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Gastrointestinal Cancers Symposium

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PROCEEDINGS

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2021 Gastrointestinal Cancers Symposium

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1 Poster Session

Population-based analysis of National Comprehensive Cancer Network (NCCN) guideline adherence for patients with anal squamous cell carcinoma in California. *First Author: Priyanka Kumar, University of California, Irvine Medical Center, Orange, CA*

Background: Oncology-specific evidence-based treatment guidelines aim to improve cancer care. Our study analyzed adherence to the National Comprehensive Cancer Network (NCCN) treatment guidelines for anal squamous cell carcinoma in California and the associated impacts on survival. **Methods:** Patients aged 18 to 79 years diagnosed with anal squamous cell carcinoma (SCC) between January 1, 2004 and December 31, 2017 with follow-up through November 30, 2018 were identified in the California Cancer Registry. Patient demographics, socioeconomic status (SES) and tumor stage were identified. We determined whether patients received NCCN guideline-adherent care (AdC) by pre-defined criteria. Odds ratios (OR) and 95% confidence intervals (CI) were estimated using logistic regression for receiving AdC. Overall survival (OS) and disease specific-survival (DSS) were calculated using Cox regression models. **Results:** Of 4,740 patients with a diagnosis of anal SCC in California, 926 (19.5%) did not receive AdC (non-AdC). Non-AdC had worse DSS (HR 1.96, 95% CI = 1.56, 2.46, $p < 0.0001$) and worse OS (HR 1.87, 95% CI = 1.66, 2.12, $p < 0.0001$). Females were more likely to receive AdC (OR 1.38, 95% CI = 1.18, 1.62, $p < 0.0001$). Medicaid patients were less likely to receive AdC (OR 0.75, 95% CI = 0.57, 1.00, p = 0.0476). Patients with the lowest SES were less likely to receive AdC (OR 0.65, 95% CI = 0.50, 0.83, p = 0.0007). Characteristics associated with DSS and OS included female gender, black race, Medicare/Medicaid, and SES (particularly, lower-middle SES). **Conclusions:** NCCN guideline-adherent care was associated with improved disease-specific and overall survival in anal SCC patients in California. Research Sponsor: Dept of Medicine, UC Irvine.

2 Poster Session

Chemotherapy use in early-stage anal canal squamous cell carcinoma and its impact on outcome. *First Author: Deanna Huffman, Allegheny Health Network, Pittsburgh, PA*

Background: The standard of care for non-metastatic squamous cell carcinoma of the anal canal (SCCA) is concurrent chemoradiotherapy with high rates of local control. There is some thought that perhaps chemotherapy can be omitted for the earliest stages without worse outcomes. We used the National Cancer Database (NCDB) to identify predictors of chemotherapy receipt or omission to assess the impact on outcomes. **Methods:** We queried the NCDB from 2004-2016 for patients with cT1N0M0 SCCA treated non-operatively with radiation with and without chemotherapy and at least 2 months of follow-up. Logistic regression was used to generate predictors of chemotherapy use. Cox regression identified predictors of survival. Propensity matching was done to help account for indication bias. **Results:** We identified 2,959 patients meeting eligibility, of which 8% (n = 237) were treated without chemotherapy. The vast majority (n = 2722, 92%) were recorded as having multi-agent chemotherapy. Median radiation dose was 50.4 Gy (IQR 45-54) in 28 fractions (IQR 49.4-59.4) with chemotherapy and 54.0 Gy (IQR 49.4-59.4) in 30 fractions (IQR 25-33) in those who had chemotherapy omitted. Predictors of omission of chemotherapy were older age (OR 0.66, 95% CI [0.49-0.90], P = 0.0087), higher comorbidity score (OR 0.62, 95% CI [0.38-0.99], P = 0.0442), African American race (OR 0.57, 95% CI [0.36-0.90], P = 0.0156) and more remote year of treatment (OR 1.1 for years 2004-2006). Predictors of survival were younger age (HR 1.73 for age > 58 years, 95% CI [1.41-2.11], $P < 0.001$), multi-agent chemotherapy use (HR 0.48, 95% CI [0.38-0.62], $P < 0.0001$), higher income (HR 0.57, 95% CI [0.40-0.81], P = 0.0016), female gender (HR 0.68, 95% CI [0.57-0.82], P = 0.0016), and private insurance (HR 0.54, 95% CI [0.34-0.87], P = 0.0104). After propensity matching, overall survival at 120 months for patients treated with and without chemotherapy was 86% and 65%, respectively ($p < 0.0001$). **Conclusions:** Chemotherapy is utilized the majority of the time in early stage SCCA. Being mindful of the limitations of a retrospective database analysis, our results suggest an association with worse survival outcomes when chemotherapy is omitted. Research Sponsor: None.

4 General Session

NACRE: A randomized study comparing short course radiotherapy with radiochemotherapy for locally advanced rectal cancers in the elderly—Preliminary results. *First Author: Eric Francois, Department of Medical Oncology, Centre Antoine-Lacassagne, Nice, France*

Background: Neoadjuvant therapy followed by total mesorectal surgery is the standard of care for locally advanced rectal carcinoma (RC). In the elderly, often underrepresented in clinical trials, but who represent a very large number of patients, therapeutic proposals are not based on high levels of evidence. The NACRE study investigated the role of short course radiotherapy with delayed surgery in this population. **Methods:** The PRODIGE 42-GERICO 12 NACRE is a multicenter randomized clinical trial aimed at comparing Arm A preop radiochemotherapy (RCT) (50 Gy, 2Gy/fraction [fr]; 25 fr + capecitabine) and delayed surgery and Arm B short course radiotherapy (25 gy, 5Gy/fr, 5fr) and delayed surgery. Eligible patients (pts) had cT3 or cT4 (or cT2 of the very low rectum), M0 rectal adenocarcinomas <12 cm from the anal verge, age ≥75years, and WHO PS ≤2. Randomization was stratified by center, T (T2/T3-T4) stage and Age (≤80 or >80 years). Two primary end-points will be analyzed according to the hierarchical sequential procedure: firstly R0 resection rate (non-inferiority test with a 8% non-inferiority margin), secondly preservation of autonomy using IADL score (superiority test with 15% absolute difference margin); secondary end-point will be survival and toxicity. We present here the results for R0 resection, survival and toxicities. **Results:** 29 sites randomized 101 patients from 01/2016 to 08/2019, 59 were males (58.4%), median age was 80 years (range 75-91). Pts characteristics were well balanced. 14% of pts in arm A did not receive all of the planned neoadjuvant treatment compared to 0% in arm B. The R0 resection rate in arm B (86.0% [IC95% 73-94%]) was not-inferior to the R0 resection rate in arm A (89.8% [ic95% 77-97%]), p=0.04 (non inferiority test). With a median follow-up of 15.8 months (CI95%: 14.8-26.0), the 6 months death rate was 10.0% (CI95%: 3.0-22.0) in arm A and 3.92% (CI95%: 0 -13.0) in arm B. There is a significant difference in overall survival between the two arm in favor of arm B (p=0.04, LogRank test), and there is a trend in favor of arm B for specific survival (p=0.06 LogRank test). Disease free survival is not statistically different (p=0.9). 13 serious adverse events were observed in arm A during preoperative phase, 7 in arm B, 16 and 10 respectively during the post-operative phase. **Conclusions:** These preliminary results show that short course radiotherapy with delayed surgery is associated with better compliance than radiochemotherapy in elderly patients and could give an advantage in overall survival. This regimen may be preferred in elderly patients. Clinical trial information: NCT02551237. Research Sponsor: French PHRC (Programme Hospitalier de Recherche Clinique).

5 General Session

A delayed path to diagnosis: Findings from young-onset colorectal cancer patients and survivors. *Laura Diane Porter, Colorectal Cancer Alliance, Cheverly, MD*

Background: Colorectal cancer (CRC) is the second-leading cause of cancer-related death among males and females in the US. Despite a decrease in overall incidence and mortality, there has been an alarming increase of CRC diagnosis among young adults (20-49 years old). In an article from 2014, authors predicted an increase in colon cancer diagnosis in people under the age of 50 with the largest increase in the 20-34-year age group of 37.8% and 90.0% by 2020 and 2030, respectively. The increase for rectal cancer is higher in the 20-34-year age group by 2020 and 2030 it is estimated to increase by 49.7% and 124.2% respectively. The Colorectal Cancer Alliance launched a comprehensive survey for Young-Onset Colorectal Cancer (YO-CRC) patients and survivors to capture self-reported experiences of this often overlooked population. **Methods:** The survey was completed by 1089 patients, survivors and caregivers. Questions were designed based on several established and validated instruments, including AYA-HOPE, EORTC-QOL-30, EORTC-CR-29, EORTC-SHC-22, PROMIS-29, FACT-C, and COH-47. The final survey instrument and study plan were reviewed and approved by the Aspire, Inc. Institutional Review Board. **Results:** Most respondents (62%) waited 3-12 months before visiting a doctor after they noticed symptoms. Furthermore, when patients visited their doctors, most indicated that they were initially misdiagnosed. Many patients reported they had to see multiple doctors and had multiple appointments before they were correctly diagnosed with YO-CRC. The majority of the respondents (75%) saw at least 2 physicians, and about 20% saw 4 physicians or more, prior to their diagnosis. Patients who saw 3 or more physicians prior to diagnosis were more likely to be diagnosed with advanced disease. **Conclusions:** The findings expose a critical issue of YO-CRC patients being diagnosed at late stages. This is often due to multiple challenges around misinformation and medical providers dismissing symptoms and not trusting the patients' self-knowledge. Medical professionals need to be aware of the possibility of colorectal cancer more readily and screen patients regardless of age. The Colorectal Cancer Alliance is dedicated to working with all stakeholders and is committed to supporting researchers who are leaders in the field to better understand YO-CRC, as well as research that looks at improved therapies for those in treatment to improve outcomes. Research Sponsor: None.

6 Oral Abstract Session

KEYNOTE-177: Phase III randomized study of pembrolizumab versus chemotherapy for microsatellite instability-high advanced colorectal cancer. *First Author: Kai-Keen Shiu, University College Hospital, NHS Foundation Trust, London, United Kingdom*

Background: KEYNOTE-177 (NCT02563002) evaluated the antitumor activity of pembrolizumab (pembro) vs chemotherapy ± bevacizumab or cetuximab (chemo) as first-line therapy for patients with microsatellite-instability high/mismatch repair deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC). We present results of the final PFS analysis and analysis of PFS2. **Methods:** Patients with locally-determined MSI-H/dMMR mCRC and ECOG PS 0 or 1 were randomized 1:1 to first-line pembro 200 mg Q3W for up to 2 years or investigator's choice of mFOLFOX6 or FOLFIRI Q2W ± bevacizumab or cetuximab (chosen before randomization). Treatment continued until progression, unacceptable toxicity, patient/investigator decision to withdraw, or completion of 35 cycles (pembro only). Patients receiving chemo could crossover to pembro for up to 35 cycles after confirmed PD. Primary end points were PFS (RECIST v1.1, central review) and OS. Secondary end points included ORR (RECIST v1.1, central review) and safety. Exploratory endpoints included duration of response (DOR), PFS2 (time from randomization to progression on next line of therapy or any cause death), and health-related quality of life (HRQoL). Data cutoff was Feb 19, 2020. **Results:** At data cutoff a total of 307 patients were randomized (153 to pembro, 154 to chemo). Median (range) study follow-up was 32.4 mo (24.0-48.3). Pembro was superior to chemo for PFS (median 16.5 mo vs 8.2 mo; HR 0.60; 95% CI, 0.45-0.80; *P*= 0.0002). The 12- and 24-mo PFS rates were 55.3% and 48.3% with pembro vs 37.3% and 18.6% with chemo. Confirmed ORR was 43.8% vs 33.1%; median (range) DOR was not reached (2.3+ to 41.4+) with pembro vs 10.6 mo (2.8 to 37.5+) with chemo. PFS2 was longer with pembro vs chemo (median not reached vs 23.5 mo [HR 0.63; 95% CI, 0.45-0.88]). OS analysis is ongoing. Grade ≥3 treatment related adverse event (TRAE) rates were 22% vs 66% for pembro vs chemo. There were no grade 5 TRAEs in the pembro arm and 1 grade 5 intestinal perforation in the chemo arm. HRQoL scores were improved with pembro vs chemo. **Conclusions:** Pembro provided a statistically significant improvement in PFS vs chemo as first-line therapy for patients with MSI-H/dMMR mCRC, with fewer TRAEs observed. Furthermore, pembro provided a clinically meaningful improvement in PFS2 for patients with MSI-H/dMMR mCRC. Clinical trial information: NCT02563002. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USAh.

7 Rapid Abstract Session

Phase II study of ipilimumab, nivolumab, and panitumumab in patients with *KRAS/NRAS/BRAF* wild-type (WT) microsatellite stable (MSS) metastatic colorectal cancer (mCRC). *First Author: Michael Sangmin Lee, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Panitumumab is a monoclonal antibody (mAb) targeting the epidermal growth factor receptor (EGFR) and is a standard therapy in KRAS/NRAS/BRAF WT mCRC. Preclinical data shows that anti-EGFR therapy causes a tumor-specific adaptive immune response and immunogenic apoptosis, with functional adaptive immunity required to mediate efficacy. However, resistance to anti-EGFR antibody therapy inevitably develops and is associated with increased expression of CTLA-4 and PD-L1. We hypothesized that addition of ipilimumab (anti-CTLA-4) and nivolumab (anti-PD-1) to panitumumab will increase response rate in patients with KRAS/NRAS/BRAF WT MSS mCRC. **Methods:** LCCC1632 was a multicenter, single-arm, Simon's two stage phase II clinical trial with a pre-specified safety run-in of panitumumab, ipilimumab, and nivolumab in KRAS/NRAS/BRAF WT, MSS mCRC (NCT03442569). Eligible patients must have received 1-2 prior lines of therapy and no prior anti-EGFR or immune checkpoint inhibitor therapy. Subjects received ipilimumab 1 mg/kg IV q6wk, nivolumab 240 mg IV q2wk, and panitumumab 6 mg/kg IV q2wk until progression, toxicity, or patient withdrawal. The primary endpoint was response rate at 12 weeks per RECIST 1.1, and key secondary endpoints included progression-free survival and duration of response. **Results:** A total of 56 subjects were enrolled 3/2018-6/2020. This included the 6-subject safety run-in, with 0/6 dose-limiting toxicities in first 12 weeks. The first stage of the Simon's two-stage clinical trial (n=32) had sufficient response rate to merit full enrollment. There were 7 unevaluable subjects for the primary endpoint of 12-week response rate. Among 49 evaluable subjects, 12-week response rate was 35% (95% CI 21-48; n=17 responses). Twenty subjects had at least an unconfirmed response at any time. Median PFS was 5.7 months (95% CI 5.5-7.9). There was one treatment-related grade 5 adverse event of myocarditis. The most common treatment-related grade 3-4 AEs included lipase increased (9%), amylase increased (7%), ALT increased (5%), AST increased (5%), diarrhea (5%), hypophosphatemia (5%), and maculopapular rash (5%). **Conclusions:** The combination of panitumumab, ipilimumab, and nivolumab demonstrated evidence of activity and met its prespecified primary endpoint of 12-wk response rate criteria to merit further study. The PFS in this single-arm study compares favorably to expected PFS for anti-EGFR monotherapy in RAS wild-type patients, and results suggest activity of immune checkpoint inhibitors combined with anti-EGFR therapy in MSS mCRC. Clinical trial information: NCT03442569. Research Sponsor: Amgen, Bristol-Myers Squibb.

8 Oral Abstract Session

NRG-GI002: A phase II clinical trial platform using total neoadjuvant therapy (TNT) in locally advanced rectal cancer (LARC)—Pembrolizumab experimental arm (EA) primary results. *First Author: Osama E. Rahma, NRG Oncology, and Dana-Farber Cancer Institute/Alliance, Boston, MA*

Background: This NCTN multi-arm randomized phase II modular clinical trial platform utilizes TNT with parallel EAs in LARC. EAs are not intended for direct comparison, but rather to test a variety of sensitizers or hypotheses in a consistent and homogenous high-risk pt population with correlative biomarkers. Here we report the primary and available secondary endpoints (EPs). **Methods:** Stage II/III LARC pts (with ONE or more of the following: distal location [cT3-4 ≤5cm from anal verge, any N]; bulky [any cT4 or tumor within 3mm of mesorectal fascia]; high risk for metastatic disease [cN2]; or not a sphincter-sparing surgery [SSS] candidate) were randomized to neoadjuvant FOLFOX x 4mo → chemoRT (capecitabine with 50.4Gy +/- pembrolizumab 200mg IV Q3 wks x 6 doses) → surgery 8-12 wks following last dose of radiotherapy. Primary EP: Improvement in Neoadjuvant Rectal Cancer (NAR) score for EA *v* control potentially representing a 3-4% absolute OS improvement. Secondary EPs: Comparisons of OS, DFS, toxicity, pCR, cCR, therapy completion, negative surgical margins, sphincter sparing surgery (SSS), and exploratory assessments of molecular and radiographic predictors of response and distant failure. Binary EPs compared by Fisher's exact test. Reported p-values are two-sided. **Results:** From 8/2018-5/2019, 185 pts were randomized to control (n=95) or pembrolizumab (n= 90). Baseline characteristics were relatively well balanced. 137 pts were evaluable for NAR (68 control, 69 pembrolizumab). Mean NAR was 14.08 for control (95% CI: 10.7-17.4) *v* 11.53 for pembrolizumab (CI: 8.5-14.6) (p=0.26). pCR=29.4% *v* 31.9% (p=0.75); cCR=13.6% *v* 13.9% (p=0.95); and SSS=71.0% v 59.4% (p=0.15). The side effects on Arm 3 were consistent with both CRT and pembrolizumab safety profile. Grade 3/4 AEs were slightly increased on the pembrolizumab arm during and after CRT (48.2 *v* 37.3%). There were 2 deaths during FOLFOX, one on the control arm due to sepsis; the other on the EA due to pneumonia. There were no statistically significant differences in RT (fractions, dose, boost fractions, or boost dose), FOLFOX or capecitabine doses. **Conclusions:** Pembrolizumab added to chemoRT as part of TNT was safe and without unexpected short-term toxicities but failed to improve the NAR score. The secondary endpoints including PFS and OS have not been reached. Correlative analysis for both T-cell and myeloid cell populations in the tissue and blood in addition to comprehensive cytokine analysis is ongoing. NCT02921256. Support: U10CA180868, -180822; UG1-189867; U24-196067. Clinical trial information: NCT02921256. Research Sponsor: U.S. National Institutes of Health.

9 Oral Abstract Session

Safety and efficacy of anti-PD-1 antibody dostarlimab in patients (pts) with mismatch repair-deficient (dMMR) solid cancers: Results from GARNET study. *First Author: Thierry Andre, Sorbonne Université and Hôpital Saint Antoine, Paris, France*

Background: Dostarlimab is a humanized anti-PD-1 monoclonal antibody that binds the PD-1 receptor, blocking interaction with ligands PD-L1 and PD-L2. The ongoing phase 1 GARNET study (NCT02715284) is evaluating dostarlimab in pts with advanced solid tumors. Here we present safety and efficacy data from cohort F. **Methods:** Cohort F of the GARNET trial enrolled pts with dMMR or POLEmut non-endometrial solid tumors; the majority were gastrointestinal (GI) in origin. Pts must have progressed per blinded independent central review (BICR) following prior systemic therapy for advanced disease and had dMMR status by local immunohistochemistry. Pts received 500 mg dostarlimab Q3W for 4 cycles and 1000 mg Q6W until discontinuation. Objective response rate (ORR) and duration of response (DOR) were assessed by BICR per RECIST v1.1. Pts were included in the efficacy analysis if they received ≥1 dose of dostarlimab, had measurable disease at baseline, and 6 mo of follow up. All pts who received ≥1 dose were included in the safety analysis. **Results:** 144 pts were included in the safety analysis, with 106 dMMR pts in the efficacy analysis (1 POLEmut pt with a confirmed PR was not included in this population). Of the 106 pts, 99 (93.4%) had GI tumors. Confirmed ORR in dMMR pts was 38.7% (95% CI: 29.4, 48.6), with a complete response rate of 7.5%. ORR was consistent across tumor type (Table). At the data cutoff, median duration of follow-up (n = 107; dMMR and POLEmut pts) was 12.4 months and median DOR was not reached. The Kaplan–Meier estimated probability of maintaining response at 12 and 18 months was 91.0% and 80.9% respectively. Treatment-related adverse events (TRAEs) were reported in 68.8% of pts; 8.3% of pts experienced at least 1 grade ≥3 TRAE. The most common was lipase increased in 2 (1.4%) pts. Treatment-related serious AEs (SAEs) were reported in 6 (5.5%) pts, and 2 pts (1.8%) discontinued dostarlimab due to a TRAE. No deaths were attributed to dostarlimab. **Conclusions:** Dostarlimab demonstrated durable antitumor activity in a cohort of dMMR solid tumor pts, the majority of whom had GI cancers. The safety profile was consistent with other cohorts in GARNET, with immune-related TRAEs infrequent and low grade. Clinical trial information: NCT02715284. Research Sponsor: GlaxoSmithKline.

		Confirmed ORR (RECIST v1.1)	
Tumor type	**N**	**n (%)**	**95% CI***
Overall	**106**	**41 (38.7)**	**29.4–48.6**
CRC	**69**	**25 (36.2)**	**25.0–48.7**
Non-CRC	**37**	**16 (43.2)**	**27.1–60.5**
Small Intestinal Cancer	12	4 (33.3)	(9.9-65.1)
Gastric Cancer	8	3 (37.5)	(8.5-75.5)
Pancreatic Carcinoma	4	0	(0.0-60.2)
Liver Cancer	2	PR, PD	
Ovarian Cancer	2	PR, SD	
Adrenal Cortical	1	PR	
Biliary Neoplasm	1	CR	
Breast Cancer	1	CR	
Esophageal Cancer	1	PD	
Gallbladder	1	1	CR
Genital Neoplasm Malignant Female	1	PR	
Pleural	1	PR	
Renal Cell Carcinoma	1	SD	
Unknown Origin (Possibly GI tract)	1	PR	

*Exact, 2-sided 95% CI for the binomial proportion.

CR = complete response, PR = partial response, SD = stable disease, PD = progressive disease.

10 Rapid Abstract Session

Prognostic value of tumor deposits in stage III colon cancer patients, a post-hoc analysis of CALGB/SWOG 80702 phase III study. *First Author: Romain Cohen, Department of Health Science Research, Mayo Clinic, Rochester, MN*

Background: In colon cancer, tumor deposits (TD) have been associated with worse prognosis, but they are included in the TNM staging system only in the absence of lymph node metastasis (i.e., stage III pN1c tumors). Here we aimed at evaluating the prognostic value of TD and the impact of the addition of TD in the count of lymph node metastases in patients with stage III colon cancer from the CALGB/SWOG 80702 phase III trial (NCT01150045). **Methods:** Pathological reports of all patients were reviewed for the presence and the count of TD, primary tumor sidedness, lymphovascular invasion and perineural invasion. Cases without available pathological report or without specific information of TD were excluded. Prognostic associations were evaluated by multi-variable Cox models adjusting for treatment arm, T-stage, N-stage, lymphovascular invasion, perineural invasion and lymph node ratio. **Results:** Overall, 2028 patients were included, with 524 (26%) TD-positive and 1504 (74%) TD-negative stage III tumors. Of the TD-positive patients, 80 (15.4%) were node negative (i.e., pN1c), 239 (46.1%) were pN1a/b and 200 (38.55%) were pN2. 17.2% and 37.0% of all pN1a/b and pN2 tumors had TD. Overall median follow-up was 69.3 months. The presence of TD was associated with poorer DFS (adjusted hazard ratio (aHR) = 1.59, 95%CI 1.28-1.91) and OS (aHR = 1.52, 95%CI 1.18-1.95) in the overall population. The negative effect of TD on DFS and OS was observed for both pN1a/b and pN2 groups and confirmed in multivariate Cox model. Among TD-positive patients, the number of TD had a linear negative effect on DFS and OS. Adding TD to the count of lymph node metastases, 104 of 1570 (6.6%) patients initially considered as pN1 were re-staged as pN2. Re-staged pN2 patients experienced worse DFS (3-year DFS rate: 65.5% versus 80.3%, P = .0003) and OS (5-year OS rate: 69.1 versus 87.8%, P = .0005) than patients confirmed as pN1. Re-staged pN2 patients had similar DFS than patients initially staged as pN2 (3-year DFS rate: 65.5% versus 63.1%, P = .1992). OS curves of these 2 groups crossed, with better outcomes during the first 3 years of follow-up but poorer 5-year estimates for re-staged pN2 patients (5-year OS rate: 69.1% versus 74.8%, P = .0436). **Conclusions:** TD are found in more than one fourth of stage III colon cancer specimens. The number of TD has a linear deleterious effect on patients' prognosis. Adding the number of TD to the count of lymph node metastases improves the prognostication accuracy of the TNM staging. Support: U10CA180821, U10CA180882; https://acknowledgments.alliancefound.org. Clinical trial information: NCT01150045. Research Sponsor: U.S. National Institutes of Health.

11 Oral Abstract Session

Circulating tumor DNA analysis for assessment of recurrence risk, benefit of adjuvant therapy, and early relapse detection after treatment in colorectal cancer patients. *First Author: Tenna V Henriksen, Department of Molecular and Clinical Medicine, Aarhus University Hospital, Aarhus, Denmark*

Background: Timely detection of recurrence, as well as identification of patients at high risk of recurrence after surgery and after completion of adjuvant therapy, are major challenges in the treatment of colorectal cancer (CRC). Postsurgical circulating tumor DNA (ctDNA) analysis is a promising tool for the identification of patients with minimal residual disease (MRD) and a high risk of recurrence. The objective of this prospective, multicenter study was to determine whether serial postsurgical ctDNA analysis could identify the patients at high risk of recurrence, provide an assessment of adjuvant therapy efficacy and detect relapse earlier than standard-of-care radiological imaging. **Methods:** The cohort comprises 265 stage I-III CRC patients, the to-date largest cohort assessed for ctDNA. All patients had the tumor resected and a subset of 62.6% (166 /265) was additionally treated with ACT. Plasma samples (n = 1503) were collected at various time points for a median follow-up of 28.4 months (range: 1.2-51.0 months). Individual tumors and matched germline DNA were whole-exome sequenced and somatic single nucleotide variants (SNVs) were identified. Personalized multiplex PCR assays were designed to track tumor-specific SNVs (Signatera, bespoke mPCR NGS assay) in each patient's plasma sample. **Results:** Postoperative ctDNA status prior to ACT was assessed in 218 patients, of which 9.17% (20/218) were identified to be MRD-positive and 75% (15/20) eventually relapsed. The remaining 25% (5/20) of MRD-positive patients that did not relapse, received ACT. In contrast, only 13.6% (27/198) of MRD-negative cases relapsed (HR: 11: 95% CI: 5.7-20; $p < 0.001$). Longitudinal ctDNA-positive status, post-definitive therapy (n = 202) was associated with a HR of 36 (95% CI: 16-81; $p < 0.001$). For a subset of 155 patients postoperative CEA and ctDNA measurements were compared, wherein, ctDNA-positive status was found to be significantly associated with RFS (HR, 7.1; 95% CI, 3.4-15; $P < 0.001$) compared to CEA (HR, 1.2; 95% CI, 0.46-3.1; P = 0.73). Serial ctDNA analysis detected MRD up to a median of 8 months (0.56 - 21.6 months) ahead of radiologic relapse. **Conclusion:** Postoperative ctDNA positive status was associated with markedly reduced RFS compared to CEA. The study also shows that effective therapy can be curative in a portion of MRD-positive patients. In a longitudinal setting, ctDNA analysis predicted the risk of recurrence and is a more reliable biomarker for treatment response monitoring. Research Sponsor: The Danish Council for Independent Research, The Novo Nordisk Foundation, The Danish Cancer Society, and Natera, Inc.

12 Rapid Abstract Session

Does non-TME surgery of rectal cancer compromise the chance of cure? Preliminary surgical salvage data from OPERA phase III randomized trial. *First Author: Arthur Sun Myint, Clatterbridge Cancer Centre, Merseyside, United Kingdom*

Background: Non-operative modality (NOM) treatment of rectal cancer is gaining popularity as it avoids extirpative TME surgery and a stoma. OPERA trial was set up to evaluate the role of dose escalation using Contact X-ray brachytherapy [CXB] in improving the chance of organ preservation compared to the standard of care (EBCRT and TME surgery). We report on the preliminary surgical salvage data for treatment failures in the OPERA trial (NCT02505750). **Methods:** OPERA is a European phase 3 randomised trial between (Arm A- standard arm) EBCRT 45Gy/25/5weeks with oral capecitabine 825mg/m^2 and EBRT boost of 9Gy/5/5 days randomised against (Arm B- experimental arm) EBCRT followed by CXB boost (90 Gy/3/4 weeks). Patients were assessed at 14, 20 and 24 weeks. Watch & wait policy was adopted for patients with cCR at 24 weeks after randomisation and surgery (TME or local excision) was offered for residual disease and also for local regrowth (recurrence) at a later date. **Results:** From July 2015 –June 2020, 148 patients were randomised of which 144 were evaluable (table). There were 71 patients in Arm A (standard) and 73 patients in Arm B (experimental). Median follow-up was 19 months (range 2-36 m). Overall clinical complete response (cCR) was observed in 103 out of 127 evaluable patients (81%) at 24 week in both arms (blinded). Surgery was carried out in 36/ 127 (28%) patients with suspected residual tumour. Further 13 patients had salvage surgery at a later date for local regrowth. At 19 months, 49/144 (34%) patients in total cohort had surgery. Local excision was carried out in 24 /49(49%) of which 3 proceeded to TME surgery due to R (1) or ypT2 adverse histology. TME surgery was carried out in 28/49 of which 8/28 (28.6%) had APER and 20/28(71.4%) had AR. In total, organ preservation (blinded) was achieved in 116/144 (80.5%) for the whole cohort. Kaplan Meier estimate of TME free survival is 76% at 19 months. **Conclusions:** Non-TME surgical treatment for cT2-cT3a-b rectal cancer is feasible in those who are fit and wish to avoid surgery (Watch & Wait). Those who needed surgery can be offered salvage surgery immediately for local residual disease or for local regrowth at a later date. Organ preservation of 80.5% (blinded) can be achieved without compromising their chance of cure. Clinical trial information: NCT02505750. Research Sponsor: French Research Authority, France.

Patients characteristics (at baseline).

Gender	**Male** **Female**	**88 (61%)** **56 (39%)**
Age	68 years	[40-92] years
T stage	cT2	92(63.9%)
	cT3a/b	52(36.1%)
Size (greatest diameter)	<3 cm	62(43%)
	>3cm	82(57%)
Location in rectum	<6cm from AV	106(73.6%)
	>6cm from AV	38(26.4%)

13 Rapid Abstract Session

Effect of treatment disparities on survival in disadvantaged black and white patients with stage IV colorectal cancer (CRC). *First Author: Douglas S. Swords, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Non-Hispanic Black patients (NHBs) and low socioeconomic status (SES) non-Hispanic White patients (NHWs) have worse cancer outcomes. In most cancers, the relative importance of treatment disparities vs. other pathways are undefined. We estimated the proportion of overall survival (OS) disparities mediated by treatment disparities in NHBs and NHWs with stage IV CRC. **Methods:** We queried the National Cancer Database for NHBs and NHBs (aged 18-80) diagnosed with stage IV CRC in 2010-16. Zip code SES was defined as low (quartile 1 income *and* education), high (quartile 4 income *and* education), and middle. Exclusions were missing SES, chemotherapy contraindications/refusal, unknown treatment, and < 60 days follow-up. From available variables, we examined 3 plausible treatment mediators of OS: chemotherapy, metastatectomy, and treatment at > 1 CoC facility. Primary tumor resection was not analyzed to avoid immortal time bias. We used inverse odds ratio weighting (IORW) to estimate the *proportion mediated* (*PM*) while adjusting for sex, age, cancer history, comorbidities, year, tumor location, grade, LVI, CEA, and KRAS status. **Results:** Among 70,773 patients, the rate of low SES was 3.6-fold higher among NHBs than NHWs. There were graded associations between higher SES and rates of each mediator (Cuzick trend tests, all $p \leqslant 0.01$). Furthermore, low and middle SES NHB and NHWs all had significantly lower rates of each mediator than high SES NHWs (Table, part A). 5-yr OS ranged from 14.5% in low SES NHBs to 21.9% in high SES NHWs. Low and middle SES NHWs and all NHBs had shorter adjusted OS than high SES NHWs (Table, part B). *PMs* were higher for low and middle SES NHBs vs. NHWs (27-28% vs. 19-22%). PMs were largest for metastasectomy (9.9-16.1%) and smallest for chemotherapy (5.0-7.9%). **Conclusions:** Treatment disparities mediate at least 20-30% of OS disparities in NHBs and NHWs with stage IV CRC. These estimates may represent the lower bound of true PMs since many aspects of treatment quality were unmeasured. These findings imply that policies addressing treatment disparities are projected to partially close survival gaps. Research Sponsor: None.

	NHB			**NHW**		
SES	**Low n=3,823 (31.9%)**	**Middle n=7,358 (61.4%)**	**High n=801 (6.7%)**	**Low n=5,187 (8.8%)**	**Middle n=41,721 (71.0%)**	***High (REF) n=11,883 (20.2%)***
Part A: Mediators by race and SES. Bold values indicate statistical significance vs. high SES White patients (chi square).						
Chemo, %	**86.5**	**87.8**	**89.3**	**87.7**	**89.8**	*91.8*
Metastatectomy, %	**12.5**	**12.9**	*17.3*	**13.7**	**15.7**	*18.2*
Tx at >1 CoC facility, %	**8.7**	**11.2**	**12.7**	**13.0**	**13.7**	*17.8*
Part B: IORW mediation analysis. HRs represent adjusted effect sizes for high SES NHWs vs. other groups. Bold values indicate statistical significance.						
Adj HR (95% CI)	**0.76 (0.71, 0.80)**	**0.79 (0.75, 0.83)**	**0.88 (0.78, 0.97)**	**0.75 (0.71, 0.79)**	**0.88 (0.85, 0.90)**	*REF*
***PM*, % (95% CI)**	**28.2 (21.1, 35.4)**	**26.9 (19.9, 33.9)**	1.8 (-238, 242)	**19.0 (13.9, 24.0)**	**22.2 (15.1, 29.4)**	

14 Rapid Abstract Session

Phase II study evaluating trifluridine/tipiracil + bevacizumab and capecitabine + bevacizumab in first-line unresectable metastatic colorectal cancer (mCRC) patients who are noneligible for intensive therapy (TASCO1): Results of the final analysis on the overall survival. *First Author: Eric Van Cutsem, University Hospital Gasthuisberg and University of Leuven, Leuven, Belgium*

Background: Our phase II randomized study was conducted in patients with previously untreated unresectable mCRC not eligible to receive standard oxaliplatin- or irinotecan- based chemotherapy regimens. The results of the primary study analysis were reported earlier and demonstrated a promising efficacy in terms of progression-free survival (PFS) and an acceptable safety profile for the combination of trifluridine/tipiracil + bevacizumab (E. Van Cutsem et al. *Ann. Oncol.* 2020). Here we present the final end-of-study analysis on the overall survival (OS). **Methods:** Eligible patients were randomized in 1:1 ratio to receive either trifluridine/tipiracil administered orally at 35 mg/m^2/dose bid from days 1-5 and days 8-12, and bevacizumab at 5 mg/kg on days 1 and 15 of a 28-day treatment cycle (TT-B), or capecitabine administered orally at 1250 or 1000 mg/m^2/dose bid (according to the patient's status) from days 1-14 and bevacizumab at 7.5 mg/kg on day 1 of a 21-day treatment cycle (C-B). Cycles were repeated until documented disease progression, unacceptable toxicity, or investigator's/patient's decision. Following the treatment discontinuation, all patients were followed for OS until the end-of-study, which was defined as the date of the withdrawal visit for the last patient. In the absence of death confirmation or for patients alive as of the end-of-study date, survival time was censored at the date of their last study follow-up. For the OS analysis the HR and the corresponding 2-sided 80% and 2-sided 95% CIs for TT-B versus C-B were estimated using a Cox proportional hazard model adjusting for the stratification factors based on IWRS data. OS was summarized using Kaplan-Meier curves and further characterized in terms of the median and survival probabilities at 6, 12, 18, and 24 months along with the corresponding 2-sided 80% and 2-sided 95% CI (Brookmeyer and Crowley CI for median and Kalbfleisch and Prentice CI for survival probabilities). **Results:** From April 2016 to March 2017, 153 patients were randomized and followed until end-of-study on September 1, 2020. Twenty-one patients, 11 from TT-B and 10 from C-B, were alive and censored for the analysis. Median OS was 22.31 months in TT-B and 17.67 months in C-B with HR 0.78 (95% CI, 0.55, 1.10). Survival probability at 18 months in TT-B was 0.62 (95% CI, 0.50, 0.72), and 0.47 (95% CI, 0.35, 0.57) in C-B. **Conclusions:** Our study demonstrated earlier a median PFS of 9.2 months for TT-B and 7.8 months for C-B when administered to patients with previously untreated unresectable mCRC ineligible for standard combination chemotherapy. The final study analysis performed on OS, the main secondary endpoint, provided further evidence for TT-B as a noteworthy valuable regimen in this population settings. Clinical trial information: NCT02743221. Research Sponsor: Servier; Taiho.

15 Rapid Abstract Session

Maintenance treatment with cetuximab versus observation in *RAS* wild-type metastatic colorectal cancer: Results of the randomized phase II PRODIGE 28-time UNICANCER study. *First Author: Valerie Boige, Gustave Roussy, Villejuif, France*

Background: Compared to observation, maintenance therapy with a fluoropyrimidine +/- bevacizumab showed significant improvement in progression-free survival (PFS) but not in overall survival (OS) in patients with unresectable metastatic colorectal cancer (mCRC) and disease control after first-line doublet chemotherapy (CT) +/- bevacizumab. Few studies are available on the role of maintenance therapy after induction anti-EGFR-based CT, and the benefit from anti-EGFR maintenance monotherapy during CT-free intervals (CFI) in patients with *RAS* wild-type (wt) mCRC. **Methods:** *RAS* wt unresectable mCRC patients with controlled disease after FOLFIRI + cetuximab (8 cycles) were randomized (1:1) to receive maintenance with bi-weekly cetuximab alone (arm A) or observation (arm B) until disease progression (PD)/unacceptable toxicity/death. Randomization was stratified according to tumor response, center, baseline Köhne Score, CEA and platelet count. In case of tumor progression during the CFI, FOLFIRI + cetuximab was to be reintroduced for 8 cycles, followed by a new CFI. Tumor response was assessed per RECIST1.1 every 8 weeks. The primary objective of this multicenter non-comparative randomized phase II trial was 6-month PFS rate after initiation of maintenance therapy. A total of 134 randomized and evaluable patients (67 per arm) were required (Fleming's one-step design, one-sided α=5%, β=20%, H0: 40%; H1: 55%). Secondary endpoints were overall response rate (ORR), time to strategy failure, PFS, OS, safety, quality of life, circulating tumor cells and circulating tumor DNA detection and dynamic changes during treatment. **Results:** From January 2014 to April 2019, 214 patients were included and 139 randomized (67 arm A/72 arm B) in 35 centers. Baseline characteristics were: males, 67%/69%; median age, 64/68 years; ECOG PS 0, 54%/46%; previous adjuvant therapy, 25%/14%; single metastatic site, 58%/47%; right-sided primary, 24%/18%. The ORR in the overall and the randomized population was 55% and 72%, respectively. The median follow-up was 30 months. The 6-month PFS rate after initiation of maintenance therapy was 30% 95%CI[19; 42] in the maintenance arm, and 6% 95%CI[2;14] in the observation arm, with a median PFS of 5.3 95%CI[3.7;6.5] and 2.0 95%CI[1.8; 2.8] months, respectively. Any grade treatment-related toxicity, including skin rash (40%/4%), diarrhea (33%/8%), and hypomagnesemia (46%/10%) was more frequent in arm A. **Conclusions:** Based on the study hypothesis, the cetuximab maintenance arm did not meet the primary objective. However, the clinically meaningful difference in PFS without any overlap in the confidence intervals between the two arms warrants further investigation. Clinical trial information: NCT02404935. Research Sponsor: MERCK SERONO S.A.S.

16 Poster Session

Adjuvant chemotherapy (AC) choices: An analysis of elderly Australian patients with stage III colorectal cancer (CRC). *First Author: Oliver Piercey, Peter MacCallum Cancer Centre, Parkville, Australia*

Background: The optimal adjuvant treatment regimen for stage III CRC patients aged ≥70 years remains unclear. Subgroup analyses of randomised trials support the use of single agent fluoropyrimidines (FP) but no survival benefit has been observed for the addition of oxaliplatin. This study assessed rates of AC use in elderly patients with stage III CRC, analysed reasons why elderly patients did not receive AC and compared disease free survival (DFS) between those who did and did not receive AC. **Methods:** Data was analysed from the ACCORD-CRC registry, which prospectively collects treatment and outcome data from patients with CRC in Australia. All patients aged ≥70 years with resected stage III CRC from seven institutions between January 2005 and December 2018 were included. Where patients did not receive AC, reasons for this were documented prospectively. Using univariate analysis, baseline demographics and clinicopathological variables were compared between patients who were and were not offered AC. Differences were defined as statistically significant if a two-tailed p value was < 0.05. DFS was defined as time from surgical resection to time of recurrence and cases of death without recurrence were censored at the time of death. **Results:** Data was obtained for 685 patients; median age was 78 years (range 70-97). AC was offered to 72% of patients; these patients were significantly more likely to be aged 70-74y (34% vs 12%, $p < 0.0001$), have an ECOG score of 0-1 (88% vs 57%, $p < 0.0001$), have proficient mismatch repair (pMMR) (87 vs 75%, p = 0.01) and T1-3 tumours (74% vs 65%, p = 0.02) compared to patients not offered AC. Nodal status and tumour differentiation did not differ significantly. 15% of patients offered AC declined systemic treatment. The most frequent documented reasons for not offering AC were age plus comorbidities, followed by comorbidities alone and age alone (42%, 29% and 23%, respectively). Of the patients who commenced AC, 27% received oxaliplatin-FP. These patients were significantly more likely to be aged 70-74y (71% vs 28%, $p < 0.0001$), have an ECOG score of 0-1 (94% vs 87%, p = 0.04), have N2 disease (39% vs 26%, p = 0.02) and poorly differentiated tumours (42% vs 29%, p = 0.02) compared to those receiving FP alone. T-stage and MMR status did not differ significantly. After median follow up of 32 months, the 3-year DFS rate was higher for patients who received AC compared to those who did not (71% vs 64%; HR 0.72, p = 0.046) but no significant difference was observed for the addition of oxaliplatin (75% vs 69%; HR 0.76, p = 0.18) compared to FP alone. **Conclusions:** In this real world cohort, approximately 75% of elderly patients with stage III CRC were offered AC. Younger age, better performance status, pMMR and lower T stage were significantly associated with physicians offering elderly patients AC. Those who received AC had improved DFS compared to those who did not. Research Sponsor: None.

17 Poster Session

Understanding factors associated with hospital admission for colon cancer diagnosis and staging work up. *First Author: Jacob B Schriner, Department of Surgery, Montefiore Medical Center, Bronx, NY*

Background: Cancer diagnosis, staging work up and treatment need to be done in a timely manner but are rarely emergencies. Cancer work up during a hospital admission is costly and can take away resources that are needed for more urgent patients. We aim to understand factors related to cancer work up in the hospital inpatient setting. **Methods:** Patients with a new diagnosis of colon cancer at a single academic institution in 2018 were identified using cancer registry. Patients were excluded if they had cancer other than carcinoma or if data on more than half of their work up was not available for review. A chart review was performed to obtain factors including their demographics, details on their cancer presentation, diagnostic and staging work up and treatment. Patients were considered to have had inpatient work up (Inpt_WU) if 50% or more of their cancer related diagnostic, staging and pre-treatment work up was conducted during a hospital admission, and included imaging, bloodwork, evaluation by consultants. Inpt_WU and non-Inpt_WU patients were compared. Logistic regression model was used calculate odds ratio (OR) and 95% confidence intervals (CI) to identify associations with Inpt_WU. **Results:** Data on 121 newly diagnosed colorectal cancer patients were analyzed. Inpt_WU occurred in 63 (52%) of the cohort. Inpt_WU and non-Inpt_WU patients required the same median number of work-up events [6, interquartile range (IQR) 5, 6]. Inpt_WU patients were more likely to initially present to the emergency department (ED: 91% vs 16%, $p<0.001$), have Medicaid insurance (40% vs 17%, $p=0.018$), be functionally dependent (30% vs 16%, $p=0.091$), have more defined symptoms (75% vs 45% $p=0.001$), and have greater cancer severity (metastatic disease 33% vs 17%, $p=0.004$). The median time between presentation and treatment initiation was markedly less for Inpt_WU compared to non-Inpt_WU [11 days (IQR 5, 24) vs 48 (IQR 37, 81), $p<0.001$]. The logistic model showed that ED presentation had over 40-fold higher odds of Inpt_WU (OR 41.2, 95% CI 12.1-177.4) after adjusting for comorbidities, insurance, functional status, symptoms, and cancer severity. **Conclusions:** The cancer diagnostic and pre-treatment workup process was markedly expedited when done during hospital admission. Most cancers presenting to the ED as the initial location of presentation resulted in admission and cancer work up in the hospital. Further studies are needed to explore whether all of these patients necessitate inpatient admission, and whether healthcare systems can be modified to mimic the efficiency of in-hospital workup. Research Sponsor: None.

18 Poster Session

Racial disparity in KRAS mutation frequency and outcomes in colorectal cancer (CRC): A U.S. population based study. *First Author: Jeffrey Bien, Stanford Cancer Center, Stanford, CA*

Background: Racial disparity in CRC survival outcome is well documented. Although the reasons for disparity are unclear, a combination of differences in access to care, quality of care, differential treatment response, and underlying cancer biology are implicated. Further, recent studies have observed differences in KRAS mutation frequency between race/ethnic groups. KRAS mutation in metastatic CRC portends a worse response to EGFR-directed therapy, and predicts a poorer prognosis. In this study, we examined whether racial/ethnic differences in KRAS mutation frequency might impact CRC outcomes on a population-based level. **Methods:** We examined data from 202,237 CRC patients in the Surveillance, Epidemiology, and End Results (SEER) registry between 2010 and 2015. The differences in tumor mutation status by stage and race/ethnicity were examined by χ^2 testing. Cause-specific survival (CSS) and overall survival by mutation status were plotted by Kaplan-Meir curves. A multivariable Cox-proportional hazards model was used to construct hazard ratios and 95% confidence intervals (CI) using patient demographics, tumor characteristics, and KRAS mutation status. **Results:** Overall, about 9% of patients (n = 18,248) in the SEER registry had KRAS status available. In this cohort, tumors from Non-Hispanic Black (NHB) (48%) or Hispanic patients (44%) carried a greater KRAS mutation (mKRAS) rate when compared against Non-Hispanic White (NHW) (39%) or Asian or Pacific Islander (API) patients (37%) ($p < 0.01$). The assessment of the impact of mKRAS within each race/ethnic group, comparing patients with mKRAS versus wild-type KRAS (wKRAS) on CSS risk show a 7% risk increase for NHW, (HR = 1.07; 95%CI:1.02-1.12), a 15% risk increase for NHB, (HR = 1.15; 95%CI: 1.04-1.26) and no significant increase among API, (HR = 1.02; 95%CI:0.92-1.4). Among patients with wKRAS, with NHW for reference, the risk of CSS is 11% higher among NHB (HR = 1.11; 95%CI:1.00-1.23), 14% higher for Hispanic, (HR = 1.14; 95% CI:1.02-1.26) and no significant difference observed among API, (HR = 1.03; 95%CI: 0.91-1.16). Evaluation of the interaction between race/ethnicity and KRAS status on the CSS risk shows an increase of: 11% for mKRAS NHW, (HR = 1.11; 95%CI:1.00-1.23), 13% risk for NHB (HR = 1.13; 95%CI:1.01-1.25), 11% for Hispanic wKRAS, (HR = 1.11; 95%CI:1.04-1.18), 31% for Hispanic mKRAS (HR = 1.31; 95%CI:1.18-1.145), 16% for wKRAS API (HR = 1.16; 95%CI:1.03-1.29). In contrast, no significant difference in risk is seen for NHB nor API patients, HR = 1.02 (95%CI:0.90-1.14) and 1.04 (95%CI: 0.91-1.20) respectively. **Conclusions:** mKRAS, compared to wKRAS, connotes worse CSS among NHW and NHB patients. Among wKRAS, NHB and Hispanic patients still experience higher mortality risk. This data suggests the negative prognosis heretofore associated with mKRAS may be linked to race/ethnicity and worthy of further study. Research Sponsor: None.

19 Poster Session

Impact of socioeconomic status (SES) on colorectal cancer patient survival: An analysis of 890,867 patients in the National Cancer Database (NCDB). *First Author: Mohamed E. Salem, Levine Cancer Institute, Atrium Health, Charlotte, NC*

Background: SES has been associated with outcomes in cancer patients (pts). We examined associations between SES and survival of pts with colorectal cancers (CRC). **Methods:** The NCDB was used to examine the association of SES status with clinicopathological features and outcomes of colorectal cancer pts, categorized by the income and education level of their area of residence. Logistic regression, Cox proportional hazard model, and chi-square test were used to examine the differences between groups. **Results:** A retrospective analysis of 890,867 pts with CRC (right-sided 34.1%, transverse 11.9%, left-sided 46.2%, and rectal 7.8%) diagnosed between 2004 and 2016, was conducted. About half the pts were male (51.4%); 84.3% were white, 11.2% black, and 4.5% of other races. Overall, 30.8% of pts lived in the highest and 18.4% in the lowest income areas. Twenty-three percent lived in areas comprising the highest high school graduation rate areas (>93%), while 17.4% lived in the lowest (< 79%). Compared to pts living in high-income areas, pts living in the lowest income areas were more likely to be black (OR 6.2, 6.1-6.3), present at a younger age (18-30 yrs vs. >70 yrs; OR 1.28, 1.18-1.39), have T3/T4 disease at presentation (OR 1.03, 95% CI 1.02-1.04), left-sided tumors (OR 1.05, 1.04-1.06), higher Charlson-Deyo score (OR 1.34, 1.33-1.36), and have Medicaid (OR: 3.9, 3.8-4.0) or no health insurance (OR: 2.9, 2.8-3.0). Tumor location and grade, stage, age, sex, race, ethnicity, income, education, insurance status, Charlson-Deyo score, and type of treatment center were independent predictors for survival in the multivariate analysis. Pts living in the lowest income and lowest education areas had a 13% and 4% higher risk of death, respectively, compared to pts in the highest income areas and education areas. Black pts had a 7% increased risk of death. Pts with Medicaid and no insurance coverage had a 44% and 29% increased risk of death, respectively, compared to pts with private insurance. **Conclusions:** CRC pts living in areas of low income and low education had worse survival. Insurance status and type of treatment center also have a strong impact on survival. Sociodemographic characteristics need to be taken into account and studied further, with the aim of improving outcomes for all pts. Research Sponsor: None.

