approved in combination with 5-FU/FA (5-fluorouracil/toxic acid; FOLF0X) for metastatic as well as in adjuvant colorectal cancer (CRC) treatment. CIPN is a common adverse event, after OXA, comprising pain, hyperesthesia, allodynia, and impairment of motor function. CIPN incidence is very high in CRC patients treated with FOLFOX6 (mFOLFOX6) for up to 6 months, randomized in a 1:1 ratio, each arm n = 140: A: CAL (5 mg/kg) + mFOLFOX6 chemotherapy B: PLC + mFOLFOX6 chemotherapy POLAR M Patients with metastatic colorectal cancer (mCRC), who are indicated for first-line mFOLFOX6 chemotherapy for up to 6 months, randomized in a 1:1 ratio, each arm n = 140: A: CAL (5 mg/kg) + mFOLFOX6 chemotherapy B: PLC + mFOLFOX6 chemotherapy POLAR M Patients with metastatic colorectal cancer (mCRC), who are indicated for first-line mFOLFOX6 chemotherapy for up to 3 months, without any pre-planned treatment breaks and will be randomized in a 1:1 ratio, each arm n = 140: A=CAL (2 mg/kg) + mFOLFOX6 chemotherapy B: CAL (5 mg/kg) + mFOLFOX6 chemotherapy C: PLC + mFOLFOX6 chemotherapy. Primary objective is to compare CAL versus PLC with respect to the proportion of patients with moderate or severe CIPN. The primary endpoint is: patient reported symptoms as proportion of pts scoring 3 or 4 in at least 1 of the first 4 items of the FACT/GOG-NTX-13 (i.e., FACT/GOG-NTX-4, relating numbness, tingling or discomfort in hands and/or feet, assessed 9 months after the first dose of chemotherapy. In addition to conventional safety endpoints, Principal Recruitment/Screening and All Survival are assessed in the POLAR M study. In the POLAR A study Disease Free Survival is one additional safety endpoint assessed. Results are expected during second half of 2020. Clinical trial information: NCT03364729.

TPS723 Trials in Progress Poster Session (Board #08), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Nintedanib in metastatic appendiceal carcinoma. First Author: Birenda Kc, Levine Cancer Institute, Atrium Health, Charlotte, NC

Background: Appendiceal carcinomas are rare with an incidence of about 0.12 cases per 1,000,000 people per year. There is limited, mostly retrospective data in the treatment of metastatic appendiceal carcinomas. Generally, fluoropyrimidine-based therapy is used in the first line, adapting regimens for metastatic colorectal cancer. However, beyond progression, no treatment option is available. In appendiceal cancer, high endothelial growth factor receptor (VEGFR2) expression has been correlated with poor survival. Moreover, malignant ascites has been demonstrated to be associated with elevated levels of VEGF. Nintedanib targets an oral tyrosine kinase inhibitor of VEGFR which demonstrated activity in lung and ovarian cancer in clinical trials, and has undergone investigation in heavily pretreated metastatic colorectal cancer. Given the analogies between appendiceal and colorectal cancer and potentially ovarian cancer, and the limited information about the optimal treatment of metastatic appendiceal carcinomas, further investigation with nintedanib is warranted. Methods: This is a single arm, open label, investigator initiated, two-stage phase II trial (NCT03287947) in metastatic appendiceal cancer patients after failure (defined as progression on or within 6 months or intolerance) of initial fluoropyrimidine-based therapy and at least one measurable site of disease. The trial started enrolling patients in June 2018, and up to 39 subjects will be enrolled. They will be treated with 200 mg of oral nintedanib twice daily and undergo disease evaluation every 12 weeks. The primary objective of this study is to evaluate the composite of objective response and stable disease (CR/SD) rate (DCR), the composite of objective response and stable disease per RECIST 1.1. Secondary objectives include evaluation of safety and toxicity, objective response rate (ORR), 6-month progression free survival (PFS) and overall survival (OS). DCR, ORR & 6-month PFS will be estimated with the corresponding 95% Clopper-Pearson confidence interval. PFS & OS will be estimated using Kaplan-Meier techniques. Exploratory objectives include evaluation of serum VEGF, as well as qualitative and quantitative correlative assessments of molecular and radiographic predictors of response and distant failure. Target accrual is 79 evaluable pts/arm with additional EAs added through protocol amendments. NCT02992356. Support: U10CA180868, 180822, UG189687, U24196067; AbbVie, Merck. Clinical trial information: NCT02921256.
TPS724
Trials in Progress Poster Session (Board #Q09),
Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM
CO.28: Neoadjuvant Chemotherapy, Excision and Observation (NEO) for early rectal cancer. First Author: Hagen F. Kennecke, Virginia Mason Hospital and Medical Center, Seattle, WA

Background: CO.28 is a phase II study which aims to determine if patients with stage I/I rectal cancer can be treated with induction chemotherapy (FOLFOX/CAPOX) and organ-preserving transanal microsurgery. Prior studies have explored the use of pelvic chemoradiation followed by transanal microsurgery as a means to increase organ preservation. However, pre-operative radiation may have acute and prolonged impacts such as wound complications and adverse on sphincter, sexual and urinary function. Moreover, patients who develop recurrence following this strategy are difficult to salvage as re-irradiation is not usually an option. There is virtually no prospective experience of neo-adjuvant FOLFOX/CAPOX chemotherapy for excision for early rectal tumors. Methods: The primary objective is to determine the rate of organ preservation and the trial will be successful if more than 65% of patients avoid a formal rectal resection. In this two-staged phase II trial, patients are eligible if they have clinical NO and T1-3aN0 MO rectal tumors and no pathologic high risk features. After 6 cycles of q2weekly FOLFOX or 4 cycles of CAPOX, rectal endoscopy and pelvic MRI are repeated and if there is evidence of tumor regression, patients proceed to tumor excision by Transanal Endoscopic Microsurgery (TEM) or Transanal Minimally Invasive Surgery (TAMIS). It is required that participating surgeons have a minimum experience of 20 TEM/TAMIS procedures and they are asked to submit an unedited video for central review. Pathologic ypT0 or ypT1N0 tumors are assigned to observation while ypT2+ or any ypN+ tumors are treated with radical surgery and total mesorectal excision (TME). Pre-operative pelvic radiation is suggested only for ypT3+ or node positive tumors. Endoscopic and cross-sectional imaging is repeated every 4-6 months for 36 months. Circulating tumor DNA (ctDNA) will be correlated with tumor response and relapse. A total of 58 patients will be accrued. Study Progress: The study was activated in Canada in late 2017 and at select US Cancer Centers in 2018, with total accrual to date of 4 patients. (NCT03259035)! Clinical trial information: NCT03259035.

TPS725
Trials in Progress Poster Session (Board #Q10),
Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM
Phase Ib study of talimogene laherparepvec (T-VEC) injection into liver metastases (LMs) in combination with intravenous (IV) atezolizumab in patients (pts) with metastatic triple-negative breast cancer (TNBC) or colorectal cancer (CRC). First Author: J. Randolph Hecht, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA

Background: T-VEC is a genetically modified, oncolytic herpes simplex virus type 1 designed to selectively replicate within tumors and produce GM-CSF to enhance systemic antitumor immune responses. Atezolizumab is a monoclonal antibody checkpoint inhibitor (CPI) that targets PD-L1. The safety of intraperative administration of T-VEC has been demonstrated in a prior clinical trial (NCT02595097). A previous trial of T-VEC in combination with a CPI in advanced melanoma demonstrated improved responses compared to those with a CPI alone (Pauzner et al., JCO, 2016, 34:2619-26). We hypothesize that T-VEC combined with a CPI may also be effective in other tumor types. This phase Ib, multicenter study evaluates the safety of intraoperative injection of T-VEC in combination with IV atezolizumab in pts with TNBC or CRC with LMs. Methods: The study will enroll up to 36 pts in two parallel cohorts (18 TNBC, 18 CRC) at sites in the USA, Europe, and Australia. The primary objective is to evaluate the incidence of dose-limiting toxicities (DLTs). Secondary objectives include objective response rate, lesion-level responses in injected and un.injected tumors, progression-free survival, and overall survival. Key eligibility criteria include: age ≥ 18 years, confirmed diagnosis of TNBC or CRC with LMs, ECOG performance status 0/1, adequate organ function, and no evidence of tumor activity with checkpoint inhibitor use. This phase I trial is expected to enroll 47 total pts to achieve 10% is assessed as appropriate evidence for the subset of stage IV pts, and exploratory assess-