Multivariate analysis.

		Hazard Ratio (95% CI)	*P*-value
Median Household Income	Lowest	**1.13** (1.11-1.14)	**<0.001**
Highest (ref)	Middle	1.06 (1.05-1.07)	
High School Graduation Rate	Low vs high rate	1.04 (1.03-1.06)	
Insurance	Medicaid	**1.44** (1.42-1.46)	
Private (ref)	Not insured	**1.29** (1.27-1.31)	
	Medicare	1.13 (1.12-1.14)	
Sex	Male vs Female	1.15 (1.14-1.15)	
Race	Black vs White	1.07 (1.06-1.08)	
Type of Treatment Center	Community	1.16 (1.15-1.17)	
Academic (ref)	Comprehensive Community	1.11 (1.10-1.12)	
	Integrated Network	1.10 (1.09-1.11)	
Charlson-Deyo Comorbidity	Any vs No Comorbidity	1.31 (1.31-1.32)	

20 Poster Session

Racial disparities negatively impact outcomes for patients with early-onset colorectal cancer independent of income or education status. *First Author: Suneel Deepak Kamath, Cleveland Clinic Taussig Cancer Institute, Cleveland, OH*

Background: The incidence of colorectal cancer (CRC) in patients under age 50 is rising for reasons that are incompletely understood. We examined the effects of health disparities and socioeconomic factors on outcomes for patients with early-onset CRC compared to older-onset CRC. **Methods:** Patients with CRC from 2004-2015 in the National Cancer Database were included and categorized by age under or over 50 years. Differences in demographic, disease and treatment characteristics and socioeconomic factors between younger and older patients were assessed by Chi-square test. The effect of age, race, ethnicity, insurance status, community median income and community educational attainment on overall survival (OS) were assessed using Cox models. Subgroup analyses were carried out by factors with significant interactions with race. Bonferonni correction was used when indicated. **Results:** The study population comprised 1,061,204 patients, 108,058 (10.2%) of whom were under age 50. The proportion of patients diagnosed under age 50 increased over time: 9.4% in 2004-2006, 10.1% in 2007-2009, 10.5% in 2010-2012 and 10.7% in 2013-2015. Compared to older patients, young patients were more likely to be Black (15.1% vs. 11.3%) or Hispanic (8.6% vs. 4.6%) and to be diagnosed with stage 4 disease (24.9% vs. 17.0%), $p < 0.0001$ for all. Age $<$ 50 years was associated with improved median OS (157.4 vs. 64.2 months, $p < 0.0001$).). Black patients had the worst median OS (58.3 months) compared to White (67.0 months), Hispanic (91.6 months) or Asian (104.9 months) patients, $p < 0.0001$. Within the subgroup of early-onset CRC patients with private insurance, Blacks had worse OS compared to White patients at multiple community income and education levels. Older CRC patients did not demonstrate the same disparities. Asian and Hispanic patients had equivalent or better OS compared to White patients regardless of insurance type, income or education level. These data are shown in the Table. **Conclusions:** Early-onset CRC continues to increase. Patients with early-onset CRC are more likely to be Black or Hispanic and to present with stage 4 cancer compared to older patients. Alarmingly, Black patients showed worse OS compared to White patients in all income subgroups, even with private insurance. Much more work is needed to address the environmental factors and health disparities that lead to these outcomes. Research Sponsor: None.

Community Median Income	Community Proportion without High School Degree	Comparison	OS Hazard Ratio	P value
< $38,000	≥ 21%	Black vs. White	1.31	< 0.0001
		Hispanic vs. White	0.89	0.18
		Asian vs. White	1.45	0.06
$38,000-63,000	7.0-12.9%	Black vs. White	1.41	< 0.0001
		Hispanic vs. White	0.81	0.07
		Asian vs. White	1.05	0.70
> $63,000	7.0-12.9%	Black vs. White	1.38	< 0.0001
		Hispanic vs. White	0.89	0.25
		Asian vs. White	1.0	0.95

21 Poster Session

Racial ethnic disparities in clinical/pathological features, treatment, and survival among patients with early-onset colorectal cancer. *First Author: Michael Lyudmer, Albert Einstein College of Medicine, Bronx, NY*

Background: Globally, the incidence of early-onset colorectal cancer has risen. Racial disparities in colorectal cancer (CRC) are well-described, however data in EO by race/ethnicity is lacking. We aim to compare the presenting features, treatment, and survival features of patients with metastatic early-onset CRC (EO). **Methods:** Patients with metastatic CRC diagnosed between 2010-2019 at two NYC hospitals were identified by tumor registry (n = 646). Clinical/pathological features, treatment and survival data was collected by chart review and compared between Non-Hispanic Whites (NHW), Non-Hispanic Blacks (NHB) and Hispanics (H) using Chi-square or Fisher's exact test. Kaplan Meier curves were plotted to compare overall survival (OS) among groups. Stata v15 was used for statistical analysis. **Results:** Of 646 CRC patients, 126 (21.5%) were NHW, NHB or H diagnosed with EO with a frequency ranging from 16.6% in NHW to 26.1% in H. Non statistically significant lower frequencies of male gender, low/moderate grade, left-sided tumors,and higher frequency of *KRAS* mutations were seen in NHB (Table). Metastectomy was performed in 20 patients (13.9%) and did not differ between groups. There was no difference in the use of chemotherapy or biologics in general (Table), but NHW were more likely to get cetuximab than NHB (OR:4.5, p = 0.02) and H (OR: 4.7, p = 0.02).There were no differences in median OS (1.8 vs. 2.2 vs. 2 years, p = 0.9)or 1-year OS (72% vs 72.3% vs 70.8%) in NHW, NHB and H, respectively. A lower 5-year OS was seen in NBH (14.5%) and Hispanics (24.4%) compared to NHW (44%). **Conclusions:** EO-CRC is more frequently seen in minority racial/ethnic groups. Despite no differences in the use of chemotherapy or biologic treatment in general, NHB have a lower 5-year survival rate compared to NHW and H. Research Sponsor: None.

n (%)	EO NHW n = 25	EO NHB N = 54	EO H n = 47	p
Male gender	15 (60)	24 (44.4)	17 (36.2)	0.15
Low/mod grade	11 (55)	32 (72.7)	25 (65.8)	0.37
Left-sided	11 (78.6)	21 (75)	25 (83.3)	0.75
***KRAS* mutant**	4 (33.3)	19 (51.4)	14 (46.7)	0.55
Oxaliplatin-based	10 (62.5)	29 (70.7)	21 (61.8)	0.68
Irinotecan-based	6 (42.9)	16 (44.4)	15 (44.1)	0.99
Biologics	19 (76)	33 (61.1)	36 (76.6)	0.18
Cetuximab	9 (64.3)	10 (28.6)	10 (27.8)	**0.04**
5-y OS	44%	14.5%	24.4%	

22 Poster Session

AABH (aspartyl (asparaginyl) β-hydroxylase) as a serum biomarker for colorectal cancer diagnosis and prognosis. *First Author: Mahmood Moshiri, Next Pharma Inc., Richmond Hill, ON, Canada*

Background: Colorectal cancer (CRC) is the third most common type of cancer diagnosed in the US. The National Comprehensive Cancer Network (NCCN) and the American Cancer Society (ACS) recommend that men and women begin colorectal cancer screening at age 50 or younger if they are at high risk. One of the following screening procedures is recommended: tests for fecal blood annually, a colonoscopy every 5 years, fecal occult blood tests in conjunction with colonoscopy every 5 years, a double-contrast barium enema every 5 years or a colonoscopy every 10 years. Fecal blood tests and colonoscopy are preferred over either test alone. Despite these recommendations, according to The Surveillance, Epidemiology and End Results Data Base (SEER), only 41% of colon cancers are diagnosed when the cancer is still confined to its primary site, 36% are diagnosed when the tumor has spread directly from its primary site or to regional lymph nodes, 19% are diagnosed when the cancer has already metastasized (4% unknown). The corresponding 5-year relative survival rates are 89.8% for localized disease, 67.7% for regional disease, and 10.3% for metastatic disease. **Methods:** Neither the NCCN nor the ACS recommends that a blood test be done as part of screening. This is due to the fact that, until now, there has not been a blood test with adequate sensitivity or specificity for this purpose. We have investigated the utility of aspartyl (asparaginyl) β-hydroxylase (AABH) as a screening test for colorectal cancer. **Results:** AABH has been detected by immunohistochemical staining (IHC) on the cell surface of a broad range of cancers including CRC. It has been detected by IHC in $>$ 99% of tumor specimens tested (n $>$ 2300) but has not been found in adjacent normal tissue and in tissue samples from people who do not have cancer. This observation and the observation that AABH is found in the serum of patients with cancer, but not in the serum of people who are cancer-free, led the development of a sandwich ELISA to measure AABH in serum. In the current study we have utilized the serum assay to quantify AABH levels in patients diagnosed with CRC and compared these values with those of people who did not have a diagnosis of cancer. Increased levels of AABH were found in the serum of 99% of patients with CRC (n = 175). In individuals not known to have cancer, AABH was essentially undetectable in serum (n = 213, specificity = 96%). **Conclusions:** AABH was identified in serum from patients with CRC irrespective of stage. Serum AABH levels for stages I, II, III and IV (local, regional, advanced regional and metastatic) were higher than 0.30 ng/mL (Cut off level). Thus, our data indicate that by measuring AABH in the serum, we should be able to detect colorectal cancer in most individuals at an earlier stage than it is currently detected. Hence, we believe that the broad application of this test could result in a much better 5-year survival for the majority of patients with colorectal cancer. Research Sponsor: Next Pharma Inc.

23 Poster Session

Human oral microbiome dysbiosis as a novel tool for detecting noninvasive biomarkers for colorectal cancer. *First Author: Cheng Kong, Shanghai Tenth People's Hospital, Tongji University, Shnaghai, China*

Background: The oral microbiome may play an important role in colorectal carcinogenesis. However, few studies have investigated the association between oral microbiome and the development of colorectal cancer (CRC). We aimed to investigate whether oral health–colorectal tumor association has an underlying microbial basis, in the quest for novel non-invasive biomarkers for CRC. **Methods:** We collected oral swab samples from 161 patients with CRC, 34 patients with colorectal adenoma (CRA), and 58 healthy volunteers. The oral microbiota was assessed using 16S rRNA sequencing. The oral microbiome was characterized, microbial markers were identified, and colorectal tumor (CRA and CRC) classifiers were constructed and validated. **Results:** Oral microbial composition and diversity were significantly different among the three groups; the CRA group had the highest diversity. Analysis of the functional potential of oral microbiota demonstrated that the pathway involving cell motility was overrepresented in the CRA and CRC groups relative to that in the healthy controls. Moreover, a random forest model was constructed based on oral microbial markers, which could distinguish the colorectal tumor groups from the healthy controls and achieve a powerful classification potential in the discovery and validation cohorts. **Conclusions:** This study suggests a potential association between oral microbiome dysbiosis and colorectal cancer. Oral microbiota-based biomarkers may be helpful in predicting the risk of developing CRA and CRC. Research Sponsor: National Natural Science Foundation of China.

24 Poster Session

Analytical and clinical validation of the TruCheck platform for diagnostic triaging of symptomatic cases suspected of colorectal cancer. *First Author: Dadasaheb B Akolkar, Datar Cancer Genetics, Nashik, India*

Background: Trucheck is a non-invasive approach for diagnostic triaging of symptomatic individuals who are suspected of Colorectal Cancer (CRC) and have been advised an invasive biopsy. Trucheck evaluates blood samples for presence of Circulating Ensembles of Tumor Associated Cells (C-ETACs: $EpCAM^{+}$, $Pan\text{-}CK^{+}$, $CD45^{\pm}$) originating from a primary Colorectal Adenocarcinoma (CR-AD: CDX-2, CK-20, Muc2); such C-ETACs are unexpected in asymptomatic individuals as well as in individuals with benign Colorectal conditions. **Methods:** For Analytical Validation, spike-recovery analysis was performed using control cells / cell lines for EpCAM (SKBR-3), Pan-CK (SKBR-3), CD45 (PBMCs), CDX2 (CaCO2), CK20 (HCT15) and MUC2 (SW620) to determine the Sensitivity, Specificity, Accuracy, Limit of Detection, Linearity and Precision. Clinical Validations were performed using 15 mL blood samples from 587 participants. An initial Retrospective Clinical Pre-validation was based on blood samples from 350 known cases of CR-AD and 20 cases of non-CRC. The Prospective Clinical Validation was performed on blood samples collected prior to any invasive procedures from 217 symptomatic cases suspected of CRC. **Results:** Analytical Validation indicated 100% Sensitivity, 100% Specificity, 100% Accuracy, 90% Precision and significant linearity ($R^2 \geq 0.98$) for all ICC markers. Clinical Pre-validation indicated 84.9 % Sensitivity and 100% Specificity for CR-AD v/s non-CRC. In the Prospective Clinical Validation cohort, histopathological evaluation (HPE) of biopsied tumor tissue indicated benign Colorectal conditions in 10 cases and CR-AD 207 of the 217 suspected cases. Based on HPE as the standard, the Trucheck approach had 90.3% Sensitivity, 100% Specificity and 95.2% Accuracy. **Conclusions:** Symptomatic individuals suspected of CRC may benefit from the sensitive and specific non-invasive Trucheck approach. Individuals positive for CR-AD-specific C-ETACs can be prioritized for further clinical procedures while C-ETAC negative individuals can be considered for alternate diagnoses. The Trucheck approach can eliminate the need for (and risks associated with) invasive colon biopsies in a significant proportion of suspected cases and is especially useful where Research Sponsor: None.

25 Poster Session

***Colonosight*: Multitarget RNA-FIT assay for noninvasive detection of advanced colorectal neoplasia.** *First Author: Erica Kay Barnell, Washington University School of Medicine, St. Louis, MO*

Background: Effective colorectal cancer (CRC) prevention and screening requires sensitive detection of all advanced neoplasias (colorectal cancer and advanced adenomas). Existing noninvasive screening approaches cannot accurately detect precancerous adenomas with high sensitivity. Here we describe a multi-factor assay (RNA-FIT test) that combines 8 stool-derived eukaryotic RNA (seRNA) biomarkers, patient demographic information (smoking status), and a fecal immunochemical test (FIT) to sensitively detect advanced colorectal neoplasias and other precancerous adenomas in a 1,305 average risk (45-75 age) prospective cohort. **Methods:** Average-risk patients undergoing colorectal cancer screening were prospectively evaluated with the RNA-FIT assay prior to an optical colonoscopy. RNA-FIT test results were generated using an ordinal regression model and results were compared to the colonoscopy findings. The model was initially assessed via 5-fold internal cross-validation of the training set and the ultimate model performance was assessed on a hold out testing set. **Results:** Of the 1,305 eligible patients recruited, 939 were included in the training set and 366 samples were reserved for the hold out testing set. When evaluating all 5 folds of the training set, internal cross validation attained a 61% sensitivity for advanced neoplasias (n = 69), 22% sensitivity for other adenomas (n = 279), 80% specificity for hyperplastic polyps (n = 155) and 86% specificity for no findings on a colonoscopy (n = 436). When employed on the testing set, the RNA-FIT test attained a 62% sensitivity for advanced neoplasias (n = 52), 27% sensitivity for other adenomas (n = 139), 78% specificity for hyperplastic polyps (n = 74) and 84% specificity for no findings on a colonoscopy (n = 101). Sensitivity for colorectal cancer and advanced adenomas with high-grade dysplasia / carcinoma *in-situ* was 100% in both the training set (n = 6) and hold out testing set (n = 5). Sensitivity for villous / tubulovillous adenomas was 65% in the training set (n = 23) and 60% in the hold out testing set (n = 15). Additional retrospective sample collection from patients with CRC is ongoing to further validate assay sensitivity for CRC. **Conclusions:** The RNA-FIT assay demonstrated clinically relevant detection of all advanced neoplasia, including early carcinomas, advanced adenomas, and other precancerous lesions. This assay could represent a noninvasive option to prevent colorectal cancer development through precancerous adenoma detection. Research Sponsor: Geneoscopy Inc.

26 Poster Session

Comparison of immune activity profiles of microsatellite instable colon tumors to microsatellite stable tumors having high ColoType CMS1-score. *First Author: Steven Allen Buechler, University of Notre Dame, Notre Dame, IN*

Background: Microsatellite instable (MSI) metastatic colorectal cancer (CRC) tumors have been found to be responsive to immune checkpoint inhibitors. Most MSI tumors are in consensus molecular subtype CMS1. Here, in a search for microsatellite stable (MSS) samples that may respond to checkpoint inhibitors, we used the ColoType CMS1-score to identify microsatellite stable (MSS) CRC tumors that have immune activity profiles similar to MSI tumors. **Methods:** This study was performed in Affymetrix cohort (n = 1,888) of primary CRC tumor samples assayed with hgu133plus2 Affymetrix microarrays. Degrees of infiltration of populations of immune cells were assessed with MCPcounter. Gene Set Enrichment Analysis (GSEA) using the Hallmark gene sets was used to compare biological features between subsets of samples. An 18-gene genomic score (PembroSig) of Ayers, et al, was used to predict response to Pembrolizumab. ColoType 40-gene signature identifies the CMS of a CRC tumor using values of continuous scores, one score for each of CMS1-4. CMS1+ denotes the samples with CMS1-score sufficiently high to predict it is in CMS1. A genomic score was used to predict MSI status for all samples in Affymetrix cohort; MSI predictions using said score had 97% agreement with clinically determined MSI status for 749 Affymetrix cohort samples. **Results:** The MSI score predicted 240 MSI samples in Affymetrix cohort, and 211 MSS samples in CMS1+ (CMS1+/MSS). The union of MSI and CMS1+/MSS compared to other samples exhibited elevated infiltration of cytotoxic lymphocytes ($p < 0.0001$) and CD8 T-cells ($p < 0.0001$), activity of interferon-gamma ($p = 0.006$) and interferon-alpha signaling ($p = 0.012$), inflammatory response ($p = 0.012$), and elevated PembroSig score ($p < 0.0001$). CMS1+/MSS compared to MSI showed no significance difference in any of these measures. None of the immune regulatory genes PD-1, PD-L1, PD-L2, CTLA4, LAG3, and IDO1 were differentially expressed between CMS1+/MSS and MSI. Of note, the only Hallmark gene sets enriched in MSI compared to CMS1+/MSS were DNA repair ($p = 0.002$) and MYC targets V1 ($p = 0.009$) and V2 ($p = 0.013$). We further analyzed the biological differences between MSI samples in CMS1+ (CMS1+/MSI, n = 190) and MSI samples not in CMS1+ (CMS1-/MSI, n = 50). We found that CMS1+/MSI compared to CMS1-/MSI exhibited elevated cytotoxic lymphocyte infiltration ($p < 0.0001$), interferon-gamma activity ($p = 0.027$), and PembroSig score ($p < 0.0001$), highlighting the relationship between immune activity and CMS1-score. **Conclusions:** ColoType CMS1-score identified MSS samples in Affymetrix cohort (11%) with similar immune activity as MSI samples (13%) and equivalently high values of a genomic score predictive of Pembrolizumab response. Research Sponsor: None.

27 Poster Session

Cross-sectional adherence with the multitarget stool DNA test for colorectal cancer screening in a large, national study of insured patients. *First Author: Lesley-Ann Miller-Wilson, Exact Sciences Corporation, Madison, WI*

Background: Colorectal cancer (CRC) is the second most deadly and fourth most frequently diagnosed cancer in the United States. Early detection can improve CRC outcomes, but overall screening rates (62%) remain below the 80% goal set by the National Colorectal Cancer Roundtable. Multiple options are endorsed for average-risk CRC screening, including the multi-target stool DNA (mt-sDNA) test, which includes patient and provider navigation support. Cross-sectional adherence with the mt-sDNA test was previously reported in a large Medicare population (71%). In the current study we investigated cross-sectional adherence with the mt-sDNA test in a broader, national sample of insured patients. **Methods:** Aggregate data from Exact Sciences Laboratories LLC (ESL; Madison, WI) were retrospectively analyzed in compliance with HIPAA requirements. Study participants included individuals ages 50 years and older who were covered by commercial insurance or Medicare, had a valid mt-sDNA test order placed between January 1–December 31, 2018, and received a test kit shipped from ESL. Cross-sectional adherence, defined as successful completion and return of the test kit within 365 days of the shipment date, was assessed overall and by patient- and provider-level factors. **Results:** In total, 1,420,460 participants met the study criteria (61.2% women; mean age 65.7 years). Overall cross-sectional adherence was 66.8%. Adherence was 72.1% in participants with Traditional Medicare, 69.1% in participants with Medicare Advantage, and 61.9% in participants with commercial insurance ($p<0.001$). Adherence increased by participant age ($p<0.001$): 60.8% for ages 50-64, 71.3% for ages 65-75, and 74.7% for ages 76+ years. For Traditional Medicare patients, ages 65-75, adherence was 73.6%. Participants with mt-sDNA tests ordered placed by gastroenterologists had a higher adherence rate (78.3%) than those with orders placed by primary care clinicians (67.2%) ($p<0.001$). Adherence rates were highest among patients with ordering providers in the Pacific region (71.4%) and West North Central region (70.1%), and lowest in the Mid-Atlantic region (65.7%), New England (65.2%), West South Central region (64.6%), and Puerto Rico and US territories (60.7%). **Conclusions:** Novel data from this large, national sample of insured patients demonstrate high cross-sectional adherence with the mt-sDNA test (66.8%), supporting the substantial contribution this guideline-endorsed option plays in average-risk CRC screening. At the patient-level, adherence increased with patient age, and was highest in those covered by Traditional Medicare. Provider-level stratification showed the highest adherence for mt-sDNA tests ordered by gastroenterologists. This study adds to data regarding the impact of accompanying navigation support and at-home convenience of mt-sDNA on screening completion rates. Research Sponsor: This study was funded by Exact Sciences Corporation.

28 Poster Session

The impact of changes in service delivery in patients with colorectal cancer during the first peak of the COVID-19 pandemic. *First Author: Konstantinos Kamposioras, The Christie NHS Foundation Trust, Manchester, United Kingdom*

Background: Increased levels of anxiety and distress in both patients and physicians have been reported in response to the significant impact COVID-19 has on cancer service delivery globally. We aimed to investigate how these changes have been perceived by patients diagnosed with colorectal cancer and identify determinants of increased anxiety. **Methods:** Survey (32-item) of consecutive patients diagnosed with colorectal cancer attending a large tertiary comprehensive cancer centre in the United Kingdom (18 May to 1 July 2020). Self-reported GAD-7 (both paper/electronic forms) was used as a screening tool for anxiety. Statistical analyses of associations: Chi-square, Fisher's exact, and uni- and multi-variable analyses were performed using SPSS v19 and R. **Results:** A total of 143 patients (response rate 67%), 82% male, and median age of 61-70 years were included. Majority of patients had telephone consultation (78%), including 40% who had scan results discussed over the phone; with favourable feedback received with both respectively. Twenty-three patients (18%) were considered to have anxiety, with 7 (6%) scoring for moderate or severe anxiety. Three items asked patients if they had concerns about getting COVID-19, were worried that COVID-19 would have effect on mental health, and affect their experience of cancer care. Patients answering positively to any of these items were most likely to have anxiety; multivariate analysis – OR 2.361 (95% CI 1.187-4.694, p=0.014), 3.219 (95% CI 1.401-7.395, p=0.006) and 3.206 (95% CI 1.036-9.920, p=0.043), respectively. Majority of the patients did not feel that they needed support during the pandemic period and hence the available well-being services were not used. Patients felt that friends and family had been very supportive but less so the primary care services ($p<0.05$). However, they felt they were supported by the clinical team. **Conclusions:** At our centre, during the first-peak of COVID-19 pandemic in the UK, patients with colorectal cancer did not display increased rates of significant anxiety. The findings of this survey suggests that some service changes implemented, including increased telephone follow-up, may have already improved the overall experience of cancer care. Importantly, patients were much more concerned about their cancer treatment than COVID-19, emphasising the need to continue to provide comprehensive cancer care even if we get a "2nd wave" of COVID-19. Research Sponsor: None.

29 Poster Session

Understanding the impact of COVID-19 on the colorectal cancer community: Barriers and opportunities for care. *First Author: Reese Garcia, Fight Colorectal Cancer, Springfield, MO*

Background: The novel coronavirus (COVID-19) has caused numerous disruptions across the cancer prevention and treatment landscape. Conservative modeling studies examining the effect of COVID-19 on cancer screening and treatment for breast and colorectal cancer (CRC) suggest that there will be 10,000 excess deaths from both cancers combined over the next decade. The goal of this analysis was to better understand the impact of COVID-19 on the CRC community, including gaps and opportunities for improving access to care and survivorship needs, and to advocate for the best possible care through policy, education and engagement of the entire cancer ecosystem. **Methods:** In April 2020, Fight Colorectal Cancer (Fight CRC) distributed an online survey to the colorectal cancer community. The survey was distributed through social media channels and targeted emails from April 24-May 5, 2020. Virtual focus groups were also conducted to gather rich qualitative data from cancer patients and caregivers about their experiences during the novel coronavirus pandemic. **Results:** In total, 222 individuals responded to the survey (survivors = 68%, caregiver = 12%, first degree family member = 8%, other = 8%), and 10 CRC survivors participated in focus groups (stage III = 30%, stage IV = 70%). Treatment disruptions and mental health were prevalent themes in both the survey and focus group. Over one-third of survey respondents indicated facing treatment disruptions (37%) and a majority (78%) of colorectal cancer patients reported feeling nervous and anxious. Another primary concern among respondents was access to care. Patients on Medicare were more likely than patients on private insurance to report having difficulties affording food and basic supplies. People living in rural areas were more likely to have greater concerns about maintaining a supportive network than those living in suburban areas. **Conclusions:** People with cancer face unique challenges as a result of the novel coronavirus, including treatment disruptions, increased feelings of anxiety, and financial concerns. Numerous health inequities also exist among low-income and rural patient groups. Identifying the barriers that patients face provides an opportunity to address the nuanced needs of the colorectal cancer community. Clinicians, supportive care providers, and advocacy organizations can tailor care delivery, increase access to care, and prepare patients for the future with reliable and accurate resources amidst a pandemic. Research Sponsor: None.

30 Poster Session

Quantifying the impact of the COVID-19 pandemic on gastrointestinal cancer care delivery. *First Author: Nicholas Perkons, University of Pennsylvania, Philadelphia, PA*

Background: Changes in healthcare utilization and delivery during the first months of the COVID-19 pandemic have altered the presentation, treatment, and management of patients with gastrointestinal (GI) malignancies. We hypothesize this has contributed to diagnostic and treatment delays that will increase disease morbidity and mortality. **Methods:** We performed a retrospective cohort study comparing healthcare utilization of patients with diagnosed GI malignancy (ICD10: C15-C26) during and prior to the COVID-19 pandemic within our health system. Deidentified patient encounter parameters were collected for the first 20 weeks of both 2019 and 2020, including the number of: new patient visits (NPVs), hospital admissions, and specialty encounters. Difference-in-difference analyses adjusted for week-specific and year-specific effects quantified the impact of the COVID-19 pandemic on care delivery, with week 11 of 2020 marking the start of the pandemic period. **Results:** The 2019 and 2020 cohorts of patients had similar demographic compositions on the basis of sex and ethnicity (2019: n = 23,536, 56.8% M, 70.4/16.3/1.9% White/Black/Hispanic; 2020: n = 25,773, 57.0% M, 70.3/16.3/2.0% White/Black/Hispanic). Across all GI malignancies, the COVID-19 pandemic period was associated with a significant decrease in NPVs (-50.0/week, -45% from 2019, $p < 1e-3$). Colorectal cancer (CRC) had the largest decrease in NPVs among GI malignancies (-25.3/week, -53% from 2019, $p < 1e-4$). Of note, there was a parallel decrease in colonoscopies during this time (-682/week, -91% from 2019, $p < 1e-11$). For patients with diagnosed GI malignancies, the COVID-19 pandemic was associated with statistically significant declines in hospital admissions (-31.7/week, -37% from 2019, $p < 1e-5$), radiology encounters (-177/week, -38% from 2019, $p < 1e-6$), radiation oncology encounters (-18.2/week, -12% from 2019, $p < 0.01$), chemotherapy infusion visits (-62.2/week, -17% from 2019, $p < 1e-4$), and surgery encounters (-71.1/week, -15.7% from 2019, $p < 0.01$). Subgroup analyses revealed these reductions were most significant in patients with CRC (radiology encounters, surgery encounters, hospital admissions), anal cancer (radiation oncology encounters), and pancreatic cancer (chemotherapy infusion visits). **Conclusions:** These data demonstrate that the COVID-19 pandemic is associated with significant disruptions to care delivery. While these effects were appreciated broadly across GI malignancies, CRC—diagnosed and managed by periodic screening—has been affected most acutely. The precipitous drop in screening colonoscopies likely contributed to the decline in NPVs, specialty encounters and hospital admissions. These findings underscore the importance of reinstating regular GI cancer screening and management. Future work will assess the impact of these and other changes to cancer care delivery on long term morbidity and mortality. Research Sponsor: U.S. National Institutes of Health.

31 Poster Session

The impact of primary tumor sidedness on survival in early-onset colorectal cancer by stage: A National Veterans Affairs retrospective analysis. *First Author: Ibrahim Azar, Karmanos Cancer Institute, Detroit, MI*

Background: The incidence of early-onset colorectal cancer (EOCRC) is rising. Left-sided colorectal cancer (LCC) is associated with better survival and response to therapy compared to right-sided colon cancer (RCC) in the metastatic setting. Current NCCN guidelines recommend the addition of EGFR inhibitors to KRAS/NRAS wild-type metastatic CRC originating from the left-side only. Whether primary tumor sidedness impacts survival in loco-regional disease and in EOCRC is of clinical interest. **Methods:** Data from the National VA Cancer Cube Registry was studied. 65,940 cases of CRC were diagnosed between 2001 and 2015. EOCRC (2,096 cases) was defined as CRC diagnosis at age <50 years. ICD codes C18 to C20 were used to delineate patients with RCC vs. LCC. RCC was defined as cancer from the cecum to the hepatic flexure (C18.0-C18.3), LCC from the splenic flexure to the rectum (C18.5-18.CRC; C19 & C20). Transverse cancer (C18.4), overlapping and unidentified sites (C18.8; C18.9) were excluded. **Results:** EOCRC is more likely to originate from the left-side (66.65% LCC in EOCRC vs. 58.77% in the whole CRC dataset). Overall, LCC has better 5-year OS than RCC in Stage I, III and better 1-year OS in stage IV (Table). Stage II RCC has better 5-year OS than LCC (RC 53.39% vs LC 49.28%). In EOCRC, there is no statistically significant difference between LCC and RCC in Stages I-III. Stage IV EOCRC patients with LCC and RCC have a 1-year OS of 73.23% and 59.84%, respectively. **Conclusions:** EOCRC is more likely than CRC to originate from the left side. In EORCRC patients, LCC is associated with better OS than RCC only in patients with metastatic disease. In the overall population, LCC is associated with better OS in all states except Stage II. The better prognosis of Stage II RCC might be due to the reported high incidence of MSI-high tumors in this subpopulation. Research Sponsor: None.

		Overall population			Early-Onset CRC		
		RCC	LCC	p-value	RCC<50	LCC<50	p-value
	n	30.28% (19969)	58.77% (38754)	-	23.62% (495)	66.65% (1397)	-
Stage I	5-yr OS	58.01% (2643)	61.67% (6661)	<0.0001	68.89% (59)	69.21% (209)	0.6033
Stage II	5-yr OS	53.39% (2459)	49.28% (3500)	<0.0001	45.30% (61)	54.96% (122)	0.3428
Stage III	5-yr OS	42.10% (1718)	46.10% (3191)	<0.0001	45.30% (53)	41.94% (155)	0.0991
Stage IV	1-yr OS	49.49% (1713)	57.79% (3501)	<0.0001	59.84% (73)	73.23% (238)	0.0086

32 Poster Session

Changes in treatment and outcomes of stage II/III rectal cancer patients treated with trimodality therapy (TT) between 2006-2016: An NCDB analysis. *First Author: Hagen F. Kennecke, Virginia Mason Medical Center, Seattle, WA*

Background: Trimodality therapy (TT) remains standard for stage 2/3 rectal cancer and emerging evidence supports better outcomes with total neoadjuvant therapy (TNT) than similar therapy given post-operatively (Post-op). Real-world practice patterns and sequence of TT have significant implications on rectal cancer quality of care, outcomes and clinical trial design, and are not well described. **Methods:** The National Cancer Database was used to identify patients with clinical (c) stage 2/3 rectal adenocarcinoma diagnosed between 2006-2016, while pathologic (p) stage 2/3 was used when c stage was missing. Patients were included if they received Chemo/Radiation (C/RT), single or multiagent (SA or MA) chemotherapy (CT) and surgery. TNT was defined as receipt of pre-op C/RT and MA CT and no post-op therapy. Survival analyses were performed using Kaplan-Meier (KM) estimates and Cox univariate and multivariate hazard ratios (HRs) adjusted for TNT group, sex, race, year of diagnosis, stage, facility type, and age of diagnosis. Five-year KM survival proportions were limited to years 2006-2012, while Cox HRs were estimated from 2006 to 2015. **Results:** Of 32,467 patients who received TT, 8883 (27%) received TNT and 23,584 were classified no-TNT. TNT and no-TNT cohorts were numerically similar in age, race and gender. A significantly higher proportion of pStages 0-2 patients were observed in the TNT vs the no-TNT cohorts (61% vs. 48%, $p < .001$). In analysis of annual treatment patterns of the whole cohort, a gradual reduction in Post-op C/RT was observed between 2006 (28%) and 2016 (8%, $p < .001$), while use of TNT and MA CT did not increase. A migration to lower pStages 0/1/2/3 was seen between 2006 (1/10/31/57%, respectively) and 2016 (3/22/29/45%) (2016) ($p < .001$). Five-year OS analysis showed superior OS for Pre-op vs Post-op C/RT (74 vs 69%, HR = .81, $p < .001$), and MA CT vs. SA CT (76 vs 71%, HR = 0.79, $p < .001$) but inferior 5-y OS for the TNT vs. no-TNT cohorts (74 vs 78%, HR = 1.17, $p < .001$). **Conclusions:** Between 2006-16, a minority of patients treated with TT for stage 2/3 rectal cancer received TNT which did not increase over time. Significant annual shifts from Post-op C/RT to Pre-op C/RT, and migration to lower pStages were seen during this time period. Pre-op C/RT and MA CT were associated with improved OS, while TNT patients experienced inferior OS vs. the no-TNT cohort, possibly related to confounding factors in this observational cohort; multivariate sub-group analysis to be presented. Emerging evidence in support of TNT may further change treatment patterns and outcomes. Research Sponsor: None.

TOTAL N = 32,467	Category	TNT N = 8883	no TNT N = 23,584	p-value
Mean Age (y)		58	57	< .001
cStage	2	41%	39%	< .003
	3	59%	61%	
pStage	0-2	62%	49%	< .001
	3	38%	51%	
SA CT	Yes	0	25%	< .001
MA CT	Yes	100%	75%	
Pre-op C/RT	Yes	100%	80%	< .001
Post-op C/RT	Yes	0	20%	
Academic Facility		34%	32%	< .001
Community Type Facility		60%	62%	
Other Facility Type		6%	6%	

33 Poster Session

Real-world data on overall survival associated with biweekly versus weekly cetuximab among metastatic colorectal cancer (mCRC) patients in the United States. *First Author: Himani Agg, Eli Lilly and Company, Indianapolis, IN*

Background: Cetuximab 250mg/m^2 weekly (Q1W) after an initial dose of 400mg/m^2 is approved for treatment of K-Ras wild-type mCRC. In real world 29% of patients received cetuximab 500mg/m^2 biweekly (Q2W). In this study overall survival (OS) associated with Q2W vs Q1W dosing of cetuximab for mCRC in real world was compared. **Methods:** This study utilized Flatiron Health electronic health record-derived database to identify adult patients with stage IV or recurrent K-Ras wild-type mCRC who received cetuximab+FOLFIRI/FOLFOX/irinotecan, or cetuximab monotherapy in first, second or third-line therapy from 01/01/2013 to 12/31/2019. Patients were assigned to Q1W or Q2W cohort if they had 70% or more cetuximab infusions with a gap of 4-10 days or 11-18 days from previous infusion. Patients who did not fall into either cohort were excluded from analysis. Propensity score (PS) matching was used to balance cohorts on their baseline demographic, clinical and treatment characteristics. Kaplan-Meier methods and Cox proportional hazards regressions were used to compare OS. **Results:** Baseline characteristics for Q2W (N = 422) vs Q1W (N = 653) cohorts before PS matching- median age 62 vs 65 years, male 58.5% vs 59.3%, white 68.3% vs 66.5%, stage IV 56.6% vs 58.5%, ECOG PS 0/1 61.6% vs 52.1%, ECOG PS 2+ 9.2% vs 9.5%. After PS matching, baseline characteristics were balanced. Hazard ratios (HRs) comparing OS in PS-matched Q2W vs Q1W cohorts were not significant for overall or line of therapy populations (Table). **Conclusions:** Weekly and biweekly cetuximab had comparable effectiveness in this real-world study. Research Sponsor: Eli Lilly and Company.

Q1W vs Q2W OS.

Population	Cohorts Reference: Q1W	N	Median OS (95% CI), month	HR (95% CI)	Log-rank p-value
Overall	Q1W	364	14.34 (12.80, 16.02)		0.246
	Q2W	364	17.24 (15.33, 18.82)	0.90 (0.75, 1.08)	
First-line	Q1W	121	23.36 (13.09, 32.17)		0.347
	Q2W	121	29.14 (17.76, 36.91)	0.86 (0.62, 1.18)	
Second-line	Q1W	159	12.93 (11.05, 14.70)		0.504
	Q2W	159	15.39 (11.94, 18.68)	0.92 (0.71, 1.19)	
Third-line	Q1W	70	12.53 (9.80, 15.56)		0.883
	Q2W	70	12.83 (9.44, 15.53)	0.97 (0.65, 1.44)	

34 Poster Session

Health-related quality of life and time from diagnosis among young adult colorectal cancer survivors. *First Author: Kimberly Ann Miller, University of Southern California, Los Angeles, CA*

Background: Incidence of colorectal cancer (CRC) in patients under 50 years of age is rising. Quality of life in survivorship is not well-described in this population. We compared health-related quality of life (HRQoL) in CRC survivors ≤ 50 years old who were 6-18 months or 19-36 months from initial diagnosis or relapse. **Methods:** A cross-sectional online survey was administered in collaboration with a national organization for young CRC survivors. The Functional Assessment of Cancer Therapy (FACT-C) was used to measure HRQoL, which assesses HRQoL globally, including a CRC specific scale, and emotional, physical, social, and functional well-being domains. T-tests were conducted to compare HRQoL between survivors who were 6-18 months versus 19-36 months from diagnosis/relapse. **Results:** This sample (n=308) had a mean age of 33.76 SD±6.68; 201 (65.3%) were male; tumor location was colon or rectal in 41.7% and 58.3%, respectively. The majority (55.23%) were diagnosed with stage 2 disease; 98.0% were non-metastatic. 42.2% experienced relapse; 25% had an ostomy. Most survivors were 6-18 months (N=189; 61.4%) from diagnosis/relapse, and key demographics and disease characteristics did not significantly differ between those who were shorter versus longer time from diagnosis/relapse. The mean global HRQoL score was 67.3 out of a possible score of 136. Across domains, scores were low, with social well-being the highest (15.15/28) and emotional well-being the lowest (11.44/24). Social well-being was significantly higher among survivors who were 6-18 months from diagnosis/relapse compared to those 19-36 months (15.98 for 6-18 months vs. 13.83 for 19-36; $p<0.01$), as was functional well-being (13.20 for 6-18 months vs. 11.12 for 19-36; $p<0.01$). Emotional well-being and physical well-being did not significantly differ between groups. **Conclusions:** Overall HRQoL scores were low among younger CRC survivors, and social and functional well-being were significantly worse for those longer from diagnosis. Appropriate counseling and other targeted interventions are necessary to maintain HRQoL over time in this at-risk population. Research Sponsor: Aflac Children's Oncology Group.

Means and T-tests to compare HRQoL among colorectal cancer survivors age 50 and under (N=308).

	Total Mean (SD)	95% CI	6-18 mos dx N=189 Mean (SD)	19-36 mos dx N=119 Mean (SD)	*t*
FACT-C Global (0-136)	67.34 (19.23)	65.18-69.50**	68.91 (17.99)	64.86 (20.87)	-1.80
Colorectal cancer scale (0-28)	14.20 (3.23)	13.84-14.56**	14.48 (3.27)	13.76 (3.13)	-1.86
Physical well-being (0-28)	14.17 (5.76)	13.53-14.82**	13.90 (4.97)	14.61 (6.82)	1.05
Social well-being (0-28)	15.15 (5.46)	14.54-15.76**	15.98 (4.87)	13.83 (6.06)	-3.41**
Emotional well-being (0-24)	11.44 (4.47)	10.94-11.94 **	11.38 (4.37)	11.54 (4.64)	0.31
Functional well-being (0-28)	12.40 (5.53)	11.78-13.02**	13.20 (5.43)	11.12 (5.46)	-3.26**

*$p<0.05$; **$p<0.01$

35 Poster Session

Survival analysis of colorectal cancer patients treated with first-line modified FOLFOX6 with or without bolus fluorouracil. *First Author: Walid Labib Shaib, Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA*

Background: The combination of oxaliplatin, bolus 5-FU (b5FU), infusional 5-FU (5-FUCI), and leucovorin (LV) is the preferred first line treatment option for mCRC. This study evaluates the impact of b5FU on survival in first line therapy for mCRC patients treated with mFOLFOX6. **Methods:** This was a retrospective chart review of patients ≥ 18 years old with mCRC receiving palliative first line mFOLFOX6 chemotherapy with or without b5FU/ LV from January 1, 2010 through June 1, 2019 at Winship Cancer Institute, Emory University. Data collection included the following: demographics (age, race, gender), disease characteristics (tumor sidedness), microsatellite status, KRAS status, BRAF status, addition of monoclonal antibodies (bevacizumab, panitumumab), ECOG PS, grade 3/4 neutropenic events, addition of growth factors, and treatment delays. The primary endpoint was PFS. The multivariable Cox proportional hazards model for PFS and OS was performed with selected covariates of interest. **Results:** A total of 252 patients with mCRC met the inclusion criteria. Median follow-up time was 2.4 years. 161 patients (64%) received mFOLFOX6 with b5FU/LV and 91 patients (36%) received mFOLFOX6 with no b5FU/LV. More cycles were delivered in the b5FU group as compared to the non-b5FU group (mean, 4.8 v. 3.8 cycles, respectively; $p < 0.001$). There were no differences in grade 3 and 4 neutropenic events between groups. Growth factor usage was numerically higher in the bolus group though not significantly different ($p = 0.06$). No difference was observed in treatment delays between groups ($p = 0.83$). There was no statistical difference in PFS between treatment groups (1.1 years in the b5FU/LV group v. 0.8 years (95% CI, 0.6-1.0) in the no 5-FU/LV bolus group; $p = 0.076$). The median OS was 2.5 years in the b5FU/LV group compared to 1.8 years in the no b5FU/LV group ($p = 0.012$). On univariate analysis, tumor sidedness and performance status were significantly different between groups. On multivariate analysis, none of the variables were significantly different between groups. **Conclusions:** The omission of the b5FU/LV from mFOLFOX6 does not significantly impact PFS, toxicity or treatment delays. However, OS is significantly shorter when the b5FU/LV is omitted suggesting the clinical importance of maintaining bolus administration with 5-FUCI in the first line palliative treatment of mCRC. Research Sponsor: None.

36 Poster Session

Defining optimal selection criteria to improve prognosis and avoid futility in surgical resection of colorectal peritoneal metastases. *First Author: Lana Bijelic, Department of Oncological Surgery, Hospital Sant Joan Despí, Moises Broggi, Catalonian Regional Peritoneal Surface Malignancy Program, Barcelona, Spain*

Background: Surgical resection of peritoneal metastases of colorectal cancer (CRC PM) may benefit some patients similar to hepatic metastases. This approach remains controversial in part due to inconsistent selection criteria and reported outcomes. The impact of preoperative clinical characteristics and tumor molecular profiles on survival among surgically treated patients is incompletely understood. The aim of this study was to investigate the relationship between possible predictive variables and survival in a large cohort of patients treated on a standardized clinical pathway and to develop a clinically useful patient selection tool. **Methods:** This retrospective cohort study utilized the database of the Catalonian peritoneal metastases regional program, established in 2006. The program provides treatment for all PM patients within an autonomous region with a population of 7.5 million and includes a single dedicated high volume surgical unit. We included all adult patients with surgically resected CRC PM. The clinical pathway includes the administration of perioperative (neoadjuvant and adjuvant) systemic chemotherapy and has historically included a dose of heated intraoperative intraperitoneal chemotherapy (HIPEC) at the time of surgery. Demographic and clinical data was analyzed with descriptive statistics. Survival and the associated predictors were analyzed with the Cox proportional hazard model with HRs used to create a predictive nomogram. **Results:** A total of 538 patients (mean age 59) have been treated with surgery and a complete resection (CC0) was achieved in 94% of cases. Planned preoperative systemic chemotherapy was delivered in 95% of cases, consistent with the clinical pathway. Surgical morbidity was low (urgent reoperation 6.1%, postoperative return to the ICU 2.4%, 30-day readmission 4.3%) as was 30-day mortality (0.4%). After a median follow up of 27.5 months, the median overall survival (OS) was 43.1 months. It varied considerably by subgroup: patients with low peritoneal tumor burden had the highest OS (median 49 months) and those with signet ring cell subtype the lowest (median 19 months). Factors independently associated with survival were: N stage at diagnosis, histological subtype, quantified peritoneal tumor burden (PCI score) and presence of visceral involvement. A selection tool and predictive nomogram were designed incorporating the results of the multivariable analysis. **Conclusions:** A set of clinical variables can be identified that independently influences patient survival after surgical resection of CRC PM that should be used as selection criteria when considering surgery. With optimized patient selection and treatment within a specialized center, excellent survival and low morbidity can be anticipated following surgery for CRC PM. Research Sponsor: None.

37 Poster Session

Preliminary safety analysis of phase II open-label NIVACOR trial (GOIRC-03-2018) in patients with advanced colorectal cancer RAS or BRAF mutated. *First Author: Angela Damato, Medical Oncology Unit, Clinical Cancer Center, AUSL-IRCCS Reggio Emilia, Reggio Emilia, Italy*

Background: NIVACOR trial is an open-label, multicentric Italian phase II trial of FOLFOXIRI/bevacizumab in association with an anti-PD1 antibody, nivolumab, in patients (pts) with metastatic colorectal cancer (mCRC). We report preliminary safety analysis by an Independent Monitoring Committee. **Methods:** Pts with mCRC RAS or BRAF mutated, regardless microsatellite status and eligible to receive a first line treatment will be enrolled. FOLFOXIRI/bevacizumab (BEV) in association with nivolumab (NIV) was administered every 2 weeks for 8 cycles (induction) followed by BEV plus NIV every 2 weeks (maintenance) until PD or unacceptable toxicities. BEV was administered intravenously at dose of 5 mg/kg and NIV intravenously as a flat dose of 240 mg every 2 weeks. The primary endpoint was the ORR. The safety is assessed after the inclusion of the 10th patient, receiving ≥1 dose. **Results:** As of September 20, 2020, 25/70 pts are enrolled. The first 10 pts were evaluated for preliminary safety analysis. Median age was 58 years (32-66), 60% of pts were male, median cycles of treatment was 5.5 (1-9). 100% were KRAS G12D mut and BRAF wild type, respectively, and 2% MSI-H/dMMR. 7/10 pts experienced at least one AE related to FOLFOXIRI/BEV and 2/10 related to NIV. The most frequent grade 1-2 AEs related to FOLFOXIRI/BEV were nausea and vomiting 4(57%), fatigue 5(71%), and diarrhea 5(71%); 3(43%) pts had grade 3-4 neutropenia, and 1(14%) febrile neutropenia. Only 2 pts developed grade 1-2 AEs related to NIV represented by rash (50%) and salivary gland infection (50%); no grade 3-4 was reported. One of pts with dose delay because of serious AES (proteinuria) BEV related, and one patient discontinued due to serious AEs (ileo-urethral fistula) not related to NIV. **Conclusions:** Combination of FOLFOXIRI/BEV and NIV was generally well tolerated and showed an acceptable toxicity profile. The final analysis will be scheduled at the end of enrollment. Clinical trial information: NCT04072198. Research Sponsor: Bristol-Myers SquibbPharmaceutical/Biotech Company.

38 Poster Session

Impact of systemic inflammation and sarcopenia on prognosis of metastatic colorectal cancer. *First Author: David da Silva Dias, Centro Hospitalar Universitário do Algarve, Faro, Portugal*

Background: Systemic inflammation, evaluated with neutrophil-to-lymphocyte ratio (NLR), and sarcopenia, assessed with skeletal muscle index (SMI), appear to predict mortality in many cancers, although the optimal cut-offs are still a matter of debate. The goal of this study is to evaluate the cut-offs of NLR and SMI and their prognostic value on metastatic colorectal cancer (mCRC) under first line treatment. **Methods:** Retrospective cohort analysis of patients with mCRC under first-line treatment in two hospital units, between January 2015 and December 2018. Muscle mass area (MMA) was detected on computed tomography, on L3 segment, with *ImageJ software*. SMI was determined as MMA/height^2. Statistical analysis was performed with *IBM SPSS v25 software*. **Results:** 178 patients were analysed, with mean age of 62 (±11) years old. 65% were male and 62.9% had ECOG PS 0. Two thirds of patients presented metastasis in a single organ, mainly in liver. The cut-off values were established based on ROC analysis. Systemic inflammation was defined as NLR > 2.80 and sarcopenia was defined by SMI < 49.12 cm^2/m^2 for men and <35.85 cm^2/m^2 for women. 52% of patients presented sarcopenia. In a multivariate analysis using a Cox regression model, an association was observed between overall survival and ECOG PS (p=0.014; HR 5.46, CI 95% [1.42-21.10]), systemic inflammation (p=0,038; HR 2.20, CI 95% [1,05-4.62]) and sarcopenia (p=0.01; HR 4.73, CI 95% [1.85-12.09]). **Conclusions:** In this study, sarcopenia and systemic inflammation showed independent prognostic value on patients with mCRC. Future prospective studies are necessary to establish a definitive cut-off value for application in clinical practice. Research Sponsor: None.