TPS726
Trials in Progress Poster Session (Board #Q01),
Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM
Evaluation of health-related quality of life (HRoQL) in patients with metastatic colorectal cancer (mCRC): A prospective, multicenter, open-label, double-arm trial of trifluridine/tipiracil (FTD/TPI) versus best supportive care (BSC). First Author: Meinolf Karthaus, Klinikum Neuperlach, Munich, Germany

Background: The RECOURSE trial in pts with refractory mCRC showed improvement in OS (7.1 vs 5.3 mo, p=0.001), but had no formal assessment of QoL. Thus, the TALLISUR trial is designed to investigate the HRoQL in pts treated with FTD/TPI and those who are treated with BSC alone on patient’s request while being suitable for treatment (Tx) with FTD/TPI prospectively. This novel design of a double-arm trial with BSC as appropriate comparative Tx is addressing assessment requirements (i.e. data on survival, morbidity and QoL) for the German Federal Joint Committee (GBA). Methods: Pts who have been previously treated with, or are not candidates for available CtX including 5-FU, oxaliplatin, irinotecan, anti-VEGFr, and anti-EGFR-agents with adequate organ functions independent from their ECOG status. Tx is FTD/TPI 35 mg/m² 1/15 and up to 4 mL of 10⁶ plaque forming units (PFU)/ml on day 1 and up to 4 mL of 10⁶ PFU/mL every 21 days thereafter; atezolizumab 1200 mg IV will be given on day 1 and every 21 days thereafter. The DLT-evaluation period is the first two cycles (1 cycle = 21 days). Interim safety analysis will occur after the first 6-pts have become DLT evaluable. Up to six cycles of T-VEC will be given with an additional 6 cycles allowed. After cycle three, nonrehab lesions may be injected, subject to protocol-defined criteria. The study opened for enrollment in January 2018. (NCT03256344)! Clinical trial information: NCT03256344.

TPS727
Trials in Progress Poster Session (Board #Q02),
Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM
NSABP FR-2: Phase II study of durvalumab following neoadjuvant chemothera
type in stage II-IV rectal cancer. First Author: Thomas J. George, NSABP Foundation, and The University of Florida, Gainesville, FL

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 neotigenic presentation, modulate the tumor microenvironment, and increase the likelihood of anti-tumor activity with checkpoint inhibitor 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 addition of pre-treatment diagnostic tumor available for profiling who are undergoing CRT with intentions to proceed to surgical resection. Stage IV disease must be limited such that the primary pelvic tumor requires definitive management. Standard ineligibility criteria include active infections, systemic steroid use, or other conditions making immunotherapy 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 a demonstrated improvement in Neo-
eoadjuvant Chemotherapy, Excision and Observation (NEO) for early rectal cancer. First Author: Hagen F. Kennecke, Virginia Mason Hospital and Medical Center, Seattle, WA
TP5728
Trials in Progress Poster Session (Board #Q03), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Colorectal Cancer Metastatic dMMR Immuno-Therapy (COMMITY) study (NCT02997228). A randomized phase III study of mFOLFOX6/bevacizumab combination chemotherapy with or without atezolizumab or atezolizumab monotherapy in the first-line treatment of patients (pts) with deficient DNA mismatch repair (dMMR) colorectal cancer (mCRC). First Author: James J. Lee, MD, PhD, University of Pittsburgh Medical Center Cancer Pavilion, Pittsburgh, PA.

Background: Deficient DNA mismatch repair (dMMR) colorectal cancer (CRC) cells are highly immunogenic. Preclinical data showed that oxaliplatin-containing chemotherapy combined with anti-VEGF enhances antitumor activity of programmed cell death-1 (PD-1) pathway blockade in murine CRC models. Prior phase I study showed mFOLFOX6/bevacizumab (bev) + atezolizumab (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 to promote tumor regression.

Methods: This is a prospective randomized phase III open-label trial. Pts (N=348) with mCRC will be randomized to 3 trial arms (1:1:1): mFOLFOX6/bev; atezolizumab monotherapy; or mFOLFOX6/bev + atezolizumab. Stratification factors include BRAFV600E status, metastatic site, and prior adjuvant CRC therapy. Primary objective is to evaluate efficacy of mFOLFOX6/bev/atezolizumab vs mFOLFOX6/bev.; secondary endpoints include disease control rate, disease control rate during all treatment on-study, and overall survival.

Principal investigator: N/A. Clinical trial information: NCT02997228.

TP5729
Trials in Progress Poster Session (Board #Q04), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

PD-I antibody combined with COX inhibitor in MSI-H/dMMR or high TMB colorectal cancer: A single arm phase II study. First Author: Zehua Wu, Sixth Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China.

Background: Programmed death protein 1 (PD-I) antibody has been approved in patients with MSI-H/dMMR colorectal cancer and has achieved significant efficacy. It’s also reported that tumor mutation burden (TMB) may be another biomarker of response to PD-I therapy. But there were about 50-60% of patients with MSI-H/dMMR were insensitive to PD-I antibody. Cyclooxygenase (COX) inhibitor has been reported to prevent adverse events in colorectal and it is safe for most of the patients. Preclinical data demonstrate that inhibition of COX synergizes with anti-PD-1 blockade in inducing eradication of tumors.

Methods: This single arm, phase II trial will assess the efficacy and safety of combination of PD-I antibody and COX inhibitor in patients with MSI-H/dMMR or high TMB colorectal cancer. Patients diagnosed with MSI-H/dMMR or high TMB colorectal cancer which was unreatactable and had at least one lines of chemotherapy fail or refuse to receive chemotherapy were eligible. Eligible patients were assigned to receive BATEO6 (100 mg every once three weeks) plus COX inhibitor (aspirin 200 mg every day or Celebrex 400 mg every day). Chest/abdomen/pelvis CT with every 4 weeks will be performed to monitor the clinical response. The primary endpoint is objective response rate (ORR). Secondary endpoints include progression-free survival (PFS), overall survival (OS), disease control rate (DCR), and safety of response. Adverse events are graded per NCI CTCAE v4.03 and will be monitored for 30 days after treatment. Patients will be followed for survival. Planned enrolment is 54 patients. Clinical trial information: NCT03638297.

TP5730
Trials in Progress Poster Session (Board #O05), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

A phase I/II multicenter study of ABO-009 (nab-sirolimus) combined with FOLFOX and bevacizumab as first-line (IL) therapy in patients (pts) with metastatic colorectal cancer (mCRC) with or without PTEN loss. First Author: Sunil Sharma, University of Utah Huntsman Cancer Institute, Salt Lake City, UT.

Background: Very few treatment options are available for pts with mCRC beside the standard of care (SOC), 5-Fluorouracil based chemotherapy + bevacizumab. Immunotherapy is an option for pts with microsatellite instability (~5% of mCRC). The central role of the PI3K/mTOR pathway in cancer biology, including CRC, suggests that mTOR inhibition along with chemotherapy may improve antitumor activity in the metastatic setting. A recent phase I/I study showed combination of antitumor activity of everolimus + SOC as IL treatment for mCRC (96% progression-free [PF] rate at six months at the maximum tolerated dose [MTD], and 86% ORR for pts with PF on treatment (Girace, ASCO 2022). The goal of this prospective, single arm phase III study is to evaluate the efficacy and safety of ABO-009, a novel mTOR inhibitor, + SOC as IL treatment for mCRC.