39 Poster Session

Real-world genomic and treatment landscape in advanced colorectal cancer identifies treatment differences pre- and post-ctDNA genomic profiling. *First Author: Junhua Yu, Guardant Health, Redwood City, CA*

Background: Clinical insights gained from real-world data have led to numerous advances in oncology including new and expanded drug approvals and an understanding of real-world clinical utilization. In this precision oncology age, integrating real-world clinical data with genomic data can lead to further advancements. We aimed to understand the genomic and treatment landscape in advanced colorectal cancer (aCRC) by leveraging a uniquely large and detailed clinical-genomic database. **Methods:** The GuardantINFORM (Guardant Health) database comprises aggregated commercial payer health claims and de-identified records from over 100,000 individuals with comprehensive ctDNA results (Guardant360). GuardantINFORM was queried for patients (pts) with a diagnosis of CRC. Pts with fewer than two pharmacy claims prior to or after the first ctDNA test were excluded from the regimen analysis. Latest claims data was truncated as of 8/31/2020. **Results:** 10,845 pts had a total of 13,510 ctDNA tests (1 – 19 tests/pt). The first ctDNA test date was from 06/2014 - 06/2020. The majority of pts had one ctDNA test (86.7%) while 5% had three or more tests. 87.9% of ctDNA tests had at least one genomic alteration identified, with the distribution of alterations consistent with prior reports (Table). 78% of pts had at least two pharmacy claims before and/or after the first ctDNA test. Of those pts with at least one CRC treatment, the most commonly prescribed CRC regimens up to one year prior to the first ctDNA test were FOLFOX +/- bevacizumab (16%, 18%), FOLFIRI +/- bevacizumab (17%, 11%), capecitabine (15%), 5-FU (12%), and regorafenib (5.2%). Anti-EGFR mono and combination therapy was reported in 6% and 16% of pts pre ctDNA testing. Immune checkpoint inhibitor (ICPi) mono and combination therapy was reported in 2% and 0.5% of pts. The most commonly prescribed CRC regimens post first ctDNA test were capecitabine (16%), FOLIRI +/- bevacizumab (15%, 13%), tipiracil and trifluridine (15%), FOLFOX +/- bevacizumab (12%, 14%), 5-FU (11%), and regorafenib (10%). Anti-EGFR mono and combination therapy was reported in 8% and 18% of pts post ctDNA testing. ICPi mono and combination therapy was reported in 5% and 1% of pts. **Conclusions:** Using a large and uniquely detailed clinical-genomic dataset, we produced results that replicate the observed distribution of ctDNA identified mutations present in aCRC. This genomic information combined with real-world clinical data provides valuable insights into the variety of longitudinal treatments, including before and after comprehensive ctDNA genomic profiling, allowing for detailed outcomes research, especially focused on precision oncology. Research Sponsor: Guardant Health.

Gene	Percentage of tests	Most common alteration type
TP53	59%	Missense (77%)
APC	52%	Nonsense (67%)
KRAS	38%	Missense (95%)
PIK3CA	19%	Missense (81%)
BRAF	17%	Missense (54%)
SMAD4	12%	Missense (78%)
MET	10%	CNG (44%)

40 Poster Session

The pattern of brain metastasis in colorectal cancer: Efficacy of metastasectomy, chemotherapy. *First Author: Suleyman Yasin Goksu, University of Texas Southwestern Medical Center, Dallas, TX*

Background: Colorectal cancer patients with brain metastases experience poor outcomes; however treatment strategies are understudied. In this study, we investigated the impact of different treatments for colorectal cancer patients with brain metastases. **Methods:** We identified stage 4 colorectal adenocarcinoma patients with brain metastasis using the National Cancer Database diagnosed between 2010 and 2015. Patients with unknown survival data, other histologies, and multiple primary sites were excluded. Patients with and without brain metastasis were compared using the Chi-square test. Kaplan-Meier method was performed to calculate univariable overall survival (OS). We used the Cox regression model for multivariable analysis after adjusting by age, race/ethnicity, comorbidity score, surgery, chemotherapy, and radiotherapy. **Results:** Among 75,901 patients with stage 4 colorectal adenocarcinoma, 1.6% had brain metastasis. Patients with brain metastasis were more likely to have bone (23% vs. 5%, $p < 0.001$) and lung metastasis (52% vs. 21%, $p < 0.001$), but less likely to have liver metastasis (56% vs. 72%, $p < 0.001$) compared to patients without brain metastasis. Patients with brain metastasis had higher KRAS mutation rate (54% vs. 43%, $p < 0.001$). Patients with brain metastasis were more likely to be age $\geq$ 50 years (85% vs. 83%, p = 0.01), white race (76% vs. 71%, p = 0.001), and receive radiotherapy (63% vs. 12%, $p < 0.001$). Total 26.4% of patients with brain metastasis underwent metastasectomy, and those patients had better OS compared to patients with non-metastasectomy (median OS 12 vs. 4 months, $p < 0.001$). Median OS in all patients with brain metastasis was 5.5 months. Patients with brain metastasis who received multiagent chemotherapy had improved OS compared with patients who received single-agent chemotherapy (mOS 13 vs. 6 months, $p < 0.001$). Patients with brain metastasis who received brain radiotherapy had better OS (mOS 6.3 vs. 3.7 months, p = 0.005) than those who did not. On multivariable analysis, metastasectomy (HR 0.65 95% CI [0.57-0.75]) and receipt of multiagent chemotherapy (HR 0.68 95% CI [0.54-0.86]) were associated with favorable prognosis, but brain radiotherapy was not (HR 1.04 95% CI [0.91-1.19]). **Conclusions:** Brain metastases are rare in colorectal cancer but portend poor survival. Lung and bone metastases are found more frequently in these patients. Treatment with metastasectomy or multiagent chemotherapy is associated with improved overall survival. Research Sponsor: None.

41 Poster Session

Evaluating the clinical utility of universal screening to identify Lynch syndrome in stage III/III colorectal cancer patients: A prospective observational study in Japan. *First Author: Yasuaki Yamamoto, Department of Colorectal Surgery, National Cancer Center Hospital East, Kashiwa, Japan*

Background: Universal screening for Lynch syndrome (LS) by identifying deficient DNA mismatch repair (MMR) in the tumor tissue of all new colorectal cancer (CRC) patients is widely accepted. The population prevalence of LS is approximately 3% in Western countries, whereas it is approximately 0.7% in Japan. In addition, the number of relatives diagnosed per proband is 3.6 in Western countries, whereas there are even fewer diagnoses per proband in Japan. To address the issue of LS remaining largely underdiagnosed in Japan, we prospectively evaluated the clinical utility of universal screening of LS in CRC patients. **Methods:** From March 2016 to August 2019, all consecutive new cases of stage II/III CRC underwent immunohistochemistry (IHC) screening for MMR using MLH1, MSH2, MSH6, and PMS2 antibodies. The patients negative for both MLH1 and PMS2 (MLH1-/PMS2-) were subjected to reflex testing for *BRAF* V600E mutation. Patients with both MLH1-/PMS2- and *BRAF* negative (cohort A, n = 14) and those with other IHC patterns (cohort B, n = 13) were referred for genetic counseling (GC) and genetic testing (GT). Furthermore, relatives of probands with confirmed LS were referred for GC/GT if they were willing. **Results:** Overall, 591 pts were enrolled in this study. Patient background were as follows: > 70 y/o, 35%; right-sided/left-sided colon/rectum, 24%/24%/53%; and cStage II/III, 65%/35%. Of 591 patients, 40 (6.8%) had MMR deficiency. Of 27 patients with MLH1-/PMS2-, 24 underwent *BRAF* reflex testing; only 10 of these patients tested positive for mutation. Of 27 patients recommended for GC, 25 were referred for GC and 22 for GT, which revealed 12 LS cases (2%, mutation genes: MLH1/PMS2/MSH2; 4/2/6). The frequency of LS diagnosis with respect to patient background was as follows: > 70/≤70 y, 1.0/2.6%; right-sided/left-sided colon/rectum, 5.8/0/1.3%; and cStage II/III, 2.6/1.0%. Interestingly, only 3 (25%) of 12 patients who underwent GC/GT in cohort A had LS compared with 9 (90%) of 10 patients in cohort B ($p = 0.004$). Moreover, among 11 relatives of 5 families who were willing to undergo GC/GT, six (55%) had LS, of whom two were first-degree relatives (33%), one was a second-degree relative (50%), and three were third-degree relatives (100%). **Conclusions:** This study showed that universal screening of LS in CRC patients is significantly useful in Japan. Furthermore, implementing a reflex testing strategy demonstrated high adherence to guidelines and the appropriateness of our referrals for GC/GT. Research Sponsor: None.

42 Poster Session

Characteristics and outcomes for fecal occult blood test (FOBT) screen detected (SD) versus non-screen detected (NSD) colorectal cancer (CRC). *First Author: Shehara Ramyalini Mendis, Walter & Eliza Hall Institute of Medical Research, Melbourne, Australia*

Background: FOBT based screening for CRC has been shown in multiple studies to reduce CRC mortality. Beyond the well described earlier stage at diagnosis, other characteristics of SD cancers have not been well studied. Since 2006 Australians aged 50-74 have regularly been mailed an immunochemical FOBT via the National Bowel Cancer Screening Program (NBCSP), with participation rate stable around 40%. **Methods:** To explore patient (pt), tumour, treatment and outcome data for SD compared to NSD, we examined a multi-site CRC database where prospectively collected data includes method of detection. Categories include SD via the NBCSP, cases that were symptomatic or incidentally found on imaging (NSD), and cases detected by screening outside the NBCSP (OSD). High risk features for Australian Clinicopathological Staging System (ACPS) Stage B included emergency presentation, T4, lymphovascular invasion and <12 lymph nodes examined. **Results:** Of 6969 registry pts diagnosed 06/2006-06/2020, 4107 (59%) were aged 50-74, including 473 (12%) SD, 3228 (79%) NSD and 406 (10%) OSD. SD versus NSD pts were younger (mean 62.4 v 64.2 years), had better ASA score (ASA 1-2: 79% v 66%, Odds Ratio [OR] 1.9, p<0.001), earlier stage at diagnosis (ACPS A/B/C/D = 38%/21%/28%/5% v 17%/29%/26%/21%, p<0.001), were more often left-sided (41% v 33%, OR 1.44, p<0.001) but less frequently located in the rectum (28% v 36% OR 0.70, p=0.001). There was no difference by gender. SD tumors were more often well/moderately differentiated (76% v 66%, OR 1.65, p<0.001) and less often mucinous (16% v 20%, OR 0.66, p=0.002). SD stage A tumours were more often T1 (66% v 43%, OR 0.36, p<0.001). SD stage B tumours were more often T3 (92% v 85%, OR 0.43, p=0.033), and had fewer high risk features (60% v 49%, OR 0.64, p=0.036). SD stage C pts had a similar rate of N2 disease (25% v 31%, p=0.20), but more often received adjuvant chemotherapy (96% v 86%, OR 3.6, p=0.002). De novo stage D and relapsed SD pts more often underwent metastatic resection (46% v 25%, OR 2.6, p<0.001). Relapse free survival (RFS) in stage A-C, progression free survival in stage D (PFS), and overall survival (OS) was superior for SD and is in Table. **Conclusions:** We show for the first time to our knowledge that SD CRCs have many distinct and favourable prognostic features that appear to be driving favourable stage based outcomes when compared to NSD patients. This prognostic data could inform adjuvant therapy decision making and surveillance strategies for SD CRC. Research Sponsor: None.

ACPS Stage	RFS/PFS Hazard Ratio for SD v NSD (95% CI, p value)	OS Hazard Ratio for SD v NSD (95% CI, p value)	5-yr OS SD v NSD
A	0.35 (0.11-1.13, 0.079)	0.37 (0.11-1.22, 0.10)	97% v 93%
B	0.13 (0.02-0.92, 0.041)	0.15 (0.02-1.09, 0.062)	97% v 89%
C	0.33 (0.16-0.68, 0.002)	0.40 (0.19-0.80, 0.010)	90% v 77%
D	0.38 (0.12-1.21, 0.10)	0.40 (0.20-0.77, 0.006)	45% v 14%
All Stages	0.23 (0.14-0.39, <0.001)	0.22 (0.14-0.34, <0.001)	91% v 70%

43 Poster Session

Evaluation of a sensitive blood test for the detection of colorectal advanced adenomas in a prospective cohort using a multiomics approach. *First Author: Jimmy Lin, Freenome, South San Francisco, CA*

Background: Blood-based screening tests for colorectal cancer (CRC) with high sensitivity and specificity are needed to improve adherence, facilitate early detection, and ultimately reduce mortality from CRC. Current stool-based tests have a sensitivity of 24-42% for colorectal advanced adenomas (AAs), while blood tests that rely on tumor-derived cell-free DNA (cfDNA) methylation signatures have shown limited sensitivity for AAs. Here we demonstrate the ability to detect AAs from blood using a multiomics test that incorporates both tumor- and immune-derived signatures, and compare it to the performance of a cfDNA methylation-only test. **Methods:** Participants enrolled in a prospective study (NCT03688906) were included in this analysis. The multiomics test includes signatures for cell-free nucleic acids based on next-generation sequencing, and for plasma proteins based on high-throughput multiplexed assays. Signatures are integrated computationally with a combination of convolutional neural networks and regularized logistic regression. We compared the multiomics test with one based on cfDNA methylation only. **Results:** This sub-study included 542 participants (AA: n = 122; colonoscopy-confirmed negative controls: n = 420). Participants with AA were 56% male with a mean age of 63 years, and colonoscopy-confirmed negative controls were 54% male with a mean age of 61 years. The multiomics test achieved a sensitivity of 41% (n = 50/122, 95% CI 34-48%) at 90% specificity (377/420). By contrast, the cfDNA methylation-only test achieved a sensitivity of 20% (24/122, 95% CI 15-25%) at 91% specificity (383/420). Performance was also analyzed by histological subtype and location, and superiority of the multiomics test to the cfDNA-methylation-only test was consistently observed. **Conclusions:** A novel multiomics blood test can detect colorectal AAs at a sensitivity and specificity comparable to existing stool-based tests. Combining signatures from both tumor- and immune-derived sources resulted in AA sensitivity greater than that of cfDNA-methylation alone. Research Sponsor: None.

44 Poster Session

The clinical and molecular characteristics of patients with personal or family history of gastrointestinal malignancies/polyposis and checkpoint kinase 2 (CHEK2) mutations. *First Author: Sana Ozair, University of South Alabama, Mobile, AL*

Background: Checkpoint Kinase 2 (CHEK 2) encodes the protein CHK2, a serine/threonine kinase involved in pathways that conduct DNA repair as well as apoptosis in response to initial DNA damage. Germline mutations in the CHEK2 gene are associated with several malignancies such as colon, breast, stomach, prostate, kidney, thyroid and soft tissue cancers. Here, we describe the clinical and molecular characteristics of patients with personal or family history of gastrointestinal (GI) malignancies/polyposis and CHEK2 gene mutations. **Methods:** This is an IRB-approved retrospective chart-review study. Between 2016 and 2020, 1011 unique genetic counseling visits were conducted. Germline testing was recommended by a certified genetic counselor if medically necessary. All patients with a germline CHEK2 mutation were identified (N = 16). Patients with a CHEK2 mutation and personal and family history of GI malignancies/polyposis were further explored and their clinical and molecualr characteristics are summarized. **Results:** The reasons for referral to the Cancer Genetics Counseling Services in patients with pathogenic CHEK2 mutations were personal history of colon cancer (N = 3) and family history of colon cancer (N = 4). One patient with the CHEK2 c.1100delC mutation had a personal history of juvenile polyposis syndrome and a family history of colon cancer. In our cohort, 11 out of 16 (69%) patients had a CHEK2 mutation and personal or family history of GI malignancies/polyposis. The median age was 57 years old (25-80). Six (55%) patients were males. All (100%) patients were Caucasians. Seven (64%) patients had a pathogenic germline CHEK2 mutation and 4 (36%) patients had a variant of unknown significance (VUS). Among patients with pathogenic germline CHEK2 mutations (N = 7), 5 (72%) patients had CHEK2 c.1100delC mutation, 1 (14%) patient had CHEK2 c.190G > A mutation and 1 (14%) patient had CHEK2 c.470T > C mutation. The CHEK2 VUS mutations seen in our cohort were CHEK2 c.539G > A, CHEK2 p.V395L, CHEK2 gain of exons 3-15 and CHEK2 c.1421G > A mutations. **Conclusions:** All patients in our cohort with CHEK2 mutations were Caucasians. The majority of our patients (69%) had an underlying personal or family history of GI malignancies/polyposis. In patients with personal or family history of GI malignancies/polyposis and CHEK2 mutation, 64% were found to have pathogenic CHEK2 mutations. The most common diagnosed CHEK2 mutation in our cohort was CHEK2 c.1100delC mutation. Research Sponsor: None.

45 Poster Session

Second primary cancers in patients with sporadic deficient mismatch repair (dMMR) colorectal cancer (CRC). *First Author: Ayman Alidina, Western Health, Melbourne, VIC, Australia*

Background: Patients with hereditary non polyposis colorectal cancer (HNPCC) diagnosed with CRC have an elevated risk of a second primary CRC (SPCRC) and of rapid primary cancer development. This informs both initial surgical approach and endoscopic surveillance intervals. A feature of HNPCC is dMMR, also found in 15% of sporadic CRC, where the risk of SPCRC has yet to be defined. **Methods:** We examined a multi-site comprehensive CRC database (Melbourne, Australia), where prospectively collected data includes family history (including HNPCC), histology, surgery performed and incidence of second primary cancer. Sporadic dMMR included any case with a BRAF V600E mutation, confirmed hypermethylation, negative germline testing, or age over 60 years. We explored the incidence and timing of SPCRC in patients with early stage sporadic dMMR (or MSI-H) versus pMMR cancers. **Results:** From February 2004 to December 2019, 7442 patients diagnosed with stage I-III CRC were recorded. MMR status was known in 4079 (54.8%), including 714 with dMMR colorectal cancer (17.4%) of which 575 (14.6%) were deemed sporadic dMMR. Sporadic dMMR patients were older (mean 76.2 years vs 65.9 years, p = < 0.001), more likely to be female (65.2% vs 42%, p = < 0.001) and have a right sided primary (80.9% vs 32.8%, p = < 0.001), compared to patients with pMMR CRC. A SPCRC was diagnosed in 11/575 patients (1.91%) with sporadic dMMR CRC versus 27/3365 (0.83%) patients with pMMR CRC (HR = 2.57, 95% CI 1.28 - 5.17, p = 0.008). Median time to SPCRC was 1.13 years vs 2.38 years (p = 0.49). The SPCRC diagnosed in sporadic dMMR CRC vs pMMR CRC were more likely to be dMMR ((72.7%) vs (25.9%), p = 0.03), but a similar number were stage I or II ((81.8%) vs (81.5%)) and a similar number were surveillance detected ((72.7%) vs (77.8%). **Conclusions:** Patients with sporadic dMMR appear to have a significantly elevated risk of SPCRC compared to the pMMR population and were diagnosed at a shorter interval. The SPCRC is also more likely to also be dMMR. Increased colonoscopic surveillance of patients presenting with an initial sporadic dMMR cancer should be considered where clinically appropriate. Research Sponsor: None.

46 Poster Session

The clinical and molecular characteristics of patients with personal history of colorectal cancer evaluated by cancer genetics counseling services. *First Author: Veena Krishnan, University of South Alabama, Mobile, AL*

Background: Genetic susceptibility to colorectal cancer (CRC) include well-defined hereditary syndromes such as Lynch Syndrome, Familial Adenomatous Polyposis syndrome (FAP), MUTYH-Associated Polyposis syndrome (MAP) and other less common syndromes. National Comprehensive Cancer Network (NCCN) guidelines recommend that individuals meeting certain criteria have detailed risk assessment and potential genetic testing. Here, we describe the clinical and molecular characteristics of patients with personal history of CRC evaluated by cancer genetics counseling services. **Methods:** This is an IRB-approved retrospective chart-review study. Between 2016 and 2020, 1011 unique genetic counseling visits were conducted. Germline testing was recommended by a certified genetic counselor if medically necessary. All patients with a personal history of CRC were identified (N = 52) and their clinical and molecular characteristics were summarized. **Results:** The median age is 50 years-old (29-82). Thirty-five (67%) patients were females. Caucasians, African Americans and other ethnic backgrounds represented 75%, 19% and 6% respectively. The primary tumor location was in the right colon, left colon and rectum in 29%, 37% and 27% of our cohort respectively. In 7%, the primary location of the tumor was not available. In our cohort, 11 out of 52 (21%) patients had a pathogenic germline mutation and 9 patients (17%) had a germline variant of unknown significance (VUS). Among patients with pathogenic germline mutations (N = 11), 4 patients had MSH2 mutations (MSH2 c.1759+1G > A, MSH2 c. 1687dupT, MSH2 c.1861C > T and MSH2 c.811_814delTCTG), 1 patient had a MSH6 mutation (MSH6 c.1012A > T), 1 patient had a PMS2 mutation (PMS2 c.2182_2184delACTinsG), 3 patients had CHEK2 mutations (CHEK2 c.1100delC and CHEK2 c.470T > C (p.I157T)), 2 patients had MUTYH mutations (MUTYH c.1187G > A and MUTYH c.536A > G) and 1 patient had a BRCA2 mutation (BRCA2 c.2808_2811delACAA). One patient had a CHEK2 and a MUTYH mutation. The VUS mutations in our cohort were POLE c.1645T > C, POLE c.5480C > T, c.2999G > A, MLH1 c.1628A > G, CTNNA1 c.503G > A, MSH2 c.128A > G, NBN c.16C > T, ATM c.6537T > G and AXIN2, BRCA1, NTHL1 mutations. **Conclusions:** In our cohort of patients with personal history of CRC, the majority of patients (62%) had negative germline testing. An underlying pathogenic germline mutation and VUS were identified in 21% and 17% of the patients respectively. Lynch Syndrome was the most commonly diagnosed hereditary CRC syndrome with 6 out of 11 patients found to have MMR germline mutations. Other pathogenic mutations were identified in the CHEK2, MUTYH and BRCA2 genes. Research Sponsor: None.

47 Poster Session

Germline testing of patients with personal history of colorectal polyposis by cancer genetics counseling services. *First Author: Gideon T Dosunmu, University of South Alabama Medical Center, Mobile, AL*

Background: National Comprehensive Cancer Network (NCCN) guidelines recommend that individuals with >10 adenomatous polyps, ≥2 hamartomatous polyps, or ≥5 serrated polyps proximal to the sigmoid colon have detailed risk assessment and potential genetic testing to rule out polyposis syndrome. Here, we describe germline testing of patients with a personal history of colorectal polyposis by Cancer Genetics Counseling Services. **Methods:** This is an IRB-approved retrospective chart-review study. Between 2016 and 2020, 1011 unique genetic counseling visits were conducted. Germline testing was recommended by a certified genetic counselor if medically necessary. All patients with a personal history of colorectal polyposis were identified (N=20) and their germline testing results were summarized. **Results:** The reasons for referral to the Cancer Genetics Counseling Services were personal history of >10 adenomatous polyps (N=13), personal and family history of colorectal polyposis (N=3), personal history of juvenile colorectal polyps (N=3) or personal history of ≥2 hamartomatous polyps (N=1). The median age is 58 years-old (1-84). Ten (50%) patients were females. Caucasians, African Americans and other ethnic backgrounds represented 80%, 10% and 10% respectively. In our cohort, 6 out of 20 (30%) patients had a pathogenic germline mutation, 5 (25%) patients had variant of unknown significance (VUS) and 9 (45%) patients had negative testing. Among patients with pathogenic germline mutations, 3 patients had a pathogenic APC mutation (APC c.1659G>A, APC c.2802C>A and APC c.1643dupT) and were diagnosed with Familial Adenomatous Polyposis (FAP). One patient had 2 pathogenic MUTYH mutations (MUTYH c.536A>G and MUTYH c.1187G>A) and was diagnosed with One patient had a pathogenic PTEN c.634+5G>A mutation and was diagnosed with PTEN Hamartoma Tumor Syndrome. Among the 3 patients with a personal history of juvenile colorectal polyps, one patient had a CHEK2 c.190G>A mutation while the other two had negative genetic test results. The VUS mutations in our cohort were MRE11A c.826C>T, BLM c.3478T>C, BRCA2 c.2519T>C, CHEK2 p.V395L and CTNNA1 c.392dupT. **Conclusions:** In our cohort of patients with personal history of colorectal polyposis, the majority of patients (45%) had negative germline testing. An underlying pathogenic germline mutation and VUS were identified in 30% and 25% of the patients, respectively. FAP Syndrome was the most commonly diagnosed hereditary polyposis syndrome with 3 patients found to have APC germline mutations. Other pathogenic mutations were identified in the MUTYH, PTEN and CHEK2 genes. Patients with MUTYH and PTEN mutations were diagnosed with MAP and PTEN Hamartoma Tumor Syndromes respectively. Research Sponsor: None.

49 Poster Session

Predictors of uptake of aspirin (ASA) chemoprevention in Lynch syndrome (LS). *First Author: Michael J. Hall, Fox Chase Cancer Center, Philadelphia, PA*

Background: Substantial data support efficacy of ASA in colorectal adenoma and cancer (CRC) chemoprevention. In 2011, the CaPP2 Phase 3 trial showed benefit of 600 mg ASA daily for prevention of LS-associated CRC (HR 0.41,p=0.02) in persons w/ASA adherence >2 yrs. Anecdotally, uptake of ASA by LS pts has been low, but few data exist. We examined uptake and predictors of ASA chemoprevention among LS pts receiving follow-up at our center since 2011. **Methods:** Pts evaluated by Fox Chase's Risk Assessment Program receive in-person medical recommendations and written information about cancer (CA) prevention measures including ASA. Medical records of 127 LS pts were retrospectively reviewed. Demographics, gene affected, personal Hx of CA, ASA use, and ASA dose were collected. Majority (94.5%) of cohort had documentation of ongoing LS endoscopic screening at our center—only 3.2% had no recent follow-up (past 3 yrs) and 2.4% had recently died (past 3 yrs). Chi-square tests and multivariable logistic regression were used in analyses. **Results:** Overall 24.4% (31/127) of pts reported ASA use for chemoprevention (see Table). Nearly half (48.4%) of ASA users took 81 mg ASA daily, and only 22.6% reported taking >600 mg ASA daily. ASA use was associated with older age, *MLH1/MSH2+* vs *MSH6/PMS2+*, and personal Hx of CRC. In the multivariable logistic model, older age (OR 2.80, p=0.04) and *MLH1/MSH2+* (OR 2.64,p=0.07) were significant and borderline significant, respectively. Adding race/ethnicity and gender strengthened the effect of age>60 (OR 3.11, p=0.03), and improved fit (pseudoR^2=16.8%). **Conclusions:** Uptake of ASA chemoprevention by LS pts is overall modest, but older age is associated with ASA uptake for chemoprevention. Among ASA users, fewer than 1 in 4 take the 600 mg daily dose shown effective in CaPP2. Confirmatory trials as well as efforts to elucidate barriers to ASA chemoprevention in LS are needed. Research Sponsor: None.

Univariate and multivariate predictors of aspirin uptake (n=127).

Univariate	N Total (%)	ASA use (%)	p
Age			
<40	28(22.1)	2(7.1)	**0.004**
>40-60	51(40.2)	10(19.6)	
>60	48(37.8)	19(39.6)	
Sex			
F	89(70.1)	18(20.2)	0.09
M	38(29.9)	13(34.2)	
Race/ethnicity			
Non-White and/or Hispanic	4(4.2)	4(12.9)	0.08
White non-Hispanic	92(95.8)	27(87.1)	
MMR gene			
MLH1	23(18.1)	8(34.8)	0.134[A]
MSH2	54(42.5)	16(19.6)	
MSH6	29(22.8)	3(10.3)	**0.03[B]**
PMS2	21(16.6)	4(19.1)	
Personal Hx of CRC			
N	90(70.9)	15(16.7)	**0.002**
Y	37(29.1)	16(42.3)	
Personal Hx of non-CRC LS-associated CA (those with history of CRC excluded)			
N	57 (63.3)	7 (12.3)	0.14
Y	33 (36.7)	8 (24.2)	
	OR	**95% CI**	**p**
Multivariable logistic model			
Age <40	0.33	0.06-1.77	0.20
Age >40 & <60	referent		
Age >60	3.11	1.15-8.38	**0.03**
Personal hx of CRC	1.67	0.61-4.57	0.32
F sex	0.55	0.20-1.55	0.26
***MLH1/MSH2* carrier (vs *MSH6/PMS2*)**	2.59	0.89-7.58	**0.08**
Non-White/Non-Hispanic race/ethnicity	2.85	0.59-13.74	0.19
PseudoR^2 (fit): 16.8% of variability explained			

A: p compares ASA use in all 4 genes B: p compares ASA use in *MLH1+MSH2* vs *MSH6+PMS2*

50 Poster Session

Development and clinical validation of a blood test for early detection of colorectal adenomas and cancer. *First Author: Shai Friedland, Stanford University Medical Center Gastroenterology and Hepatology, Stanford, CA*

Background: Many of the 50,000 annual colorectal cancer (CRC) deaths can be attributed to 1/3 eligible Americans not following screening guidelines or approximately 1/2 of the population not adherent to the follow-up post-polypectomy guidelines. The new understanding of the natural history and shared etiology of adenomas and CRC inform integration of clinically relevant biomarkers. The two objectives of CRC screening and surveillance are early detection to improve survival and prevention of CRC through removal of adenomas using colonoscopy. Adenomas account for 98% of actionable colonoscopies. Stool tests have low sensitivity for advanced adenomas (AA, 24-42%). **Methods:** A prospective, blinded study was conducted at the VA Palo Alto Health Care System. Patients had blood drawn prior to colonoscopy. The test analyzes two biomarkers: circulating gastrointestinal epithelial cells and somatic mutations of cell-free DNA. The probability of advanced neoplasia was obtained by ordinal/nominal logistic regression methods together with SEER-incidence rate and prior history of AA on a training set of 346 subjects. The cutpoint for the quantitative score was fixed and the remaining 112 subjects were tested. **Results:** Interim results for 458 patients with no prior diagnosis of colorectal cancer (CRC) are presented. The cohort included both screening (239) and surveillance (219) subjects. Indications for colonoscopy were 86% asymptomatic and 14% with symptoms or positive-FIT. Balanced distribution of roughly 3/4th subjects in each disease category were randomly selected for training and algorithm development and the remaining 1/4th subjects were used for validation. A cutpoint was selected to obtain a test specificity (non-neoplastic finding or negative colonoscopy) of 90% resulting in a sensitivity of 100% and 80.0% for detection of CRC and advanced neoplasia (AN = CRC+AA), respectively, on the training subjects. The area under the ROC curve is 0.91. Validation using the fixed cutpoint and 112 test subjects achieved 91.4% specificity and 100% and 75.0% sensitivity for CRC and AN. **Conclusions:** This blood test has high sensitivity for colorectal advanced neoplasia while retaining high specificity. The quantitative nature of the score has the potential to enable stratification of patients for screening or post-polypectomy surveillance colonoscopy. Research Sponsor: CellMax Life.

Study Results	# Subject Training	# Subject Validation	Training N = 346	Validation N = 112
Screening/Surveillance			176/170	63/49
			Sensitivity (95% CI)	
CRC	10	4	100% (72.3-100)	100% (51.0-100)
AA	50	16	76.0% (62.6-85.7)	68.8% (44.4-85.8)
Adenomas ≥ 1cm, high grade dysplasia, > = 25% villous				
Nonadv Adenoma	168	57	48.8% (41.4-56.3)	54.4% (41.6-66.6)
Advan Neoplasia (CRC+AA)	60	20	80.0% (68.2-88.2)	75.0% (53.1-88.8)
			Specificity (95% CI)	
All Negative (non-neoplastic finding + negative colonoscopy)	118	35	90.7% (84.1-94.7)	91.4% (77.6-97.0)

51 Poster Session

Evaluating adherence to post-treatment follow-up of colorectal cancer at a reference center in Mexico: A retrospective analysis. *First Author: Jorge Humberto Hernandez-Felix, Universidad Autonoma de Coahuila, Torreon, Mexico*

Background: Adequate post-treatment surveillance for colorectal cancer (CRC) is recommended by all major societies with the intention to improve overall survival. However, compliance is variable and has not been studied in our country. Our aim was to evaluate the adherence to post-treatment surveillance NCCN guidelines for CRC at our Institution in Mexico City. **Methods:** We retrospectively reviewed charts from patients with stage I-III CRC who were diagnosed between January 2014 and December 2016. Adherence to surveillance was evaluated for the first 3 years after completion of oncologic treatment or until recurrence, whichever came first. We used an adherence composite definition previously defined by Cooper *et al*, where adequate compliance with guidelines was considered if patients had ≥2 physician visits per year for 3 years, ≥2 CEA tests per year for 2 years, and at least one colonoscopy in the 3-years surveillance period. **Results:** We included 90 patients. Mean age at diagnosis was 62 ± 12.5 years, 53% (n=48) were male, 68% (n=62) had colon cancer and 31% (n=28) rectal cancer. According to AJCC7 19% (n=17) were Stage I, 39% (n=35) II, and 42%(n=38) III. Median score for Charslon index at diagnosis was 4 (IQR 3-6). Results of follow-up adherence are presented in Table. Just 12% (n=11) of patients had a PET/CT or any other non-indicated imaging study for surveillance. Recurrence rate at the 3rd year of surveillance was 6.6% (n=6). A bivariate analysis was performed to find clinical and demographic factors associated to adherence and individual components of surveillance, we did not find any significative association. **Conclusions:** At our institution compliance with follow-up guidelines for CRC is good and higher than reported by other centers, though individual components have a decreasing trend in adherence every year. This could be explained because in our Institution cancer surveillance is performed by a medical oncologist. The main limitation of our study is that it involves an individual reference center in Mexico; thus, extrapolating data may not be feasible. Research Sponsor: None.

Surveillance Year	1 n=90 (%)	2 n=86 (%)	3 n=84 (%)	3y Overall n=90 (%)
Medical Visits[1]	82 (91.1)	71 (77.8)	61 (72.6)	63 (70)
CEA[1]	77 (85.6)	67 (74.4)	53 (58.9)	53 (58.9)
Colonoscopy[2]	79 (87.8)	NA	NA	83 (92.2)
TC[3]	62 (68.9)	55 (61.1)	49 (54.4)	33 (36.7)
Composite adherence	NA	NA	NA	49 (54.4)

1: ≥2 per year 2: Done between 6-18 months after surveillance started 3: ≥1 per year

52 Poster Session

Examining patterns of and reasons for delays to treatment in colon cancer. *First Author: Ali Kalam, Albert Einstein College of Medicine, Bronx, NY*

Background: Delays in colon cancer (CC) treatment can impact patient outcomes. Detailed examination into the patterns and reasons for delay in the diagnostic and pre-treatment work up are understudied, hindering the development of strategies to improve timeliness of care. **Methods:** CC patients diagnosed at an urban academic institution in 2018 were investigated. Chart review yielded presentation location, diagnostic-work up, treatment and patient characteristics. Time between presentation to the healthcare provider to treatment initiation of ≥ 60 days was considered a delay (Total_Delay). Total time further examined as 3 phases: presentation to diagnosis (PtoD), diagnosis to staging completion (DtoS), and staging completion to treatment (StoT). Delays for each phase was defined as ≥ 30 days. Total_Lt60d vs non-Total_Ge60d were compared. A logistic regression model was used to calculate odds ratio (OR) and 95% confidence intervals (CI) to identify associations with Total_Ge60d. **Results:** Among 121 CC patients, the median time and interquartile range (IQR) between presentation and treatment initiation was 29 (IQR 8, 53) days. Total_Delay occurred in 21% of patients. The median time between presentation and treatment and interquartile range (IQR) for Total_Delay was 106 (IQR 82, 162) and 16 (IQR 6, 39) for non-Total_Delay. Age, sex, race, and comorbidities were similar between Total_Delay and non-Total_Delay. Total_Delay patients were generally more functionally independent (92% vs 74%, $p < .06$), presented to locations other than the emergency department (64% vs 42%, $p < .075$) and were less likely to have hospital admission work-up (20% vs 60%, $p < .001$) compared to non-Total_Delay. The logistic model showed that Total_Delay is associated with non-hospital work-up (OR 8.3, 95% CI 1.9-45.3), adjusting for comorbidities, symptoms, functional status, cancer severity, and insurance. Delays similarly occurred in all three phases for Total_Delay patients; 48% had delay during PtoD, 60% during DtoS, and 48% during StoT. The most common reason for delay by phase was the following; in the PtoD phase, 5 of 11 (46%) was due to obtaining endoscopy, in DtoS and StoT, 6 of 15 (40%) and 5 of 11 (46%), respectively, was in getting outpatient specialty appointments. Delays due to patient factors (PtoD 18%, DtoS 27%, StoT 28%) were less frequent. **Conclusions:** Delays to treatment for CC are largely driven by health systems delays. Bundling of diagnostic evaluation and pre-treatment that mimics work-up during a hospital admission may overcome delays in cancer care. Research Sponsor: None.

53 Poster Session

Adherence to clinical practice guidelines for adjuvant chemotherapy for colorectal cancer in Uruguay: A population-based study. *First Author: Santiago Fontes, Servicio de Oncología Clínica, Hospital De Clínicas, Universidad de la República, Montevideo, Uruguay*

Background: Despite surgery, the 5-year risk of systemic recurrence of colorectal cancer (CRC) in the absence of any further therapy is approximately 50 % for those with lymph node involvement and 20—30 % if the lymph nodes are negative. Adjuvant chemotherapy contributes to improved disease-free and overall survival for node-positive (stage III) or high-risk node negative (stage IIB) colon cancer. Similar benefits are observed for adjuvant chemoradiotherapy in rectal cancer. Previous research shows varied rates of adherence to published adjuvant chemotherapy Clinical Practice Guidelines (CPGs) for CRC, although population-based data is scarce. Purpose: The aim of this analysis was to assess adherence rates to adjuvant chemotherapy prescription within 16 weeks of surgery according to local and international CPGs for CRC patients treated with curative intent between 2008 and 2019 at the Uruguayan National Cancer Institute. Data regarding factors associated with chemotherapy receipt beyond 16 weeks from surgery and chemotherapy non receipt was also retrieved and analysed. **Methods:** We retrospectively reviewed medical and pathology reports of 833 patients diagnosed with CRC at our institution. Patients with stages IIB or III CRC who underwent curative-intent surgery were identified and included in the present analysis. A 16-week benchmark timeline for treatment initiation from date of surgery was considered. Fisher's exact test was used to determine factors independently associated with receipt of chemotherapy and meeting the 16-week benchmark (p 0.05). **Results:** A total of 400 patients were identified of which 72% had peritoneal colorectal tumors and 28% had sub-peritoneal rectal tumors. Approximately 70% of the latter group received neo-adjuvant chemo-radiotherapy. Considering the total cohort, 61% received adjuvant chemotherapy. Factors predicting chemotherapy receipt in the peritoneal colorectal group were age $\leq$ 70 and stage III disease. In the sub-peritoneal rectal group no significant effect was found. The 16-week benchmark was met in 72% (175) of those receiving chemotherapy and 70.6% (167) completed 6 months of systemic adjuvant treatment. A total of 156 patients (39%) did not receive adjuvant chemotherapy. The factors predicting chemotherapy non receipt were age $>$ 70 and stage IIB in the peritoneal colorectal group. **Conclusions:** This analysis of adherence to CPGs identified several factors associated with chemotherapy non receipt and chemotherapy receipt outside of timeline benchmarks from date of curative-intent surgery in Montevideo, Uruguay. The two main factors significantly associated with chemotherapy non receipt were advanced age and lower disease stage. To our knowledge, our data is the first to elucidate these specific factors in the Uruguayan CRC patient population. Research Sponsor: None.

54 Poster Session

Clinician perspectives on preemptive pharmacogenetic testing to guide chemotherapy dosing in patients with gastrointestinal malignancies. *First Author: Kelsey S. Lau-Min, Division of Hematology/Oncology, Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA*

Background: Pharmacogenetic (PGx) testing for germline variants in the *DPYD* and *UGT1A1* genes can be used to guide fluoropyrimidine and irinotecan dosing, respectively. Despite the known association between PGx variants and chemotherapy toxicity, preemptive testing prior to chemotherapy initiation is rarely performed in routine practice. **Methods:** We conducted a multi-site mixed-methods study to understand clinician attitudes toward PGx testing and to identify facilitators and barriers to using preemptive testing to guide chemotherapy dosing in patients with gastrointestinal malignancies. Each participant completed a demographic survey and semi-structured interview informed by the Consolidated Framework for Implementation Research. Interviews were analyzed using a modified grounded theory approach. **Results:** A total of 16 medical oncologists and 9 oncology pharmacists from one academic medical center and two community hospitals participated. Fifteen (60%) participants reported feeling comfortable or very comfortable with interpreting PGx test results. While clinicians expressed generally favorable attitudes toward PGx testing, many were hesitant to use it to preemptively guide chemotherapy dosing due to a perceived lack of evidence for this practice. They cited a lack of consensus chemotherapy dosing recommendations in response to PGx test results, as well as concerns about decreased drug efficacy, especially in patients treated with curative intent. Additional barriers included 1) a low prevalence of actionable PGx variants; 2) lengthy PGx test turnaround time; 3) concerns about testing costs and lack of insurance coverage; and 4) burdensome integration of PGx testing into clinical workflows. The electronic health record emerged as a potential tool for the unobtrusive integration of PGx testing into clinical practice–suggested applications included default PGx test orders for eligible patients, discrete reporting of PGx variant results, and clinical decision support to guide subsequent chemotherapy dosing. **Conclusions:** Successful adoption of preemptive PGx-guided chemotherapy dosing in patients with gastrointestinal malignancies will require a multi-level effort to demonstrate clinical effectiveness while addressing the contextual factors identified in this study. The electronic health record should be explored as a tool to integrate PGx testing into routine practice. Research Sponsor: Penn Center for Precision Medicine Implementation Grant.

55 Poster Session

Cost effectiveness of *DPYD* genotyping to screen for dihydropyrimidine dehydrogenase (DPD) deficiency prior to adjuvant chemotherapy for colon cancer. *First Author: Gabriel A. Brooks, Norris Cotton Cancer Center, Lebanon, NH*

Background: Fluoropyrimidine chemotherapy agents, including 5-fluorouracil and capecitabine, are the backbone of adjuvant treatment for colon cancer, and adjuvant chemotherapy substantially reduces recurrence and mortality after surgical resection of stage 3 colon cancer. While fluoropyrimidine chemotherapy is generally safe, the risk of severe, potentially fatal chemotherapy toxicity is substantially increased for the 2-3% of U.S. patients with DPD deficiency caused by pathogenic variants in the *DPYD* gene. *DPYD* genotype testing is readily available in the U.S. but has not been widely adopted. We evaluated the cost effectiveness of *DPYD* genotyping prior to adjuvant chemotherapy for colon cancer in the U.S. **Methods:** We constructed a Markov model to simulate screening for DPD deficiency with *DPYD* genotyping (versus no screening) among patients receiving fluoropyrimidine-based adjuvant chemotherapy for stage 3 colon cancer. Screen-positive patients were modeled to receive dose-reduced fluoropyrimidine chemotherapy. Model transition probabilities for treatment-related toxicities were derived from published clinical trial data with annotation of *DPYD* genotype and chemotherapy dosing strategy. Our analysis is from the healthcare perspective, with a time horizon of five years and an annual discount rate of 3% for future costs and benefits. Direct healthcare costs and health utilities were estimated from published sources and converted to 2020 US dollars, and post-treatment survival was modeled from SEER data. The primary outcome was the incremental cost-effectiveness ratio (ICER), defined as dollars per quality-adjusted life year (QALY). We used a value of $100,000/QALY as the cost-effectiveness threshold. One-way sensitivity analyses were used to examine model uncertainty. **Results:** Compared with no screening, screening for DPD deficiency with *DPYD* genotyping increased per-patient costs by $106 and improved quality-adjusted survival by 0.0028 QALYs, leading to an ICER of $37,300/QALY. In one-way sensitivity analyses, the ICER exceeded $100,000/QALY when the carrier frequency of pathogenic *DPYD* gene variants was less than 1.17%, and when the specificity of *DPYD* genotyping was less than 98.9%. Cost-effectiveness estimates were not sensitive to the cost of *DPYD* genotyping, the cost of toxicity-related hospitalizations, or the health utility associated with grade 3-4 toxicity. **Conclusions:** Among patients receiving adjuvant chemotherapy for stage 3 colon cancer, screening for DPD deficiency with *DPYD* genotyping is a cost-effective strategy for preventing infrequent but severe, sometimes fatal toxicities of fluoropyrimidine chemotherapy. Research Sponsor: U.S. National Institutes of Health.

56 Poster Session

Change in skeletal muscle index and its prognostic significance in conversion therapy for initially unresectable colorectal cancer. *First Author: Hiroaki Nozawa, Department of Surgical Oncology, The University of Tokyo, Tokyo, Japan*

Background: Systemic chemotherapy can cause loss of skeletal muscle mass in colorectal cancer (CRC) patients in the neoadjuvant and palliative settings. However, it is largely unknown how the body composition is changed by chemotherapy rendering unresectable CRC to resectable disease or how it affects the prognosis. This study aimed at elucidating the effects of systemic chemotherapy on skeletal muscles and survival in stage IV CRC patients who underwent conversion therapy. **Methods:** We reviewed 98 stage IV CRC patients who received systemic chemotherapy in our hospital. According to the treatment setting, patients were divided into the 'Conversion', 'Neo-adjuvant chemotherapy (NAC)', and 'Palliation' groups. The cross-sectional area of skeletal muscles at the third lumbar level and changes in the skeletal muscle index (SMI), defined as the area divided by height squared, during chemotherapy were compared among patient groups. The effects of these parameters on prognosis were analyzed in the Conversion group. **Results:** The mean SMI increased by 8.0% during chemotherapy in the Conversion group (n = 38), whereas it decreased by 6.2% in the NAC group (n = 18) and 3.7% in the Palliation group (n = 42, $p < 0.0001$). Moreover, patients with increased SMI during chemotherapy had a better overall survival (OS) than those whose SMI decreased in the Conversion group (p = 0.021). The increase in SMI was an independent predictor of favorable OS on multivariate analysis (hazard ratio: 0.26). **Conclusions:** Stage IV CRC patients who underwent conversion to resection often had an increased SMI. As such an increase in SMI further conveys a survival benefit in conversion therapy, it may be important to make efforts to preserve muscle mass by meticulous approaches, such as nutritional support, muscle exercise programs, and pharmacological intervention even during chemotherapy in patients with metastatic CRC. Research Sponsor: C: grant number; 18K07194, C: grant number; 19K09114, C: grant number; 19K09115, and Challenging Research (Exploratory): grant number: 20K21626.

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Quadruplet regimen with capecitabine, irinotecan, oxaliplatin, and bevacizumab in chemo-naive patients with metastatic colorectal cancer: Results from the safety lead-in of QUATTRO-II study. *First Author: Hideaki Bando, Department of Clinical Oncology, Aichi Cancer Center Hospital, Nagoya, Japan*

Background: FOLFOXIRI plus bevacizumab (BEV) is regarded as the standard of care for selected patients (pts) with metastatic colorectal cancer (mCRC), despite the high incidence of neutropenia and diarrhea. The AXEPT phase III study showed that the modified capecitabine (CAP) + irinotecan (IRI) + BEV (CAPIRI+BEV) [CAP 1600 mg/m^2, IRI 200 mg/m^2, and BEV 7.5 mg/kg q3wk] treatment was non-inferior to FOLFIRI+BEV, with a lower incidence of hematologic toxicity. We hypothesized that the modified CAPIRI combined with oxaliplatin (OX) and BEV (CAPOXIRI+BEV) would be more feasible than FOLFOXIRI+BEV, without compromising efficacy. **Methods:** The QUATTRO-II study is an open-label, multicenter, randomized phase II study. In Step 1, the recommended doses (RD) of OX and IRI were investigated as a safety lead-in. In Step 2, pts are randomized to either the RD of CAPOXIRI+BEV or FOLFOXIRI+BEV. In Step 1, four dose levels of CAPOXIRI (fixed dose of CAP 1600 mg/m^2 and BEV 7.5 mg/kg plus escalated or de-escalated doses of OX and IRI, q3wk) were investigated in a 3+3 manner. A dose level of $\leq$ 2/6 of dose-limiting toxicity (DLT) cases was expected as the RD. **Results:** A total of 9 pts (3 at Level 0, 6 at Level 1) were included in Step 1. The baseline characteristics were as follows: the median age was 62 years; 6 were male; 6 presented with a left-sided tumor; 8 had a performance status of 0; all wild type/*RAS* mutant/*BRAF* V600E mutant were 8/1/0; and UGT1A1 wild type/*6 single hetero/*28 single hetero were 7/0/2. In Level 0 (IRI 200 mg/m^2, OX 100 mg/m^2), one grade 4 neutropenia and one grade 3 anorexia were observed, but without DLT. In Level 1 (IRI 200 mg/m^2, OX 130 mg/m^2), two grade 4 neutropenia and one grade 3 colitis were observed, with 1 DLT (febrile neutropenia) case, fully recovered without G-CSF administration. No treatment-related deaths were observed. Although dose modifications were needed in 4 of the 6 pts, no further safety concerns related to treatment continuity were observed in the 2nd or subsequent cycles. Thus, we determined that the dose administered in Level 1 is the RD for Step 2. According to the preliminary efficacy results at 8 weeks after initiating study treatment, 6 pts achieved a partial response (2 in Level 0 and 4 in Level 1). **Conclusions:** The RD of CAPOXIRI+BEV was 200 mg/m^2 IRI, 130 mg/m^2 OX, 1600 mg/m^2 CAP, and 7.5mg/kg BEV. The randomized phase II Step (Step 2) of QUATTRO-II is ongoing. Clinical trial information: NCT04097444. Research Sponsor: Chugai pharmaceutical.

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Subgroup analyses of patients (pts) with microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC) treated with nivolumab (NIVO) plus low-dose ipilimumab (IPI) as first-line (1L) therapy: Two-year clinical update. *First Author: Heinz-Josef Lenz, USC Norris Comprehensive Cancer Center, Los Angeles, CA*

Background: In the phase 2 CheckMate 142 trial, NIVO + low-dose IPI had robust, durable clinical benefit and was well tolerated as 1L therapy for MSI-H/dMMR mCRC (median follow-up, 29.0 months [range, 24.2–33.7]) (Lenz et al. *J Clin Oncol* 2020;38:Abstract 4040; NCT02060188). Objective response rate (ORR) per investigator (INV) was achieved in 69% of pts (95% CI, 53–82); progressive disease rate was 13%. Median progression-free survival (PFS) and overall survival (OS) were not reached. Median duration of treatment was 19.1 months (95% CI, 11.1–29.0). Grade 3–4 treatment-related adverse events (TRAEs) occurred in 22% of pts. We present the post hoc subgroup analyses of efficacy and safety outcomes in pts from the same follow-up based on demographics and baseline disease characteristics. **Methods:** Pts with MSI-H/dMMR mCRC and no prior treatment for metastatic disease received NIVO 3 mg/kg Q2W + low-dose IPI 1 mg/kg Q6W until disease progression or discontinuation. ORR (primary endpoint, RECIST v1.1) and PFS were assessed per INV. Post hoc subgroup analyses of efficacy (by ECOG performance status [PS], stage at initial diagnosis, primary tumor location, and *BRAF/KRAS* mutation status) and safety (by age and ECOG PS) are presented. **Results:** Among 45 treated pts, efficacy (Table) and safety were generally consistent across evaluated subgroups. ORR was similar in pt subgroups by *BRAF/KRAS* mutation status, stage at initial diagnosis, primary tumor location, and ECOG PS (Table). Median PFS and OS were not reached (NR) in evaluated subgroups after a minimum follow-up of 24.2 months (Table). Incidence of grade 3–4 TRAEs for subgroups by age and ECOG PS were consistent with the overall population. **Conclusions:** NIVO + low-dose IPI demonstrated robust, durable clinical benefit; was well tolerated with 2-year follow-up; and was consistent in evaluated subgroups in 1L MSI-H/dMMR mCRC. Clinical trial information: NCT02060188. Research Sponsor: Bristol Myers Squibb.

Efficacy.

Overall (N = 45)	ORR, n (%) 31 (69)	Median PFS (95% CI), months NR (NE)	Median OS (95% CI), months NR (NE)
Mutation status[a]	8 (62)	NR (1.4-NE)	NR (24.2-NE)
***BRAF/KRAS*wild type (n = 13)**	13 (76)	NR (19.8-NE)	NR (19.8-NE)
***BRAF*mutant (n = 17)**	8 (80)	NR (11.1-NE)	NR (NE)
***KRAS*mutant (n = 10)**			
Initial diagnosis stage[b]	19 (68)	NR (NE)	NR (NE)
II-III (n = 28)	12 (71)	NR (1.6-NE)	NR (24.2-NE)
IV (n = 17)			
ECOG PS	17 (68)	NR (NE)	NR (NE)
0 (n = 25)	14 (70)	NR (1.6-NE)	NR (16.0-NE)
1 (n = 20)			
Primary tumor location[c]	10 (67)	NR (4.0-NE)	NR (8.1-NE)
Left-sided (n = 15)	19 (73)	NR (NE)	NR (NE)
Right-sided (n = 26)			

Median follow-up = time on study from first dose to data cutoff (29.0 months [range, 24.2-33.7])

[a]Excluded 5 pts with unknown mutation status.

[b]All pts had stage IV disease at study entry.

[c]Excluded 4 pts with uncategorized primary tumor location.

NE, not estimable.

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Final results of the ACTS-CC 02 trial: A randomized phase III trial of S-1/oxaliplatin (SOX) versus UFT/leucovorin as adjuvant chemotherapy for high-risk stage III colon cancer. *First Author: Naohiro Tomita, Division of Lower GI Surgery, Department of Surgery, Hyogo College of Medicine, Hyogo, Japan*

Background: As previously reported (Sunami E, et al. *Clin Colorectal Cancer*. 2020), the ACTS-CC 02 trial demonstrated that S-1 and oxaliplatin (SOX) was not superior to UFT/leucovorin (LV) in terms of disease-free survival (DFS) as adjuvant chemotherapy for high-risk stage III colon cancer (any T, N2, or positive nodes around the origin of the feeding arteries). We now report the final overall survival (OS) after a median follow-up of more than 6 years. **Methods:** A total of 966 patients with high-risk stage III colon cancer were randomly assigned to receive either UFT/LV (300–600 mg/day of UFT 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/m^2 of oxaliplatin on day 1 and 80–120 mg/day of S-1 according to BSA on days 1-14, every 21 days, 8 courses). The primary endpoint was DFS. Patients' data were updated in February 2020. **Results:** The subjects of this final efficacy analysis were 955 patients (478 in the UFT/LV group and 477 in the SOX group). Totally, Stage IIIA/IIIB/IIIC were 1.3%/50.2%/48.6% and T1/2/3/4 were 1.5%/4.0%/61.8%/32.7%. With median follow-up time of 74.3 months, the 5-year OS rate was 78.3% in the UFT/LV group and 79.1% in the SOX group (HR: 0.97; 95% CI: 0.76-1.24; p = 0.8175). The 5-year DFS rate was 55.2% in the UFT/LV group and 58.1% in the SOX group (HR: 0.92; 95% CI: 0.76-1.11; p = 0.3973). In an exploratory analysis, the 5-year OS rate in patients with T4 disease was 65.2% and 70.8% in the UFT/LV group and SOX group, respectively (HR: 0.81; 95% CI: 0.56-1.17), and the 5-year DFS rate was 45.4% and 50.5% (HR: 0.87; 95% CI: 0.65-1.19), respectively. Notably, in patients with T4N2b disease, the 5-year OS rate was 51.0% and 64.1% in the UFT/LV group and SOX group, (HR: 0.72; 95% CI: 0.40-1.31) and the 5-year DFS rate was 31.1% and 37.2% (HR: 0.87; 95% CI: 0.50-1.31), respectively. **Conclusions:** In Japanese patients with high-risk stage III colon cancer, the 5-year OS rate was similar in the UFT/LV group and SOX group. However, the oxaliplatin-based regimen was suggested to be more effective for DFS and OS in patients with advanced disease, such as T4N2b. Clinical trial information: JapicCTI-101073. Research Sponsor: Taiho Pharmaceutical Co, Ltd.

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Clinicopathological characteristics and impact on efficacy of three versus six months of adjuvant chemotherapy in early-onset colon cancer: ACHIEVE and ACHIEVE-2 trials. *First Author: Eiji Oki, Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan*

Background: Colorectal cancer (CRC) incidence and mortality have decreased since the 1970s but several data such as the SEER CRC registry show that the incidence of early onset colon cancer (eoCC, age 20-49) and RC keep increasing. There is limited results suggesting eoCC may have different behaviors compared to traditional CC (tCC, age $\geq$ 50). **Methods:** Individual patient data of 1,805 high-risk stage II/III colon cancer (CC) patients (pts) as the modified ITT population in ACHIEVE and ACHIEVE-2 trials were investigated. Clinicopathological features and treatment-related data were assessed by age group. Disease-free survival (DFS) was assessed by Kaplan-Meier curves and Cox multivariable models adjusted by trials, regimen, T and N. **Results:** Of the 1,805 pts, eoCC were 155 pts (8.6%). Using 5% difference between age groups as clinically meaningful cutoff, eoCC had similar gender (female, 52 vs 48%), PS (PS = 1, 1 vs 4%), risk group (high-risk, 43 vs 42%) and T stage (T4, 30 vs 30%) as tCC, while eoCC were less likely right-sided colon primary (32 vs 39%), had N1 disease (48 vs 54%), and treated by FOLFOX (16 vs 23%). Overall, eoCC significantly had a worse DFS than tCC (3y-DFS, 75 vs 82%; Adjusted Hazard Ratio = 1.40: 95% Confidence Interval, 1.00-1.95: p= 0.0478); in addition, similar DFS were observed among tCC pts (age 50-69 vs >70). eoCC experienced less neutropenia, thrombocytopenia and stomatitis, but had more diarrhea, nausea and/or vomiting. There were 38 and 297 pts with an initial relapse in eoCC and tCC, respectively. Of those, peritoneal metastases were more frequently seen in eoCC (n = 13, 34%) than in tCC (n = 63, 21%) (p = 0.097), whereas liver and lung metastases were similar between the two groups. Impact on DFS of 3 versus 6 months of adjuvant chemotherapy in eoCC (3y-DFS, 75% vs 76%) is similar to that in tCC (83% vs 81%). **Conclusions:** eoCC had unique characteristics; the difference in DFS between eoCC and tCC were potentially due to a different metastatic spread. eoCC had a different adverse event profile compared to tCC. No impact on DFS of treatment duration in eoCC was suggested. Clinical trial information: UMIN000013036. Research Sponsor: Yakult Honsha.

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Tissue and plasma tumor mutation burden (TMB) as predictive biomarkers in the CO.26 trial of durvalumab + tremelimumab (D+T) versus best supportive care (BSC) in metastatic colorectal cancer (mCRC). *First Author: Jonathan M. Loree, BC Cancer, Vancouver, BC, Canada*

Background: Pembrolizumab was recently granted tissue agnostic FDA accelerated approval for metastatic cancers with TMB≥10 mut/Mb. However, limited data supports immunotherapy in microsatellite stable (MSS) mCRC with TMB≥10 mut/Mb. We assessed tissue TMB and contrasted it to plasma derived TMB in the CO.26 trial. **Methods:** CO.26 was a phase 2 trial (2-sided α = 0.1 and 80% power) that randomized 180 patients (pts) 2:1 to D+T or BSC in refractory mCRC. Pre-treatment plasma was sequenced with the GuardantOMNI assay and archival tissue underwent exome sequencing with TMB assessed per the TMB harmonization project. MSI-H cases were excluded. For plasma TMB, we used a previously published cut point (≥28). **Results:** Overall survival (OS) but not progression free survival (PFS) was improved with D+T in the entire population. Of 180 pts, 163 were evaluable for plasma and 110 for tissue TMB. Median time between archival tissue and plasma collection was 3.1 yrs (IQR 1.9-5.1). Median tissue TMB was 6.6 muts/Mb (IQR 4.1-12.0), while median plasma TMB was 16.3 muts/Mb (IQR 9.4-25.9). Tissue and plasma TMB (r = -0.039, P = 0.69) were not correlated. Tissue TMB≥10 was not prognostic in the BSC arm (HR 1.01, 90%CI 0.52-1.92, P = 0.99) and OS was not improved in pts with tissue TMB≥10 (32/110 pts) following D+T vs BSC. A test of interaction suggested this threshold was not predictive (P = 0.85). Using a minimum P-value approach, no threshold supported high tissue TMB as predictive in MSS mCRC. In fact, the optimal cut point suggested low tissue TMB (< 4.1 muts/Mb) had the greatest benefit from D+T (P-interaction = 0.048) and pts with TMB ≥4.1 mut/Mb (HR 0.50, 90%CI 0.26-0.96, P = 0.083) trended to better OS in the BSC arm. In contrast, 35/163 pts (21%) were identified in a high plasma TMB group associated with worse OS (HR 2.56, 90%CI 1.45-4.54, P = 0.007) in the BSC arm but improved OS following D+T compared to BSC with P-interaction = 0.082. Only 1 response was noted following D+T in a pt with tissue TMB = 16 mut/Mb and plasma TMB = 13 mut/Mb. **Conclusions:** Archival tissue TMB≥10 mut/Mb does not appear predictive of D+T benefit in MSS mCRC. Plasma derived TMB may better reflect evolutionary changes following intervening therapy than archival tissue. Clinical trial information: NCT02870920. Research Sponsor: AstraZeneca, Canadian Cancer Society.

Group	OS HR (90% CI, P)	PFS HR (90% CI, P)
All Pts	0.73 (0.55-0.97, P = 0.07)	1.01 (0.76-1.34, P = 0.97)
FDA Pembrolizumab Tissue Cut Point		
Tissue TMB ≥10 mut/Mb	0.54 (0.27-1.09, P = 0.14)	0.87 (0.44-1.71, P = 0.73)
Tissue TMB < 10 mut/Mb	0.63 (0.42-0.94, P = 0.060)	0.88 (0.59-1.32, P = 0.61
Exploratory Minimum P-value Tissue Cut Point		
Tissue TMB ≥4.1 mut/Mb	0.73 (0.49-1.09, P = 0.20)	1.02 (0.69-1.52, P = 0.94)
Tissue TMB < 4.1 mut/Mb	0.35 (0.17-0.72, P = 0.017)	0.39 (0.18-0.82, P = 0.038)
Plasma		
Plasma TMB ≥28 mut/Mb	0.34 (0.18-0.63, P = 0.004)	0.72 (0.39-1.32, P = 0.37)
Plasma TMB < 28 mut/Mb	0.72 (0.51-1.02, P = 0.12)	0.97 (0.69-1.36, P = 0.88)

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Phase I dose-escalation study of MCLA-158, a first-in-class bispecific antibody targeting EGFR and LGR5, in metastatic colorectal cancer (CRC). *First Author: Guillem Argiles, Vall d'Hebron University Hospital and Institute of Oncology (VHIO), CIBERONC, TTD Group, Barcelona, Spain*

Background: The WNT and EGFR signaling pathways are oncogenic and mitogenic drivers in CRC and other cancers. MCLA-158 is an ADCC enhanced human IgG1 cLC bispecific antibody identified from functional screening of CRC patient (pt)-derived organoids (PDO). MCLA-158 exposure leads to EGFR degradation in LGR5+ cancer and exhibits potent growth inhibition of *RASmut* and *wt* CRC PDOs, while minimal inhibition is observed in non-tumoral PDOs. Blockade of metastasis initiation was seen in preclinical *in vivo* models. MCLA-158 also demonstrated tumor regression or stasis in esophageal squamous (6/6) and gastric adenocarcinoma (6/8) PDX models selected for LGR5 and EGFR expression. **Methods:** Metastatic CRC pts progressing after oxaliplatin, irinotecan and fluoropyrimidines, and EGFR monoclonal antibodies if *RASwt*, received MCLA-158 IV every 2 weeks (q2w; 4-week cycle) in a phase I study. Safety, efficacy (per RECIST 1.1), PK and ADA were assessed. WNT and EGFR pathway components were evaluated in tumor tissue. EGFR pathway mutations (ctDNA) and soluble EGFR (sEGFR) were assessed in blood. PDOs were derived from baseline biopsies and assessed for MCLA-158 responsiveness. **Results:** As of 7 September 2020, 33 pts were treated over 11 dose levels (5 to 1500 mg, flat dose). At enrollment, median age was 58 years (range 35-76), ECOG PS 0/1: 22/11, and 15 pts were *RASmut*. Pts had a median of 3 metastatic sites (range 1-12) with a median of 4 prior lines of therapy (range 1-10). A median of 2 MCLA-158 cycles (range 1-6) were administered. No dose limiting toxicity occurred. Infusion-related reactions were the most common AEs (67% of pts), occurred mostly in cycle 1 (21/22 pts), and were manageable. Other common related AEs included rash acneiform (36%), diarrhea (15%), pyrexia (9%) and asthenia/fatigue (9%). Related AEs were mostly mild or moderate; G3 related AEs were IRRs (4 pts; 12%), diarrhea and hypophosphatemia (1 pt each). The RP2D (1500 mg) was selected based on safety, PK and receptor occupancy prediction. MCLA-158 exhibited target-mediated clearance with proportional PK from 750 mg ($t_{1/2}$ ~80 h at 1500 mg). Low ADA titers were seen in 3/23 pts, with no effect on PK. Target saturation is predicted at steady state serum trough levels. No clinical responses were observed during dose escalation. No/low baseline tumor EGFR expression (0-1+ IHC) was observed in 17/30 pts and non-elevated sEGFR levels (< 4 ng/mL) in 18/22 pts. More than 1 activating mutation in EGFR signaling pathway genes were identified in ctDNA from 10/20 pts. 1/4 PDOs had > 30% growth inhibition with MCLA-158 ex vivo. MCLA-158 activity on PDOs correlated negatively with the presence of *EGFR* pathway resistance-mutations. **Conclusions:** Dual EGFR/LRG5 blockade with MCLA-158 was well tolerated, and the RP2D was 1500 mg IV q2w. Enrollment of pts with gastric and other non-CRC cancers at the RP2D continues in the expansion phase. Clinical trial information: NCT03526835. Research Sponsor: Merus NV.

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Short-course radiotherapy and subsequent CAPOX plus camrelizumab followed by delayed surgery for locally advanced rectal cancer: Short-term results of a phase II trial. *First Author: Zhenyu Lin, Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China*

Background: Chemoradiotherapy followed by radical surgery is standard treatment for patients with locally advanced rectal cancer (LARC). Short-course radiotherapy (SCRT), either with immediate or delayed surgery, provides similar oncological results compared with long-course radiotherapy with delayed surgery. Delayed surgery with the addition of neoadjuvant immunotherapy may bring better down-staging effect and minimize the risk of distant relapse. We conducted this single-arm phase 2 trial to investigate the efficacy and safety of SCRT combined with subsequent capecitabine and oxaliplatin (CAPOX) plus Camrelizumab (anti-PD-1 antibody) followed by delayed surgery in patients with LARC. **Methods:** Patients with histologically confirmed $T_{3\text{-}4}N_0M_0$ or $T_{1\text{-}4}N_+M_0$ rectal cancer, previously untreated disease, and ECOG performance status of 0-1, received SCRT (5×5 Gy) with subsequent two 21-day cycles of CAPOX (oxaliplatin 130 mg/m^2 ivgtt, d1; capecitabine 1000 mg/m^2 po bid, d1-14) plus Camrelizumab (200 mg iv drip, d1) after 1 week, followed by radical surgery after 1 week. Adjuvant therapy was decided by the investigator. The primary endpoint was pathological complete response (pCR) rate, defined as the absence of viable tumor cells in the primary tumor and lymph nodes. The study is ongoing to follow up the survival outcomes and obtain the results of next generation sequencing and PD-L1 expression. The data cutoff date was September 8, 2020. **Results:** From November 2019 to September 2020, a targeted number of patients (n = 29) were enrolled and are expected to complete the surgery by November 2020. The median age was 57 (range 31-73) years, 55% (16/29) of patients had ECOG performance status of 1, and the median distance from tumor to the anal verge was 5 (range, 1.9-9) cm. At data cutoff, 10 patients had undergone the surgery, with R0 resection rate of 100%. The pCR rate was 60% (6/10), including 56% (5/9) for those with mismatch repair-proficient, and 100% (1/1) for those with mismatch repair-deficient. Of 4 patients without pCR, 2 only received one cycle of CAPOX plus Camrelizumab due to the outbreak of COVID-19 in Wuhan, and 1 had signet-ring cell rectal carcinoma. At data cutoff, 20 patients had received at least one dose of Camrelizumab. Immune-related adverse events (irAEs) were all grade 1-2, and the most common irAE was reactive cutaneous capillary endothelial proliferation in 10 (50%) of 20 patients. Postoperative bleeding and infection occurred in 1 (10%) and 2 (20%) of 10 patients, respectively. No treatment-related death was observed. **Conclusions:** SCRT combined with subsequent CAPOX plus Camrelizumab followed by delayed surgery showed promising pCR rate with good tolerance in patients with LARC, regardless of the mismatch repair status, suggesting a candidate strategy for the neoadjuvant therapy. Clinical trial information: NCT04231552. Research Sponsor: Jiangsu Hengrui Medicine Co., Ltd.

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A single-institution experience using total neoadjuvant therapy to treat locally advanced rectal cancer. *First Author: Tyler Friedrich, University of Colorado Comprehensive Cancer Center, Aurora, CO*

Background: The management of locally advanced rectal cancer has historically included preoperative chemoradiation followed by surgery and then adjuvant chemotherapy. Recently there has been an increasing utilization of preoperative chemotherapy in addition to standard chemoradiation, a strategy known as total neoadjuvant therapy (TNT). TNT has been offered to patients at the University of Colorado Cancer Center since 2015. **Methods:** Records of all patients presenting to the University of Colorado colorectal multidisciplinary clinic since 2015 were screened for treatment with TNT. Data collected on these patients included demographic information, diagnosis and initial staging, preoperative treatment received, and surgical outcomes including treatment response and pathological stage. TNT included preoperative chemotherapy with oxaliplatin combined with either 5-FU (FOLFOX) or capecitabine (CAPOX) as well as chemoradiation, generally given with concurrent capecitabine. Patients then underwent surgical resection; if a complete clinical response was achieved with TNT, non-operative management (NOM) was offered. **Results:** A total of 81 patients thus far have undergone TNT followed by resection or, if complete clinical response and preferred by the patient, NOM. The mean age of patients was 56 years, ranging from 23 to 87, and 60% of patients were male. The majority of patients (67) had stage III disease at presentation while 1 had stage 1 (T2N0) disease, 11 had stage II disease and 2 patients had oligometastatic disease. Ultimately 13 patients (16%) opted for non-operative management after being found to have a complete clinical response following TNT. Of the 68 patients who underwent surgical resection, 21 (31%) had a pathological complete response, with another 14 (21%) with near-complete response. 28 patients (41%) had a partial treatment response and 5 (7%) had no treatment response. In total, the rate of complete clinical or pathologic response was 42%. Treatment was overall well-tolerated with 90% of patients receiving the full planned dose of radiation and 98% of patients completing all planned cycles of chemotherapy, though most of them with typical dose reductions needed. Of the patients who underwent surgery, 49 (72%) had low anterior resection and 19 (28%) had an abdominoperineal resection. Of patients with temporary ileostomies, 85% of them had their ileostomy reversed within 10 weeks of surgery. **Conclusions:** Treatment of locally advanced rectal cancer by a total neoadjuvant approach is well-tolerated and results in a high rate of clinical and pathological complete response. Research Sponsor: None.

65 Poster Session

The efficacy and safety of anlotinib in refractory colorectal cancer: A double-blinded, placebo controlled, randomized phase III ALTER0703 trial. *First Author: Yihebali Chi, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China*

Background: The efficacy of late line treatments for metastatic colorectal cancer (mCRC) is still limited. Antiangiogenic therapy is one of standard treatments in mCRC. Anlotinib is a multitarget tyrosine kinase inhibitor, mainly targets VEGFR1-3. This phase III trial was conducted to evaluate anti-tumor efficacy and safety of anlotinib monotherapy in refractory mCRC. **Methods:** Aged 18 years or older mCRC patients were enrolled in 33 Chinese hospitals. They had received at least 2 lines of chemotherapy based treatments; had ECOG PS 0-1and adequate bone marrow, liver and renal function. Enrolled patients were 2-to-1 randomly assigned into anlotinib or placebo group and stratified by previous VEGF-targeting therapy (y/n) and time from diagnosis to metastases (</≥18 months). Anlotinib (12 mg/d, oral, d1-14, q3w) or matched placebo was administered plus best supportive care. Primary end point was Overall Survival (OS). Secondary endpoints included Progression Free Survival (PFS), Objective Response Rate (ORR), Disease Control Rate (DCR), safety and quality of life. **Results:** Between December 2014 and August 2016, 421 patients were enrolled (282 in anlotinib and 137 in placebo group). By the cut-off date (August 31, 2018), the median OS was 8.6 months (95% CI 7.8-9.7) in anlotinib and 7.2 months (6.2-8.8) in placebo without statistical difference (p=0.87; HR=1.02 [0.82-1.27]). The median PFS in anlotinib group (4.1 months; 3.4-4.5) was significantly improved over that in placebo (1.5 months; 1.4-1.5), with a p<0.0001 and a HR of 0.34 (0.27-0.43). Improvements of ORR and DCR were observed in anlotinib over placebo (Table). In subgroup patients with RAS/KRAS/BRAF wildtype, the median OS was statistically prolonged in anlotinib (11.0 months; 8.6-14.1; n=103) than that in placebo (6.7 months; 3.5- 11.1; n=46), HR=0.68 (0.47, 0.99), p=0.043. 52.5% of patients in anlotinib and 19.7% in placebo group experienced grade 3 or above treatment related adverse events (TRAEs). The most common grade ≥3 anlotinib related adverse events were hypertension (20.9%), increased γ-GT (7.1%) and hand-foot syndrome (6.4%), which were recovered by reducing dosage. Only 2 patients in anlotinib group had grade 5 TRAE, which were both hemorrhage. **Conclusions:** Anlotinib could provide clinical benefits by substantially prolonged PFS with manageable toxicity for Chinese refractory mCRC patients. Although median OS did not reach significant improvement. Those with RAS/KRAS/BRAF wildtype might be the potential patients in anlotinib treatment. Clinical trial information: NCT02332499. Research Sponsor: Chia Tai Tianqing Pharmaceutical Group Co., Ltd.

Tumor response of anlotinib versus placebo.

Best response	Anlotinib (n=282)	Placebo (n=137)	P value
PR	12	1	
SD	202	41	
PD	47	73	
NE	0	1	
NA	21	21	
ORR, n(%)	12 (4.26%)	1 (0.73%)	0.0690
DCR, n(%)	214(75.89%)	42(30.66%)	<0.0001

66 Poster Session

A new radio-enhancer, PEP503 (NBTXR3), in combination with concurrent chemoradiation in locally advanced or unresectable rectal cancer: The dose-finding part of a phase I/II trial. *First Author: Jaw-Yuan Wang, Division of Colorectal Surgery, Kaohsiung Medical University Chung-Ho Memorial Hospital, Kaohsiung, Taiwan*

Background: PEP503 (as known as NBTXR3) is a novel radio-enhancer composed of functionalized hafnium oxide nanoparticles for a higher energy deposit by radiotherapy comparing to radiotherapy alone without it. A prior phase 3 study for soft tissue sarcoma has demonstrated the clinical benefit. The phase 1b part of the study aimed to test the feasibility of PEP503 intra-tumor injection and examine the safety profile of various dose levels of PEP503 in combination with concurrent chemoradiation (CCRT) for locally advanced rectal cancers. **Methods:** Patients who had rectal adenocarcinoma of T3-4 or locally unresectable disease suitable for neoadjuvant CCRT were eligible. A single administration of PEP503 intra-tumor injection with multiple needle punctures was applied 24 to 72 hours before the start of IMRT or IMAT at 50 Gy in 25 fractions in combination with capecitabine or infusion 5-FU over 5~6 weeks. Dose escalation of 4 levels of PEP503 injected volume was based on 5%, 10%, 15%, and 22% of the baseline tumor volume by MRI. Intra-tumor dispersion of nanoparticles was inspected by CT-scan and the body kinetics evaluation was performed. The total mesorectal excision was planned around 8~12 weeks later after the completion of CCRT. Preliminary efficacy including tumor response after CCRT and the pathological response with tumor regression grade (TRG) after surgery was collected. **Results:** Twenty patients were enrolled, with 7, 4, 3, and 6 patients at 5%, 10%, 15%, and 22% dose levels, respectively. An injection procedure-related dose-limiting toxicity of urinary tract infection with sepsis was reported in the first treated patient at 5%. There was no adverse event (AE) or serious AE directly caused by PEP503. The most frequently reported AEs related to CCRT across all dose levels were diarrhea (~45%), WBC decreased (~40%), and dermatitis (~25%), but all were grade 1 or 2. The safety profile of CCRT with PEP503 was similar to it of CCRT without PEP503 for rectal cancer patients. The CT scans, before and after CCRT, displayed the dispersion of PEP503 among different tumor shapes and contours without leakage to the surrounding healthy tissues. In most patients, hafnium was not detected in the circulation in 60 minutes after PEP503 injection and not found in urine. Around 70% of patients showed tumor response after the CCRT and half of the patients receiving surgery achieved good tumor regression (AJCC TRG 0 or TRG 1). In the small phase 1b dose-escalation part of the trial, the dose-dependency of the efficacy endpoints could not be assessed. **Conclusions:** Intra-tumor injection of PEP503/NBTXR3 with CCRT is feasible without additional toxicities for rectal cancer patients. The extension phase 2 of the trial to investigate the clinical benefits of PEP503 at 22% of tumor volume is ongoing in Taiwan. Clinical trial information: NCT02465593. Research Sponsor: PharmaEngine, Inc.

67 Poster Session

Application of new treatment strategies for mCRC: Effect of online education on clinician knowledge and confidence. *First Author: Geoff Roy Fisher, Medscape Global Education, New York, NY*

Background: This study determined whether online continuing medical education could improve the knowledge and confidence of cliniciansin the application of the latest strategies for the treatment of mCRC. **Methods:** A 30-minute online video panel discussion was launched for physicians outside the USA in March 2020. Data was collected to May 2020. Educational effect assessed with repeated-pairs pre-/post-activity, where individual participants served as their own control. 3 multiple-choice, knowledge questions and 1 self-efficacy, 5-point Likert scale confidence question were analyzed. Chi-squared test assessed pre- to post-activity change (5% significance level, $P < .05$). Magnitude of change in total number of correct responses overall, and for each question, were determined with Cramer's V (< .06 = Modest, 0.06-0.15 = Noticeable, .16-.26 = Considerable, > .26 = Extensive). **Results:** 108 oncologists (oncs) and 33 gastroenterologists (gastros) completed pre- and post-activity questions. A positive educational effect was observed for oncs (noticeable effect, V = .123, P < .01); average % correct increased from 71 to 81%. For gastros, there was a noticeable effect (V = .06) but P was not significant; correct responses increased from 49 to 56%. Clinicians with 3/3 answers correct increased post-activity (37 to 54% for oncs, 18 to 24%, for gastros). For oncs, improvements in % of correct responses post-activity were seen for questions on tailoring treatment to primary tumour location, outcome of the CRICKET trial on cetuximab re-challenge, and outcome of the BEACON trial in BRAF mutated mCRC (11%, 21%, and 13% relative changes, respectively). Relative changes of 25%, 18% and -17%, respectively, were observed for gastros. % of clinicians mostly or very confident with selecting optimal treatment strategy across the continuum of care improved post-activity, increasing from 33 to 58% for oncs and from 27 to 36% for gastros. **Conclusions:** This on-demand, online video panel discussion resulted in a positive education effect. However, the sample size for gastros was small and the post-activity change was not significant. Knowledge gaps remained post-activity, indicating the need for further education to support optimisation of the treatment of mCRC. Research Sponsor: Merck KGaA.

68 Poster Session

Sensitivity of HER2-amplified colorectal organotypic cancer spheroids at *ex vivo* resistance to panitumumab and trastuzumab. *First Author: Jeremy D. Kratz, University of Wisconsin-Madison, Madison, WI*

Background: HER2 amplification is an emerging biomarker in colorectal cancer (CRC) with increased copy number associated with improved clinical outcomes to HER2 targeting. RAS/RAF wildtype CRC also benefit from use of epidermal growth factor receptor inhibition (EGFRi). The sequencing of EGFRi versus HER2 inhibition in low copy number HER2 amplified CRC remains uncertain. Patient-derived cancer organoids (PDCOs) allow an *ex vivo* method to assess treatment sensitivity. We examined treatment sensitivity of a HER2 amplified PDCO at baseline and following resistance to panitumumab and trastuzumab. **Methods:** Following IRB-approval, fresh CRC tissue was cultured to maturation. After expansion, subcultures were treated with stepwise (20%) increase to physiologic C_{max} of panitumumab (230ug/mL) and trastuzumab (180ug/mL). Threshold for escalation was median relative growth of +20% at 96h. Sensitivity was assessed on primary culture (RC1), panitumumab resistance (RC1-P) and trastuzumab resistance (RC1-T) using 96h of physiologic C_{max} panitumumab, trastuzumab, and combination trastuzumab/pertuzumab. Individual sphere response was assessed for change in mean NADH autofluorescence intensity and ratio of NADH/FAD signal. Response was assessed at 96h in comparison to control using effect size of Glass's Delta (GΔ). **Results:** Molecular profiling revealed HER2 copy number of 14 with no concurrent alterations in *RAS*, *RAF*, or *PIK3CA*. Time to resistance was similar between panitumumab (55 days) and trastuzumab (51 days). RC1 had baseline growth (+116%) which was reduced with single agent panitumumab (+17%, GΔ=1.40) with intermediate sensitivity to trastuzumab (+48%, GΔ=0.95) and trastuzumab/pertuzumab (46%, GΔ=0.99). Normalized NADH/FAD ratio revealed significant metabolic response to panitumumab (-20%, GΔ=0.66) and trastuzumab/pertuzumab (-35%, GΔ=1.16) with insignificant effect of single agent trastuzumab (-14%, GΔ=0.46). Following resistance to panitumumab, RC1-P had persistent growth with trastuzumab (+68%) which improved in combination trastuzumab/pertuzumab (+34%, GΔ=1.16). Following resistance to trastuzumab, RC1-T was insensitive to EGFRi with panitumumab including persistent growth (+58%, GΔ=0.70) and unchanged metabolism (+2%, GΔ=-0.10). **Conclusions:** Therapeutic dose escalation in a single PDCO of HER2 amplified CRC suggests improved sensitivity to EGFRi and dual HER2 targeting with trastuzumab/pertuzumab. Resistance to EGFRi resulted in persistent sensitivity to dual HER2 inhibition using trastuzumab/pertuzumab, however resistance to single agent trastuzumab. Resistance to trastuzumab resulted in future insensitivity to EGFRi. Molecular profiling at resistance revealed no pathologic alterations in EGFR or ERBB2 signaling, with ongoing analysis of transcriptional changes by RNAseq. Research Sponsor: U.S. National Institutes of Health. Other Foundation.

69 Poster Session

Neoadjuvant chemotherapy with modified FOLFOXIRI for locally advanced rectal cancer: A single center phase II trial. *First Author: Wen Zhang, Department of medical oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China*

Background: Chemoradiotherapy (CRT) remains the standard treatment choice for locally advanced rectal cancer (LARC). Neoadjuvant chemotherapy alone with doublet mFOLFOX6 (folinic acid, 5-fluorouracil, and oxaliplatin) seemed not to influence recurrence free survival with the advantage of less treatment-related complications. This phase II trial was designed to evaluate the efficacy and safety of neoadjuvant triplet chemotherapy with mFOLFOXIRI (folinic acid, 5-fluorouracil, oxaliplatin, and irinotecan) in patients with LARC (NCT03443661). **Methods:** Patients with LARC received up to 5 cycles of mFOLFOXIRI (irinotecan 150 mg/m^2, oxaliplatin 85 mg/m^2, leucovorin 200 mg/m^2 were administered on Day 1, fluorouracil 2400 mg/m^2 was administered as a continuous intravenous infusion for 48 hours on Day 1, and was repeated every 14 days). Magnetic resonance imaging (MRI) was performed to assess the baseline and post-chemotherapy TN stage. Radical resection was performed within 4–6 weeks of the last dose of chemotherapy if the tumor shrank or remained stable. Adjuvant chemotherapy with mFOLFOX6 or XELOX (oxaliplatin and capecitabine) was recommended. Postoperative radiation was planned for R1 resection, ypT4b, ypN2, and positive circumferential resection margin (CRM). The primary endpoint was the pathological complete response (pCR) rate. **Results:** Between December 2015 to March 2019, a total of 50 patients were enrolled. 48 (96%) of the patients were clinically node-positive, 28 (56.5%) were CRMnvolved, and 39 (78.4%) were extramural venous invasion (EMVI)-positive. The median cycle of neoadjuvant mFOLFOXIRI chemotherapy was 5 (range, 1–5). A total of 46/50 (92%) patients underwent total mesorectal excision (TME) surgery, all with R0 resection. The pCR rate was 4.3% (2/46). Twenty-three of 46 (50%) patients achieved pathological node-negative status. The proportion of pathologically positive CRM and EMVI were 2.2% and 34.7%, respectively (table). Adjuvant radiotherapy was given to 14/46 (30.4%) patients. The most common Grade 3 or more toxicities included neutrocytopenia (50%), leukopenia (14%), and diarrhea (12%) during neoadjuvant chemotherapy. Clinical meaningful surgical morbidities included pneumonia (n=1), pelvic infection (n=1), and anastomotic fistula (n=1). With a median follow-up time of 33 months (range, 14–73 months), local recurrences and distant metastases were confirmed in 3 (6.5%) and 8 (17.4%) cases, respectively. **Conclusions:** Neoadjuvant chemotherapy with mFOLFOXIRI yielded a significant down-staging effect with an ordinary pCR rate, and seemed effective in eliminating EMVI and transforming CRM-positive to CRM-negative status in patients with LARC. The preliminary survival results are promising. This regimen could serve as a potential alternative to CRT in selected patients with LARC. Clinical trial information: NCT03443661. Research Sponsor: None.

Characteristics evaluated by MRI at baseline and after neoadjuvant chemotherapy and pathology characteristics (N=46).

Characteristics	Baseline N (%)	After neoadjuvant chemotherapy N (%)	Pathology N (%)
T Stage			
T0	0 (0)	0 (0)	2 (4.3)
T1	0 (0)	0 (0)	0 (0)
T2	0 (0)	6 (13)	4 (8.7)
T3	27 (34.7)	37 (80.4)	35 (76.1)
T4	19 (65.3)	3 (6.5)	5 (10.9)
N Stage			
N0	2 (4.3)	22 (47.8)	23 (50)
N1	22 (47.8)	19 (41.3)	12 (26.1)
N2	22 (47.8)	5 (10.7)	11 (23.9)
TNM Stage			
0	0	0	2 (4.3)
I	0	6 (13)	3 (6.5)
II	2 (4.3)	16 (34.8)	18 (39.1)
III	44 (95.7)	24 (52.2)	23 (50)
EMVI			
Positive	36 (78.4)	17 (34.7)	17 (34.7)
Negative	10 (21.6)	29 (65.3)	29 (65.3)
CRM			
Positive	26 (56.5)	4 (8.7)	1 (2.2)
Negative	20 (43.5)	42 (91.3)	45 (97.8)

70 Poster Session

ALTER-C-001: Efficacy and safety of anlotinib plus XELOX regimen as first-line treatment followed by maintenance monotherapy of anlotinib for patients with mCRC—A single-arm, multicenter, phase II clinical trial. *First Author: Jin Yan, Department of Gastrointestinal Surgery, Sichuan Cancer Hospital and Institute/The Affiliated Cancer Hospital School of Medicine, UESTC, Chengdu, China*

Background: The combination of anti-VEGF or anti-EGFR targeted drugs with chemotherapy is considered as the standard first-line therapy for metastatic colorectal cancer (mCRC), and maintenance treatment is proven to be a promising and controversial therapeutic strategy which is mainly involved bevacizumab or capecitabine. However, studies regarding the maintenance strategies based on antiangiogenic TKIs are limited currently. Anlotinib is a novel oral multi-target TKI which can inhibit both tumor angiogenesis and tumor cell proliferation simultaneously. Previous studies indicated that anlotinib demonstrated clinical benefits for patients with mCRC. This study aimed to evaluate the efficacy and safety of anlotinib plus XELOX as first-line treatment followed by anlotinib maintenance therapy for mCRC. **Methods:** ALTER-C-001 trial was an open label, single-arm, multicenter phase II study. A calculated sample size of 53 patients with previously untreated mCRC, ranging from 18-75 years old and an ECOG performance status $\leq$ 1 were planned to recruit. Eligible patients were treated with capecitabine (1000 mg/m^2, po, d1-14, q3w) and oxaliplatin (130 mg/m^2, iv, d1, q3w) plus anlotinib (10mg, po, d1~14, q3w) for 6 cycles followed by maintenance therapy of anlotinib (12mg, po, d1~14, q3w) until disease progression or intolerable adverse events (AEs). The primary endpoint was progression-free survival (PFS). Secondary endpoints were ORR, DCR, DOR and safety. **Results:** From January 2020 to September 2020, a total of 9 patients were enrolled, 6 patients were available for efficacy assessment. In best overall response assessment (all confirmed), there were 66.7% PR (4/6), 16.7% SD (1/6) and 16.7% PD (1/6). The preliminary ORR and DCR of the 6 patients was 66.7% (95% CI, 22.3-95.7%) and 83.3% (95% CI, 35.9-99.6%), respectively. The median PFS was not reached. Most treatment-related adverse events (TRAEs) were grade 1-2. Grade 3 or above TRAEs were as follows: hypertriglyceridemia (33.3%), hypertension (16.7%), neutropenia (16.7%) and lipase elevated (16.7%). No grade 5 AEs were observed. **Conclusions:** The preliminary results indicated that anlotinib plus XELOX regimen followed by anlotinib monotherapy as first-line treatment exhibited antitumor efficacy and manageable toxicity for patients with mCRC. The study is still ongoing and the data will be updated subsequently. Clinical trial information: ChiCTR1900028417. Research Sponsor: Chia Tai Tianqing Pharmaceutical Group Co., Ltd.

71 Poster Session

Initial experience of TAS-102 chemotherapy in Australian patients with chemorefractory metastatic colorectal cancer. *First Author: Azim Jalali, Personalised Oncology Division, Walter & Eliza Hall Institute of Medical Research, Melbourne, VIC, Australia*

Background: For patients with refractory metastatic colorectal cancer (mCRC) treatment with Trifluridine/Tipiracil, also known as TAS-102, improves overall survival. In Australia, TAS-102 was initially made available locally through patients self-funding, later via an industry sponsored Medicine Access Program (MAP) and then via the Pharmaceutical Benefits Scheme (PBS). This study aims to investigate the efficacy and safety of TAS-102 in real world Australian population. **Methods:** A retrospective analysis of prospectively collected data from the Treatment of Recurrent and Advanced Colorectal Cancer (TRACC) registry was undertaken. The characteristics and outcomes of patients receiving TAS-102 were assessed and compared to all TRACC patients and those enrolled in the registration study (RECOURSE). **Results:** Across 13 sites, 107 patients were treated with TAS-102 (non-PBS n = 27, PBS n = 80), The median number of patients per site was 7 (range: 1-17). The median age was 60 years (range: 31-83), compared to 67 for all TRACC patients and 63 for RECOURSE. Comparing registry TAS-102 and RECOURSE patients, 75% vs 100% were ECOG performance status 0-1, 74% vs 79% had initiated treatment more than 18 months from diagnosis of metastatic disease and 39% vs 49% were RAS wild type. Median time on treatment was 10.4 weeks (range: 1.7-32). Median clinician assessed progression-free survival was 3.3 compared to RECIST defined PFS of 2 months in RECOURSE study, while median overall survival was the same at 7.1 months. Two patients (2.3%) had febrile neutropenia and there were no treatment-related deaths in the real-world series, where TAS102 dose at treatment initiation was at clinician discretion. In the RECOURSE study there was a 4% febrile neutropenia rate and one treatment-related death. **Conclusions:** TRACC registry patients treated with TAS102 were younger than both TRACC patients overall and those from the RECOURSE trial. Less strict application of RECIST criteria and less frequent imaging may have contributed to an apparently longer PFS. However overall survival outcomes achieved with TAS102 in real world patients were comparable to findings from this pivotal trial with an acceptable rate of major adverse events. Research Sponsor: None.

72 Poster Session

Response to PD-1 and PD-L1 based immunotherapy in MSS advanced colorectal cancer is impacted by metastatic disease sites. *First Author: Marwan Fakih, City of Hope National Medical Center, Duarte, CA*

Background: Microsatellite stable (MSS) metastatic colorectal cancer (mCRC) has been associated with immunotherapy resistance. However, the impact of metastatic diseases sites on clinical outcome with checkpoint inhibition has not be adequately investigated. **Methods:** Following IRB approval (14361), we performed a retrospective study to assess the response and progression-free survival (PFS) to PD-1 or PD-L1 based therapy in patients with MSS mCRC who progressed following standard chemotherapy and targeted therapy. Patients were included if they received an FDA approved anti-PD1 or anti-PD-L1 agent, alone or in combination with other investigational agents. Exclusion criteria included concurrent cytotoxic therapy. Response and PFS were determined by RECIST guidelines. **Results:** 97 patients with refractory MSS mCRC satisfied the inclusion criteria were evaluable for analysis. 57, 17, 13, and 10 received nivolumab, atezolizumab, pembrolizumab, and durvalumab, respectively. 47, 8, 10, 10, 17 received concurrent VEGFR, MEK, CTLA-4, radiation, or other targeted therapies. Among tested variables, including age, gender, primary tumor location, ECOG status, *RAS, BRAF, APC, TP53*, TMB, and sites of metastasis, only ECOG status (0 vs. 1) and metastatic disease to the liver were associated with disease control (partial response and stable disease; p = 0.005 and $<$ 0.001 respectively). Disease control rates in patients without liver metastases (n = 43) was 56% (95% CI: 40-71%), compared with 2% (95% CI: 0.1-10%) in patients with liver metastases (n = 54) ($p < 0.001$). Also, liver involvement was predictive for PFS based on multivariate Cox regression model ($p < 0.001$). The median PFS in patients with liver involvement was 1.5 vs 4.5 months for no liver involvement (HR = 4.41, p = $<$ 0.001). Amongst patients without liver metastases, 35% (15/43) remained without progression at 6 months. These patients were characterized by lung metastases (n = 8) and/or lymph node metastases (n = 4). **Conclusions:** The presence of liver metastases is MSS mCRC is predictive for lack of benefit from PD-1/PD-L1 inhibitors. Patients without liver metastases can derive a meaningful clinical benefit, with 35% being progression-free at 6 months. Future PD-1/PD-L1 drug development should consider metastatic sites of disease in study design and development. Research Sponsor: None.

74 Poster Session

Updated data from alloSHRINK phase I first-in-human study evaluating CYAD-101, an innovative non-gene edited allogeneic CAR-T in mCRC. *First Author: Hans Prenen, University Hospital Antwerp (UZ Antwerp), Antwerp, Belgium*

Background: CYAD-101 is a first-in-class, non-gene edited allogeneic CAR T-cell product that combines the broad breadth of tumor targeting of the NKG2D-based chimeric antigen receptor (CAR) with a peptide-based approach that controls graft versus host disease (GvHD). NKG2D binds eight ligands commonly over-expressed across many tumors while the co-expressed T-cell receptor (TCR) inhibitory (TIM) peptide interferes with signaling by the endogenous TCR. A bank of CYAD-101 cells was produced from a single donor and evaluated in the AlloSHRINK phase 1 study (NCT03692429) in patients with unresectable metastatic colorectal cancer (mCRC). **Methods:** Three CYAD-101 infusions, each administered following a FOLFOX standard cycle as preconditioning chemotherapy, were tested in a 3+3 dose-escalation study (dose-levels (DL): 10^8, $3x10^8$ and 10^9 T-cells per infusion) in patients with relapsed/refractory mCRC who progressed after previous treatment with oxaliplatin-based chemotherapy, with or without irinotecan-based chemotherapy. **Results:** Fifteen patients (pts) were enrolled (3 pts at DL-1, 3 pts at DL-2, 9 pts at DL-3). No dose-limiting toxicity (DLT), Grade $\geq$ 3 related adverse events or GvHD were reported after any of the CYAD-101 infusions, thus confirming the overall good safety profile of CYAD-101 post FOLFOX. Encouraging anti-tumor activity was observed with 2 confirmed partial responses (PR), including one response in a KRAS mutated patient. In addition, 9 pts achieved stable disease (SD), with 7 SD lasting at least 3 months. The median progression-free survival in this heavily pre-treated population was 3.9 months (95% CI). Whilst engraftment of the CYAD-101 cells was observed after each infusion, the relative level of systemic cytokines appeared to be primarily modulated by cell dose with some suggestion that the magnitude of modulation might be associated with clinical response. Interestingly, preliminary analysis of the T-cell repertoire identified some evidence of TCR diversity after therapy in the patient showing the most durable partial response. **Conclusions:** These clinical results demonstrate the safety and tolerability of a fist-in-human non-gene edited allogeneic CAR T-cell treatment with early promising anti-tumor activity in advanced mCRC pts. Preliminary translational analysis present intriguing observations that the modulation of systemic cytokine levels may be associated with dose which is uncommon in CAR T-cell therapies reported to date while limited T-cell clonal diversification in the best responding patient underscores the likely central role of the adoptively transferred T-cell in driving therapeutic response in this particular patient. Extension cohort evaluating CYAD-101 following other preconditioning chemotherapy is expected to be initiated end 2020. Clinical trial information: NCT03692429. Research Sponsor: Celyad SA.

75 Poster Session

Anlotinib combined with CAPEOX in first-line treatment of patients with RAS and BRAF wild-type unresectable metastatic colorectal cancer: A single-arm, phase II study (ALTER-C-002 trial). *First Author: Ke-Feng Ding, Colorectal Surgery and oncology, Key Laboratory of Cancer Prevention and Intervention, Ministry of Education, The Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China*

Background: Anlotinib is an oral small molecule multi-target tyrosine kinase inhibitor that is designed to primarily inhibit VEGFR1/2/3, FGFR1-4, PDGFR α/β and c-Kit, with a broad spectrum of inhibitory effects on tumor angiogenesis and growth. In a previous trial, Anlotinib had been demonstrated to be safe and efficacious in advanced colorectal cancer after failure of recommended treatment. We aimed to evaluate the efficacy and safety of Anlotinib combined with CAPEOX as first-line treatment for unresectable RAS and BRAF wild-type metastatic colorectal cancer (mCRC). **Methods:** ALTER-C-002 is a single-arm phase II clinical trial. A total of 30 patients with RAS/BRAF wild-type unresectable mCRC, aged 18-75, without prior systemic treatment and ECOG performance score $\leq$ 1 will be prospectively included. Patients received Capecitabine (850 mg/m^2, p.o., on day 1-14 every 3 weeks), Oxaliplatin (130 mg/m^2, i.v., every 3 weeks) and Anlotinib (12 mg, p.o., 2 weeks on/1 week off). After 6 cycles of inducing therapy, patients will receive Capecitabine and Anlotinib as maintenance therapy until tumor progression. Primary endpoint was objective response rate (ORR); secondary endpoints included safety, disease control rate (DCR) and progression-free survival (PFS). **Results:** As of Sep.15th, 2020, 19 patients had been enrolled. 12 of 19 patients were evaluable for antitumor activity: 10 patients had partial response, 2 patients had stable disease. The ORR was 83.3% (95% CI: 51.6-97.9%), and DCR was 100% (95% CI: 73.5-108.1%). 9 patients (47.4%) developed grade III adverse events with 1 (5.3%) grade IV AE. The grade III AEs included hypertension (n = 8), diarrhea (n = 3), hypertriglyceridemia (n = 2), leukopenia and neutropenia (n = 3), alanine aminotransferase increase (n = 1), intestinal obstruction (n = 1), nausea and vomiting (n = 1), and grade IV AE was blood bilirubin increase. 1 patient received emergent surgery for relieving intestinal obstruction after 14 days of Anlotinib treatment discontinuation. No extra bleeding or wound healing risk were observed during the perioperative period. No treatment-related deaths occurred. **Conclusions:** The combination of Anlotinib and CAPEOX displayed promising antitumor activity and manageable toxicity in unresectable RAS and BRAF wild-type mCRC, which should be merited further evaluation in randomized studies. Clinical trial information: NCT04080843. Research Sponsor: None.