Methods: Eligible pts have an ECOG performance status of 0-2 and histologically confirmed measurable metastatic disease. PF progression (by IHC) and mutational status for PIK3CA, KRAS, NRAS, BRF1 by NGS is evaluated for all pts. ABO-009 is given weekly x3 every four weeks starting at 30 mg/m2 and escalation to 45 and 60 mg/m2 (3+3 design); mFOLFOX6 + bevacizumab is given every two weeks. After six cycles of therapy, cycles may change to 28-days: ABO-009 weekly x2 every three weeks and mFOLFOX6 + bevacizumab every three weeks. Pts are treated until disease progression. Tumor response is assessed by CT at baseline and every 8 weeks. New lesions are evaluated during the first 12 weeks thereafter. Phase I will enroll up to 18 pts; the primary endpoints are dose-limiting toxicities and MTD; secondary endpoints include disease control rate and safety profile. Phase II will enroll 40 pts; the primary endpoint is PF at six months, and secondary endpoints are median PF survival, overall survival, duration of response, and DCR in the intent-to-treat population and based on PTEN status. This study is now active, with first pt enrolled. The anticipated enrollment period is 12 months. This prospective phase I/II study may show evidence of efficacy and safety of ABO-009 combined with the SOC in pts with mCRC with or without PF loss to warrant a larger clinical study.

Results: N/A. Conclusions: N/A. Clinical trial information: NCT03439462.

TP5731
Trials in Progress Poster Session (Board #O06), Sat, 7:00 AM-7:55 AM and 12:15 PM-1:45 PM

Phase II study of avelumab in combination with cetuximab in pre-treated RAS wild-type metastatic colorectal cancer patients: CAVE (cetuximab-avelumab). Colon. First Author: Teresa Troiani, Medical Oncology Università degli Studi della Campania “Luigi Vanvitelli”, Naples, Italy.

Background: The immune system plays a crucial role in modulating response to monoclonal antibodies therapy in cancer. Novel immune checkpoint inhibitors have demonstrated potent efficacy alone and in combinations with cytotoxic agents in several cancers. In this regard, avelumab in combination with cetuximab might be a relevant rechallenge strategy in RAS wild-type (WT) metastatic colorectal cancer (mCRC) patients treated in first-line with chemotherapy (CT) in combination with anti-EGFR drugs and who achieved a complete or partial response. CAVE is a single arm, multi-center phase II study designed to evaluate the efficacy of avelumab and cetuximab in pre-treated RAS WT mCRC patients. Eligible patients: pathologically confirmed RAS WT mCRC treated with a first-line CT in combination with an anti-EGFR agent with a major response achieved (complete or partial), who have progressed to a second line therapy, and received no prior immunotherapy. Primary endpoint is overall survival, secondary endpoint are overall response rate according to RECIST 1.1, progression free survival and safety profile. The current study seeks to determine a median OS of 11 months (alternative hypothesis) by the experimental combination in comparison with historical median OS 8.0 (null hypothesis) with standard third line treatments, which correspond to an improvement of OS at six months from 40% to 57%. It was estimated that it would be needed to enroll 66 patients to achieve an 80% power with a one-sided 5% level test. The accrual period will be 18 months and the total duration of the study will be 36 months. Considering a potential drop-out of approximately 15% of patients, a total of 75 patients will be recruited. Seven patients have been enrolled and started treatment to date (September 15, 2018) with avelumab 10 mg/kg q14 as a one-hour i.v. infusion and cetuximab at 400 mg/m2 over two-hour and subsequently 250 mg/m2 14 as one-hour i.v. infusion or unacceptable toxicities. EudraCT number: 2017-004392-32. This study is partially supported by Merck KgA, Darmstadt, Germany. Results: N/A. Conclusions: N/A. Clinical trial information: EudraCT number: 2017-004392-32.
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