76 Poster Session

Impact of omitting fluorouracil from FOLFIRI plus bevacizumab as second-line chemotherapy for metastatic colorectal cancer patients. *First Author: Yuki Matsubara, Department of Clinical Oncology, Aichi Cancer Center Hospital, Nagoya, Japan*

Background: FOLFIRI + bevacizumab (FOLFIRI + BEV) is a standard second-line chemotherapy (Cx) for metastatic colorectal cancer (mCRC) patients (pts) who are refractory or intolerant to fluoropyrimidines (FPs) and oxaliplatin (OX). However, the efficacy of continuing FPs as second-line Cx for pts who are refractory to FPs in first-line Cx remains unclear. **Methods:** We retrospectively evaluated mCRC pts who received irinotecan (IRI) + BEV or FOLFIRI + BEV as second-line Cx at a single institution from Jan 2010 to Apr 2020. The main eligibility criteria were ECOG performance status (PS) of 0-2, known *KRAS* status, a standard initial dose of fluorouracil (5-FU) (bolus 400 mg/m^2, infusional 2400 mg/m^2) in FOLFIRI + BEV and IRI (150 mg/m^2), refractory to FPs, no prior use of IRI, and prior use of OX. We compared the efficacy and safety of IRI + BEV with those of FOLFIRI + BEV. The adjusted hazard ratios (aHRs) for progression-free survival (PFS) and overall survival (OS) were calculated using a multivariate Cox model that contained variables with $p < 0.05$ in the univariate analysis to reduce the imbalance between both the treatments. **Results:** Among the 261 pts, 107 were eligible (IRI + BEV/FOLFIRI + BEV, 31/76 pts). Pt characteristics were as follows (IRI + BEV/FOLFIRI + BEV): median age, 67/62; ECOG PS, 1–2, 55/46%; *KRAS* mutant, 45/50%; *BRAF* V600E mutant, 6/11%; right-sided tumor, 19/43%; lactate dehydrogenase (LDH) $\geq$ 400 U/L, 13/12%; PFS of first-line Cx $<$ 6 month (m), 39/30%; prior use of BEV, 84/63%. Relative dose intensity (RDI) (IRI + BEV/FOLFIRI + BEV) of IRI and BEV was similar in the groups; median RDI (range) of IRI, 80 (44–100) /83 (49–100) %; p = 0.560; median RDI of BEV, 86 (35–100) /83 (20–100) %; p = 0.681. Efficacies (IRI + BEV/FOLFIRI + BEV) after a median follow-up of 13.1/14.3 m were as follows: median PFS, 6.4/5.8 m (HR, 0.90; 95% CI, 0.57–1.38; p = 0.64; aHR, 0.82; 95% CI, 0.50-1.34; p = 0.44); median OS, 16.6/16.5 m (HR, 0.83; 95% CI, 0.51-1.32; p = 0.44; aHR, 1.01; 95% CI, 0.59-1.69; p = 0.97); objective response rate, 25.9/11.3%. Adjustment factors for PFS were prior colorectomy, number of metastatic sites, ECOG PS, liver metastasis, and the level of LDH, while those for OS were prior colorectomy, number of metastatic sites, liver metastasis, peritoneal metastasis, and the level of LDH. All subgroup analyses for PFS and OS according to the pt characteristics also showed no significant differences in the groups. All grade nausea (32/58%) and stomatitis (13/36%) and grade 3–4 neutropenia (23/58%) and febrile neutropenia (0/3%) were less common in the IRI + BEV than in the FOLFIRI + BEV group. **Conclusions:** Our study suggests that omitting 5-FU from FOLFIRI + BEV as second-line Cx for mCRC pts who are refractory to FPs may lower the occurrence of adverse events without impairing the treatment efficacy. Research Sponsor: None.

77 Poster Session

Phase II study of pembrolizumab plus capecitabine and bevacizumab in microsatellite stable (MSS) metastatic colorectal cancer (mCRC): Interim analysis. *First Author: Andrea Grace Bocobo, University of California San Francisco, Helen Diller Family Comprehensive Cancer Center, San Francisco, CA*

Background: MSS mCRC rarely responds to pembrolizumab monotherapy, but capecitabine and bevacizumab may induce immune-stimulatory effects. This study evaluates the safety, tolerability and preliminary efficacy of pembrolizumab in combination with capecitabine and bevacizumab in MSS mCRC. We present results at the planned interim analysis. **Methods:** Design: single-arm, open-label, single-site phase 2 trial with a safety lead-in to confirm the recommended phase 2 dose (RP2D) for capecitabine and expansion cohorts. Per the Simon's 2-stage design, $\leq$1 response in 29 patients (pts) requires trial suspension. Key eligibility criteria: MSS mCRC with stable disease (SD) or progressive disease (PD) on prior fluoropyrimidine-based therapy. Treatment: RP2D PO capecitabine on days 1-14 plus 200 mg IV pembrolizumab and 7.5 mg/kg IV bevacizumab on day 1 in 21-day cycles. Pts are followed for toxicity and radiographic response. **Results:** From 04/2018-09/2020, 29 pts were enrolled, of whom 15 (52%) were female; 21 (72%) white; and median age was 55 years (range 36-77 years). Prior therapies: 2 (7%) pts had SD and 27 (93%) pts had PD on fluoropyrimidine-containing regimens; 24 (83%) pts had prior exposure to bevacizumab. The RP2D for capecitabine was 1000 mg/m2 PO BID, with no dose limiting toxicities observed. Complete toxicity data are available for 25 off-treatment pts. The most common related adverse events (AEs) were palmar-plantar erythrodysesthesia (PPE) (64%) and fatigue (68%). Grade $\geq$3 related AEs occurred in 9 (36%) pts, including immune-related AEs of Grade 3 dyspnea, hypophosphatemia, and pancreatitis in 1 pt each. Treatment related AEs leading to dose interruptions, reductions, or delays occurred in 15 (60%) pts, most commonly PPE in 13 (52%) pts. No pt had a related AE leading to treatment discontinuation or death. Disposition: of 29 pts enrolled, 24 were removed for PD and 1 was removed for an unrelated AE. Best response by RECIST 1.1 in 23 evaluable pts: partial response (PR) in 2 (9%); SD in 14 (61%); PD in 7 (30%). Median time on treatment was 6 months (range 2-26 months). **Conclusions:** Combination of pembrolizumab with capecitabine and bevacizumab was found to be tolerable with an expected toxicity profile in MSS mCRC pts. With 2 responses, the study met interim analysis criteria to continue accrual. Tissue and blood-based immune correlatives are planned. Clinical trial information: NCT03396926. Research Sponsor: Merck Sharp & Dohme Corp.

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Phase I expansion study of P-cadherin-targeted 90Y-FF-21101 antibody in advanced chemorefractory colorectal and pancreatic-biliary cancers. *First Author: Devalingam Mahalingam, Northwestern University, Robert H Lurie Comprehensive Cancer Center, Chicago, IL*

Background: Overexpression of the cell-cell adhesion protein P-cadherin has been associated with a more aggressive cancer cell phenotype, cancer stem cell properties, tumor invasion and metastasis. We determined the safety and recommended Phase II dose of the yttrium-labeled P-cadherin-targeted ^{90}Y-FF-21101 monoclonal antibody (mAb) in patients (pts) with advanced tumors, and focused our expansion study in advanced colorectal (CRC) and pancreatic-biliary cancers (non-CRC tumors). We report the safety, efficacy, and correlative pharmacokinetics (PK)/pharmacodynamics (PD) in this cohort. **Methods:** Pts enrolled must have progressed on all standard therapies. 25 mCi/m^2 (8 mCi/mg mAb) ^{90}Y-FF-21101 was administered intravenously every 12 weeks (wks) until disease progression or unacceptable toxicity. Disease response was assessed based on RECIST v1.1 every 8 wks (1 cycle = 28 days). Serum mAb PK, existence of anti-drug antibodies (ADA) and tumor P-cadherin expression were also evaluated. **Results:** 31 pts [mean age 63 (range, 39-89); 14F/17M; median number of prior therapies, 3 (range, 1-11)] with CRC (18) and non-CRC tumors [pancreatic (8), cholangiocarcinoma (3), duodenal (2)] received a median of 1 (range, 1-2) dose of ^{90}Y-FF-21101. Median duration on study was 8.1 (3.9 – 27) wks (CRC) and 8 (1.1-17.1) wks (pancreatic-biliary). Myelosuppression was the most common treatment-related adverse event [thrombocytopenia (87%; Grade (Gr) 3/4 in 45%), lymphopenia (74%; Gr 3/4 in 61%), anemia (52%; Gr 3/4 in 13%), leukopenia (32%; Gr 3/4 in 16%)], in addition to fatigue (68%, 1 Gr 3) and nausea (39%, 1 Gr 3). Three pts required dose reduction to 20 mCi/m^2 with subsequent infusion after Gr 3/4 thrombocytopenia [(pancreatic (2), CRC (1)]. The clinical benefit rate in pts with CRC based on stable disease (SD) for ≥8 wks is 43.8% (7/16 pts), with a median PFS of 8.1 wks and OS of 27 wks [median PFS, 7.9 wks; OS, 17.1 wks in non-CRC]. Longer-term SD was maintained in 2 pts with CRC for 17-24 wks; one continues on treatment. Enrollment is ongoing in the non-CRC cohort. FF-21101 has a mean $t_{1/2}$ of approximately 65 hours, and post-treatment ADA titers have been observed in < 5% of pts. Tumor P-cadherin expression analysis by IHC demonstrated H-scores > 150 in 88% (14/16) of CRC pts, 75% (9/12) for non-CRC; 2 CRC pts with SD ≥17 wks had H-scores ≥190. **Conclusions:** ^{90}Y-FF-21101 administered every 12 wks demonstrated expected toxicities and has been generally well-tolerated, with preliminary evidence of benefit demonstrated in heavily pre-treated pts with advanced CRC. The optimal dose and schedule for this radioimmunotherapeutic will continue to be explored, along with pre-treatment P-cadherin expression as a predictive biomarker for disease response. Clinical trial information: NCT02454010. Research Sponsor: FUJIFILM Pharmaceuticals U.S.A., Inc.

79 Poster Session

Phase II trial of bintrafusp alfa in patients with metastatic MSI-H cancers following progression on immunotherapy. *First Author: Van K. Morris, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Microsatellite instability-high (MSI-H) tumors are characterized by deficient mismatch repair, high tumor mutation burden, and exceptional anti-tumor responses to immunotherapy. While durable disease control is often observed for advanced MSI-H cancers treated with immune checkpoint blockade (ICB), some patients (pts) experience treatment resistance. In melanoma and urothelial cancer, acquired resistance to ICB has been associated with increased signaling of the immunosuppressive TGF-β pathway. Bintrafusp alfa (BA) is a first-in-class bifunctional fusion protein composed of the extracellular domain of the TGF-βRII receptor (a TGF-β "trap") fused to a human IgG1 monoclonal antibody blocking PD-L1. **Methods:** In this phase II study (NCT03436563), pts with MSI-H metastatic solid tumors who had progressed on prior ICB were eligible. Pts received 1200 mg BA intravenously every 14 days. Paired tumor biopsies were collected for biomarker analysis. The primary objective was to estimate response rate (RR) per iRECIST. Median progression-free survival (PFS) and overall survival (OS) were calculated according to the Kaplan-Meier method. Adverse events (AEs) were assessed according to CTCAE v5.0. **Results:** 15 pts [arising from the colon/rectum (12), pancreas (1), duodenum (1), appendix (1)] were enrolled. Median duration of prior ICB before progression was 7.2 months (range, 1.8-24). All pts were evaluable for toxicity, and 14 for response. There was 1 grade 3 treatment-related AE (adrenal insufficiency) and 1 grade 5 treatment-related immune AE (hepatic failure). Median number of doses with BA was 4 (interquartile range, 2-4). There were 3 pts with stable disease and 11 with progressive disease as best response. RR was 0% (95% confidence interval (CI), 0-24%), and disease control rate was 21% (95% CI, 5-51%). Median PFS and OS were 1.8 months (95% CI, 1.5-5.7) and 9.1 months (95% CI, 5.3-not estimable), respectively. One pt with colorectal cancer demonstrated sustained stable disease (20.5 months) with BA. **Conclusions:** Dual inhibition of TGF-β and PD-L1 by BA did not demonstrate significant anti-tumor activity in the majority of pts with MSI-H metastatic cancer who had progressed on prior ICB. One pt did experience prolonged clinical benefit from BA. Ongoing correlative studies may inform on the effect of TGF-β and PD-L1 modulation by BA within the tumor microenvironment. Clinical trial information: NCT03436563. Research Sponsor: EMD SeronoU.S. National Institutes of Health.

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Interim analysis of the AVETUXIRI Trial: Avelumab combined with cetuximab and irinotecan for treatment of refractory microsatellite stable (MSS) metastatic colorectal cancer (mCRC)—A proof of concept, open-label, nonrandomized phase IIa study. *First Author: Marc Van Den Eynde, Institut Roi Albert II, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium*

Background: Immune checkpoint inhibitors have demonstrated poor efficacy in MSS mCRC. Previous research indicate that cetuximab (anti-EGFR chimeric monoclonal antibody) could initiate, independently from RAS mutation, an immunogenic tumor cell death and mediate antitumor immune response. In this trial, we aim to explore the clinical efficacy and safety of anti-PDL1 avelumab (AVE) combined with cetuximab (CET) and irinotecan (IRI) for treatment refractory MSS mCRC. **Methods:** AVETUXIRI (NCT03608046) is a multicenter academic study recruiting MSS, BRAFV600E wt, mCRC patients (pts) refractory to standard treatment (fluoropyrimidine, oxaliplatin, irinotecan and anti-EGFR treatment if RAS wt tumor) in 2 cohorts (cohort A: RAS wt - cohort B: RAS mut). In both cohorts, patients receive CET (400 mg/m2 W1, 250 mg/m2 W2, 500 mg/m2/2 weeks from W3), IRI (180 - 150 mg/m2/2 weeks from W1) and AVE (10 mg/kg/2 weeks starting from W3). Primary endpoints are overall response rate (ORR), defined as partial or complete response (PR or CR) according (i)RECIST1.1, and safety. Secondary endpoints include disease control rate (DCR), PFS and OS. Based on a Simon 2-stage design for ORR in each cohort (cohort A: P0=0.15, P1=0.33 / cohort B: P0=0.09, P1=0.25 / α = 0.1, β = 0.2 in both cohorts), 10 and 13 patients are required in the first stage of cohort A and B respectively. At least 2 pts have to reach PR or CR in each cohort to allow the continuation of the trial in the 2nd stage. **Results:** Between Oct 2018 and Jan 2020, 23 patients (median age 62 y-old, 86.9% male 78.3% left-sided, 91.3% synchronous mCRC) have been included in the first stage of the trial. No major or unexpected safety events were observed. 21.7% (5/23) of pts presented grade 3 diarrhea, all related to IRI, with complete resolution after IRI dose reduction or interruption. A reduced starting dose of IRI (150 mg/m2) was amended (09/2019) for the last included 8 pts without any grade 3-4 diarrhea occurrence. Grade 1-2 hypothyroidism was the only immune-related side effect. 3 PR were observed in cohort A and none in cohort B. DCR was 60.0% (6/10) and 61.5% (8/13) in cohort A and B respectively. Median PFS and OS were respectively 4.2 and 12.7 months (cohort A) and 3.8 and 14.0 months (cohort B). 6 months-PFS rate was 40.0% and 38.5% in cohort A and B. 12 months-OS rate was 53.3% and 57.7% in cohort A and B. The median follow-up of patients was 9.2 months. **Conclusions:** The AVETUXIRI trial met its primary efficacy endpoint for RAS wt mCRC pts justifying the study continuation in cohort A (2nd stage). No PR was observed in RAS-mut cohort. Nevertheless, encouraging data of DCR, PFS and OS observed in RAS mut cohort allow the opening of a new cohort for RAS-mut mCRC (cohort C) with PFS as primary endpoint. Clinical trial information: NCT03608046. Research Sponsor: Merck Healthcare KGaA.

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Initial experience of patients treated in a real-world clinical setting with bevacizumab-awwb: The first FDA-approved biosimilar to bevacizumab. *First Author: Ran Jin, Amgen Inc, Thousand Oaks, CA*

Background: Bevacizumab-awwb is the first anti-cancer biosimilar and the first biosimilar to bevacizumab approved by the FDA. It was launched in the United States on July 19, 2019. Bevacizumab-awwb approval was based on a phase 3 study in a predetermined sensitive population of non-squamous non-small cell lung cancer (NSCLC) patients. This study investigated initial use of bevacizumab-awwb, across its approved indications for advanced cancer management, in real-world US community and academic oncology practices. **Methods:** This retrospective observational study described demographic and clinical characteristics of patients who received bevacizumab-awwb using structured patient-level data from the nationwide de-identified Oncology Services Comprehensive Electronic Records (OSCER), a Flatiron Health EHR-derived database. The database is longitudinal, demographically and geographically diverse, and includes more than 2.2 million US cancer patients from >280 cancer clinics. This analysis included adult patients who received ≥1 bevacizumab-awwb infusion between July 30, 2019 and April 30, 2020 and focused on describing initial biosimilar uptake in cancer patient populations beyond NSCLC. **Results:** First use of bevacizumab-awwb was in mCRC and occurred within 10 days of product launch. All bevacizumab-awwb approved cancer indications were represented among 2,422 patients treated with bevacizumab-awwb. Initial use of bevacizumab-awwb across indications: mCRC (68%), NSCLC (14%), brain cancer (11%), cervical cancer (5%), metastatic renal cell carcinoma (1%). Among 1657 mCRC patients treated with bevacizumab-awwb, 55% were male with a median age of 65 years (y). Most patients were white (60%), with ECOG scores of 0/1 (84%), and median body weight was 78 kg. Among mCRC patients, 59% had received the reference product before receiving the biosimilar. Among patients with other tumor types, 42-50% had prior bevacizumab exposure. Among mCRC patients with prior exposure to bevacizumab, 67% received bevacizumab-awwb within 28 days of last infusion of reference product (Table). Demographic and clinical characteristics were comparable between patients with and without prior bevacizumab use. **Conclusions:** Early evidence suggests physicians are comfortable initiating or transitioning patients to the first FDA-approved biosimilar to bevacizumab, with little evidence that demographic characteristics differ between patients with and without previous treatment with bevacizumab. Future analyses will determine whether these patterns persist across all indications. Research Sponsor: Amgen Inc.

Percent of mCRC patients with prior bevacizumab use (n=972) according to days between final bevacizumab infusion and bevacizumab-awwb initiation.	n (%)
28 days	647 (67)
>28 days, ≤ 84 days (~3 mos)	124 (13)
>84 days, ≤ 168 days (~6 mos)	88 (9)
>168 days, ≤ 365 days (~12 mos)	67 (7)
>365 days	46 (5)

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Phase Ib/II open-label, randomized evaluation of efficacy and safety of atezolizumab plus isatuximab versus regorafenib in MORPHEUS-colorectal cancer. *First Author: Jayesh Desai, Peter MacCallum Cancer Centre, Victoria, Australia*

Background: The MORPHEUS platform consists of multiple, global, open-label, randomized Phase Ib/II trials designed to identify early efficacy signals and safety of treatment (tx) combinations across tumor types. Isatuximab (isa; anti-CD38) targets CD38 receptors expressed on immunosuppressive cells in the tumor microenvironment. We hypothesized atezolizumab (atezo; anti-PD-L1) + isa would induce an anti-tumor response beyond that of regorafenib (rego), a multi-kinase inhibitor, in patients (pts) with tx-refractory metastatic colorectal cancer (mCRC). **Methods:** This randomized Phase Ib/II trial (NCT03555149) enrolled pts with microsatellite stable/mismatched repair proficient mCRC who had received ≤ 2 prior tx lines (fluoropyrimidine-, oxaliplatin- or irinotecan-containing chemotherapy plus a biologic agent). Pts received atezo (1200 mg intravenously [IV] every 3 weeks [q3w]) + isa (10 mg/kg IV q3w) or control tx with rego (160 mg orally days 1–21; dose escalation to 160 mg during Cycle 1 allowed per institutional guidelines). The primary endpoint was objective response rate (ORR; investigator-assessed RECIST 1.1); secondary endpoints included progression-free survival (PFS), overall survival (OS), disease control rate (DCR) and safety. **Results:** Data cutoff date was March 3, 2020. Fifteen pts received atezo + isa and 13 pts received rego. Fourteen atezo + isa pts (93.3%) and 11 control arm pts (84.6%) had received 2 prior lines of tx; 9 atezo + isa pts (60.0%) and 9 control pts (69.2%) had liver metastases at enrollment. No responses were seen in either arm; 3 pts receiving atezo + isa (20.0%) and 8 control pts (61.5%) had stable disease as their best response. DCR (response and/or stable disease ≥ 12 weeks) was 6.7% with atezo + isa and 15.4% with control. One pt treated with atezo + isa beyond progression had prolonged disease stabilization. Median PFS was 1.4 mo (95% CI: 1.4, 1.8) with atezo + isa and 2.8 mo (95% CI: 1.6, 3.1) in the control arm; median OS was 5.1 mo (95% CI: 3.1, 7.8) with atezo + isa and 10.2 mo (95% CI: 4.8, not reached) with control. Tx-related adverse events (AEs, Grade 1-4) occurred in 13 atezo + isa pts (86.7%), and 12 control pts (92.3%). The most common tx-related AEs with atezo + isa were infusion-related reaction (73.3%), nausea (26.7%) and fatigue (20.0%). No Grade 5 AEs occurred in the atezo + isa arm, 1 (7.7%) was reported in the control arm (sepsis, considered unrelated to study tx). No atezo + isa pts and 1 control-arm pt (7.7%) withdrew from treatment due to a tx-related AE. Biomarker analyses did not identify any significant trends related to efficacy. **Conclusions:** In this trial, superior efficacy of atezo + isa vs rego was not shown. However, the atezo + isa combination was well tolerated, with a manageable safety profile. Clinical trial information: NCT03555149. Research Sponsor: F. Hoffmann-La Roche, Ltd.

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Incidence of hypertension and proteinuria in patients treated with bevacizumab versus bevacizumab biosimilar *First Author: Yun Man, Roswell Park Cancer Institute, Buffalo, NY*

Background: Biosimilar products are proven to have no clinically meaningful differences in terms of safety and effectiveness with the reference product, however, to our knowledge, there is limited comparative analysis regarding adverse events for the bevacizumab biosimilars and the reference product. The purpose of this study was to evaluate the incidence of hypertension and proteinuria in patients treated with reference versus biosimilar bevacizumab to potentially streamline clinical management. **Methods:** A retrospective study was conducted with data consisting of gastrointestinal cancer patients who initiated either reference bevacizumab or biosimilar bevacizumab between January 2019 and July 2020 at Roswell Park Comprehensive Cancer Center. For the primary composite endpoint, Electronic Health Records were searched for the presence or absence of hypertension and proteinuria, as well as time to event analysis. In patients treated with bevacizumab biosimilar, demographics, hypertension and proteinuria related risk factors, bevacizumab containing chemotherapy regimen, and bevacizumab dosing were also identified to assess the risk association with hypertension and proteinuria. **Results:** 75 patients were included with 42 patients received bevacizumab and 33 patients received bevacizumab biosimilar. Hypertension occurred in 52.4% of reference bevacizumab group versus 36.4% of bevacizumab biosimilar group. Median time to hypertension is 84 days (bevacizumab) versus 24.5 days (bevacizumab biosimilar) following the first treatment (p= 0.0064). Proteinuria developed in 35.7% of reference bevacizumab patients compared to 30% of bevacizumab biosimilar patients. Median onset of proteinuria was 213 days (bevacizumab) versus 53.5 days (bevacizumab biosimilar) (p= 0.0022). In patients with a history of hypertension or underlying renal dysfunction, there was an increased risk of further hypertension and proteinuria, respectively. **Conclusions:** Higher risk of hypertension and proteinuria was associated with the bevacizumab reference product group, although not statistically significant. A shorter onset of hypertension and proteinuria was associated with the bevacizumab biosimilar group. Our results need further validation in larger cohorts, especially due to the more recent implementation of bevacizumab biosimilar products. Research Sponsor: None.

	Bevacizumab (n = 42)	Bevacizumab biosimilar (n = 33)	p-value
Hypertension (%)	52.4	36.4	0.2427
Time to hypertension (median days)	84	24.5	0.0064
Number of doses to hypertension, (median doses)	5	1.5	0.0005
Proteinuria (%)	35.7	30	0.7193
Time to proteinuria (median days)	213	53.5	0.0022

84 Poster Session

Outcomes of isolated distant lymph node metastases in colorectal cancer. *First Author: Vinod Kalapurackal Mathai, Royal Hobart Hospital, Hobart, Australia*

Background: The optimal management of isolated distant lymph node metastases (IDLNM) in metastatic colorectal cancer (mCRC) is not clearly established. Small case series and prior data from the TRACC (Treatment of Recurrent and Advanced Colorectal Cancer) registry support the use of radical treatment with curative intent (local resection, chemo-radiation or stereotactic radiotherapy), which may lead to better outcomes in mCRC patients with IDLNM. Aims: This study investigates the clinical characteristics and outcomes of mCRC patients with IDLNM treated with systemic therapies plus locoregional therapy with curative intent versus systemic therapies with palliative intent. **Methods:** Clinical data were collected and reviewed from the TRACC registry, a prospective, comprehensive registry for mCRC from multiple tertiary hospitals across Australia from 01/07/2009 to 30/06/2020. Clinicopathological characteristics, treatment modalities and survival outcomes were analyzed in patients with IDLNM and compared to patients with other organ metastases. Fisher exact test was used for significance tests and Kaplan Meier curves for survival analyses. **Results:** Of 3408 mCRC patients with a median follow-up of 38.0 months, 93 (2.7%) were found to have IDLNM. Compared to mCRC with other organ metastases, patients with IDLNM were younger (mean age: 62.1 vs 65.6 years, p=0.0200), more likely to have metachronous disease (57.0% vs 38.9%, p=0.0005), be KRAS wild-type (74.6% vs 53.9%, p=0.0012) and BRAF mutant (12.9% vs 6.2%, p=0.0100). There was no overall survival difference between with IDLNM and those with other organ metastases (median OS 27.24 vs 25.92 months, p=0.2300). Twenty-four patients (25.8%) with IDLNM received treatment with curative intent, with a trend towards improved overall survival compared to those with other organ metastases treated with curative intent (73.5 vs 62.7 months, p=0.8200). Amongst mCRC patients with IDLNM, those who received treatment with curative intent had a significantly better overall survival than those treated with palliative intent (73.5months vs 23.2 months, p=0.0070). **Conclusions:** Our findings suggest that there are differences in the patterns of presentation of IDLNM and other organ metastases. Radical treatment with curative intent options should be considered for mCRC patients with IDLNM where appropriate. Research Sponsor: None.

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PARADIGM study: A multicenter, randomized, phase III study of mFOLFOX6 plus panitumumab or bevacizumab as first-line treatment in patients with *RAS* (*KRAS/NRAS*) wild-type metastatic colorectal cancer. *First Author: Takayuki Yoshino, Department of Gastroenterology and Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa, Japan*

Background: The optimal choice of monoclonal antibodies (mAbs) for first-line treatment in patients (pts) with *RAS* (*KRAS/NRAS*) wild-type metastatic colorectal cancer (mCRC) remains controversial. The meta-analyses of subgroup analyses in phase III studies of pts with *KRAS* exon 2 wild-type mCRC suggested a longer overall survival (OS) with an anti-EGFR mAb over bevacizumab in pts with *RAS* wild-type mCRC or with left-sided primary tumors. However, there has been no prospective study comparing the two mAbs in these pt populations. This randomized phase III study was originally designed to demonstrate the superiority of panitumumab versus bevacizumab, both in combination with mFOLFOX6, for *RAS* wild-type mCRC, but we have revised the protocol to analyze efficacy in pts with a left-sided primary tumor as the primary (final) analysis. **Methods:** Eligible pts are aged 20-79 years with histologically/cytologically confirmed *RAS* wild-type chemotherapy-naive mCRC, and ECOG performance status 0-1. Between May 29, 2015 and Jun 8, 2017, 823 pts were randomized 1:1 to panitumumab plus mFOLFOX6 or bevacizumab plus mFOLFOX6 by the minimization method and the randomisation was stratified by institution, age (20-64 vs. 65-79 years), and liver metastases (present vs. absent). The primary analysis was revised to adopt a hierarchical testing procedure; we first compare OS between the two arms in left-sided primary tumor population, and only if there is statistically significant difference, then ITT population analysis will be performed. In this revised plan, the expected number of deaths is 420 in the left-sided population to provide 80% power to detect an OS hazard ratio of 0.74 at a one-sided significance level of 0.02101 determined on the alpha spending function approach after one interim analysis. A large-scale exploratory biomarker substudy to identify potential biomarker candidates using tumor tissue and circulating tumor DNA is also underway (Clinical trial no.: NCT02394834). The data cut off for the primary analysis is expected to be during 1Q 2021. **Results:** Results are expected in 2021. **Conclusions:** Results are expected in 2021. Clinical trial information: NCT0239475. Research Sponsor: Takeda Pharmaceutical Company Limited.

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Safety analysis of the randomized phase II study of FOLFOXIRI plus cetuximab versus FOLFOXIRI plus bevacizumab as the first-line treatment in metastatic colorectal cancer with *RAS* wild-type tumors: The DEEPER trial (JACCRO CC-13). *First Author: Takanori Watanabe, Department of Surgery, Himeji Red Cross Hospital, Himeji, Japan*

Background: Triplet regimens, FOLFOXIRI, combined with bevacizumab (bev) or panitumumab have been shown to be superior in terms of early tumor shrinkage (ETS) and depth of response (DpR) compared to doublet regimen plus bev or triplet regimen in patients with *RAS* wild-type metastatic colorectal cancer (mCRC), in the TRIBE trial (*N Engl J Med* 2014) or VOLFI trial (*J Clin Oncol* 2019), respectively. There have been few studies which directly compared cetuximab (cet) with bev when combined with triplet regimen. Therefore, we investigated the efficacy and safety of bev vs. cet in combination with FOLFOXIRI in previously untreated mCRC patients with *RAS* wild-type tumors. **Methods:** This trial was a randomized phase II trial to evaluate modified (m)-FOLFOXIRI (irinotecan 150 mg/m^2, oxaliplatin 85 mg/m^2, 5-FU 2400 mg/m^2) plus cet vs. bev as first-line treatment in terms of the DpR during the entire course as the primary endpoint in 360 patients with *RAS* wild-type mCRC (ClinicalTrials.gov Identifier: NCT02515734). The experimental arm with cet was considered to be active if the difference of median DpR was over 12.5% compared with the bev arm, under the conditions of significance level of 0.05 and power of 0.85. Secondary endpoints included the ETS at week 8, progression-free survival, overall survival, secondary resection rate, and toxicity. **Results:** A total of 359 patients were enrolled between July 2015 and June 2019. For the safety analysis set (median age 65y, 64% male, PS0/1: 91%/9%, left/right primary: 83%/17%), 173 and 175 patients were randomly assigned to the cet and bev arms, respectively, some patients were excluded for the safety analysis due to the violation of inclusion criteria (6 for cet arm and 5 for bev). On the cutoff date of September 2020, median number of cycles administered was 10 (range, 1-51) for the cet arm and 12 (range, 1-51) for the bev arm. The incidence of severe adverse events (AEs) was 25.4% (44/173) for the cet arm and 25.7% (45/175) for the bev arm, respectively. The following AEs of grade 3-4 were observed more frequently in the cet arm compared to the bev arm: oral mucositis (9.2% vs. 2.3%), diarrhea (12.1% vs. 8.0%), dermatitis acneiform (12.1% vs. 0%), and hypomagnesemia (4.0% vs. 0%). The treatment-related death occurred in 2 patients of the cet arm, while no patients in the bev arm. The rate of treatment discontinuation due to AEs of any cause was comparable between the cet and bev arms (7% vs. 9%). **Conclusions:** This safety analysis indicated that both regimens of m-FOLFOXIRI plus cet or bev were tolerable in *RAS* wt mCRC patients although some frequent severe AEs were observed. Clinical trial information: UMIN000018217. Research Sponsor: Merck Biopharma Co., Ltd.

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Development of a cure model for the estimation of long-term outcomes in patients with microsatellite instability(MSI)-high metastatic colorectal cancer (mCRC) receiving immune-checkpoint inhibitors (ICIs). *First Author: Filippo Pietrantonio, IRCCS National Cancer Institute (INT), University of Milano, Milan, Italy*

Background: Anti-PD-(L)1-based therapy yielded unprecedented efficacy in patients with MSI-high mCRC. A relevant proportion of subjects may achieve long-term disease control when receiving ICIs, particularly anti-PD-1 plus anti-CTLA-4 combo. However, some patients still experience treatment refractoriness or short-term clinical benefit. **Methods:** We analyzed data of 163 patients with MSI-high mCRC treated with anti-PD-1 +/- anti-CTLA-4 agents. The endpoint was progression-free survival (PFS); multivariable analyses were performed using a cure model (Othus et al, CCR 2012), which allows to test which factors, including ICI type, could identify patients achieving long-term disease control. To account for biases consistent with non-random ICI assignment, we estimated a propensity score (covariates: ECOG PS, age, sex, primary tumor location, its resection, adjuvant treatment, synchronous presentation of mets, mucinous histotype, *RAS/BRAF* status, n. prior treatment lines, previous chemo, n. metastatic sites, presence of peritoneal, lung, liver, bone, brain, nodal mets), and then in the cure model we applied an inverse-probability-of-treatment-weight (IPTW) based on propensity score. A beforehand variable selection was operated using a random survival forest (RSF) model (RSF covariates: all the propensity score covariates plus ICI line and ICI type, platelets count (PLT), NLR, LDH), where we introduced a weight system in order to adjust variable selection net of ICI type. **Results:** RFS selected 5 variables: ICI type, ECOG PS, NLR, PLT and N. prior lines, the combination of which allowed to estimate the cure probability: the higher the probability the greater the chance of achieving long-term disease control. The Table shows the odds ratio estimates, defining the chance of being "cured" according to the values of the selected variables. ICI type was significantly associated with long-term disease control: patients treated with anti CTLA-4-combo achieved the highest chance of being cured, 3.41 times greater than the chance of patients treated with anti PD-1 mono. The median cure probability was as higher as 70.1% (IQR: 51.9-81.0%) with CTLA-4-combo vs 34.8% (IQR: 18.4-51.9%) with anti-PD-1 mono; the probability within treatment groups was varying according to ECOG PS, NLR, PLT and n. prior lines. **Conclusions:** Based on 5 variables including the ICI treatment type, a nomogram was built in order to estimate the cure probability in patients with MSI-high mCRC and potentially assist clinicians in their clinical practice. Research Sponsor: None.

Variable	Reference values	OR (CI95%)	Wald test p-value
ICI type	Anti-CTLA4-combo vs anti-PD-1 mono	3.41 (1.54 - 7.55)	0.045
ECOG PS	0 vs ≥1	1.81 (0.85 - 3.84)	0.371
NLR	≤3 vs > 3	1.99 (0.92 - 4.30)	0.298
PLT	100k vs 300k	3.11 (1.70 - 5.69)	0.053
N. prior lines	0 vs 2	1.65 (0.99 - 2.74)	0.334

88 Poster Session

Is antiangiogenic therapy necessary for patients with metastatic colorectal cancer (mCRC) and mutation in the *BRAF* gene? Results of the systematic review and meta-analysis. *First Author: Mikhail Fedyanin, Federal State Budgetary Institution N.N. Blokhin National Medical Research Center of Oncology of the Ministry of Health of the Russian Federation (N.N. Blokhin NMRCO), Moscow, Russian Federation*

Background: There are no direct prospective randomized studies supporting the need for antiangiogenic drugs in the treatment of patients with the m*BRAF* mCRC. However, subgroup analysis of different studies showed conflicting results. Therefore, we performed systemic review and meta-analysis to compare efficacy anti-angiogenic targeted therapy with chemotherapy and chemotherapy alone in patients with m*BRAF* mCRC in terms of progression free survival (PFS), and overall survival (OS). **Methods:** We performed a search of all prospective randomized phase III studies in PubMed, ASCO and ESMO congresses for all years before September, 2020, compared chemotherapy (CT) plus bevacizumab or aflibercept or ramucirumab and CT alone at the first-line or second-lines with information of the *BRAF* status. Primary outcome was hazard ratio (HR) for PFS and 95% confidence interval (CI); secondary–HR for OS and 95%CI. Fixed effects were used for analysis. Meta-analysis was conducted by "Review Manager" Ver. 5.3. **Results:** We identified 4 trials (AVF2107g, AGITG MAX, VELOUR and RAISE), which included 120 patients with mBRAF (anti-angiogenic plus CT–65 (54%) and CT alone–55 (46%). According to results of the meta-analysis there was a tendency for significant improvement in PFS (HR 0.64, 95% CI 0.4-1.02; p = 0.06; I^2 = 0%, p for heterogeneity 0.7; 53trials) and significant improvement in OS (HR 0.51, 95% CI 0.32-0.82; p = 0.005; I^2 = 0%, p for heterogeneity 0.52; 4 trials) in group of ani-angiogenic therapy. **Conclusions:** Addition of anti-angiogenic therapy to chemotherapy showed improvement in the PFS and OS in pts with m*BRAF* compared with chemotherapy alone. A prospective randomized trial is needed to determine the optimal regimen of systemic therapy for pts with m*BRAF* mCRC. Research Sponsor: None.

89 Poster Session

Survival outcomes of adjuvant chemotherapy in elderly patients with stage III colon cancer. *First Author: Walid Labib Shaib, Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA*

Background: The survival impact of multi-agent (MAC) as compared to single-agent (SAC) adjuvant chemotherapy (AC) in elderly patients with stage III colon cancer (CC) remains controversial. The aim of this study is to evaluate the survival outcome comparing MAC to SAC in this population utilizing the National Cancer DataBase (NCDB). **Methods:** Patients 70 years and older with pathological stage III CC were identified between 2004 and 2015 from the NCDB using ICD-O-3 morphology and topography codes: 8140-47, 8210-11, 8220-21, 8260-63, 8480-81, 8490, and C18.0-18.8 (without C18.1). Univariate and multivariable analyses were conducted and Kaplan-Meier analysis and Cox proportional hazard models were used to identify the association between MAC vs. SAC and overall survival (OS). **Results:** A total of 41,707 elderly patients (≥70 years old) with stage III CC were identified. Around half of the patients (n = 20,257; 48.5%) received AC; the majority of whom (n = 12,923, 63.8%) received MAC. The median age was 79 (range 70-90). Of the patients who received AC, the majority were female (n = 11,201, 55.3 %), Caucasians (87.4%) and had a moderately differentiated tumor grade (n = 12,619, 62.3%). Tumor size more than 4 cm was identified in 11,785 (58.2%) patients and 18,496 (91.3%) had negative surgical margins. Low-risk stage III CC constituted 50.6% (n = 10,264) of the study population. High-risk stage III CC was associated with worse OS compared to low-risk disease ($p < 0.001$). MAC was associated with better 5-year OS compared to SAC ($p < 0.001$). High-risk stage III patients who received MAC had an OS of 4.2 v. 3.4 years in SAC ($p < 0.001$). In low risk stage III, patients who received MAC had median OS of 8.5 v. 7 years in SAC ($p < 0.001$). In Univariate, male sex, positive surgical margin, insurance and facility types, age, year of diagnosistumor size, and Charlson-Deyo Score of > 2 were associated with worse OS ($p < 0.05$). **Conclusions:** Multi-agent AC is associated with better survival in stage III CC patients 70 years and older compared to SAC. Enhanced benefit of MAC was shown for both low risk and high risk stage III CC. Research Sponsor: NCDB.

90 Poster Session

Demographics and clinical characteristics of metastatic colorectal cancer patients treated with bevacizumab-awwb in real-world oncology clinics. *First Author: Richard DeClue, ConcertAI, Memphis, TN*

Background: Bevacizumab-awwb is a biosimilar to bevacizumab approved by the FDA based on evidence obtained in a phase 3 study in non-squamous non-small cell lung cancer. The present real-world evidence study evaluated experience with bevacizumab-awwb (launched 07/19/2019) in patients with metastatic colorectal cancer (mCRC) in a real-world oncology setting to gain insight into biosimilar use for a bevacizumab-awwb approved indication lacking clinical trial data. **Methods:** This retrospective analysis identified patients, age ≥ 18 years (y), within existing medical records diagnosed with mCRC who initiated bevacizumab-awwb as first- or later-line treatment. Patients were identified from the ConcertAI Definitive Oncology Dataset, a consolidated EMR database of CancerLinQ and Vector Oncology, representing geographically diverse practice locations, including rural and urban centers, within the United States. **Results:** A total of 304 patients were eligible for this analysis. First use of bevacizumab-awwb in mCRC occurred within 20 days of product launch. Most patients (n = 262, 86%) were treated in a community setting and more than half of all eligible patients received prior bevacizumab (n = 162, 53%). Among 42 patients treated in academic settings 29 (69%) had not received bevacizumab prior to receiving bevacizumab-awwb. In the 162 patients with prior bevacizumab use, 134 (83%) had no recorded disease progression between the last bevacizumab infusion and start of bevacizumab-awwb. Among these 134 patients, 111 (83%) received bevacizumab-awwb within 28 days of last bevacizumab dose. Demographic and clinical characteristics of patients stratified by prior bevacizumab use were comparable (Table). In both subgroups most patients had an adenocarcinoma histological diagnosis with primary tumors in the rectum or sigmoid colon. Overall, most frequent comorbidities of mCRC patients were diabetes (24%), chronic obstructive pulmonary disease (10%), and renal disease (8%). **Conclusions:** Patients with mCRC who received bevacizumab-awwb in this real-world oncology setting in the first year post product launch were similar regardless of prior bevacizumab use. Among patients with prior bevacizumab use, 83% continued with bevacizumab-awwb in the same line. In the subset of patients without progression post bevacizumab, most received bevacizumab-awwb within 28 days of last bevacizumab dose demonstrating use of bevacizumab-awwb in new and continuing patients. Research Sponsor: Amgen Inc.

Patient Demographic/Characteristic	No Prior Bevacizumab	Prior Bevacizumab
n = 142	n = 162	
Male, n (%)	73 (51)	98 (60)
> 65 y of age, n (%)	52 (37)	80 (49)
Median BMI at Stage IV mCRC dx, n	28	27
White race, n (%)	95 (67)	111 (69)
Public, no private insurance, n (%)	23 (16)	58 (36)
mCRC Stage IV at dx, n (%)	50 (35)	50 (31)
ECOG score 0/1 at dx, n (%)	104 (73)	116 (72)

91 Poster Session

INNOVA: Interval or neoadjuvant chemotherapy in rectal cancer—A phase II randomized study comparing interval versus neoadjuvant chemotherapy in magnetic resonance imaging-defined high-risk rectal cancer. *First Author: Ramakrishnan Ayloor Seshadri, Cancer Institute (WIA), Chennai, India*

Background: Total neoadjuvant treatment is a promising option in rectal cancer. We aim to compare neoadjuvant versus interval chemotherapy in high risk rectal cancer to identify the optimal sequencing of treatment. **Methods:** Using a Simon two-stage design, newly diagnosed MRI defined high risk rectal cancer patients were randomly assigned in a 1:1 ratio to receive three 21 day cycles of chemotherapy with Capecitabine 1000 mg/m2 and Oxaliplatin 130 mg/m2 either before (Arm A-neoadjuvant) or after (Arm B-interval) chemoradiation followed by surgery. Primary end point was the pathological complete response (pCR) following surgery. A heirarchial model was used to assess the primary and secondary end points (toxicity and compliance) and compare the two regimens. (Clinical Trial Registry of India No. CTRI/2015/01/005385). **Results:** In this single centre study conducted between November 2015 and February 2020, 42 patients were randomised in the first stage. A pCR was seen in 4 patients in Arm A and 6 in Arm B. Hence another 52 patients were randomised in the second stage of which an additional 3 and 2 patients had a pCR leading to an overall pCR of 7 and 8 patients (15.5% vs 17% and 18.4% vs 19.5% in the intent-to-treat and per-protocol populations in Arm A and B respectively. This exceeded the minimum predetermined number of 5 pCR needed to qualify for further evaluation for each arm. Grade ≥3 toxicity was observed in 2.2% of 132 cycles and 4.6% of 129 cycles of chemotherapy delivered in 45 and 43 patients in Arm A and B respectively while 11/43 (25.5%) and 10/47 (21.2%) patients experienced grade ≥3 toxicity during chemoradiation. Treatment break of > 7 days was seen in 23.2% and 29.7% of patients in Arm A and B respectively while 93.3% in Arm A and 100% of patients in Arm B completed all 3 planned cycles of pre-operative chemotherapy. A non-significant trend towards greater pathological downstaging was seen in Arm B than in Arm A (ypT1-2 39% vs 26.3%; p = 0.1 and ypN0 68.3% vs 57.9%; p = 0.5 respectively). **Conclusions:** In this phase two study, both neoadjuvant and interval chemotherapy emerged eligible for further evaluation against the standard of care in a future phase III study. Although we could not pick one winner based on pCR, toxicity or compliance, the greater downstaging observed with interval chemotherapy suggests it could play a greater role in an organ preservation approach. Clinical trial information: CTRI/2015/01/005385, UTN no: U111111650578. Research Sponsor: None.

92 Poster Session

Neoadjuvant chemoradiotherapy with capecitabine in locally advanced rectal cancer: Analysis of prognostic factors. *First Author: Jesus Romero, Department of Radiation Oncology, Puerta de Hierro Hospital, Majadahonda, Madrid, Spain*

Background: Capecitabine-based neoadjuvant chemoradiotherapy is the standard treatment for locally advanced rectal cancer (LARC). The objective of this retrospective study is to analyze overall survival (OS), local relapse free-survival (LRFS), distant metastases free-survival (DMFS) and prognostic factors. **Methods:** Between 2009 and 2018, 207 patients(p) with LARC has been treated in our hospital with neoadjuvant CRT. Clinical characteristics: Mean age: 65 y (41-87); male:129, female:78; TNM: cT2: 12p, cT3: 176p, cT4: 19p, cN0: 59p, cN1: 106p, cN2: 42p. Treatment: pelvic radiotherapy (45Gy, 1.8Gy/day) plus concomitant capecitabine (852mg/sqm/12h for 28 days). Surgery (mesorectal excision) was carried out 6-8 after the end of CRT. Statistics: Kaplan-Meier and Log-rank test. **Results:** Mean follow-up: 43 months. Downstaging:104/192 (54%). Pathological complete response: 31/192 (16%). Sphincter preservation rate was 82%. Five-year OS, LRFS and DMFS were 89.9%, 93.3% and 81.7%, respectively. Factors predicting shorter 5-y OS were: cT4 (69% vs 91% and 91% for cT1 and CT2, respectively; p=0.027), pT3-4 (85% and 64% vs 100%, 100% and 98% for pT0, pT1 and pT2, respectively; p=0.008), pathological involved nodes (pN+) (77% vs 96%; p=0.001), perineural invasion (PNI) (78% vs 95%; p=0.041), LVI (p<0.001), Ryan 3 (p<0.001), resection margin R1 (67% vs 94% for R0; p<0.001), no pCR (p=0.027) and absence of downstaging (73% vs 97%; p=0.001). Factors associated with poor 5-y DMFS were: pT3-4 (70% and 0% vs 96%,88% and 98% for pT0,pT1 and pT2, respectively; p<0.001), pN+ (68% vs 88% for pN0: p<0.001), PNI (64% vs 85%; p=0.036), Ryan 3 (49% vs 96%, 85% and 85% for Ryan 0, 1 and 2, respectively; p<0.001), R1 (33% vs 86% for R0; p<0.001) and absence of downstaging (50% vs 71%; p<0.001). CTCAE 4.0 grade 3 toxicity: 1%. No grade 4 toxicity was seen. **Conclusions:** CRT with capecitabine provides high rates of survival and sphinter preservation with excellent tolerance. Patients with adverse pathological factors (pT4, pN+, PNI, Ryan 3, R1 and absence of downstaging) have a higher risk of distant metastasis and are more likely to benefit from adjuvant chemotherapy. Research Sponsor: None.

93 Poster Session

A phase Ib study of NUC-3373 in combination with standard therapies in advanced/metastatic colorectal cancer (NuTide:302). *First Author: Andrew L. Coveler, Seattle Cancer Care Alliance/University of Washington, Seattle, WA*

Background: 5-FU is a key anti-cancer agent used across a broad range of tumors. The anti-cancer metabolite of 5-FU, fluorodeoxyuridine-monophosphate (FUDR-MP), binds and inhibits thymidylate synthase (TS), disrupting DNA synthesis and repair. 5-FU is often dosed with leucovorin (LV) to enhance the binding of FUDR-MP to TS. NUC-3373 is a targeted inhibitor of TS designed to bypass 5-FU resistance mechanisms associated with transport, activation and breakdown and avoid the generation of toxic metabolites such as FUTP and FBAL. NUC-3373 has a longer plasma $t_{1/2}$ (~10 hours) than 5-FU (8-14 minutes), generating substantially higher intracellular levels of FUDR-MP and lower levels of the toxic metabolites FUTP and FBAL. Part 1 interim data from the NuTide:302 study demonstrated NUC-3373's favorable PK and safety profile was unaffected by LV. Therefore, all subsequent patients in NuTide:302 are receiving NUC-3373 + LV. Here we present the next data series from NuTide:302. **Methods:** NuTide:302 is a 3-part, Phase Ib study in patients with advanced CRC who have relapsed after ≥2 prior lines of fluoropyrimidine- containing therapies. In Part 1, patients are receiving NUC-3373 with or without LV. In Part 2, NUC-3373 +LV is being administered in dose-escalation cohorts with either oxaliplatin (NUFOX) or irinotecan (NUFIRI). In Part 3, the NUFOX and NUFIRI regimens selected from Part 2 will be combined with biologics targeting VEGF and EGFR pathways. **Results:** 36 patients have been treated in Part 1: 21 received 1500 mg/m^2 NUC-3373 ± LV q2w; 11 received 1500 mg/m^{2}NUC-3373 + LV q1w; and 4 received 2500 mg/m^2 NUC-3373 + LV q1w. Clinical activity has been observed including tumor shrinkages and stabilization of disease for up to 5 months following rapid progression (≤2 months) on prior lines of therapy. One fluoropyrimidine-refractory patient demonstrated a 28% reduction in target lesions and achieved a stable disease of 5 months after rapid progression on CAPOX (2 months) and FOLFIRI (1.5 months). Safety data for all patients treated with NUC-3373 ± LV in Part 1 of NuTide:302 is shown below. Updated data on the clinical activity and safety of NUC-3373 will be presented. Clinical trial information: NCT03428958. **Conclusions:** NUC-3373 ± LV has shown clinical activity in heavily pretreated CRC patients, including tumor shrinkage in a fluoropyrimidine-refractory patient. The safety profile of NUC-3373 ± LV is very encouraging: no neutropenia or hand-foot syndrome of any grade and no diarrhea or mucositis above Grade 2. NUC-3373 +LV is currently being dose escalated further in Part 1 and dosed with either oxaliplatin (NUFOX) or irinotecan (NUFIRI) in Part 2 of NuTide:302. Research Sponsor: NuCana.

	AEs Related to Treatment n = 36	
	All Grades (%)	G3 or G4 (%)
Diarrhea	30	0
Nausea	44	3
Vomiting	33	0
Mucositis/Stomatitis	6	0
Hand-foot syndrome	0	0
Dermatitis	6	0
Fatigue/lethargy	36	3
Anemia	6	3
Neutropenia	0	0
Elevated bilirubin	3	3

94 Poster Session

LEAP-005: A phase II multicohort study of lenvatinib plus pembrolizumab in patients with previously treated selected solid tumors—Results from the colorectal cancer cohort. *First Author: Carlos Gomez-Roca, Institut Claudius Regaud, Toulouse/Iuct, France*

Background: Pembrolizumab (pembro), an anti-PD-1 antibody, is approved for the treatment of patients (pts) with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair (MMR) deficient colorectal cancer, both as first-line treatment and after progression following treatment with fluoropyrimidine, oxaliplatin, and irinotecan. The combination of lenvatinib, a multiple receptor tyrosine kinase inhibitor, and anti-PD-1 treatment showed synergistic antitumor activity in preclinical models. LEAP-005 (NCT03797326) is evaluating the efficacy and safety of lenvatinib plus pembro in pts with previously treated advanced solid tumors. We present findings from the colorectal cancer cohort. **Methods:** In this nonrandomized, open-label, phase 2 study, adult pts (aged ≥18 y) with histologically/cytologically documented metastatic and/or unresectable colorectal cancer, non-MSI-H/pMMR tumor per local determination, previous treatment with oxaliplatin and irinotecan in separate lines of therapy, measurable disease per RECIST v1.1, ECOG PS of 0–1, and a tissue sample evaluable for PD-L1 expression were eligible. Pts received lenvatinib 20 mg QD plus pembro 200 mg Q3W for up to 35 cycles of pembro (~2 y) or until confirmed disease progression, unacceptable toxicity, or withdrawal of consent. Treatment with lenvatinib could continue beyond 2 y in pts with clinical benefit. Primary endpoints were ORR (per RECIST v1.1 by blinded independent central review) and safety. Secondary endpoints included disease control rate (DCR), duration of response (DOR), PFS, and OS. Tumor imaging was performed Q9W from treatment initiation for 54 wks, then Q12W to week 102, and Q24W thereafter. **Results:** 32 pts with colorectal cancer received treatment with lenvatinib plus pembro (median age, 56 y [range, 36-77]; male, 81%; 3L, 91%); median time from first dose to data cutoff (April 10, 2020) was 10.6 mos (range, 5.9-13.1) ORR was 22% (95% CI, 9-40; Table). Grade 3-5 treatment-related AEs occurred in 16 (50%) pts. Treatment-related AEs led to treatment discontinuation in 3 pts (grade 2 ischemic stroke [n = 1], grade 3 increased liver transaminases [n = 1], grade 5 intestinal perforation [n = 1]). Efficacy Results. Clinical trial information: NCT03797326. NR, not reached [a]Confirmation was not required for best overall response of SD, but a final visit response of SD or better must have occurred ≥6 wks after starting study treatment **Conclusions:** In pts with previously treated advanced non-MSI-H/pMMR colorectal cancer, lenvatinib plus pembro demonstrated promising antitumor activity and a manageable safety profile. Enrollment in the colorectal cohort was expanded to 100 pts. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Outcome	N = 32
ORR (CR+PR), % (95% CI)	22 (9-40)
DCR (CR+PR+SD[a]), % (95% CI)	47 (29-65)
DOR, median (range), mos	NR (2.1+-10.4+)
PFS, median (95% CI), mos	2.3 (2.0-5.2)
OS, median (95% CI), mos	7.5 (3.9-NR)

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Phase II trial of nivolumab and metformin in patients with treatment refractory microsatellite stable metastatic colorectal cancer. *First Author: Mehmet Akce, Department of Hematology and Medical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA*

Background: Preclinical data suggests metformin can improve immune exhaustion of tumor infiltrating lymphocytes and potentiate the effects of PD-1 blockade. By normalizing the hypoxic TME, metformin was shown to improve cytotoxic T cell function and efficacy of anti-PD-1 antibody in highly aggressive B16 melanoma and MC38 colon adenocarcinoma tumor models. Based on this preclinical rationale we conducted a phase II study with nivolumab and metformin combination in treatment refractory MSS metastatic colorectal cancer (mCRC). **Methods:** Nivolumab 480 mg IV every 4 weeks and Metformin 1000 mg po twice daily was administered in 28-day cycles following a 14-day metformin only lead-in phase.Eligible patients included stage IV metastatic treatment refractory MSS mCRC (patients must have received oxaliplatin, irinotecan, and fluoropyrimidine), age ≥18 years, ECOG PS 0-1, adequate organ function, no prior anti PD-1 agent. The primary endpoint was overall response rate (ORR). Secondary endpoints included overall survival (OS) and progression free survival (PFS). Simon's two-stage Minimax design was employed (H_0: ORR =4%; H_1: ORR=15%; alpha = 0.1; power =80%). If ≥1 objective response was observed in the first evaluable 18 patients, 10 additional patients would be included in the cohort. ≥3 objective responders in 28 patients would be required to be considered positive study. Pre-treatment and on-treatment research biopsies and correlative peripheral blood specimens were collected. **Results:** A total of 24 patients were enrolled, 6 patients were replaced per protocol, and 18 patients had evaluable disease. Of the 18 evaluable patients 11/18 (61%) were female, median age 58 [IQR 50-67]. 2 patients had prolonged stable disease (4 and 10 cycles). No patients had objective response based on RECIST 1.1. Median OS and PFS was 5.1 months [95% CI (2-11.7)] and 2.3 months [95% CI (1.7-2.4)], respectively. Most common grade 3 and 4 toxicities were anemia (n=2) and diarrhea (n=2). **Conclusions:** In treatment refractory MSS mCRCnivolumab and metformin combination was well tolerated. Two patients achieved stable disease, but no objective response was seen; therefore, the study did not proceed with the second stage of enrollment. Immunologic correlative analysis of this study is ongoing. Clinical trial information: NCT03800602. Research Sponsor: Bristol-Myers Squibb.

96 Poster Session

Implementation of hepatic artery infusion (HAI) chemotherapy for unresectable colorectal liver metastases (CRLM): The University of Miami experience. *First Author: Agustin Pimentel, University of Miami Sylvester Comprehensive Cancer Center, Miami, FL*

Background: In patients with unresectable liver-confined CRLM, regional chemotherapy via HAI in combination with modern systemic chemotherapy (CT) can achieve hepatic disease control and expand surgical resectability. We describe patient selection and early outcomes following implementation of a HAI program at our tertiary referral academic center. **Methods:** We analyzed demographics, previous systemic treatment, primary tumor location, molecular profiling, extent of hepatic/extrahepatic disease, perioperative HAI outcomes (toxicity, conversion to resection/ablation, radiographic response), and overall survival (OS) in CRLM patients selected for HAI treatment (01/2018–06/2020) after multidisciplinary review. **Results:** Of 35 patients with unresectable CRLM (primary: colon, n = 24; rectum, n = 11) selected for HAI, 57% were heavily pre-treated (with at least 2 lines of pre-HAI systemic chemotherapy), 71% had a Fong clinical risk score ≥3, 86% presented with synchronous disease, 80% had bilobar metastasis, and 86% had > 5 tumors. All tumors were microsatellite stable, with 20% harboring *KRAS/NRAS* mutations and none had class I/II *BRAF* mutations. HAI was initiated at a median 14 (IQR 3, 64) months after CRLM diagnosis, and administered for a median of 7 (range 2, 16) cycles; 91% of patients (31/34) received concurrent HAI and systemic chemotherapy. Although most (69%) patients experienced some degree of hepatic toxicity during HAI therapy resulting in FUDR dose reduction and steroid administration, biliary sclerosis requiring intervention was observed in only 3 (9%) of patients. The overall perioperative morbidity was 17%, and there were no surgical-related 90-day mortalities following HAI pump placement. Excluding patients who initiated HAI treatment within the last 3 months of the study period (n = 3), 13 of 32 patients (41%) were rendered disease-free in the liver following complete resection and/or ablation in combination with HAI/systemic chemotherapy; in the remaining 19 patients (59%), hepatic progression-free survival was 7.3 months (IQR 4, 12). At a median follow-up of 11.2 months, post-HAI median OS for the overall cohort was 12.3 (IQR 7, 20) months. Patients undergoing complete resection/ablation demonstrated improved survival compared with those with progressive disease (median 20 vs 12 months, respectively). **Conclusions:** Implementation of a HAI program for multimodality liver-directed management of unresectable CRLM is feasible and is associated with meaningful clinical outcomes unlikely to be achieved with systemic therapy alone in heavily pre-treated patients. Research Sponsor: None.

97 Poster Session

Targeted multiplex proteomics (TMP) and genomics of early-onset colorectal cancer (EO-CRC). *First Author: Audrey E. Kam, Rush University Medical Center, Chicago, IL*

Background: The incidence and mortality of early-onset colorectal cancer (EO-CRC) is on the rise. Consequently, there is an urgent unmet need to better understand their unique tumor biology to expand therapeutic options and improve clinical outcomes. **Methods:** Exploratory Targeted multiplex proteomics (TMP) and targeted 648 gene panel was performed on specimens from 35 patients with resected colon cancer diagnosed at age < = 40 years. TMP panel consisted of 72 proteins involved in differentiation, tumorigenesis, and response to chemotherapy, targeted therapy, and immunotherapy. Clinicopathologic and genomic data were also collected. **Results:** The median age of diagnosis was 33 years. The cohort included 15 male and 20 female patients. 20 (57%) had left-sided tumors and 6 (17%) had stage IV disease. Notable genomic alterations included mutations in: BRAF V600E (2/35); RAS (15/35); PIK3CA exon 9 or 20 (5/35); and ERBB2 (2/35). One patient exhibited ERBB2 amplification. 9/35 tumors were MSI-H. TMP analysis revealed overexpression of chemotherapy resistance proteins in several patients: ALDH1A1: 16/35; ERCC1: 1/35; GART: 26/35; MDR1: 9/35; MGMT: 5/35; RRM1: 6/35; TUBB3: 1/35; TYMS: 2/35; XRCC1: 11/35. In contrast, some tumors exhibited elevated biomarkers of chemosensitivity: hENT1: 8/35; DHFR: 12/35; TYMP: 15/35; OPRT: 8/35; SLFN11: 1/35; TLE: 11/35; TOPO1: 12/35; TOPO2A: 1/35. Protein targets of cell signaling pathways were overexpressed in a number of tumors: CAT: 16/35; CAV-1: 6/35; CBL: 2/35; E-Cadherin: 19/35; HSP90A: 16/35; HSP90B: 18/35; MET: 5/35; NQO1: 18/35; paxillin: 4/35; SRC: 21/35; STAT3: 11/35. Regarding EGFR and KRAS, none of the tumors exhibited elevated protein expression level. Furthermore, RAS mutational status did not correlate with the level of EGFR or KRAS protein expression. Antibody drug conjugate biomarkers were observed. HER2 overexpression was noted in one patient who had a confirmed ERBB2 amplification. Regarding immunotherapy targets, PDL-1 protein was not overexpressed in any tumor, whereas MSLN and TROP2 were elevated in 1/35 and 2/35 patients, respectively. **Conclusions:** TMP analysis of EO-CRC patients revealed marked heterogeneity in the expression of proteins involved in differentiation, tumorigenesis, and response to chemotherapy, targeted therapy, and immunotherapy. Differential protein expression may provide insight into therapeutic vulnerabilities for EO-CRC. Furthermore, the discordance between detected genomic alterations and protein expression levels highlights the complementary nature of genomic sequencing and TMP analysis. Research Sponsor: None.

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Polymorphisms of pluripotency transcription factors for predicting cetuximab efficacy in metastatic colorectal cancer: Data from FIRE-3 and TRIBE trials. *First Author: Hiroyuki Arai, Division of Medical Oncology, USC Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, CA*

Background: Cancer stem cells are subpopulation of cancer cells characterized by the self-renewal ability, and primarily maintained by a network of pluripotency transcription factors (PTFs). Despite their chemo-resistant phenotype, recent clinical trials data show cetuximab (Cet) is more beneficial for a subset of metastatic colorectal cancer (mCRC) categorized in a mesenchymal/stem-like subtype based on transcriptomic classifications. We investigated whether single nucleotide polymorphisms (SNPs) in PTF encoding genes have predictive values for the efficacy of Cet in mCRC patients. **Methods:** Genomic and clinical data from three independent cohorts of patient treated with first-line chemotherapy (n = 451, in total) were tested: Cet cohort (FOLFIRI+Cet arm in FIRE-3 trial, n = 129); bevacizumab (Bev) cohort 1 (FOLFIRI+Bev arm in FIRE-3 trial, n = 107) and Bev cohort 2 (FOLFIRI+Bev arm in TRIBE trial, n = 215), as controls. Genomic DNA extracted from blood samples was genotyped using an OncoArray (Illumina, Inc., San Diego, CA, USA). Eight SNPs in PTF encoding genes (*NANOG* rs11055786, *NANOG* rs11055767, *NANOGP8* rs2168958, *NANOGP8* rs9944179, *POU5F1* rs3130501, *POU5F1* rs3130932, *SOX2* rs11915160, and *MYC* rs3891248) were tested for association with progression-free survival (PFS) and overall survival (OS), using Cox proportional hazards model. **Results:** In the Cet cohort, three SNPs were significantly associated with PFS in univariate analysis: *NANOG* rs11055767 (C/C vs any A allele, hazard ratio [HR] = 0.62, 95% confidence interval [CI] = 0.42–0.94, log-rank p = 0.02), *NANOGP8* rs2168958 (A/A vs any C allele, HR = 2.12, 95% CI = 1.36–3.29, log-rank $p < 0.01$), and *NANOGP8* rs9944179 (G/G vs any A allele, HR = 3.68, 95% CI = 1.46–9.31, log-rank $p < 0.01$). Multivariate analysis confirmed the significance in *NANOGP8* rs2168958 and *NANOGP8* rs9944179. Furthermore, two SNPs were significantly associated with OS in multivariate analysis: *POU5F1* rs313051 (G/G vs any A allele, HR = 0.46, 95% CI = 0.22–0.99, adjusted p = 0.04) and *POU5F1* rs3130932 (A/A vs any C allele, HR = 0.46, 95% CI = 0.22–0.93, adjusted p = 0.03). Both in the Bev cohorts 1 and 2, no significant associations between the SNPs and clinical outcomes were observed. **Conclusions:** The current findings suggest that polymorphisms in the PTF genes could be predictive markers for Cet in patients with mCRC. Further studies are warranted to validate the predictive utility. Research Sponsor: This work was supported by the National Cancer Institute [P30CA 014089 to HJL], Gloria Borges WunderGlo Foundation, Dhont Family Foundation, Victoria and Philip Wilson Research Fund, San Pedro Peninsula Cancer Guild, and Daniel Butler Research Fund.

99 Poster Session

Folate pathway gene expression in metastatic colorectal cancer patients treated with arfolitixorin/5-FU-based chemotherapy. *First Author: Roger Tell, Isofol Medical AB, Gothenburg, Sweden*

Background: Arfolitixorin is the natural, biologically active form of the marketed folates and is expected to be efficacious in a larger proportion of patients with less inter- and intra-individual variability compared with e.g. leucovorin. We have previously found a positive correlation between survival and expression of folate pathway genes in stage III/IV CRC treated with 5-fluorouracil/leucovorin (5-FU/LV). Low expression of folate-related genes may lead to poor response to 5-FU/LV-based treatment, since suboptimal transport and metabolization of LV yield insufficient active [6R]-5,10-methylenetetrahydrofolate and weak inhibition of the target enzyme thymidylate synthase (TYMS). The aim of the present study was to investigate possible confounders and biomarkers of arfolitixorin/5-FU-based treatment in relation to safety and response in a phase I/IIa metastatic colorectal cancer (mCRC) trial. **Methods:** ISO-CC-005 is a multi-center, phase I/IIa study in mCRC patients eligible for 5-FU/folate therapy alone or in combination with irinotecan or oxaliplatin ± bevacizumab. Patients were also treated with different doses of arfolitixorin as a single or double bolus. The study investigated safety and tolerability of arfolitixorin, and anti-tumor activity was evaluated by overall response rate (ORR) per RECIST v1.1 after 4 cycles of chemotherapy. RNA was prepared from FFPE tumor tissue, reverse transcribed and used for gene expression profiling. The following genes of interest were evaluated: *ABCC3*, *MTHFD2*, *SLC46A1*, *SLC19A1*, *SLC25A32* and *TYMS*. An ANOVA test was used to rule out potential biases in the baseline expression levels of the genes and to assess the potential association with clinical response. **Results:** Eighty-one (77.1%) of 105 patients provided material for this analysis. A lower pre-treatment expression of TYMS was associated with clinical benefit (PR and SD; p = 0.021). No clear association was identified between the gene expression markers and the number of adverse events. Gender was not significantly associated with differences in gene expression. **Conclusions:** Low pre-treatment expression levels of TYMS were associated with clinical benefit (PR and SD) following treatment. Given the role of this gene in the folate metabolic pathways we plan to further assess its predictive potential on a larger cohort during our ongoing global phase III AGENT study. In parallel an assessment of the expression of the other candidate genes on specific patient sub-groups is currently ongoing. These studies will provide additional cues on the use of these genes as predictive markers for treatment outcome and their role in the mode of action of the drug. Clinical trial information: NCT02244632. Research Sponsor: Isofol Medical AB.

100 Poster Session

Translational research of VOLTAGE-A: Efficacy predictors of preoperative chemoradiotherapy and consolidation nivolumab in patients with both microsatellite stable and microsatellite instability-high locally advanced rectal cancer. *First Author: Koji Inamori, Department of Colorectal Surgery, National Cancer Center Hospital East, Kashiwa, Japan*

Background: In VOLTAGE-A, chemoradiotherapy (CRT; 50.4Gy with capecitabine, 1,650mg/m^2) followed by five cycles of consolidation nivolumab (nivo) (240mg q2 weeks) showed 30% pathological complete response [pCR; AJCC tumor regression grade (TRG) 0] and 38% major pathological responses (AJCC TRG 0-1) in patients with microsatellite stable (MSS) locally advanced primary rectal cancer (LARC). In addition, 60% pCR was observed in patients with microsatellite instability-high (MSI-H) LARC. In this study, we aimed to determine the predictive biomarkers for efficacy of sequential preoperative CRT and consolidation nivo. **Methods:** Serial tumor biopsies were performed at four time points: pre-CRT; post-CRT; post-3 cycles of nivo; and pre-surgery. We analyzed the immune status of the patients by flow cytometry using the collected tumor-infiltrating lymphocytes (TILs) dissociated from tumor samples. Whole exome and RNA sequencing analyses were conducted using the extracted DNA and RNA from tumor, respectively. The PD-L1 status of tumor samples was also evaluated by *in vitro* diagnostic immunohistochemistry staining. **Results:** Of the 38 MSS patients whose PD-L1 tumor proportion score (TPS) was analyzable in pre-CRT samples, the pCR rates were 67% (6/9) and 17% (5/29) in positive (≥1%) and negative PD-L1 status (p = 0.009), respectively. Among the 24 MSS patients whose samples were serially collected, the pCR rates according to CD8$^+$ T cells/effector regulatory T cells (CD8/eTreg) ratio in TILs of pre-CRT samples ≥2.5 and < 2.5 were 78% (7/9) and 13% (2/15), respectively (p = 0.003). The CD8/eTreg ratio in TILs was consistently high in patients with pCR during the study treatments. Ki-67 and PD-1 expression by CD8$^+$ T cells in TILs was significantly high in pre-CRT samples from patients TRG 0-1. Conversely, in patients with TRG 2-3, CTLA-4 expression by both CD4$^+$ T cells and CD8$^+$ T cells in TILs was significantly high after five cycles of nivo, suggesting the potential resistance mechanisms of nivo monotherapy. Of the 21 MSS patients whose consensus molecular subtype (CMS) was analyzable, those with CMS1 and CMS3 tumors achieved 100% (2/2) and 60% (4/6) TRG 0-1, respectively. In contrast, patients with CMS2 and CMS4 tumors achieved 43% (3/7) and 29% (2/7) TRG 0-1, respectively. The tumor mutational burden (TMB) of pre-CRT samples in five MSI-H patients was higher than that in the 24 MSS patients (median: 13.2 vs. 0.99 mutation/Mbp, p < 0.0001). Among MSS patients, TMB was higher in patients with TRG 0-1 than in patients with TRG 2-3 (median: 1.45 vs. 0.84 mutation/Mbp, p = 0.016). **Conclusions:** Positive PD-L1 TPS; high CD8/eTreg ratio; Ki-67, PD-1, and CTLA-4 expression by CD8$^+$ T cells in TILs; CMS 1 or 3; and high TMB can be good predictors of efficacy of preoperative CRT followed by nivo. Clinical trial information: NCT02948348. Research Sponsor: ONO PHARMACEUTICAL CO., LTD.

101 Poster Session

The effects of neoadjuvant chemoradiation on exosomal markers (CD63 and CD9) expression in patients with locally advanced rectal adenocarcinoma. *First Author: Moh'd M. Khushman, Medical Oncology, The University of South Alabama, Mitchell Cancer Institute, Mobile, AL*

Background: Exosomes mediate intercellular communications and have pivotal roles in cancer development. CD63 and CD9 are widely accepted exosomal markers. The effect of concurrent chemoradiation on the expression of exosomal markers is unknown. Here we explored the effect of neoadjuvant concurrent chemoradiation (NCCR) on exosomal markers (CD63 and CD9) expression in patients with locally advanced rectal cancer (LARC). **Methods:** Between 2015 and 2018, 33 patients had LARC treated with NCCR and had pre NCCR biopsy and post NCCR resected rectum examined for exosomal markers expression using immunohistochemistry. Two pathologists independently scored CD63 and CD9 staining in the tumor. Staining intensity was graded from 1-3. Staining percentage was estimated in 10% increments. Mean quick-score (Q-score) was calculated (intensity x percentage). Un-Paired t test was used for statistical analysis. **Results:** In our cohort, median age was 59 years. Males represented 79% of the patients. Caucasians, African American and other ethnic groups represented 70%, 27% and 3% respectively.The mean tumor CD63 score in pre NCCR biopsy vs post NCCR resected rectum was 106 vs 165 (p = 0.0022). The mean tumor CD9 score in pre NCCR biopsy vs post NCCR resected rectum was 136 vs 215 (p < 0.0001). The exosomal markers expression in the adjacent normal mucosa (ANM) from pre NCCR biopsy and post NCCR resected rectum was only performed in16 out of 33 patients (due to ANM tissue availability). The mean ANM CD63 score in pre NCCR biopsy vs post NCCR resected rectum was 166 vs 183 (p = 0.37). The mean ANM CD9 score in pre NCCR biopsy vs post NCCR resected rectum was 104 vs 145 (p = 0.0897). **Conclusions:** In patients with LARC, the expression of exosomal markers (CD63 and CD9) increased after treatment with NCCR. Our results show that the expression of CD63 and CD9 is relatively higher in rectal cancer specimens treated with NCCR and thus suggest a possible role of these exosomes in adaptive response to NCCR. Further follow-up and laboratory studies are required to precisely understand the underlying mechanism(s). Research Sponsor: None.

102 Poster Session

Minimal residual disease (MRD) detection with circulating tumor DNA (ctDNA) from personalized assays in stage II-III colorectal cancer patients in a U.K. multicenter prospective study (TRACC). *First Author: Gayathri Anandappa, The Royal Marsden NHS Foundation Trust, London, United Kingdom*

Background: Numerous studies have shown the clinical utility of ctDNA, a non-invasive biomarker to detect MRD and stratify CRC patients who are more likely to relapse. We present an analysis of MRD detection in CRC patients from a prospective multicentre UK study, who were monitored pre- and post-surgery before adjuvant chemotherapy (ACT). **Methods:** The study recruited patients diagnosed with stage II-III CRC (n=122), including a subset of rectal patients who underwent trimodality treatment (TMT). All patients had their primary tumor resected and 56% (68/122) received ACT. Paired plasma samples (n=244) were collected before surgery/neaodjuvant chemoradiotherapy and after surgery; median follow-up for survival was 15.48 months (0.16 - 42.1 months). Individual tumors and matched germline DNA were whole-exome sequenced and somatic single nucleotide variants (SNVs) identified. Multiplex PCR assays were designed to track tumor-specific SNVs (Signatera, bespoke mPCR NGS assay) in plasma samples. The study evaluated ctDNA status and clinical outcomes including radiologic imaging. Cox regression was used to calculate recurrence-free survival (RFS) in patients stratified by post-op ctDNA status. Patients were also stratified into low and high-risk groups based on the clinicopathological features. Multivariate analysis was performed with covariates: ctDNA, age, gender, laterality, stage, number of lymph node resected, MSI & TMB. **Results:** Pre-treatment ctDNA was detected in 93.4% (100/107) of patients. Post-operative ctDNA status prior to ACT was assessed in 107 patients, of whom, 13% (14/107) were MRD-positive (MRDpos). Of the MRDpos patients 42.9% (6/14) eventually relapsed. In contrast, only 8.6% (8/93) of MRD-negative (MRDneg) cases relapsed (HR: 10; 95% CI: 3.3-30; p<0.001). MRD rates stratified by risk features in each of the stages with respective recurrence rates are shown in Table. In stage III patients (n=64), 45.4% (5/11) of the MRDpos patients relapsed, whilst only 17% (9/53) of the MRDneg cases relapsed (HR: 9; 95% CI:2.6-32; p<0.0001). In the multivariate analysis, ctDNA status was the most significant prognostic factor associated with RFS (HR: 28.8, 95% CI: 3.5-234.1; p<0.001). **Conclusions:** Postoperative ctDNA analysis with tumor informed assay enables detection of CRC patients at high-risk of recurrence. Early detection of MRD could guide ACT decisions in intervention trials and is currently underway in TRACC. Clinical trial information: NCT04050345. Research Sponsor: National Institute of Health Research Biomedical Research Centre & Royal Marsden Hospital NHS Foundation Trust GI & Lymphoma Unit, Pharmaceutical/Biotech Company.

MRD and recurrence rates (n=107)

Setting	MRD detection rates at the first post-op time point	Recurrence rates	
		MRDpos	MRDneg
Stage II (Low risk)	1/31 (3.2%)	0/1 (0%)	0/30 (0%)
Stage II (High risk)	2/15 (13.3%)	1/2(50%)	0/13 (0%)
Stage III (Low risk)	3/20 (15%)	0/3 (0%)	2/17 (11.7%)
Stage III (High risk)	7/19 (36.8%)	4/7 (57.1%)	3/12 (25%)
TMT group	1/22 (4.5%)	1/1 (100%)	3/21 (14.2%)

103 Poster Session

Single nucleotide polymorphisms (SNPs) in endoplasmic reticulum (ER) stress response genes to predict first-line treatment outcome in patients (pts) with metastatic colorectal cancer (mCRC): Data from the MAVERICC and FIRE-3 trials. *First Author: Francesca Battaglin, Division of Medical Oncology, USC Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, CA*

Background: ER stress, triggered by the disruption of intracellular protein homeostasis, promotes the activation of a highly conserved adaptive program called unfolded protein response (UPR). UPR signaling has been reported to contribute to tumor initiation and progression, as well as microenvironment remodeling and chemoresistance in multiple cancer types, including CRC. Several studies point to a direct role of the UPR in tumor angiogenesis and an interaction with EGFR signaling. We therefore hypothesized that genetic variants in ER stress response genes may predict first-line treatment outcome in mCRC pts. **Methods:** The impact on outcome of 17 functional SNPs in 8 core genes of the ER stress response pathway (*IRE1*, *PERK*, *ATF6*, *XBP1*, *CHOP*, *GRP78*, *GADD34*, *ATF4*) was analyzed on a total of 560 pts enrolled in two independent randomized first-line trials: MAVERICC (FOLFIRI/bevacizumab, [bev] n = 163; FOLFOX6/bev, n = 161), and FIRE-3 (FOLFIRI/bev, n = 107; FOLFIRI/cetuximab [cet], n = 129). Genomic DNA from blood samples of pts was genotyped through the OncoArray, a custom array manufactured by Illumina. The association between SNPs and clinical outcomes was evaluated using Cox regression and log-rank tests. The SNP*treatment interaction was assessed in both trials. **Results:** *IRE1* rs16947383 any T allele variant was associated with shorter progression free survival (PFS) and overall survival (OS) compared to the C/C genotype in pts treated with FOLFIRI/bev in the MAVERICC trial both in uni- and multivariate analysis: 10.5 vs 14.1 months for PFS, adjusted hazard ratio (HR) 1.83, 95% confidence interval (CI) 1.12-2.99, adjusted *P*-value = 0.02; 23.8 vs 38.4 months for OS, adjusted HR 2.12, 95%CI 1.1-4.09, adjusted *P*-value = 0.02. The association with OS was validated in the FIRE-3 FOLFIRI/bev arm where any T allele carriers showed significantly shorter OS compared to the C/C genotype in both uni- and multivariate analysis: 21.1 vs 44.2 months, adjusted HR 2.06, 95%CI 1.01-4.18, adjusted *P*-value = 0.05. This effect was not observed in MAVERICC FOLFOX6 and FIRE-3 cet cohorts. A significant interaction was found between *IRE1* rs16947383 and treatment on OS in both trials: *P* = 0.04 in MAVERICC (FOLFIRI vs FOLFOX6), and *P* = 0.03 in FIRE-3 (bev vs cet). In the MAVERICC FOLFOX6/bev arm, *XBP1* rs2239815 and *PERK* rs6731022 SNPs were associated with shorter PFS and OS, while *GADD34* rs610308 with longer OS, in multivariable analysis ($P < 0.05$). **Conclusions:** Our results provide evidence that germline polymorphisms in ER stress response genes may have a predictive value in mCRC pts receiving first-line bev-based treatment and contribute to modulate anti-VEGF efficacy. Research Sponsor: National Cancer Institute P30CA014089, Gloria Borges WunderGlo Foundation, Dhont Family Foundation, Victoria and Philip Wilson Research Fund, San Pedro Peninsula Cancer Guild, and Daniel Butler Research Fund.

104 Poster Session

Chemoradiation-induced molecular alterations and associated outcomes in patients with rectal cancer. *First Author: Mohamed E. Salem, Levine Cancer Institute, Atrium Health, Charlotte, NC*

Background: Molecular changes and associated acquired resistance of rectal tumors following chemoradiotherapy (CRT) have not been well studied. We aimed to examine CRT-induced molecular changes and prognostic associations in rectal cancer patients (pts) undergoing preoperative CRT followed by surgery. **Methods:** A paired analysis using pre-CRT biopsies and the corresponding post-CRT resected tissues of rectal cancer patients undergoing preoperative CRT followed by surgery was performed. Pre- and post-CRT tumor samples underwent next-generation sequencing (NGS) by Tempus xT assay, which detects a panel of 596 gene mutations, including single nucleotide variants, insertions/deletions, copy number amplifications, and gene rearrangements. The cancer driver gene was detected based on positional clustering of gained mutations using OncodriveCLUST. The paired t-test was used to examine differences in tumor mutational burden (TMB) and microsatellite instability (MSI) between pre- and post-CRT samples. **Results:** In total, 61pts of median age 61yrs–75% white, 18% black, and 57% male–with localized rectal cancer were studied. NGS testing was performed in 57 pt tumor samples; 43 pts had pre-CRT samples, 48 pts had post-CRT samples, and 34 pts had paired samples. The most frequent genetic alterations seen in the 43 pre-CRT tumor samples were *APC* (37.2%), *ARID1B* (30.2%), *KMT2C* (30.2%), *ZFXH3* (25.6%), *FLT4* (20.9%), *MLLT3* (20.9%), and *TP53* (20.9%), whereas in the 48 post-CRT tumor samples, the most frequent mutations were *APC* (54.2%), *TP53* (35.4%), *KRAS* (27.1%), *MKI67* (25.0%), *KMT2C* (18.8%), *APOB* (14.6%), and *CEBPA* (12.5%). Comparing the pre- and post-CRT samples, no significant differences in TMB (median: 5.0 mut/MB vs. 3.3 mut/MB, p=0.922) or MSI status by NGS (p=0.069) were observed. Among the 34 pts with paired samples, 26.5% (9/34) relapsed, and 17.6% (6/34) died. When examining tumor mutation changes between pre- and post-CRT samples (table), the most common gained mutations were seen in *APC* (29.4%), *MKI67* (26.5%), *KTM2C* (17.6%), and *TP53* (17.67%); and most common losses were in *ARID1B* (26.5%), *ZFHX3* (26.5%), *FLT4* (21.0%) and *GATA6* (21.0%). Of the gained mutations, OncodriveCLUST analysis showed that *MKI67* potentially carries a driver mutation (pG866V) at exon 12 (p = 0.045), which exclusively existed in the two relapsed pts. **Conclusions:** Our data suggest that CRT did not alter MSI status nor the level of TMB. However, CRT did result in gained molecular alterations that could be responsible for treatment resistance and predict relapse. Gained *MKI67* mutation may be a prognostic biomarker for relapse after CRT. Further prospective studies are needed to validate these findings. Research Sponsor: Levine Cancer Inst.

Gained mutation N = 34 (%)	Gained mutations in Relapsed patients N=9 (%)
***APC* 29.4**	*APC* 33.3
***MKI67* 26.5**	*BCR* 22.2
***KMT2C* 17.6**	*FAM104A* 22.2
***TP53* 17.6**	*KRAS* 22.2
***APOB* 14.7**	***MKI67* 22.2**
***GNAS* 14.7**	*TP53* 22.2
***BCLAF1* 11.8**	
***CEBPA* 11.8**	
***CYP2D6* 11.8**	
***FOXL2* 11.8**	

ABSTRACT WITHDRAWN

106 Poster Session

Characteristics of genomic alterations in circulating tumor DNA (ctDNA) in patients (Pts) with advanced gastrointestinal (GI) cancers in nationwide large-scale ctDNA screening: SCRUM-Japan Monstar-Screen. *First Author: Yoshiaki Nakamura, Department of Gastroenterology and Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa, Japan*

Background: Analysis of ctDNA has been utilized in pts with advanced GI cancer for identification of genomic alterations for targeted therapy. However, the characteristics of ctDNA genomic alterations of GI cancers compared to non-GI cancers remains unclear. **Methods:** Pts with advanced solid tumors were eligible in MONSTAR-SCREEN, a nationwide ctDNA screening project in Japan. Plasma samples were analyzed by an NGS-based 70-gene ctDNA assay, FoundationOne Liquid (F1L) at a CLIA-certified and CAP-accredited laboratory since Jul 2019. For treatment-naïve pts, tumor tissue samples were analyzed by FoundationOne CDx (F1CDx), a 324-gene tissue-based panel. **Results:** As of Jun 18 2020, out of enrolled 540 pts with advanced solid tumor, 470 pts, consisting of 133 with advanced GI cancers (67 colorectal, 48 gastric, 14 esophageal, 2 gastrointestinal tumor (GIST) and 2 small intestinal) and 337 non-GI cancers (103 hepatobiliary and pancreatic, 70 genitourinary, 64 breast, 46 head and neck, 33 gynecologic, and 21 skin), had an available ctDNA result. Sequencing success rate was similar between GI and non-GI cancers (91.7% vs. 89.3%, P = 0.50). GI cancers had a significantly higher ctDNA level (maximum variant allele fraction) than non-GI cancers (median, 11.8% vs. 0.57%; P = 1.6E-7). The most frequently altered genes were *TP53* (73%), *APC* (73%), *KRAS* (30%), *BRAF* (15%), and *PIK3CA* (12%) in colorectal cancer, *TP53* (44%), *KRAS* (19%), *PIK3CA* (15%), *ATM* (10%), and *ERBB2* (10%) in gastric cancer, and *TP53* (79%), *ATM* (21%), *ERBB2* (21%) in esophageal cancer. Mutations in genes in pathways related to RAS/RAF/MEK (39.1 % vs. 21.4 %, P = 1.8E-4), receptor tyrosine kinase (20.3% vs 11.9%, P = 0.027), p53 (66.2% vs 49.6%, P = 0.0014), and Wnt (41.4% vs 4.7%, P = 4.4E-21) were significantly enriched in GI cancers compared to non-GI cancers. Tumor tissue samples were analyzed using F1CDx for 63 treatment-naïve pts, in which 51 (31.3%) of 132 alterations identified by F1L were not detected by F1CDx. **Conclusions:** GI cancers had higher ctDNA levels and distinct characteristics of ctDNA genomic alterations from non-GI cancers with an enrichment in several oncogenic pathways. One-third of ctDNA alterations were detected in only ctDNA, indicating the potential of ctDNA analysis to identify heterogenous genomic alterations in advanced GI cancer. Clinical trial information: UMIN000036749. Research Sponsor: SCRUM-Japan Funds.

108 Poster Session

Tumor bulk as a prognostic biomarker and predictor of benefit from anti-EGFR therapy in patients with metastatic colorectal cancer: Analysis of 476 patients from the ARCAD Clinical Trials Program. *First Author: Benjamin Adam Weinberg, Ruesch Center for the Cure of Gastrointestinal Cancers, Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC*

Background: Primary tumor sidedness has emerged as a prognostic and predictive biomarker for patients (pts) with metastatic colorectal cancer (mCRC). Tumor bulk has also been postulated to predict response to anti-EGFR therapy. We sought to evaluate the role of tumor bulk as a predictive biomarker to anti-EGFR therapy in pts with left- (LS) and right-sided (RS) mCRC. **Methods:** Data from 476 pts with mCRC enrolled across 2 first-line trials of anti-EGFR plus chemotherapy versus chemotherapy were pooled. Pts were included if there was available information on tumor sidedness and tumor bulk. All were *KRAS* wild-type and *BRAF* wild-type or unknown *BRAF* status. The right colon was defined as the cecum through the transverse colon, and the left colon as the splenic flexure through the rectum. Tumor bulk was the mean tumor size of target lesions at baseline, bulky defined as $>$ 3.5 cm. Overall survival (OS) and progression-free survival (PFS) were assessed using Kaplan-Meier and Cox models adjusting for performance status (PS), platelet count, primary tumor (PT) resection, number of metastatic sites, and stratified by study. **Results:** Pts with bulky tumors (211, 44%) had higher PS, white blood cell and platelet counts, higher CEA, fewer sites of metastatic disease, more liver than lung metastases, and fewer had PT resection. OS and PFS medians in months (mos) are presented in the table with 95% confidence intervals (95%CIs). Bulky tumors had inferior median OS compared with non-bulky (mOS, 17.9 vs. 21.3 mos, HR_{adj} 1.33, 95% CI 1.05-1.69, P = 0.016) although median PFS was similar (mPFS, 8.6 vs. 8.7 mos, HR_{adj} 1.15, 95% CI 0.92-1.42, P = 0.21). **Conclusions:** Tumor bulk is an independent prognostic factor for OS in *KRAS* wild-type and *BRAF* wild-type or unknown *BRAF* status pts. Pts with non-bulky RS tumors have survival outcomes similar to pts with bulky LS tumors. Although the mPFS for pts with RS tumors treated with anti-EGFR therapy was the lowest across subgroups, this finding was not statistically significant. Further research is warranted into whether pts with bulky RS tumors benefit from anti-EGFR therapy. Clinical trial information: NCT00182715, NCT00640081. Research Sponsor: None.

	mPFS (95%CI)			mOS (95%CI)		
	w/o anti-EGFR	w/ anti-EGFR	all	w/o anti-EGFR	w/ anti-EGFR	all
LS bulky (N = 148)	9.0 (8.4-10.5)	8.9 (6.5-10.2)	8.9 (8.1-9.8)	19.4 (15.9-22.5)	17.4 (15.6-24.6)	18.3 (16.6-21.2)*
RS bulky (N = 63)	8.0 (4.3-11.1)	6.1 (5.4-9.4)	7.4 (5.8-9.2)	13.5 (9.8-24.1)	13.0 (8.8-26.1)	13.4 (9.8-20.7)
LS non-bulky (N = 192)	9.2 (8.4-11.3)	8.7 (8.3-10.8)	8.9 (8.4-10.6)	23.0 (20.7-28.3)	22.1 (17.8-27.0)	22.4 (20.3-26.7)*
RS non-bulky (N = 73)	8.1 (6.6-10.3)	7.8 (7.0-10.5)	8.1 (7.1-9.0)	18.6 (13.2-31.4)	18.3 (10.1-25.1)	18.6 (13.8-24.8)

*$P_{adj} \leq 0.05$.

109 Poster Session

Genomic profiling of gastrointestinal cancers by comprehensive tumor-normal sequencing. *First Author: Fadel S. Alyaqoub, Ashion Analytics, Phoenix, AZ*

Background: Gastrointestinal cancers (GIC) account for 26% of global cancer incidence and 35% of cancer-related deaths. We investigated the molecular landscape and therapeutic targets across 18 types of GIC using whole exome (WES) and whole transcriptome sequencing (WTS). **Methods:** GEM ExTra assay was performed on 603 paired samples (ages 18-90 years, median = 61 years). Targeted sequence coverage was 180X for germline DNA and 400X for tumor DNA. Reportable somatic alterations included single base substitutions, indels, Copy Number Alterations, gene fusions, alternate transcripts, as well as tumor mutational burden (TMB) and microsatellite instability (MSI) status. Germline subtraction identified somatic-specific alterations. **Results:** Analysis of 603 GIC patient samples, including esophageal, gastric cancer (GC), biliary tract (BT), pancreatic cancer (PC), colorectal cancer (CRC), and other cancers, identified 434 actionable targets. The median number of alterations was 3 per GIC patient. The 5 most common actionable alterations were in APC, KRAS, CDKN2A, ARID1A and PIK3CA. Activation of Wnt signaling was found in 264/603 (44%), with the majority being in CRC cases. Alterations in cell cycle genes including CDKN2A, CDK4/6 and others were noted in 129/603 (21%) cases, with the majority in PC, suggesting benefit from CDK4/6 inhibitors. Activation of PI3K/PTEN/Akt/mTOR pathway was noted in 105/603 (17%), with the majority harbored in CRC, suggesting benefit from targeting this pathway. ERBB2 amplification and mutations were noted in 22/603 (4%) across different GIC tumor types. Alterations in homologous recombination genes predicting platinum and PARP inhibitor response was noted in 181/603 (30%) samples distributed across GIC subtypes. KRAS (G12C) mutation was found in 7% of all KRAS mutations across GIC subtypes, thus allowing patients to enroll in clinical trials with G12C-specific inhibitors. The majority of cases with MSI- and TMB-high status were identified in GC and CRC tumors and may be predictive of response to immunotherapy. WTS identified actionable fusions, including FGFR1/2/3 and novel NRG1 fusions in BT cancers. **Conclusions:** Our study revealed actionable targets used in patient selection for precision therapies, in addition to other mutational profiles of clinical significance. Overall, comprehensive genomic profiling enabled detection of established and novel actionable alterations, including fusions, which may have gone undetected using hotspot panels. Research Sponsor: None.

110 Poster Session

Epigenetic regulation of the Wnt-signaling pathway in CIMP-H *BRAF*V600E mCRC. *First Author: Hey Min Lee, University of Texas MD Anderson Cancer Center, Houston, TX*

Background: *BRAF*V600E mutation identifies mCRC patients with poor prognosis with only little benefit from standard therapy. Analysis from TCGA revealed that 89% of *BRAF*V600E CRC tumors were associated with a high CpG island methylator phenotype (CIMP-H), which may result in epigenetic silencing of tumor suppressor genes, while only 29% of *BRAF* wild-type tumors are CIMP-H. In this study, we define key pathways regulated by global DNA hypermethylation in the context of *BRAF*V600E mutation. **Methods:** We analyzed the TCGA Illumina 450k array methylation datasets and RNA-sequencing datasets for 97 CIMP-H CRC tumors (27 *BRAF*V600E; 69 *BRAF* WT) identified by five universal CIMP annotations (*p14, p16, MLH1, MINT1, MINT2, MINT31*). We defined differential methylation profile according to *BRAF* mutation status and calculated Spearman correlation between methylation and gene expression to identify CIMP-H *BRAF*-associated genes. Next, pathways enriched with CIMP-H *BRAF*V600E tumors were defined using PANTHER pathway analysis. Additionally, β-catenin IHC were conducted on 145 MD Anderson CRC patient samples and compared by CIMP and *BRAF* status. **Results:** *BRAF* mutation is associated with lower rates of *APC* mutation as has previously been shown (32%, 82%). We identified 6,097 differentially methylated probes by *BRAF* mutation status (FDR = 10^{-4}), and as expected, our data suggests a higher methylation profile in *BRAF*V600E mutated tumors compared to *BRAF* WT. Intriguingly, CIMP-H *BRAF*-associated genes showed enrichment in the Wnt-signaling and cadherin signaling pathways ($p < 0.0001$ (FDR $<$ 0.0001)). Despite the epigenetic Wnt-signaling, nuclear β-catenin expression (as a measure of Wnt activity) in CIMP-H and *BRAF* tumors remains lower than for non-CIMP, and *BRAF* wild-type ($p = 0.0003$ for comparison of CIMP). **Conclusions:** Genes under methylation regulation in the BRAF-mutant context showed enrichment in Wnt-signaling pathway. Since *BRAF*V600E CRC tumors have a low association with *APC* mutation, this data suggests role of epigenetic regulation of the Wnt-pathway activation. However, as measured by nuclear β-catenin, Wnt activation in these tumors is not as high as traditional *APC*-mutated CRC tumors. CIMP-H tumors with *BRAF*V600E mutation is a unique subset of CRC tumor that have Wnt-pathway activation regulated by epigenetic modifications more than a β-catenin activation. Research Sponsor: U.S. National Institutes of Health.

111 Poster Session

Artificial intelligence-assisted immunohistochemical (IHC) evaluation of tumor amphiregulin (AREG) and epiregulin (EREG) expression as a combined predictive biomarker for panitumumab (Pan) therapy benefit in *RAS* wild-type (wt) metastatic colorectal cancer (mCRC): Analysis within the phase III PICCOLO trial. *First Author: Christopher Williams, Leeds Institute of Medical Research at St James's, University of Leeds, Leeds, United Kingdom*

Background: High tumor mRNA levels of the EGFR ligands, AREG and EREG are associated with anti-EGFR agent response in patients (pts) with *RAS*-wt mCRC, regardless of tumor location. However, ligand RNA assays have not been adopted into routine clinical practice due to issues with analytical precision and practicality. Here we test whether AREG and EREG expression assessed by IHC can predict benefit from Pan. **Methods:** A retrospective biomarker study within the PICCOLO trial (NCT00389870; irinotecan [Ir] ± Pan in fluoropyrimidine-resistant *RAS*-wt mCRC). AREG and EREG positive tumor cells were assessed by IHC in all *RAS*-wt patients with available tumor tissue. Pathologists annotated tumor areas on digital images of glass slides. Artificial intelligence (AI) algorithms calculated the percentage of tumor cells staining positive for AREG and EREG within the tumor areas. More than 50% AREG and/or EREG tumor cell positivity was regarded as high ligand expression. The primary endpoint was progression-free survival (PFS) and secondary endpoints were RECIST response rate (RR) and overall survival (OS). **Results:** 274 *RAS*-wt pts had available tumor tissue. High ligand expression (n = 132) was associated with significant PFS benefit from IrPan compared with Ir (8.0 vs 3.2 months; HR 0.54 [0.37-0.79]; p = 0.001); whereas low ligand expression (n = 142) was not (3.4 vs 4.4 months; HR 1.05 [95% CI, 0.74-1.49]; p = 0.78). The ligand-treatment interaction was significant (p = 0.02) and independent of *BRAF*-mutation status and primary tumor location. Likewise RR was significantly improved in pts with high ligand expression (IrPan vs Ir: 48% vs 6%; risk ratio, 7.8 [2.90-20.69]; p < 0.0001) but not those with low ligand expression (IrPan vs Ir: 25% vs 14%; risk ratio, 1.8 [95% CI, 0.89-3.65]; p = 0.10) (interaction p = 0.01). Lesser effect was seen on OS. **Conclusions:** IHC assessment of AREG and EREG identified pts who did or did not benefit from Pan, as has been previously demonstrated through mRNA quantification. IHC represents a more practicable technique as it can be provided at the point of care and is associated with shorter turn-around times. AREG and EREG IHC may be of use in routine practice to identify patients who would benefit from anti-EGFR therapy and those for whom alternative treatment strategies should be explored. Research Sponsor: Roche Tissue DiagnosticsOther Government Agency.

112 Poster Session

SCRUM-Japan genesis virtual sequencing (VSQ) project: A novel algorithm combining deep learning (DL) with pathological diagnostics to enable the prediction of *BRAF* mutations and microsatellite instability (MSI) in advanced colorectal cancer (CRC). *First Author: Satoshi Fujii, Division of Pathology, Exploratory Oncology Research & Clinical Trial Center, National Cancer Center, Kashiwa, Japan*

Background: Numerous genetic and epigenetic abnormalities may lead to various morphologies of cancer. However, exactly which gene abnormality causes which morphology is unknown. The VSQ Project aims at investigating a novel algorithm by synergistically fusing DL technology and pathological diagnostics for the prediction of cancer genome abnormalities. This was achieved by elucidating the association between the morphological findings and genetic abnormalities, including *BRAF* V600E mutations and MSI status directly linked to the therapeutic strategies for advanced CRC patients (pts). **Methods:** Clinicopathological-genomic integrated DB derived from SCRUM-Japan GI-SCREEN, a nation-wide cancer genome screening project including CRC, were used. A total of 1,657 images of thin sections (one representative image per pt) cut from formalin-fixed and paraffin-embedded (FFPE) tissue specimens from primary or metastatic tumors with genetic abnormalities confirmed by next-generation sequencing (NGS) were investigated; 1,234 and 423 images (one per pt) were used for training and validation cohorts, respectively. First, we developed image-prediction models based on the morphological features precisely annotated by the single central pathologist, and then constructed the DL algorithms (gene-prediction models) that enabled the prediction of gene abnormalities by using images filtered by the image-prediction models. **Results:** We achieved high accuracy of AUC > 0.90 for 12 features among the 33 morphological features analyzed. Next, we created several DL algorithms that enabled the prediction of *BRAF* mutations and MSI. The prediction level reached a high accuracy of AUC = 0.955 for the *BRAF* mutations and AUC = 0.857 for MSI in the training cohort. We verified the AUCs in the validation cohort and achieved AUC = 0.831 and 0.883 for *BRAF* mutations and MSI, respectively. **Conclusions:** Our findings suggest that VSQ can appropriately predict *BRAF* mutation and MSI status in advanced CRC, potentially without performing NGS tests. VSQ may also enable prompt initiation of systemic treatments in CRC patients as well as establish an unprecedented next-generation pathology in the near future. Research Sponsor: None.

113 Poster Session

Real-world data evaluating immunotherapy markers and checkpoint inhibitor response among GI cancers in a large community-based oncology network. *First Author: Carissa Jones, Sarah Cannon Research Institute, Nashville, TN*

Background: Checkpoint inhibitor (CPI) therapies have shown prolonged survival in patients (pts) with microsatellite instability (MSI). Tumor mutation burden (TMB) has also been associated with benefit from CPIs, with pembrolizumab recently approved for solid tumors with a TMB of ≥10 muts/mb. However, the validity of a tissue-agnostic approach has been debated given the high degree of TMB variation across tumor types. We sought to evaluate the impact of TMB and MSI on CPI response in pts with advanced gastrointestinal (GI) cancers who received NGS profiling. **Methods:** Patients within the Sarah Cannon network with GI cancer and comprehensive next generation sequencing (NGS) data were identified through Genospace, Sarah Cannon's clinicogenomic analytics platform. Microsatellite (MS) status [high (MSI-H) vs. stable (MSS)] was defined by NGS. TMB-high (TMB-H) was defined as ≥10 muts/mb. Kaplan-Meier estimates were used to examine time to treatment failure (TTF), defined as the time from therapy start to start of next therapy, death, or loss to follow-up. **Results:** We identified 5,788 pts with GI cancers who received NGS, of which 48% (N=3,603) had colorectal cancer (CRC). MS status was evaluated on 4,219 (66%) NGS reports, TMB on 2,922 (46%) reports, and both on 2,863 (45%) reports. MSI-H and TMB-H co-occurred on 127 reports (4%), MSS/TMB-H occurred on 312 reports (11%), and MSS/TMB-Low (TMB-L) occurred on 2,424 reports (85%). No reports were MSI-H/TMB-L. Overall, 580 pts (14%) received CPI therapy (N=52 MSI-H/TMB-H, N=41 MSS/TMB-H, N=215 MSS/TMB-L). Independent of line of therapy or tumor type, TTF was significantly shorter for CPI vs. non-CPI therapies [median TTF (mTTF)=151 vs. 238 days, respectively, $p=3.4x10^{-9}$]. As expected, MSI-H was also associated with longer CPI TTF compared to MSS (mTTF=727 vs. 124 days, $p=3.1x10^{-11}$). Due to small sample sizes, further analyses were focused on pts with CRC (Table). TMB-H was independently associated with longer CPI TTF compared to TMB-L (Table, $p=9.2x10^{-10}$). Similarly, the co-occurrence of MSI-H/TMB-H was also associated with longer CPI TTF (Table). However, there was no difference in CPI TTF for MSS/TMB-H and MSS/TMB-L (Table, p=0.45). All pts who received non-CPI therapies, regardless of MS/TMB group, had longer TTF than MSS/TMB-H and MSS/TMB-L pts who received CPI (Table). mTTF [days (N)] for pts with CRC by biomarker. **Conclusions:** Despite recent tissue-agnostic approvals, TMB does not appear to be a good biomarker of CPI response in pts with CRC. Rather, time to CPI failure is associated with the co-occurrence of TMB-H with MSI-H. Continued research is needed to identify better biomarkers of response to immunotherapy in GI cancers. Research Sponsor: None.

Biomarker	CPI mTTF	Non-CPI mTTF
TMB-H	Not reached (NR) (59)	231 (205)
TMB-L	94 (74)	296 (1036)
MSI-H/TMB-H	NR (41)	190 (71)
MSS/TMB-H	107 (17)	238 (129)
MSS/TMB-L	90 (74)	295 (1027)

114 Poster Session

Multifocal extramural venous invasion detected with an elastin stain as a predictor of cancer-specific outcomes in stage I-III resected colorectal cancer (CRC). *First Author: David Patrick Cyr, Department of Surgery, University of Toronto, Toronto, ON, Canada*

Background: ExtraMural Venous Invasion (EMVI) is considered an indicator of poor prognosis in patients who have undergone resection of primary CRC, but its use has not been widely adopted in staging systems or nomograms. Staining for elastin may facilitate the accurate detection of EMVI and minimize interobserver variability, as well as enable the assessment of specific features of EMVI including focality and size. We examined the prognostic potential of EMVI detected by elastin staining at a tertiary center that performs a high volume of CRC resections. **Methods:** This is a single-institution, observational study of consecutive patients who underwent resection of primary CRC between 01/2011 and 12/2016 (n=556). All pathology specimens were re-assessed by expert reviewers who were blinded to patient outcomes. Venous invasion was detected using an elastin trichrome stain and classified as IntraMural or ExtraMural. The number of VI foci, as well as the maximum foci width and length, were also determined. Disease-specific and recurrence-free survival (DSS, RFS) were estimated using the Kaplan-Meier method and group differences were assessed using the log-rank test. Cox proportional-hazard models were used to calculate hazard ratios (HR) and 95% CI. For the present analysis, patients with stage IV (n=86) CRC were excluded. **Results:** The cohort for analysis included 470 patients (264M, 206F; TNM 8th edition Stage I/II n=291; Stage III n=179) with a median follow-up time of 63 months (0.1-114). EMVI was detected in 33% of all cases (20% in Stage I/II vs. 55% in Stage III; $p<0.0001$). For the entire cohort, DSS and RFS at 5 years were 86% and 76%, respectively. The presence of EMVI was associated with significantly worse DSS and RFS at 5-years (73% and 54%) compared to patients with no VI (92% and 85%) or IMVI alone (93% and 89%; $p<0.0001$). The majority of EMVI was multifocal (69%) vs. unifocal (31%). Interestingly, multifocal EMVI was prognostic for worse 5-year DSS (65%), whereas unifocal EMVI was similar to the absence of EMVI (91% and 92%, respectively; $p<0.0001$). A Cox-proportional hazards model showed worsening DSS with increasing number of detected EMVI foci (1 focus: HR 1.1, 2-4 foci: HR 3.3, >4 foci: HR 7.9; $p<0.0001$). A similar trend was observed for RFS. Neither the maximum width or length of EMVI foci were prognostic of DSS or RFS. **Conclusions:** To our knowledge, the prognostic role of EMVI focality in CRC has not been previously explored. In this cohort of Stage I - III CRC patients, multifocal EMVI as assessed by elastin staining was a powerful predictor of cancer-specific death and recurrence-free survival. Elastin staining, which improves the accuracy and objectivity of EMVI detection, may allow validation of EMVI as an independent prognostic variable that should be incorporated into staging systems and nomograms. Research Sponsor: None.

115 Poster Session

Predicting resistance to first-line FOLFOX plus bevacizumab in metastatic colorectal cancer: Final results of the multicenter, international PERMAD trial. *First Author: Thomas Seufferlein, Department of Medicine I, Hospital of the University Ulm, Ulm, Germany*

Background: Antiangiogenic agents, in particular monoclonal antibodies (mAbs) against VEGF, a major driver of tumor angiogenesis, are widely used in cancer therapy including metastatic colorectal cancer (mCRC). However, some patients do not profit from antiangiogenic treatments (AT), other patients benefit initially, but subsequently develop resistance not only to chemotherapy but also to AT. So far, no biomarkers are available to predict resistance to AT. Having an accurate assessment of imminent resistance to an AT may e.g. enable to respond by treating the patient with a more broadly acting antiangiogenic agent and thereby further delay resistance to the treatment and at the same time avoid employing a not anymore efficacious treatment. We hypothesized that repeated analysis of multiple cytokines related to angiogenesis together with machine learning approaches may enable an accurate prediction of anti-VEGF resistance during first-line treatment of mCRC patients with FOLFOX plus bevacizumab. The PERMAD trial aimed at establishing a CAF marker combination that enables the prediction of treatment resistance of patients with mCRC receiving Bevacizumab plus mFOLFOX6 in a palliative first-line setting about three months prior to radiological progress using an omics approach and bioinformatics. **Methods:** A phase I/II biomarker trial was conducted, including 15 centers in Germany and Austria. All mCRC patients included were treatment naïve and received FOLFOX plus Bevacizumab treatment. 102 different, preselected CAFs were prospectively collected and centrally analyzed in plasma samples (n = 647) obtained prior to treatment and biweekly until radiological progress determined by CT scan every 2 months. The values of CAFs affected in a similar fashion by both chemotherapy and disease progress were excluded. Using the remaining CAFs we employed a random forest predictor to define a combination of 5 CAF (CAF marker combination) whose change in values/pattern correlated with subsequent progress 3 months prior to radiological progress according to RECIST 1.1. **Results:** Using the samples described above and a random forest predictor we established a CAF marker combination comprising 5 CAF whose specific change in value/pattern over time indicated treatment resistance 3 months prior to radiological progress. The model allowed to differentiate timepoints without progress from timepoints predicting progress 100 days before radiological progress with an accuracy of 83%, a sensitivity of 76% and specificity of 88%. **Conclusions:** Using advanced bioinformatics, we identified a CAF marker combination that points out treatment resistance to FOLFOX plus Bevacizumab in patients with mCRC 3 months prior to radiological progress. Clinical trial information: NCT02331927. Research Sponsor: Sanofi.

116 Poster Session

GDF15 expression in metastatic colorectal cancer. *First Author: Priya Jayachandran, Division of Medical Oncology, USC Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, CA*

Background: Cachexia affects many cancer patients. Growth differentiation factor-15 (GDF15) is a protein that regulates weight and the stress response of cells. The GDF15 gene encodes a ligand of TGF-beta that triggers cachexia and modulates the progression from tumorigenesis to metastasis. Inhibition of GDF15 with an antibody restored muscle mass and fat in animal models. Serum levels rise in proportion to the progression of colon cancer, predict outcome, and have been correlated with CEA. **Methods:** We retrospectively reviewed 7607 CRC tumors profiled by Caris Life Sciences (Phoenix, AZ) from 2019 to 2020. Profiling included whole transcriptome sequencing (RNA-Seq by NovoSeq). Tumor mutational burden, mismatch repair status, and pathway genomic alterations were evaluated. QuantiSEQ was used to assess immune cell infiltration in the tumor microenvironment. **Results:** GDF15 expression ranged from 0 to 593 transcripts per million (TPM) with median of 30 (IQR = 15.02). There was no association with age, sex, or primary tumor sidedness. MSI-H/dMMR tumors had higher GDF15 expression (median 37 vs 30, p = 0.0004); TMB > = 17 tumors was seen in 5.9% of bottom quartile (Q1) GDF15 expressors and 8.3% of top quartile (Q4). PDL1 IHC positivity was inversely correlated with GDF15 expression (7.1% in Q1 vs. 2.6% in Q4, $p < 0.0001$). Genomic alterations associated with higher GDF15 expression (Q4 vs Q1) included genes on TGF-B (SMAD2/4), PI3K (PIK3CA, MTOR), chromatin remodeling (ARID1A, KMT2C), DDR (ATM) and Wnt pathway (APC); those inversely associated included MYC CNA and TP53. Q1 tumors had higher CNA of ERBB2 and FGFR1. Relative neutrophils and NK cells in the TME increased from Q1 to Q4 ($p < 0.001$). There was a decrease in CD8+ T-cells and Treg cells from Q1 to Q4. **Conclusions:** GDF15 expression correlates with increased dMMR/MSI-H and TMB, but not with PDL1 expression. Mutations and activated pathways associated with GDF15 expression may explain increased cachexia with more aggressive disease. The association with chromatin remodeling may warrant therapies targeting histone modification and epigenetics. The increase in NK cells but decrease in CD8+ T cells in the TME with increasing GDF15 suggests approaches to treatment. Higher CD8+ lymphocyte counts correlate with PFS with immunotherapy. Anti-PD-L1 therapy reinvigorates the killing function of $CD8^+$ T cells. The decrease in CD8+ T cells and PDL1 positivity with rising GDF15 suggests worse outcome and a lack of response to anti-PDL1 therapy. NK cell checkpoint inhibitors, CARs, and an anti-GFRAL antibody are now in clinical trials and might be utilized in high GDF15 cancers. GDF15 is emerging as a target in the treatment of obesity and cachexia and as a prognostic marker in oncology. Understanding its expression in metastatic colon cancer may reveal which patients could benefit from developing anti-GDF15 targeted therapies against cancer progression. Research Sponsor: None.

117 Poster Session

ctDNA-based mutational landscape following anti-EGFR antibodies in metastatic colorectal cancer (mCRC) to uncover novel resistance mechanisms in the CCTG CO.26 trial. *First Author: James T. Topham, Genome Sciences Center, Vancouver, BC, Canada*

Background: Previous studies have identified MAPK and PIK3CA/AKT/mTOR pathways as common mechanisms of acquired resistance to anti-EGFR antibodies (EGFRab) in mCRC. However, such alterations do not account for all patients that become treatment resistant. Using paired whole-exome (WES; tissue) and circulating tumor DNA (ctDNA; plasma) sequencing, we performed characterization of the EGFRab resistance landscape in patients with mCRC. **Methods:** Post-treatment (ctDNA; plasma) sequencing was performed for 169 patients with mCRC, with 112 (66%) patients also receiving pre-treatment (WES; primary tumor) sequencing as part of the CO.26 trial. 66 (39%) patients received EGFRab previously at a median of 132.0 days prior to plasma sampling. Using bespoke bioinformatics pipelines (WES) coupled with the GuardantOMNI assay (plasma), we compared somatic mutation (SNV/indel, CNV and fusion) frequencies between pre- and post-EGFRab timepoints, and contrasted results between the two groups. **Results:** Significant increases in *de novo* acquisition of *EGFR* (p = 5.6e-4), *KRAS* (p = 0.011), *ZNF217* (p = 0.0022), *MAP2K1* (p = 0.0078) and *LRP1B* (p = 0.017) SNV/indels were unique to the EGFRab group and often occurred as multiple, low allele frequency events in the same patient. *De novo* copy number amplification of known resistance genes *EGFR*/*BRAF*/*MET* were observed in EGFRab-treated patients ($p < 0.05$), along with *SMO* (p = 6.8e-7), PTEN inhibitory gene *PREX2* (p = 5.6e-4), *FLT3* (p = 2.0e-5), *NOTCH4* (p = 6.3e-5), *ERBB2* (7.4e-4), *KMT2A* (p = 3.7e-4) and *ARID1B* (p = 0.0014). Genes impacted by fusion events in EGFRab-treated patients included *BRAF-KIAA1549* (1 patient) and *MET-CAV1* (1 patient), and these events were not detected in matched pre-treatment samples. EGFRab-treated patients were found to acquire a combination of multiple (≥5) mutation events (SNV/indel, CNV or fusion) at much higher frequency compared to non-EGFRab-treated patients (67% versus 25% of patients, p = 8.7e-8). Tumor mutation burden (TMB) was not significantly different (p = 0.71) between treatment groups prior to therapy initiation, while post-treatment TMB was significantly higher (p = 1.8e-7) in EGFRab-treated patients (median 25.4 versus 13.1 mut/mb). **Conclusions:** In addition to previously established resistance pathways, we identified acquired alterations in additional genes such as *SMO*, *PREX2* and epigenetic modifiers *KMT2A*/*ARID1B* in EGFRab-treated patients. Moreover, we highlight the phenomenon by which EGFRab-treated tumors acquire multiple concurrent resistance mutations and heightened TMB. Our analysis provides novel insight into the landscape of resistance mechanisms to EGFRab in mCRC while highlighting the potential role for immunotherapy post-EGFRab. Clinical trial information: NCT02870920. Research Sponsor: Canadian Cancer Society.

118 Poster Session

Genetic variants involved in the lipid metabolism pathway to predict outcome in patients (pts) with metastatic colorectal cancer (mCRC): Data from FIRE-3 and MAVERICC trials. *First Author: Jingyuan Wang, Division of Medical Oncology, USC Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, CA*

Background: Antiangiogenic drug (AAD)-triggered oxygen and nutrient depletion through suppression of angiogenesis switches the glucose-dependent metabolism to lipid-dependent metabolism. Blocking fatty acid oxidation can enhance AAD-mediated anti-tumor effects in colorectal cancer. Previous reports suggested that polymorphisms of the lipid metabolism-related genes are associated with the increased risk of CRC and poor clinical outcome in CRC. Therefore, we hypothesized that genetic variants in the lipid metabolism pathway may predict first-line treatment outcome in mCRC pts. **Methods:** Genomic DNA from blood samples of pts enrolled in two independent randomized trials, FIRE-3 and MAVERICC, was genotyped through the OncoArray, a customized array manufactured by Illumina including approximately 530K SNP markers. The impact on outcome of 25 selected SNPs in 10 genes involved in the lipid metabolism pathway (CD36, FABP4, LPCAT1, LPCAT2, PPARG, CPT1A, ACSS2, SREBF1, FASN, ACACA) was analyzed. Those treated with FOLFIRI/ bevacizumab (bev) in FIRE-3 (n = 107) and MAVERICC (n = 163) served as discovery and validation cohorts respectively, while FIRE-3 FOLFIRI/ cetuximab (cet) (n = 129) arm was used as the control. Interaction between each SNP and treatment was evaluated in FIRE-3 (FOLFIRI/bev arm vs. FOLFIRI/cet arm). **Results:** In the discovery (FIRE-3 bev) cohort, pts with FASN rs4485435 any C allele (N = 21) showed significantly shorter progression-free survival (PFS) (8.69 vs 13.48 months) compared to carriers of G/G (N = 62) in both univariate (hazard ratio [HR] = 2.88; 95% confidence interval [CI]: 1.57-5.29; p = 0.00037) and multivariate (HR = 2.87; 95%CI 1.4-5.9; p = 0.00675) analyses. These data were validated in the MAVERICC bev cohort in multivariate analysis (11.17 vs 14.06 months; HR = 2.07; 95%CI: 1.15-3.74; p = 0.02). Pts carrying any T allele in PPARG rs3856806 (N = 36) showed significantly longer overall survival (OS) (Not reached vs 42 months) than carriers of C/C (n = 93) in the FIRE-3 cet cohort in both univariate (HR = 0.4; 95%CI 0.17-0.92; p = 0.03) and multivariate (HR = 0.37; 95%CI 0.15-0.93; p = 0.02) analyses, but the association was not observed in the bev cohort of MAVERICC and FIRE-3. In the comparison of bev arm vs cet arm in FIRE-3, interactions were shown with FASN rs4485435 (p = 0.017) on PFS and PPARG rs3856806 (p = 0.059) on OS. **Conclusions:** Our study demonstrates for the first time that FASN polymorphism could predict outcomes of bev-based treatment in mCRC patients; Meanwhile PPARG polymorphism could predict outcomes of cet-based treatment in mCRC patients. These findings support a possible role of the lipid metabolism pathway in contributing to resistance to anti-VEGF/EGFR treatment. Research Sponsor: The National Cancer Institute [P30CA 014089 to H.-J.L.], Gloria Borges WunderGlo Foundation, Dhont Family Foundation, Victoria and Philip Wilson Research Fund, San Pedro Peninsula Cancer Guild.

119 Poster Session

Utility of circulating tumor DNA in the clinical management of patients with *BRAF*^{V600E} metastatic colorectal cancer. *First Author: Van K. Morris, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Molecular profiling is critical for oncologists in personalizing treatment decisions for patients (pts) with metastatic colorectal cancer (mCRC). In contrast to archival tumor tissue specimens classically used profiling, sequencing of circulating tumor DNA (ctDNA) is more sensitive at quantifying low mutation allele frequencies and characterize "real time" tumor biology. We assessed the relationship between detection of *BRAF*^{V600E} mutations in ctDNA and the clinical management of pts with mCRC. **Methods:** We retrospectively analyzed mCRC patients evaluated at MD Anderson Cancer Center with *BRAF*^{V600E} mutations on ctDNA. ctDNA was isolated and sequenced for somatic mutations using a 70-gene next-generation sequencing assay (MD Anderson/GuardantHealth LB70 panel). Variant allele frequency (VAF) was characterized as the ratio of mutant reads: total reads for a given gene. *BRAF*^{V600E} mutations were classified as "clonal" if the relative VAF (rVAF) exceeded 50% of the maximum VAF. "Major" and "minor" subclonal mutations were called for a rVAF of 10-50% and $<$ 10%, respectively. Associations between *BRAF*^{V600E} clonality and treatment decision were performed using a Fisher's exact test. Survival outcomes were estimated using the Kaplan-Meier method. **Results:** 64 patients with mCRC had a *BRAF*^{V600E} mutation detected in ctDNA. Concordance between tissue and ctDNA for *BRAF*^{V600E} mutation was occurred in 44/55 (80%) patients with evaluable tumor specimen. There were 9 patients with *BRAF*^{V600E} mutations identified in the absence of evaluable tumor tissue. Median VAF for *BRAF*^{V600E} in the ctDNA was 3.6% (interquartile range, 0.50 - 17%). The majority of patients had a clonal *BRAF*^{V600E} mutation (50/64, 78%). There were 3 (5%) and 11 (17%) patients with major subclonal and minor subclonal *BRAF*^{V600E} mutations, respectively. Among patients with minor subclonal *BRAF*^{V600E} mutations, 91% (10/11) had developed resistance to anti-EGFR therapies for management of *RAS*$^{wild\text{-}type}$ mCRC. Discordance between tissue and ctDNA *BRAF*^{V600E} status was associated with minor subclones (odds ratio (OR) 56, $p < .0001$). Clonal *BRAF*^{V600E} mutations in the ctDNA were associated with a higher likelihood for treatment with BRAF targeted therapies (OR 5.8, p = .008). Median progression-free survival among 37 evaluable patients was 6.4 months. **Conclusions:** Reported VAF in the ctDNA served to stratify *BRAF*^{V600E} according to relative clonality. Lower VAF was linked to acquired resistance to anti-EGFR therapies, whereas higher VAF was associated with receipt of matched targeted therapies for *BRAF*^{V600E} mCRC. ctDNA technologies for identifying *BRAF*^{V600E} mutations are feasible and informative for conducting relevant molecular profiling for patients with mCRC. Research Sponsor: None.

120 Poster Session

Expression of PD-L1 and PD-L2 in colorectal cancer (CRC): A post-hoc integrated analysis of SCRUM-Japan GI-SCREEN CRC. *First Author: Satoshi Yuki, Department of Gastroenterology and Hepatology, Hokkaido University Hospital, Sapporo, Japan*

Background: PD-1, PD-L1/L2 axis is responsible for cancer immune escape which facilitate disease progression. However, expression of these proteins in CRC and its significance in clinical prognosis are yet to be fully clarified. **Methods:** This was a post-hoc analysis using FFPE tumor samples from the Nationwide Cancer Genome Screening Project, SCRUM-Japan GI-SCREEN for metastatic CRC. Patients (Pts) with MSI-H or *BRAF* V600E mutant tumors were prioritized to be included. PD-L1 (22C3) and PD-L2 expressions were centrally assessed using immunohistochemical assays at QualTek and Neo-Genomics, respectively. Tumor infiltrating lymphocytes (TILs) were morphologically evaluated by H&E staining. Clinical information including biomarker status and overall survival (OS) were extracted from SCRUM-Japan GI-SCREEN database. **Results:** In total, 200 pts were included in this study with a median age of 65 (range, 29-88) years; male/female (116/84); MSI status MSI-H/non-MSI-H/unknown (8/189/3); *RAS* wild-type/mutant (113/87); and *BRAF* V600E wild-type/mutant (173/27). Positivity rate of PD-L1 in tumor cells (TC), immune cells (IC), PD-L2 on TC and IC were 10.8%, 46.9%, 0% and 20.3%, respectively. Expression of PD-L1 on TC or IC and PD-L2 on IC were associated with TIL (p = 0.023, p = 0.009, respectively). PD-L1 on TC was highly seen in *BRAF* V600E-mutated tumors (p = 0.043), but not related to other factors including *RAS* and MSI status. The pts with PD-L1+ tumors on TC or IC had longer OS than those with PD-L1- (Median, 31.9 vs 23.5 months; HR = 0.67, 95% CI, 0.46–0.99; p = 0.040), while OS in pts with PD-L2+ tumors was similar to that with PD-L2- (Median, 21.4 vs 27.3 months; HR = 0.87, 95% CI, 0.53–1.44; p = 0.60). The PD-L1 expression was also associated with the longer OS in pts with *BRAF* wild-type or non-MSI-H tumors. **Conclusions:** Our study suggested different prognostic impact of PD-L1 and PD-L2 expression in CRC pts, which require further evaluations as potential therapeutic targets for CRC. Clinical trial information: UMIN000016343. Research Sponsor: MSD.

121 Poster Session

Relationship of HER2 alteration and MSI status in colorectal adenocarcinoma. *First Author: Miao-zhen Qiu, Sun Yat-sen University Cancer Center, Guangzhou, China*

Background: The impact of HER2 somatic mutations in colorectal carcinoma (CRC) has not been well studied and its relationship with MSI-H is an open question. **Methods:** From February 2017 to February 2020, CRC patients who received tumor specimens next-generation sequencing and detail record of clinic-pathologic information were enrolled. HER2 alteration and its relationship with MSI-H were analyzed. **Results:** There were totally 55 patients (7.5%) with HER2 alteration including 29 (4.0%) HER2 somatic mutations, 24 (3.3%) HER2 gene amplification, and 2 patients (0.2%) with both HER2 mutations and amplification. For HER2 mutated cases, 48.3% were MSI-H, while none of HER2 amplification cases were MSI-H. MSI-H was found in 5.2% in our cohort and 36.8% MSI-H patients were HER2 mutated. MSI-H had less frequency of lung metastasis. The mPFS for first line chemotherapy was significantly higher in MSS cases than in MSI-H cases, 11.5 months vs 3.5 months, P = 0.032. MSI-H patients with HER2 mutation had significantly worse mPFS for PD-1 antibody than those without HER2 alteration, P = 0.036. **Conclusions:** High MSI-H rate is found in HER2 mutated cases but no MSI-H in HER2 amplification cases. MSI-H patients with HER2 mutated had worse PFS for PD-1 antibody than those without. Research Sponsor: None.

122 Poster Session

Impact of adjuvant chemotherapy and patient age on patterns of metastatic recurrence in stage III colorectal cancer. *First Author: Grace Gard, Walter & Eliza Hall Institute of Medical Research, Melbourne, Australia*

Background: The patterns of metastatic relapse for Stage III colorectal cancer (CRC) are known to be influenced by the primary site and mutation status. Whether the use of adjuvant therapy also influences recurrence patterns, due to a variable chemotherapy impact by metastatic site, has yet to be explored. Patient age 70 years has consistently been associated with a lack of benefit from the addition of oxaliplatin to a fluoropyrimidine (FP) chemotherapy. **Methods:** Data from a multi-site CRC database that prospectively captures, patient, tumour, treatment and outcome data was examined. Patients with de novo metastatic or multiple primary tumours were excluded. Patterns of recurrence were analysed by receipt of surgery and adjuvant chemotherapy (S + AC) or surgery alone (S alone) and by age 70 years and $<$70 years old. **Results:** Of 701 patients with stage III colon cancer 397 were male, median age was 68 years (range 33-83) and 574 (81%) were ECOG 0-1. S + AC was administered in 555 (79%), including 228 treated with a FP alone and 324 treated with an oxaliplatin doublet. Metastatic relapse was delayed in S + AC patients, occurring at a median of 17.81 vs 9.43 months ($p<$ 001). Liver metastases were the most common site of relapse overall (40%) and numerically less common in the S + AC group (38% vs 46%, p = 0.06). Brain metastases were less common in S + AC patients (1% vs 3.5%, p = 0.04). When analysed by primary tumour side the only significant finding was that for patients with a right-side primary (n= 208, 76% had S + AC), S+ AC was associated with a lower rate of lung metastases (28% vs 41% p = 0.046). 318 of the 701 (45%) of this relapsed cohort were 70 years old, 220 (69%) of these patients had S + AC. In both the older and younger cohort metastatic relapse was delayed with S + AC (18.7 vs 11.3 months, $p < 0.001$, 17.08 vs. 6.01 months, $p < 0.001$) and liver metastases were the most common site of relapse (41% vs 38%, p=0.56). Similar rates of lung metastases (40% vs 34%, p=0.1), peritoneal disease (20% vs 22%, p=0.57) and brain metastases (2.2% vs 0.8%, p=0.13) were seen in the 70 years old and $<$70 years old patients, with no evident interaction between chemotherapy use and age with respect to recurrence sites. **Conclusions:** S + AC for stage III colon cancer in this community series delayed time to recurrence and resulted in numerically lower recurrence rates at all disease sites. Brain metastases although uncommon were less frequent in S + AC patients. Patients with a right sided primary had a lower incidence of lung metastases following S + AC patient cohort. There was no significant impact of age on recurrence patterns. Research Sponsor: None.

123 Poster Session

CD8$^+$ tumor-infiltrating lymphocyte infiltration prediction with radiomic signature in locally advanced rectal cancer. *First Author: Eui Kyu Chie, Seoul National University College of Medicine, Seoul, South Korea*

Background: Despite increasing use of cancer immunotherapies, no biomarker relevant to anti-tumor immunity has been developed in rectal cancer. The present study aims to develop a radiomic signature to predict the infiltration of CD8$^+$ tumor-infiltrating lymphocytes (TILs). **Methods:** In total, 131 patients undergoing neoadjuvant chemoradiotherapy (CRT) from 2005 to 2012 were analyzed. The study included pre-CRT dataset A (n = 113; n = 75 and 38 for training and validation) and post-CRT datasets B (n = 32; predominance of tumor) and C (n = 20; pure fibrosis). To build the radiomic signature, 38 features selected from pre-CRT T2-weighted MRI scans were incorporated into the least absolute shrinkage and selection operator method. **Results:** Higher CD8$^+$ TIL infiltration was associated with better overall and progression-free survival (P = 0.01 and 0.03, respectively). In pre-CRT dataset A, the area under the receiver operating characteristic curve values of radiomic score for predicting CD8$^+$ TILs were 0.760 and 0.729 for training and validation subsets, respectively. A significant correlation was observed between the radiomic signature and CD8$^+$ TIL density in the post-CRT dataset B (Pearson's R = –0.372, P = 0.036), whereas no association was found within the dataset C accounting for pure fibrosis after CRT (Pearson's R = –0.069, P = 0.77). **Conclusions:** We established the MRI-derived radiomic signature for predicting CD8$^+$ TIL infiltration in the contemporary treatment era of rectal cancer. The noninvasive characterization of tumor immune status would provide insights into the role of radiomic-pathology modeling to predict the local immune phenotypes. Research Sponsor: National Research Foundation of Korea.

124 Poster Session

The impact of neoadjuvant chemotherapy (NACT) on the tumor immune microenvironment (TME) in patients with colorectal cancer with liver metastases (CRCLM). *First Author: Medhavi Gupta, Roswell Park Cancer Institute, Dept. of Medicine, Buffalo, NY*

Background: Microsatellite stable (MSS) colorectal cancer and CRCLM are highly resistant to current immunotherapeutic approaches. Understanding the TME and the impact of standard chemotherapeutics is of utmost importance in developing optimal therapeutic strategies. Data is limited on the impact of NACT in the TME. In this study, we sought to explore the effects of chemotherapy on the proportions of different immune cell populations [Total leukohematopoetic cells, CD45+, T cell markers, CD3+, CD8+, and macrophage (M) markers, CD163+, CD68+)], as well as to assess their prognostic capacity. **Methods:** CRCLM pts who underwent liver resection were divided in 2 groups: pts who had NACT within 4 months of liver resection [NACT (+)] and no NACT [NACT (-)]. Whole slide staining of metastatectomy specimen for CD3, CD8, CD68, CD163, and CD45 was done. Cellular density within representative tumor core sections was analyzed. Retrospective chart review was done to obtain clinical data. Disease free (DFS), relapse free (RFS), and overall survival (OS) were analyzed using Kaplan Meir methods. Association between markers and outcomes was evaluated using Cox Regression Models. **Results:** A total of 43 pts were studied [NACT (+), n= 14; NACT (-), n=29). There were no significant differences in baseline characteristics between the two groups, including age, primary site, T stage, N stage, and grade. Median OS was 48 months. Outcomes were not significantly different with use of NACT. Within the NACT (+) CRCLM significant increases were seen in densities of CD3, CD8, CD45 and CD163 cells. Densities of CD8 cells were strongly correlated to CD163 cell densities ([r] 0.77, p < .0001). The NACT (+) cohort saw significantly increased ratios of T-cells/ macrophages as compared to NACT (-) (CD3/CD68, CD3/CD163, CD8/CD163). High CD45 density was associated with improved OS (HR = 0.28, p = 0.006). CD3, CD8, CD68, and CD163 were not independently associated with OS. However, both the ratio of CD3/CD68 and CD3/163 were associated with improved OS (HR 0.44, p=0.03 and HR 0.27, p=0.03 respectively). Conversely, CD68/45 and CD163/CD45 ratios were associated with a worse OS (HR 1.42, p=0.05 and HR 1.43, p=0.03 respectively). No difference was seen in cellular populations based on the type of NACT received: oxaliplatin vs irinotecan. **Conclusions:** Our study highlights that the administration of NACT is associated with favorable changes in LM TME. While there is a general increase in leukocytes (CD45), the density of CD3+ and CD8+ T cells is particularly increased. Further, this increase is proportionately greater than the concurrent increases on monocytoid populations, reflected by increased CD3/CD163 and CD8/CD163 ratios. Ratios of T-cells/ macrophages are predictive of survival. This study was partly supported by the American Cancer Society Grant, 126771-IRG-14-194-11-IRG. Research Sponsor: American Cancer Society Internal Research Grant #126771-IRG-14-194-11-IRG.

125 Poster Session

Impact of primary tumor size/horizontal extent on survival in colorectal cancer. *First Author: Olatunji B. Alese, Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA*

Background: Pathologic staging in colorectal cancer (CRC) is crucial in patient management. Data regarding the impact of size/horizontal tumor extent is limited, contradictory and currently excluded from the American Joint Committee on Cancer (AJCC) staging model. However, a previously published SEER analysis showed that AJCC stages I and IIIA have similar 2- and 5- year survival rates, and worse rates for stage II. Using the largest cohort to date, we report the impact of primary tumor size on CRC survival. **Methods:** Data were obtained from all US hospitals that contributed to the National Cancer Database (NCDB) between 2010 and 2015. Univariate and multivariate analyses were performed to identify factors associated with patient outcome. Kaplan-Meier analysis and Cox proportional hazards models were used to assess the association between tumor/patient characteristics and overall survival (OS). **Results:** A total of 61,145 patients were identified with a similar gender distribution (M/F: 50.9%/49.1%). The mean age was 62.7years (SD+/-14.1) and 82% were non-Hispanic Whites. Majority had colon primary (82.7%) and 82.4% had microsatellite stable (MSS) disease. Distribution across stages I-IV was 20.1%, 32.1%, 34.7% and 13.2% respectively. Among the total study population, AJCC stage correlated closely with OS on multivariate analysis (HR 1.49, 2.29, 8.38 for stages II to IV compared to stage I), while the distinguishing power for tumor size was relatively mild (HR 1.19 and 1.33 for 5-10 cm and >5cm compared to <5cm). Among patients with stage II disease, tumors >10cm were associated with worse survival compared to those <5cm (HR 1.2; 1.03-1.39; p=0.22). Stage III disease also had differential survival rates; patients with tumors 5-10cm (HR 1.21; 1.14-1.28; p<0.001) and >10cm (HR 1.57; 1.37-1.80; p<0.001) had worse survival than those <5cm. Patients with stage II who did not receive adjuvant chemotherapy (CTX) had worse survival outcomes (HR 1.29; 1.08-1.55; p=0.005) compared to stage III disease who did. Accounting for tumor size, there was no statistically significant survival differences between stage I patients and stages II and III patients who received adjuvant chemotherapy. **Conclusions:** Tumors larger than 10cm have inferior outcomes among patients in the same AJCC stages. Stage II patients without adjuvant CTX did worse than stage III with CTX. Further studies are needed to clarify the role of tumor size in staging models. Research Sponsor: None.

Survival among patients with stage I CRC (colon vs. Rectal) vs. stage II +/- adjuvant chemotherapy (CTX) vs. stage III + CTX.

Group	No. of Subject	Median Survival (95% CI)	12-month Survival (95% CI)
Stage I T2N0 (Rectal – without CTX)	775	NR (NR, NR)	96.8% (95.3%, 97.9%)
Stage I T2N0 (colon - without CTX)	5222	NR (92.6, NR)	95.1% (94.5%, 95.7%)
Stage II with CTX	6591	NR (90.7, NR)	97.4% (97.0%, 97.8%)
Stage II without CTX	13016	NR (91, NR)	92.7% (92.2%, 93.1%)
Stage III with CTX	16658	NR (91.7, NR)	95.8% (95.5%, 96.1%)

126 Poster Session

Differential gain of chromosomal regions 20q or 13q with loss of 8p and 18q differentiates disease-free survival in colorectal cancer. *First Author: Hsueh-Ping Chao, Livestrong Cancer Institutes, University of Texas at Austin Dell Medical School, Austin, TX*

Background: In microsatellite stable (MSS) colorectal cancer (CRC) cases, frequent amplifications in 13q and 20q regions have been reported with limited understanding of their potential role for prognosis and treatment. Based on an internal research molecular tumor board case analysis of a KRAS WT, MSS left-sided (LS), metastatic CRC patient, we noted 50% of the 11 listed variants of unknown significance were on 20q. This study aims to investigate the potential prognostic role for gain of 20q chromosomal regions relative to other chromosomal imbalances using a retrospective cohort. **Methods:** We performed a genome-wide CN cluster analysis using the TCGA data with resulting patient clusters compared based on Kaplan-Meier estimated disease-free interval (DFI) in months (mos) using a log-rank. We examined associations between CN-derived clusters and CRC phenotypes. **Results:** Using TCGA data, we identified four CN-derived patient clusters of which two had significantly different DFI's. One longer DFI cluster (n = 83; median DFI = 28mos) was defined by a signature of copy neutral genes along Chr8p and 18q regions. The shorter DFI cluster (n = 46; median DFI = 20mos) was defined by a signature of Chr8p and 18q regions of loss. The two clusters significantly differed in terms of site (85% right-sided in the shorter vs. 85% LS in the longer DFI cluster) and MS status (81% MSS in the shorter vs. 72% MSI in the longer DFI cluster) with no significant differences in age (mean of 70 years at diagnosis) and KRAS status (around 50% WT) between clusters. The shorter DFI was able to be further differentiated based on gain of chromosomal regions 20q (n = 26; median DFI = 24mos) and 13q (n = 20; median DFI = 18mos). No significant differences in mean age, tumor stage, site, and MS status between the shorter DFI subgroups were noted. Enriched pathways in the Chr20q gain sub-cluster include cell differentiation (Hippo, Rap1, VEGF), whereas metabolic signaling pathways via AGE-RAGE and AMPK, as well as cell growth and malignant transformation via RAS are enriched in the Chr13q gain sub-cluster. **Conclusions:** Clinical sequencing is able to identify regions of gain in Chr20q and Chr13q as part of VUS's. Gain of Chr20q has been reported with better survival in mCRC patients. Gain of chromosomal region 20q and loss of 18q has been reported to discriminate between Lynch Syndrome and familial colorectal cancer. Herein, we show that gain of the 20q region with 18q and 8p regions of loss is associated with shorter DFI and gain of 13q region with loss of 8p even worse prognosis. Research Sponsor: None.

127 Poster Session

Utilization of liquid biopsy for advanced gastrointesinal malignancies in a community oncology practice. *First Author: Niraj K. Gupta, St. Vincent Hospital, Indianapolis, IN*

Background: Liquid biopsy (LB) offers a non-invasive alternative for obtaining genomic signature of malignancies to develop a tailor-made treatment plan. We evaluated the feasibility and impact on clinical management of liquid biopsies performed on patients with advanced gastrointestinal malignancies in a community setting. **Methods:** A retrospective chart review of adult patients with stage-IV gastrointestinal malignancies was conducted to gather all the pertinent information, including diagnoses, treatment regimens, results of liquid biopsies and any impact on further management. **Results:** Data on 42 liquid biopsies performed between Aug 2018 and Mar 2020 was collected. M:F ratio was 1.4: 1. Median age was 57yrs (range 31-86). The diagnoses were; Colo-rectal Ca 22(54.7%), pancreatic 9(21.9%), gastric 2(4.7%), biliary 2(4.7%), HCC 2(4.7%), Appendix 1 (2.3%), CUP 1(2.3%) and others 3(7.1%). One (2.3%) LBs was done before first line treatment and 41(97.7%) were done after the failure of first line treatment. There was insufficient sample in the bx to do tissue-NGS for the pt. who had LB before starting treatments. Majority of LBs, 37(88%) were done after the failure of second line/later treatments compared to 5(12%) done after failing the first line treatment. Patient preference and technical challenge to obtain adequate tissue were the commonest reasons for getting the LBs. Results were available in all (100%) the cases. Median turnaround time was 8 days (range:7-13). The commonest mutations were TP53,APC, KRAS, PIK3CA, BRAF, SMAD4. BRCA-2 was identified in 1 pancreatic ca pt. MSI-H was noted in 3 patients; 2 with Colon ca, and 1 with CUP. An actionable alteration was seen in, 40 (95.2%) of the patients. A FDA approved target-matched drug was available for 27/40(67.5%) pts., if we also consider off-label usage. For those who had an alteration, but no FDA approved target-matched drug was available, 13/40 (32.5%), a clinical trial was available for all 13/13 (100%) of the pts.. 43% of those who had a FDA approved target-matched treatment available, but not approved for their disease, were able to receive the drug off-protocol. Two out of 13(15.3%) of the pts. who had a clinical trial available, were enrolled on a study. **Conclusions:** Liquid biopsies can be efficiently utilized in a community oncology practice. It offers an attractive option to gather genomic information of malignant cells in patients with advanced GI malignancies to be able to deliver state of the art care to all patients, including those who may not have a convenient access to a tertiary center. Research Sponsor: None.

128 Poster Session

Global BRAF testing practices in metastatic colorectal cancer. *First Author: Scott Kopetz, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: The BRAF V600E mutation is a marker of poor prognosis in patients with metastatic colorectal cancer (mCRC). Targeted therapy, such as encorafenib plus cetuximab, is approved in the US/Europe for the treatment (tx) of BRAF V600E-mutated mCRC and demonstrated improved survival vs historical standard of care (SOC). Determining BRAF mutation status in mCRC is recommended by NCCN and ESMO guidelines although adherence to guidelines may not be uniform. This report's objective is to communicate global survey results of mCRC BRAF testing practices. Identifying regions where BRAF testing is not SOC may help identify where education efforts are needed improve effective tx decision making. **Methods:** Oncology tx centers were identified from a registry and public information. Centers were selected for research experience, historic data quality, and estimated mCRC patients. A BRAF testing practices survey using an online platform of verified centers was conducted March-August 2020; 395 centers/38 countries have responded thus far. **Results:** Respondents indicated BRAF-mutation testing is performed as SOC for patients with mCRC in most regions; Eastern Europe and South America are exceptions: only 47% (45/95) and 45% (9/20) of centers, respectively routinely performed mutation testing. Most test tumor tissue, few test both tumor tissue or blood, and none conduct blood mutation testing only. Most regions perform BRAF testing at initial diagnosis or confirmation of advanced disease. Individual country statistics will be presented. **Conclusions:** BRAF testing has global variability, impacting tx decisions. Increased awareness and routine testing may lead to informed decisions regarding targeted therapies, such as encorafenib plus cetuximab where approved, in patients with BRAF V600E-mutant mCRC. Research Sponsor: Pfizer; Ashwin Gollerkeri, Ashwin.Gollerkeri@pfizer.com, 303-381-6600, Pharmaceutical/Biotech Company.

	East Asia	Australasia	Eastern Europe	Northern & Western Europe	Africa, India, & Middle East	North America	South America
Is mCRC BRAF mutation testing performed as SOC at your practice? Yes, n/N (%)	52/56 (93)	15/17 (88)	45/95 (47)	111/114 (97)	22/33 (67)	52/60 (87)	9/20 (45)
Typical timing of BRAF testing? n/N (%)							
At initial histological dx, any stage	26/56 (46)	7/17 (41)	14/95 (15)	22/114 (19)	4/33 (12)	20/60 (33)	1/20 (5)
At initial radiological confirmation of advanced/metastatic disease prior to 1L tx	25/56 (45)	8/17 (47)	33/95 (35)	90/114 (79)	16/33 (48)	31/60 (52)	9/20 (45)
Upon progress following 1L SOC tx	3/56 (5)	0	11/95 (12)	2/114 (2)	4/33 (12)	2/60 (3)	3/20 (15)
Not performed/only done in clinical trial setting	2/56 (4)	2/17 (12)	37/95 (39)	0	9/33 (27)	7/60 (12)	7/20 (35)
('Yes' to routine BRAF testing) What type of testing? n/N (%)							
Tumor tissue	37/52 (71)	15/15 (100)	40/45 (89)	95/111 (86)	15/22 (68)	33/52 (63)	6/9 (67)
Blood	0	0	0	0	0	0	0
Both tumor tissue or blood	15/52 (29)	0	5/45 (11)	16/111 (14)	7/22 (32)	19/52 (37)	3/9 (33)

129 Poster Session

Targetable mutations in gastrointestinal malignancies: A comparison of RAS mutant and RAS wild type tumors. *First Author: Jamie Randall, Inova Fairfax Hospital, Fairfax, VA*

Background: KRAS and NRAS (RAS) mutations are considered driver mutations in gastrointestinal malignancies such as colorectal and pancreatic cancer. Our institution obtains broad molecular testing (commercial panels with full exon coverage of at least 300 genes) for all stage IV gastrointestinal malignancies that are reviewed at an internal molecular tumor board (MTB). The MTB subjectively felt there was less benefit from comprehensive molecular testing in RAS mutant tumors and wished to quantify this using standardized analysis according to validated guidelines. **Methods:** We performed a retrospective cohort study of 209 consecutive genomic sequencing results of advanced gastrointestinal malignancies at our institution dating from March 2016 until December 2019. We compared the number of "targetable" mutations in the RAS mutant and wild type (WT) malignancies, as analyzed by an interpretation service according to the Association of Molecular Pathology (AMP) guidelines. A lower AMP score corresponds to a higher level of evidence as a predictive biomarker. We also compared molecular tumor board specific recommendations for each group (excluding recommendations regarding RAS such as EGFR mAbs). **Results:** There were 134 RAS mutant and 75 RAS WT cases. Alterations with AMP scores of 1A,1B, and 1C were more commonly seen in the RAS WT population 18/75 and 9/134 respectively (24.0% versus 6.7% p-value=0.0004). 39 of 75 cases in RAS WT and 27/134 in RAS mutant (52.0 versus 20.1%, p-value <0.0001) cohort had at least one alteration that was deemed actionable by our institution's current MTB criteria. **Conclusions:** Actionable mutations were significantly less common in the RAS mutant versus RAS WT population, and further studies assessing the value of comprehensive genomic testing in RAS mutant gastrointestinal malignancies may be warranted. Research Sponsor: None.

Mutations deemed "targetable" by the Inova Schar Cancer Institute MTB.

Mutation	Number seen in RAS mutant cases	Number seen in RAS WT cases
BRAF V600E	0	10
BRAF non-V600	2	3
ATM alteration	6	3
BRCA1/BRCA2	2	8
ERBB2 alterations	4	6
MSI high	1	0
TMB high	6	8
RET fusion	0	1
TSC1/2	2	0
NTRK fusion	1	0
MTOR	3	0

130 Poster Session

Identification of transcriptomic determinants to predict the efficacy of anti-EGFR treatment of colorectal cancer patients. *First Author: Saikat Chowdhury, University of Texas MD Anderson Cancer Center, Houston, TX*

Background: It is now well known that in colorectal cancer (CRC) activating mutations in *KRAS, NRAS,* and *BRAF* confer resistance to anti-EGFR therapy. However, only ~ 40% of patients with RAS^{WT} ($KRAS^{WT}/NRAS^{WT}/BRAF^{WT}$) tumors respond to therapy. We have used transcriptomic data in addition to somatic mutations to decipher intrinsic resistance mechanisms and identify novel biomarkers of anti-EGFR response in CRC. **Methods:** The transcriptomic profiles of metastatic CRC patients treated with the anti-EGFR drug cetuximab plus chemotherapy (n = 193) or as a single agent (n = 80) were retrospectively obtained from two independent clinical cohorts (Okita et al., 2018; & Khambata-Ford et al., 2007). Tumor samples were further divided into RAS^{WT} and RAS^{Mut} groups and subsequently in four consensus molecular subtypes (CMS) based on their transcriptomic profile. The transcriptomic profiles of cetuximab treated CRC cell lines (n = 148, Medico et al., 2015) and PDX models (n = 230, Bertotti et al., 2015) were used for validation. **Results:** In RAS^{WT} population of cetuximab plus chemotherapy cohort, the disease control rates (DCR) observed for cetuximab in the second line were 92% (33/36) for CMS2 and 83% (15/18) for CMS4 tumors relative to 50% (2/4) and 59% (13/22) for CMS1 and CMS3 respectively (Chi-square test p-value = 0.037). Similarly, in cetuximab single agent cohort, the DCR were 0% (0/4), 68% (15/22), and 29% (5/17) for CMS1, CMS2, and CMS4, respectively (Chi-square test p-value = 0.029). In the preclinical study of 148 CRC cell lines, 60% (12/20) of CMS2 cell lines with RAS^{WT} genes were sensitive to cetuximab, versus no sensitive cell lines from other CMS (CMS1 = 0/4; CMS3 = 0/5; CMS4 = 0/12). In the PDX study, 84% (11/13) of CMS2 tumor showed clinical benefit, followed by CMS4 with 75% (6/8) in RAS^{WT} group (CMS1 = 2/5; CMS3 = 2/4). Gene Set Enrichment Analysis (GSEA) of tumor tissue samples identified that Myc (NES = 1.32, FDR = 0.3), E2F (NES = 2.24, FDR = 0.02), and mTOR (NES = 1.54, FDR = 0.1) pathways were active in the cetuximab refractory RAS^{WT} CMS2 patients relative to cetuximab sensitive tumors. Similarly, these pathways were also activated (FDR $\leq$ 0.05) in cetuximab resistant RAS^{WT} cell lines and PDX models, suggesting that preclinical models are appropriate for testing of potential therapeutic combinations to overcome resistance to anti-EGFR therapy. **Conclusions:** Resistance to anti-EGFR therapy in extended RAS^{WT} CRC tumors is mediated in part by transcriptional activation and can be predicted by consensus molecular subtype (CMS) and quantifying transcriptional states of Myc, E2F, and mTOR pathway gene sets. Research Sponsor: Cancer Prevention and Research Institute of Texas (CPRIT).

131 Poster Session

Circulating tumor DNA in identifying resistant subclones post EGFR blockade: Implications for EGFR rechallenge. *First Author: Adithya Chennamadhavuni, University of Iowa, Iowa City, IA*

Background: For patients with metastatic RAS/RAF wild-type refractory colorectal cancer anti-EGFR therapy can be reused in subsequent lines of therapy. However, it is not entirely clear if all patients derive benefit. Increasingly it is been recognized that these patients acquire mechanisms of resistance which can be detected on circulating tumor DNA-based testing. We present a series of patients who had serial testing post EGFR therapy showing its feasibility and value. This would have implications for EGFR rechallenge. **Methods:** We reviewed records for patients who initially were noted to have tissue RAS/RAF Wild type who received prior anti-EGFR therapy and then subsequently had at least 1 circulating tumor DNA-based testing. Included a result of patients who had comprehensive NGS based profiling for both tissue as well as ctDNA. **Results:** Median duration of initial prior anti EGFR therapy was around 10 months. Table shows results of patient's tissue based genomic testing in parallel with the serial circulating tumor DNA-based testing that was done later when subsequent lines of therapy were being decided. As noted, known acquired mechanisms of resistance were noted in 100% of the cases. These included KRAS, NRAS, extracellular domain mutations in EGFR and BRAF mutations. Interestingly the levels of the sub-clones expressed as variant allele fraction percentage varied and decreased over time in relation to timing of the prior EGFR exposure. Additionally, these were noted to be polyclonal and the number of clones also varied including some disappearing over time during non-EGFR based therapy (EGFR holiday). **Conclusions:** Patient's post EGFR blockade may have multiple mechanisms of acquired resistance that can be easily detected on noninvasive liquid biopsies. These patients likely will not benefit from EGFR rechallenge based on the results of the recently reported CRICKET (NCT02296203) and CAVE (EudraCT number: 2017-004392-32) clinical trials. Rechecking liquid biopsy plasma RAS/RAF status is one thing that may be incorporated into practice with EGFR rechallenge only if acquired mechanisms of resistance are absent. Research Sponsor: None.

	APC	TP53	KRAS	NRAS	BRAF	EGFR
Patient 1						
Tissue NGS	+	+				
ctDNA – T1*		+	+		+	+
ctDNA – T2	+	+	+			
Patient 2						
Tissue NGS	+	+				
ctDNA – T1*	+	+				
ctDNA – T2						
ctDNA – T3	+	+	+			
Patient 3						
Tissue NGS	+	+				
ctDNA – T1*	+	+				+
ctDNA – T2	+	+	+			+
ctDNA – T3	+		+			+
ctDNA – T4	+	+				+
Patient 4						
Tissue NGS	+	+				
ctDNA – T1*	+	+	+			
ctDNA – T2	+	+	+			
ctDNA – T3	+	+	+		+	
ctDNA – T4	+	+	+	+		
Patient 5						
Tissue NGS	+	+				
ctDNA – T1*	+	+				+
ctDNA – T2	+	+				+
ctDNA – T3	+	+				+
Patient 6						
Tissue NGS	+	+				
ctDNA – T1*	+	+	+		+	
ctDNA – T2	+	+	+		+	
ctDNA – T3	+	+	+		+	

*+ indicates the timepoint where the named clones were detected.

132 Poster Session

Overall survival based on MSI and BRAF mutation status for stage II/III colorectal cancer. *First Author: Sophiya Karki, University of Kansas Medical Center, Kansas City, KS*

Background: Colorectal cancer (CRC) is the second leading cause of cancer-associated deaths in the United States. Some of the poor prognostic factors for metastatic CRC (mCRC) include BRAF V600E mutation and microsatellite instability (MSI) that result from mutation or loss of mismatch-repair genes. While the prognostic value of MSI-high CRC for early-stage patients treated with resection and adjuvant chemotherapy is favorable, the prognostic value of BRAF mutation is still unclear. Furthermore, the impact of BRAF mutation with concurrent microsatellite instability on overall survival has not been well investigated. **Methods:** Here, we collected BRAF mutation status and MSI status of stage II/III CRC patients (n=106) treated at the University of Kansas Cancer Center between September 2009 and July 2020 and compared overall survival between 4 subtypes: MSI-H/BRAF mutant (n=16), MSS/BRAF mutant (n=4), MSI-H/BRAF WT (n=17) and MSS/BRAF WT (n=69), further stratifying patients by age at diagnosis and tumor location. Molecular data were obtained from molecular oncology laboratory as PCR or IHC-based or acquired from outside records. Subgroup analyses were done for stage II and stage III cancers. **Results:** Table shows the patient characteristics. From our preliminary analysis, MSI-H CRC was found to be primarily a right-sided tumor (MSI-H/BRAF mutant: 94% and MSI-H/BRAF WT 76%). On the contrary, MSS CRC had a more heterogenous localization, spanning left colon, right colon and rectum. In our patient cohort, median survival was not reached for stage II patients whereas for stage III patients, BRAF mutation was associated with poor median survival irrespective of MSI status (MSS/BRAF mutant: 27 months and MSI-H/BRAF mutant 29 months). Median overall survival was found to be 87 months, not reached, 27 months and 29 months for MSS/BRAF WT, MSI-H/BRAF WT, MSS/BRAF mutant and MSI-H/BRAF mutant, respectively. Although associated with poor survival, MSI-H/BRAF mutant displayed later age at diagnosis (mean age 73) compared to MSS/BRAF mutant (mean age 60, p-value<0.029). **Conclusions:** Our finding suggests that BRAF mutation has poor prognosis even at earlier stages of the disease and that MSS/BRAF mutation, in particular, has the worst prognostic features. These findings highlight the need for BRAF-targeted therapy for CRC at any stage. Due to small sample size, however, our results warrant validation in a larger cohort. Research Sponsor: None.

Baseline characteristics according to MSI/BRAF status.

N=106	Total n=69 (65%)	MSS/BRAF WT n=17 (16%)	MSI-H/BRAF WT n=4 (4%)	MSS/BRAF mutant n=16 (15%)	MSI-H/BRAF mutant
Age, y					
<65	58	47	7	3	1
65-75	17	3	4	0	10
>75	31	19	6	1	5
Sex					
Female	55	32	9	3	11
Male	51	37	8	1	5
Location					
Colon	87	51	16	4	16
Rectum	19	18	1	0	0
Clining Stage					
II	40	19	11	0	10
III	66	50	6	4	6
Tumor Location					
Right	52	22	13	2	15
Left	24	18	3	2	1
Rectum	25	24	1		
Not specified	5	5			

133 Poster Session

Cost-effectiveness of cetuximab + FOLFIRI versus bevacizumab + FOLFIRI in the first-line treatment of *RAS* wild-type metastatic colorectal cancer in China. *First Author: Ilse Van Oostrum, Ingress Health, Rotterdam, Netherlands*

Background: Adding cetuximab to FOLFIRI chemotherapy (cet+CT) as first-line (1L) treatment for *RAS* wild-type (wt) metastatic colorectal cancer (mCRC) has been reported as cost-effective vs bevacizumab + FOLFIRI (bev+CT) in multiple jurisdictions. This study determined the cost-effectiveness (CE) of cet+CT for patients with mCRC in China. **Methods:** A published 3-health-state (nonprogressive, progressive, death) CE model was adapted to reflect Chinese patient characteristics, health state utilities, unit costs, and discounting rates, applying FIRE-3 trial–based resource utilization and adverse event rates. Progression-free and overall survival estimates were based on published FIRE-3 trial simulations to statistically adjust for available later-line treatment modalities in China vs those observed in FIRE-3.[1] Cetuximab and bevacizumab costs were based on up-to-date prices after the 2019 national reimbursement drug listing negotiations. Incremental CE ratios (ICERs) are given as cost (Chinese Yuan [¥]) per life-year (LY) and quality-adjusted LY (QALY) gained. The willingness-to-pay (WTP) threshold was ¥193,931, equivalent to 3 times the gross domestic product per capita, following WHO guidance. **Results:** Overall costs/costs restricted to 1L treatment were ¥483,771/¥249,619 (cet+CT) and ¥366,036/¥156,802 (bev+CT). Health effects were 3.32/2.68 (cet+CT) and 2.39/1.94 (bev+CT) LYs/QALYs gained. Discounted ICERs for cet+CT vs bev+CT were ¥148,311 and ¥186,517 per LY and QALY gained in deterministic analysis. cet+CT had a 71.8% (LY) and 52.5% (QALY) probability of being cost-effective. Treatment duration with a biologic in 1L, utilities in 3L treatment, and duration of 2L treatment were the main outcome drivers. **Conclusions:** Projections suggest that cet+CT is cost-effective vs bev+CT for 1L treatment of patients with *RAS* wt mCRC in China, with ICERs below the current WTP threshold in deterministic and probabilistic sensitivity analyses. [1] Van Oostrum I, et al. *Value Health*. 2020;23(Suppl 1): S8. Research Sponsor: Merck KGaA.

134 Poster Session

Microsatellite instability in colorectal cancer: An analysis of the National Cancer Database. *First Author: Kamelah Abushalha, Doctors Without Borders, Amman, Jordan*

Background: High-frequency microsatellite instability (MSI-H) accounts for roughly 15% of all cases of colorectal cancer (CRC). Studies suggest a significant non-adherence to routine MSI testing in patients diagnosed with CRC despite universal guidelines. **Methods:** We used the NCDB to identify adults with MSI-H status CRC from 2010-2015 with the following histologic subtypes: mucinous and not otherwise specified adenocarcinoma, and medullary carcinoma. The primary site was localized to the right colon, left colon, and rectum; demographic factors, clinicopathologic features, and treatments were identified. Patients were stratified by site and discrete and continuous variable comparisons were made using the chi-square and Mann-Whitney test, respectively. Survival was examined with the Kaplan-Meier method and a Cox proportional hazards regression model. A logistic regression model was used to examine MSI status. All analyses were conducted with SAS version 9.4. **Results:** A total of 5364 patients were identified and stratified by site into 3 groups: right colon (n = 4004, 74.6%), left colon (n = 890, 16.59%) and rectum (n = 470, 8.76%). Compared to the left colon and rectum, right colon patients were more likely to be older females with larger tumors and less likely to receive chemoradiation. After adjusting for all else, we found statistical evidence that female vs. male gender (OR = 1.47; 95% CI: 1.24 to 1.73), Black vs. White race (OR = 0.61; 0.45 to 0.83), left vs. right colon (OR = 0.33, 0.27 to 0.41), rectum vs. right colon (OR = 0.08, 0.05 to 0.13), mucinous adenocarcinoma vs. adenocarcinoma (OR = 2.37, 1.92 to 2.93), medullary carcinoma vs. adenocarcinoma (OR = 8.86, 4.56 to 17.22), positive vs. negative k-RAS mutation (OR = 0.49, 0.41 to 0.59), and positive vs. negative CEA status (OR = 0.79, 0.66 to 0.94) were factors associated with MSI-H status. Improved survival was associated were Hispanic white race, stage 1, and free surgical margins within a multivariable context. Factors associated with poor survival: increased Charlson/Deyo score, advanced stage, lymphovascular invasion, and positive CEA status. **Conclusions:** In settings where resources are scarce and universal testing is not possible, there is a benefit from MSI testing in female patients, those with right-sided colon cancer, mucinous adenocarcinoma, and medullary carcinoma. Research Sponsor: None.

135 Poster Session

Trends in hospitalizations among patients with colorectal cancer: Results from the National Inpatient Sample (2007 through 2017). *First Author: Udhayvir Singh Grewal, Louisiana State University Health Sciences Center, Shreveport, LA*

Background: Colorectal cancer is the second leading cause of cancer-related deaths in the United States with a rising incidence, especially in young adults. Care for patients with colorectal cancer is associated with significant health care costs and expenditures. We analyzed trends in admissions and outcomes related to hospitalizations in patients with colorectal cancer. **Methods:** We retrospectively interrogated the National Inpatient Sample for admissions in patients with colorectal cancer from 2007 – 2017. Records were stratified based upon the anatomical site and were analyzed for various inpatient outcomes. SAS version 9.4 (SAS Institute Inc.) was used for statistical analysis. **Results:** A total of 1,962,705 admissions were identified. About 50.2% patients were males, 64.4% were white and median age was 67.7 (53.8-81.6). Majority (47.8%) of the admissions that were coded for anatomical location of malignancy were for ascending colon cancer. 60.7% of the admissions were non-elective and Medicare was the primary payer for 58.6% of admissions. Most patients admitted for colon cancer belonged to the lower income quartile (28.3%) and were concentrated in large (58.9%), urban teaching hospitals (53.4%) in Southern US (38.8%). Hypertension (53.6%) and diabetes mellitus (18.6%) were the most common co-morbidities ($p < 0.0001$). Average in-hospital mortality was 4.9% and was lower in patients with ascending colon cancer (2.9, $p < 0.001$). Median length of stay was 5 days, but was higher in patients with transverse colon cancer (9 days, $p < 0.0001$). Median cost of hospitalization was found to be $12,295 and was significantly higher for patients with descending colon malignancy ($16,369, $p < 0.0001$). The number of annual hospitalizations stayed steady overall; the number of annual hospitalizations increased by 98.6% for rectosigmoid cancer. **Conclusions:** Despite highest number of hospitalizations, patients with ascending colon cancer had lowest in-hospital mortality. Cost of hospitalization and median length of stay were highest for patients with descending colon and transverse colon respectively. Number of annual hospitalizations has significantly increased for rectosigmoid cancer. Our findings may help inform physicians and healthcare administrators to devise appropriate strategies to efficiently channelize healthcare resources in order to decrease the overall economic burden associated with hospitalizations in patients with colorectal cancer. Research Sponsor: None.

136 Poster Session

Inoperable stage IV colorectal cancer with intact primary tumor in patients receiving palliative chemotherapy: Does the response to chemotherapy correlate between primary and metastatic sites? An Irish cancer center experience. *First Author: Ruba Hamed, Department of Medical Oncology University Hospital Limerick, Limerick, Ireland*

Background: Colorectal cancer (CRC) is the 3rd most common malignancy in Ireland with over 2700 cases annually. Approximately 20% are diagnosed with stage IV disease. The aim of this study is to evaluate the response to chemotherapy at primary and metastatic sites and review the frequency of intervention required to palliate the intact primary tumour in patients with stage 4 inoperable CRC in an Irish tertiary referral centre. **Methods:** A retrospective review of medical records was completed, identifying stage 4 CRC patients with primary tumour in situ diagnosed between January 2014 and December 2019, treated with chemotherapy (oxaliplatin or irinotecan based +/- bevacizumab or EGFR monoclonal antibody). Data and survival analysis were obtained using Kaplan-Meier methods. **Results:** 50 eligible patients were identified; 60% male, 40% female with a median age of 62 years. 2% had a transverse colonic primary, 32% right and 44% left sided and 22% had a rectal primary. 36% presented with liver metastasis only, 4% lung metastasis alone and 20% both. 48% were KRAS, 4% NRAS and 4% BRAF mutation positive while 1 patient was identified as having microsatellite instability. All patient received first-line chemotherapy either oxaliplatin or irinotecan based, 18% with the addition of Bevacizumab and 24% with EGFR monoclonal antibody. Overall response to first-line chemotherapy at the primary site and metastatic sites was assessed radiologically; 42% displaying a partial response, 36% had stable disease while 18% had progression at primary site. At the metastatic sites 50% responded, 10% stable disease and 40% progressed. Complication at primary tumour site included: obstruction 12%, with perforation in 6%, bleeding 10%, pain at tumour site in 6%, and one patient developed an abscess. Overall, after chemotherapy 76% of all patients did not require further intervention to manage primary site. 6% underwent curative surgery with resection of primary and metastatic lesions. Of those who had palliative intervention; 10% underwent palliative colostomy/ileostomy, 12% palliative radiotherapy, and 2% both. Overall survival was 14 months. At time of analysis 14% were alive, 10% receiving treatment and 4% on radiological surveillance. **Conclusions:** This retrospective study confirms that palliative chemotherapy +/- targeted therapy is effective in controlling the primary tumour in stage 4 inoperable CRC. In addition, it reveals a nearly 80% partial response or stable disease radiologically at the primary site after first-line chemotherapy. Furthermore, progression was significantly lower at primary site compared to distant metastasis (18% vs 40%). Almost 75% did not require palliative intervention for their primary tumour. Overall survival in our centre is higher compared to internationally observed data. Research Sponsor: None.

137 Poster Session

Continuing education curriculums and outcomes on progressive metastatic colorectal cancer treatment. *First Author: Kinjal Parikh, Medscape Oncology, New York, NY*

Background: The treatment armamentarium for patients with metastatic colorectal cancer (mCRC) has expanded significantly and treatment options for progressive disease remain limited. As data from clinical trials or subgroup analyses become available, landmark trials are published, and guideline recommendations or clinical utility of these therapies change, continuing medical education (CME) for oncologists is necessary to ensure that eligible patients continue to receive effective therapies. **Methods:** A series of 7 activities launched from 2016-2020 to reach a global oncology audience in the care of patients with mCRC. The educational activities included multimodality approaches with didactics, cases, simulations, and panel discussions. Educational effectiveness was assessed with repeated paired pre/post assessment where learners served as their own controls to measure changes in knowledge, competence, confidence, and performance. Oncologists who completed both the pre- and post-CME questions or who made relevant clinical decisions in the simulation activity were included in analysis and McNemar's tests were conducted to assess statistical significance of the results with $p < .05$ being considered significant. The first activity launched on 6/8/2016 and the data reported were collected through 7/20/20. **Results:** As of 7/20/2020, 59,595 learners participated in the activities, including 18,634 total physician learners with 5,862 oncologists. Significant improvements in knowledge, competence, and confidence among oncologists, measured as relative % changes in correct responses or confidence from pre- to post-CME, were seen (n=60-214) [% pre, % post, p value]: 11%: knowledge regarding therapies for progressive disease in mCRC (83; 92; $p < .05$); 17%: knowledge of clinical trials assessing impact of patient/disease specific aspects on treatment selection (63; 74; $p < .001$); 11%: competence selecting therapy (55; 61; $p < .05$); 41%: confidence selecting therapy (34; 48; $p < .001$); 24%: confidence addressing communication barriers in mCRC (50; 62; $p < .01$). Significant improvement in performance of oncologists, measured as absolute % changes in pre- to post-CME correct responses were seen (n = 46) [% pre, % post, p value]: 28%: starting preferred treatment options (24; 52; $p < .01$); 18%: prescribing regorafenib (24; 43; $p < .01$); 9%: prescribing trifluridine + tipiracil (0; 9; $p < .05$). **Conclusions:** This series of online, expert-led, CME-certified educational activities resulted in significant improvement in knowledge, competence, confidence, and performance among learners regarding the management of patients with progressive metastatic colorectal cancer over time. These results demonstrate the effectiveness of on-demand education as new data emerge and indications expand to reinforce existing knowledge, close persistent gaps, and increase confidence in managing these patients. Research Sponsor: Bayer, Taiho Oncology.

138 Poster Session

Severe lymphopenia predicts poorer survival in patients with rectal cancer undergoing neoadjuvant chemoradiation. *First Author: Daniel W Kim, Massachusetts General Hospital, Boston, MA*

Background: Chemoradiation (CRT) induced lymphopenia is common and associated with poorer survival in multiple solid malignancies. The objective of this study was to evaluate the prognostic impact of lymphopenia in patients with rectal cancer undergoing neoadjuvant CRT. We hypothesized that severe lymphopenia would correlate with worse survival. **Methods:** The inclusion criteria for this single-institution retrospective study were: 1) biopsy-proven diagnosis of rectal adenocarcinoma, 2) receipt of neoadjuvant CRT followed by surgery, and 3) absolute lymphocyte count (ALC) available prior to and within 12 weeks of CRT. In general, CRT consisted of 5-fluorouracil or capecitabine and RT with 50.4 Gy over 28 fractions. Lymphopenia was graded according to CTCAE v5.0. The primary variable of interest was ALC nadir within 12 weeks of CRT, dichotomized by ALC of < 0.5 k/μl (Grade 3 lymphopenia). The primary endpoint was overall survival (OS). Cox modeling and Kaplan-Meier methods were used to perform survival analyses. **Results:** 193 patients were identified. Median follow-up for the entire cohort was 68 months. Median age was 58. 62% were male, 82% were Caucasian, and 90% had ECOG $\leq$1. Median tumor distance from anal verge was 8 cm. Overall clinical stage was 1 or 2 in 23% and 3 in 77%. Median baseline CEA was 3.2 ng/ml. 83% received chemotherapy following RT. Following CRT, 70% underwent low anterior resection and 30% underwent abdominoperineal resection. Median baseline ALC for the entire cohort was 1.7 k/ul. ALC nadir within 12 weeks of initiating CRT was < 0.5 k/ul among 110 (57%) patients. Patients who developed severe lymphopenia with CRT had a lower baseline hemoglobin (median 13.3 vs. 14.0 g/dl, p = 0.022) and lower baseline ALC (median 1.6 vs. 1.8 k/ul, p = 0.010) compared to those who did not develop severe lymphopenia. There were no differences in disease and treatment characteristics between the two groups. On multivariable Cox model, severe lymphopenia was significantly associated with increased hazards of death (HR = 3.52 [95% CI 1.47-8.44], p = 0.005). Receipt of chemotherapy post-CRT (HR = 0.22 [95% CI 0.09-0.54], p = 0.001) predicted better OS while higher pathologic T (HR = 8.01 [95% CI 2.98-17.21], $p < 0.001$) and N stage (HR = 9.43 [95% CI 3.19-27.86], $p < 0.001$) and positive surgical margin (HR = 3.77 [95% CI 1.13-12.62], p = 0.031) predicted worse OS. The 5-year OS was 79% vs. 92% in the cohort with vs. without severe lymphopenia, respectively (log-rank p = 0.001). **Conclusions:** CRT-induced lymphopenia is common and severe lymphopenia may be a prognostic marker of poorer survival in rectal cancer. Closer observation in high-risk patients and treatment modifications may be potential approaches to mitigating CRT-induced lymphopenia. Our findings also suggest an important role of the host immunity in rectal cancer outcomes, supporting the ongoing efforts of immunotherapy trials in rectal cancer. Research Sponsor: None.

139 Poster Session

A National Cancer Database (NCDB) analysis of the impact of nonmetastatic colon cancer sidedness on survival. *First Author: Deven Patel, Cedars-Sinai Medical Center, Los Angeles, CA*

Background: Differences in embryological origin and tumor biology distinguish right-sided colon cancer (RCC) from left-sided colon cancer (LCC). Previous studies characterizing the prognostic impact of colon cancer laterality on clinical outcomes in non-metastatic colon cancer have been conflicting, thus closer examination is needed. **Methods:** Using the NCDB, patients with stage I-III colon cancer between 2004-2014 were stratified according to tumor location; RCC vs. LCC. Patient (pt) and tumor characteristics were compared in univariate analysis, survival (OS) was estimated by Kaplan-Meier (KM) curves and Cox proportional hazards modeling. Binomial logistic regression analysis was utilized to identify variables associated with colon cancer laterality. **Results:** Of the 342,735 pts who met inclusion criteria, 210,343 (61.4%) were diagnosed with RCC, and 132,392 (38.6%) with LCC. Pts with RCC were older (mean 71.6 vs. 66.4 years, $p < 0.001$) and predominantly female (65% vs. 35%, $p < 0.001$) compared to those with LCC. A trend towards poorer OS was seen in pts with RCC (mean 91.0 mos [95% CI: 90.2-91.8]) compared to LCC (112.2 mos [95% CI: 110.9-113.6]) in unadjusted analysis. On Cox multivariable adjusted analyses there was a significant but minimal impact on OS and laterality (hazard ratio or HR [LCC as ref] 0.978, 95% CI 0.967-0.989 $p < 0.0001$). Multiple unadjusted KM survival analyses showed RCC with T4 disease, high-grade, LVI/PNI, positive margins, N0-N2 disease, tumor deposits, and receipt of adjuvant chemotherapy had poorer OS than those features in LCC (all $p < 0.0001$). Binomial logistic regression showed RCCs were significantly more likely to be higher grade (odds ratio or OR 2.024) and MSI-H (OR 2.010) with trends (nonsignificant) towards more likely having N1-2 positive disease, LVI, less receipt of adjuvant chemotherapy, and fewer tumor deposits. **Conclusions:** The impact of sidedness on prognosis in stage I-III colon cancer is complex. In this large, population-based study, RCC tends to be associated with more adverse prognostic features than LCC. More investigation into the biologic differences between RCC and LCC is warranted and how they impact phenotype and survival. Research Sponsor: None.

140 Poster Session

Impact and utility of COLONTOWN, an online CRC patient and caregiver support group in clinical trial design. *First Author: Manju George, Colontown/Paltown Development Foundation, Crownsville, MD*

Background: Online cancer patient and caregiver support groups have burgeoned in the recent years; many provide critical emotional support and experiential wisdom to newly diagnosed patients. We outline below our experience engaging patients in clinical trial design working with COLONTOWN, a 5000+ member, online colorectal cancer (CRC) patient and caregiver support and educational community. Effective trial design is a complicated and lengthy process that requires input from multiple sources. Complex trial design can be particularly challenging, where opinions are mixed and a clear path forward may not be visible. Informed patient perspectives from support groups can be invaluable in such situations. **Methods:** Principal Investigators (PIs) for the oligometastatic CRC ERASure trial and the Janus rectal cancer trial worked with the lead author, a patient who is the Scientific Director of COLONTOWN. An interactive survey strategy was adopted and followed to solicit group feedback. COLONTOWN members (n = 70-120) were enthusiastic to participate and share the logic behind poll choices, and their personal experiences. Poll participation led to additional scientific discussion and improved community engagement around the survey questions. Poll data and highlights of the discussion were collected and passed on to study PIs in a de-identified manner. **Results:** Feedback from COLONTOWN helped PIs gauge patient enthusiasm for trial concepts and provide patient perspective and clarity to controversial questions in study design. This was particularly useful where data to support more than one option was available and the guidance from the NCI Task Force or cooperative group was split. The perspective from COLONTOWN was invaluable and used alongside NCI Task Force and cooperative group feedback to make decisions to move the trial concept forward. **Conclusions:** Support groups such as COLONTOWN are a versatile, valuable, underutilized and available resource that can be used to tap into patient perspectives during any clinical trial design process. Ideally, when utilized early, structured patient input can provide unique insights to PIs developing clinical trial concepts that could eliminate barriers and shorten the inception part of trial design. Increased awareness and knowledge of trial design support provided by such cancer communities could facilitate the development of patient-friendly trials to promote better accrual. Research Sponsor: None.

141 Poster Session

Factors associated with long-term survival in patients with early-onset and standard-onset colorectal cancer. *First Author: Riya Jayesh Patel, Jacobi Medical Center, Bronx, NY*

Background: Differences in incidence, clinical features, and survival between early-onset (EO) and standard-onset (SO) colorectal cancer (CRC) are well-established. Factors associated with longer survival have not been reported. We aim to determine clinical and treatment factors associated with longer survival in patients (pts) with metastatic EO and SO CRC. **Methods:** Pts with metastatic CRC diagnosed between 2010-2019 at two NYC hospitals were identified by tumor registry and classified as EO (diagnosis at < 50 years) or SO (diagnosis at ≥ 50 years). Median overall survival (OS) was calculated for each group using Kaplan Meier curves. Long-term survival was defined as OS > 2 years (EO-CTC median OS). Data was collected by chart review and compared between short vs long-term survivors in EO and SO CRC pts independently. Stata v15 was used for statistical analysis. **Results:** Of 646 pts, 144 (22.3%) had EO and 502 (77.7%) had SO. High grade tumors were more likely in EO (33.3% vs 24%, OR: 1.59, p = 0.04) than SO; whereas no differences were seen in gender, sidedness, *KRAS* mutation or chemotherapy. Biologics were used more frequently in EO than SO (OR = 1.7; p = 0.008]. Median OS was 2.1 and 1.9 years in EO and SO. There were 53 (36.8%) and 175 (35.1%) long-term survivors in EO and SO groups. In pts with SO, metastasectomy, irinotecan-based chemotherapy and use of biologics were significantly associated with long-term survival, whereas metastasectomy was the only associated factor in pts with EO. **Conclusions:** Metastatectomy was the only factor associated with longer survival in both EO and SO groups. Other clinical/pathological and treatment-related factors associated with long-term survival among SO-CRC were not associated with long-term survival among EO-CRC patients. Research Sponsor: None.

N (%)	All N = 646	EO-Short N = 91	EO-Long N = 53	p	SO-Short N = 324	SO-Long N = 175	p
Male gender	302 (46.8)	47 (51.7)	19 (35.9)	0.07	143 (44.1)	92 (52.6)	0.07
NHB race	256 (39.6)	35 (44.9)	19 (39.6)	0.25	134 (45.3)	65 (40.1)	0.44
Left-sided	253 (76.2)	38 (70.4)	26 (83.9)	0.17	36 (26.5)	22 (20)	0.235
***KRAS* (n = 354)**	167 (47.2)	20 (39.2)	19 (42.2)	0.76	59 (43.7)	41 (33.9)	0.108
Metastasectomy	67 (10.4)	7 (7.7)	13 (24.5)	0.005	15 (4.6)	32 (18.3)	< 0.001
Oxa-based	274 (65.1)	47 (70.1)	26 (63.4)	0.47	128 (64.7)	71 (63.4)	0.83
Irino-based	177 (46.6)	28 (46.7)	16 (43.2)	0.74	69 (40.8)	64 (57.7)	0.006
Biologic	401 (62.1)	65 (71.4)	38 (71.7)	0.97	165 (50.9)	132 (75.43)	< 0.001
Bevacizumab	354 (74.2)	57 (79.2)	37 (77.1)	0.79	144 (67.3)	115 (82.1)	0.002

TPS142 Trials in Progress Poster Session

Evaluation of the ctDNA LUNAR-2 Test In an Average Patient Screening Episode (ECLIPSE). *First Author: Victoria M. Raymond, Guardant Health, Inc., Redwood City, CA*

Background: Population-wide colorectal cancer (CRC) screening has been recommended by the United States Preventive Task Force (USPSTF) since 2008. Despite multiple CRC screening options, screening compliance rates have plateaued well below the 80% compliance goal set by leading health organizations. Almost 1 in 3 Americans are non-compliant with screening recommendations, citing reasons that screening is time consuming, unpleasant, and in the case of colonoscopy, invasive. The potential exists for a blood-based CRC screening test with high sensitivity and specificity to improve uptake and adherence to CRC screening. **Methods:** ECLIPSE (**E**valuation of the **c**tDNA **L**UNAR-2 Test **I**n an Average **P**atient **S**creening **E**pisode; NCT# 04136002) is a prospective, observational, multi-center study being conducted in the United States. The primary objective is performance of a proprietary blood-based circulating tumor DNA (ctDNA) test (LUNAR-2, Guardant Health, Redwood City, CA) developed to detect CRC in a screen-relevant, average risk population as compared to colonoscopy reference. ECLIPSE involves collection of whole blood prior to a standard of care screening colonoscopy and associated preparation from 10,000 subjects. Eligibility criteria include average risk adults age 45-84 without prior history of cancer, inflammatory bowel disease, or familial predisposition to CRC, and have not received recent CRC screening. Primary outcomes are sensitivity of CRC detection and specificity of advanced neoplasia (AN) detection. Health-related outcomes at one and two-years will be collected as secondary endpoints to investigate the possibility of incidental non-CRC cases and interval CRC cases that had not reached a clinical threshold for detection at time of colonoscopy. Additional secondary objectives are positive predictive value and negative predictive value for AN detection and sensitivity of advanced adenoma detection. Enrollment began in October 2019, continues at over 130 sites nationwide, and is on track for the 24-month enrollment goal. Study enrollment remained open despite the COVID-19 pandemic. Study features including mobile phlebotomy and remote site monitoring were implemented. This contributed to successful study execution during COVID-19, as demonstrated by the enrollment rebound observed as early as June 2020 which saw higher enrollment than prior months, even pre-COVID. Clinical trial information: NCT# 04136002. Research Sponsor: Guardant Health.

TPS143 Trials in Progress Poster Session

PULSE: A randomized phase II open label study of panitumumab rechallenge versus standard therapy after progression on anti-EGFR therapy in patients with *RAS* wild-type metastatic colorectal cancer (mCRC). *First Author: John H. Strickler, Duke University Medical Center, Durham, NC*

Background: Patients with *KRAS* and *NRAS* (*RAS*) wild-type mCRC benefit from the epidermal growth factor receptor (EGFR) monoclonal antibodies (Abs) panitumumab and cetuximab, but nearly all patients experience resistance. Blood-based profiling of cell free DNA (cfDNA) can identify genomic alterations that drive acquired EGFR Ab resistance. After discontinuation of anti-EGFR Abs, acquired genomic alterations decay over time to undetectable levels. Some studies have suggested clinical benefit from EGFR Ab rechallenge, but there is limited evidence that EGFR Ab rechallenge improves survival compared to standard of care (SOC) therapies. We hypothesize that cfDNA profiling will identify patients appropriate for panitumumab rechallenge, and that these molecularly selected patients will have improved survival compared to current SOC therapies. **Methods:** This is a randomized phase II, open label study designed to compare the overall survival (OS) of panitumumab rechallenge versus SOC (investigator choice TAS-102 or regorafenib). Secondary objectives include comparisons of progression free survival, objective response rate, clinical benefit rate, and quality of life as measured by the linear analogue self-assessment (LASA) questionnaire. Eligible patients have radiographically measurable *KRAS*, *NRAS*, and *BRAF* codon 600 wild-type mCRC based on tumor tissue testing, and must have experienced progression or intolerance to treatment with a fluoropyrimidine, oxaliplatin, irinotecan, an anti-VEGF Ab, and an anti-PD-1 Ab if the tumor has mismatch repair deficiency or is MSI-H. Progression after at least 4 months treatment with an anti-EGFR Ab is required. All patients must be enrolled in the COLOMATE cfDNA screening protocol (NCT03765736) and meet molecular eligibility based on Guardant360 cfDNA profiling (absence of amplification of *ERBB2*, *KRAS*, *NRAS*, and *MET*; absence of mutations of *BRAF*, *EGFR*, *ERBB2*, *KRAS*, *NRAS*, and *MET* [mutant allele frequency $>$ 0.5%]). Greater than 90 days must have elapsed between the most recent treatment with an anti-EGFR Ab and cfDNA profiling. Dosing for all study drugs is according to clinical SOC. 120 patients will be randomized 1:1 to panitumumab rechallenge or SOC. With 83 OS events, this study will have 80% power to detect an improvement in median OS from 6.5 to 10 months (HR=0.65; 1-sided α= 0.15). This study began enrollment in 6/2020. Recruitment is ongoing at 16 sites in the Academic and Community Cancer Research United (ACCRU) network (ACCRU-GI-1623). Clinical trial information: NCT03992456. Research Sponsor: Amgen.

TPS144 Trials in Progress Poster Session

A multicenter phase Ib/II study of DNA-PK inhibitor peposertib (M3814) in combination with capecitabine and radiotherapy in patients with locally advanced rectal cancer. *First Author: Paul Bernard Romesser, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Perioperative radiotherapy and chemotherapy, followed by total mesorectal excision, is the standard of care for patients with locally advanced rectal cancer (LARC). However, 1/3 of these patients still develop distant metastases, indicating the need for more effective therapies. In addition, strategies that increase pathological complete response rates are needed to enable non-surgical management of LARC. DNA-dependent protein kinase (DNA-PK) regulates a key DNA damage repair pathway for double-strand break repair. Peposertib (M3814), a potent, selective, orally administered DNA-PK inhibitor, has been shown to potentiate the effect of ionizing radiation in a human colon cancer xenograft model and several colon cancer cell lines. Peposertib is being investigated in several different trials across multiple indications. This Phase Ib/II study (NCT03770689) aims to evaluate the safety, tolerability, pharmacokinetics (PK), and efficacy of the neoadjuvant treatment combination of peposertib, capecitabine, and radiotherapy (RT) in patients with LARC. **Methods:** Patients aged $\geq$18 years with histologically confirmed and resectable Stage II/III rectal adenocarcinoma are eligible. Induction chemotherapy is permitted, but residual disease must first be documented by MRI, digital rectal examination and endoscopy. Patients who received other anticancer therapies or those with prior pelvic RT are excluded. At open-label Phase Ib (open), 18–30 patients (n = 3 per cohort) will receive peposertib + capecitabine (orally, 825 mg/m^2 twice daily [BID]) + RT (45–50.4 Gy), 5 days/week. Peposertib 50 mg once daily (QD) was the starting dose. Additional dose levels will range between 100—800 mg QD. Dose escalation is determined by the safety monitoring committee and guided by a Bayesian 2-parameter logistic regression model. At Phase II (planned), 150 patients will be randomized (1:1) to receive oral capecitabine (825 mg/m^2 BID) + RT (45–50 Gy), with either oral peposertib (recommended phase II dose [RP2D] or placebo, QD for 5 days/week. Primary objectives are to define a maximum tolerated dose and RP2D (Phase Ib), and to evaluate the efficacy of peposertib + capecitabine + RT in terms of pathological/clinical complete response (Phase II). Secondary objectives include assessment of antitumor activity (Phase Ib), quality of life outcomes (Phase II), and PK of peposertib, and the safety and tolerability of the combination therapy (both phases). To date, one patient has received peposertib 50 mg QD, six patients peposertib 100 mg QD, three patients peposertib 150 mg QD, and three patients peposertib 250 mg QD. Clinical trial information: NCT03770689. Research Sponsor: Merck KGaA, Darmstadt, Germany.

TPS145 Trials in Progress Poster Session

BOLD-100-001 (TRIO039): A phase Ib dose-escalation study of BOLD-100 in combination with FOLFOX chemotherapy in patients with advanced gastrointestinal solid tumors. *First Author: Grainne M. O'Kane, Princess Margaret Cancer Centre, Toronto, ON, Canada*

Background: Although most cancers are initially susceptible to existing anticancer therapies, over time cancer cells develop resistance. BOLD-100 is a first-in-class therapy that targets the GRP78 pathway, a major regulator of cellular stress and resistance. This therapy suppresses drug resistance, survival and proliferation by restraining stress-induced upregulation of GRP78 in tumor cells, leading to inhibition of the cell survival response. BOLD-100 successfully completed a Phase 1 monotherapy trial, with a manageable safety profile; it has demonstrated synergy in established preclinical models in combination with a wide variety of anticancer therapies and shown to restore sensitivity of drug-resistant cell lines. **Methods:** BOLD-100-001 is a multicenter, prospective, two-stage, non-randomized Phase 1b dose escalation and expansion study of BOLD-100 in combination with FOLFOX chemotherapy for selected advanced solid gastrointestinal (GI) tumors: colorectal (CRC), pancreatic (PANC), gastric (GC) and bile duct cancers (BDC). Each patient will receive BOLD-100 along with FOLFOX chemotherapy on Day 1 of each 14-day cycle. In the dose-escalation phase (Part A), patients will be enrolled to determine the combination recommended dose using a standard 3+3 design. In the dose-expansion phase (Part B), up to 80 patients with selected GI tumors will be enrolled in 5 cohorts (comprising the 4 GI cancers referred) and treated with BOLD-100 at the recommended dose and FOLFOX, until progressive disease or unacceptable toxicity. In Part A dose-escalation, the primary objective is to assess the safety, tolerability and maximum tolerated dose. The Part B dose-expansion will assess the efficacy (progression free survival, overall survival and response rate), of FOLFOX chemotherapy plus BOLD-100. Secondary objectives in Part A and B include the assessment of pharmacokinetic and pharmacodynamic parameters and potential biomarkers predictive of efficacy. Eligible patients will have previously treated histologically/cytologically confirmed metastatic/unresectable GI tumor (CRC, PANC, GC or BDC), measurable disease per RECIST criteria, an ECOG performance score of 0 or 1, and adequate organ function. In Part A, no formal statistical hypotheses will be tested; analysis of the data will focus on comparisons of safety and dose-limiting toxicities between cohorts and only descriptive methods will be used. In Part B, Bayesian modelling will be used to continually reassess the efficacy endpoints: progression free survival, overall survival and objective response rates. The study was opened for enrollment in August 2020; approximately 25-30 patients will be screened to achieve up to 20 patients in Part A and up to 80 patients will be enrolled in Part B with a maximum of 25 patients per arm. Clinical trial information: NCT04421820. Research Sponsor: Bold therapeutics.

TPS146 Trials in Progress Poster Session

KRYSTAL-2: A phase I/II trial of adagrasib (MRTX849) in combination with TNO155 in patients with advanced solid tumors with KRAS G12C mutation. *First Author: Joshua K. Sabari, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: KRAS is the most frequently mutated oncogene in cancer and a key mediator of the RAS/MAPK signaling cascade that promotes cellular growth and proliferation. KRAS G12C tumor mutations occur in approximately 14% of patients with lung adenocarcinoma and 3-4% of colorectal adenocarinoma. SHP2 is a phosphatase that acts as a key mediator of signaling from receptor tyrosine kinases (RTKs) to downstream RAS/MAPK pathways. Adagrasib (MRTX849) is a specific small-molecule investigational inhibitor of KRAS G12C that covalently binds to and locks mutant KRAS in its GDP-bound inactive form. Adagrasib has been optimized for a long half-life and extensive tissue distribution to enable inhibition throughout the entire dosing interval. Preliminary results from a Phase 1/2 study of adagrasib demonstrated promising antitumor activity and tolerability across multiple KRAS G12C tumor types. TNO155 is a selective inhibitor of SHP2 with demonstrated inhibition of RTK signaling and significant antitumor activity in preclinical models. Preclinical studies have shown that resistance to KRAS G12C inhibition may be mediated by SHP2-dependent feedback loops. Because KRAS G12C retains some level of cycling between GTP- and GDP-bound states, KRAS G12C that is not bound by inhibitor can activate downstream signaling. Active SHP2 functions to increase the active state of RAS proteins (including mutant KRAS) and also increases ERK pathway activation. Therefore, the addition of TNO155 to adagrasib may augment antitumor activity and overcome resistance by inhibiting cycling to GTP-bound KRAS and/or through inhibition of feedback activation and more comprehensively inhibiting downstream ERK signaling. In KRAS G12C human tumor models, adagrasib combined with a SHP2 inhibitor demonstrated greater activity compared to each agent alone. These data provide support for clinical evaluation of this combination in KRAS G12C tumors. **Methods:** KRYSTAL-2 is a multicenter Phase 1/2 study evaluating adagrasib and TNO155 in patients with advanced solid tumors harboring a KRAS G12C mutation. Overall objectives of the trial include evaluating safety, tolerability, and PK. The Phase 1 portion will evaluate adagrasib and TNO155 utilizing a modified Toxicity Probability Interval dose escalation design to identify maximum tolerated dose and recommended Phase 2 dose. The Phase 2 portion utilizes a Simon's optimal two-stage design to evaluate the clinical activity of adagrasib with TNO155 in 2 cohorts of up to 108 patients—CRC (54 patients) and NSCLC (54 patients). Efficacy endpoints include Objective Response Rate (RECIST 1.1), Duration of Response (DOR), Progression-free Survival (PFS), and Overall Survival (OS). The study is currently enrolling and patients will receive study treatment until disease progression, unacceptable adverse events, patient withdrawal, or death. Clinical trial information: NCT04330664. Research Sponsor: Mirati Therapeutics, Inc.

TPS147 Trials in Progress Poster Session

Conversion from unresectable to resectable liver metastases in real-world patients with liver-only metastatic colorectal cancer (mCRC) treated with FOLFOXIRI plus bevacizumab: The Conversion trial. *First Author: Shahid Ahmed, University of Saskatchewan, Saskatoon, SK, Canada*

Background: Patients with mCRC generally have a limited life expectancy, however, a small number of patients with liver-only mCRC could be cured following metastasectomy. In highly selected patients with mCRC, FOLFOXIRI (5FU, oxaliplatin, and irinotecan) plus bev results in high response rates. However, very limited evidence is available about efficacy of this regimen in real-world patients with liver-only mCRC. Furthermore, there is paucity of biomarkers that predict liver metastasectomy in such patients. The current study aims a) to evaluate rate of conversion from unresectable to resectable liver metastases in real-world patients with liver-only mCRC following FOLFOXIRI-bev, b) to identify predictive markers including an early PET-FDG response that correlate with curative surgery, & c) to determine disease control rate, overall survival, quality of life, treatment toxicities, and cost-effectiveness of surgery. **Methods:** In this pragmatic phase 2 study, 37 patients with liver-only unresectable mCRC who are deemed eligible for FOLFOXIRI-bev by their oncologist will be recruited at the two major cancer centers in Saskatchewan. Patients will receive FOLFOXIRI-bev every two weeks for a total of 12 cycles and will undergo periodic imaging tests. The resectability of liver metastases will be determined by a multidisciplinary team. For those patients who are not able to undergo a curative surgery, a doublet chemotherapy regimen ±bev will be continued at the discretion of treating oncologist. . The prognostic and predictive value of mutations in specific genes involved in cell proliferation, cell death resistance, angiogenesis, and invasion in colorectal cancer along with the relationship between the abundance and characteristics of exRNA and conversion rate and survival will be assessed. Logistic regression and Cox proportional analyses will be performed to assess correlation between an eight-week FDG-PET/CT response to chemotherapy and other biomarkers and rate of removal of metastases and survival, respectively. This pragmatic study will help to determine conversion rate in real-world patients with FOLFOXIRI plus bev and role of early FDG-PET/CT scan response and other biomarkers in predicting metastasectomy along with cost-effectiveness of this approach. Clinical trial information: NCT03401294. Research Sponsor: Canadian Institute of Health Research (CIHR).

TPS148 Trials in Progress Poster Session

Phase II/III study of circulating tumor DNA as a predictive biomarker in adjuvant chemotherapy in patients with stage II colon cancer: NRG-GI005 (COBRA). *First Author: Van K. Morris, NRG Oncology, and UT-MD Anderson Cancer Center, Houston, TX*

Background: There are currently no validated predictive biomarkers for stage II resected colon cancer (CC) after adjuvant chemotherapy. However, circulating tumor DNA (ctDNA) that is shed into the bloodstream represents a highly specific and sensitive approach for identifying microscopic or residual tumor cells. For patients (pts) with CC, the detection of ctDNA is associated with persistent disease after resection and may outperform traditional clinical and pathological features as a prognostic factor to assess risk for recurrence. We hypothesize that for pts whose stage II colon cancer has been resected and who have no traditional high-risk features, a positive ctDNA status may identify those who will benefit from adjuvant chemotherapy. **Methods:** In this prospective phase II/III clinical trial, pts (N=1,408) with resected stage II CC without traditional high-risk features and whom the evaluating oncologist deems suitable for no adjuvant chemotherapy will be randomized 1:1 into 2 arms: standard-of-care/observation (Arm A), or prospective testing for ctDNA (Arm B). Postoperative blood will be analyzed for ctDNA with the GuardantHealth LUNAR panel, covering CC-relevant mutations and CC-specific methylation profiling. Pts in Arm B with ctDNA detected will be treated with 6 months of adjuvant (FOLFOX) chemotherapy. For all pts in Arm A, ctDNA status will be analyzed retrospectively at the time of endpoint analysis. The primary endpoints are clearance of ctDNA with adjuvant chemotherapy (phase II) and recurrence-free survival (RFS) for "ctDNA-detected" pts treated with or without adjuvant chemotherapy (phase III). Secondary endpoints will include time-to-event outcomes (OS, RFS, TTR) by ctDNA marker status and treatment, prevalence of detectable ctDNA in stage II CC, and rates of compliance with assigned intervention. Archived normal and matched tumor and blood samples will be collected for exploratory correlative research. The trial is actively accruing towards the phase II endpoint across all US and Canadian cooperative groups. Support: U10-CA-180868, -180822; UG1CA-189867; GuardantHealth. Clinical trial information: NCT04068103. Research Sponsor: U.S. National Institutes of HealthPharmaceutical/Biotech Company.

TPS149 Trials in Progress Poster Session

Tepotinib plus cetuximab in patients (pts) with RAS/BRAF wild-type left-sided metastatic colorectal cancer (mCRC) and acquired resistance to anti-EGFR antibody therapy due to MET amplification (METamp). *First Author: Josep Tabernero, Vall d'Hebron University Hospital and Institute of Oncology (VIHO), Barcelona, Spain*

Background: *MET*amp is a secondary, or co-driving, genetic change in pts with mCRC and acquired resistance to anti-EGFR therapy, which can contribute to disease progression. In EGFR-resistant pts with mCRC and *MET*amp, MET inhibition + an anti-EGFR agent could achieve disease control by targeting emerging MET pathway activation and maintaining EGFR pathway inhibition. Tepotinib is an oral, once-daily, highly selective, potent MET tyrosine kinase inhibitor (TKI). Tepotinib + the EGFR TKI gefitinib demonstrated improved outcomes in pts with *EGFR*-mutant *MET*amp non-small cell lung cancer and acquired EGFR TKI resistance vs chemotherapy (INSIGHT: NCT01982955). In these pts, progression-free survival (PFS) was 16.6 vs 4.2 months (HR = 0.13; 90% CI: 0.04, 0.43) and overall survival (OS) was 37.3 vs 13.1 months (HR = 0.08; 90% CI: 0.01, 0.51). In pts with mCRC and acquired resistance to anti-EGFR antibody therapy due to *MET*amp, tepotinib + anti-EGFR antibody cetuximab may be active and therefore provide an effective therapeutic option. **Methods:** This Phase II, multicenter, single-arm, open-label study will assess preliminary antitumor activity, safety and tolerability, and explore pharmacokinetic (PK) profiles of tepotinib + cetuximab in pts with *RAS/BRAF* wild-type left-sided mCRC and acquired resistance to anti-EGFR antibody-targeted therapy due to *MET*amp. A safety run-in (6-12 pts) will evaluate the recommended Phase II dose of tepotinib to be used in combination with cetuximab (endpoint: dose-limiting toxicities). Enrollment is based on a confirmed advanced left-sided CRC diagnosis, with *RAS/BRAF* wild-type, documented previous anti-EGFR therapy and acquired resistance on the most recent anti-EGFR antibody and *MET*amp confirmed by liquid and/or tissue biopsy. Pts must be ≥18 years old and have an Eastern Cooperative Oncology Group performance status of 0/1 and normal organ function. The study will screen sufficient pts to account for setting-specific *MET*amp heterogenicity. Approximately 42 pts are planned to receive study treatment: ~22 in Cohort A (tepotinib second-line, outside US) and 20 in Cohort B (tepotinib ≥third-line, US only). Primary endpoint: investigator-assessed objective response (RECIST 1.1). Secondary endpoints are investigator-assessed duration of response (DoR) and PFS (RECIST 1.1), OS, tolerability and safety (NCI-CTCAE v5.0) and cetuximab immunogenicity (measured by antidrug antibody assays at the start and end of treatment). Additional endpoints include assessment of tepotinib and cetuximab PK profiles and expression of biomarkers of resistance (from blood and/or tissue samples). Retrospective assessment of best overall response, DoR and PFS by an independent review committee may be conducted. No formal statistical hypothesis will be tested in this exploratory study. Clinical trial information: NCT04515394. Research Sponsor: Merck KGaA, Darmstadt, Germany.

TPS150 Trials in Progress Poster Session

ARC-9: Phase Ib/II study to evaluate etrumadenant (AB928)-based treatment combinations in patients with metastatic colorectal cancer (mCRC). *First Author: Michael Cecchini, Yale University, New Haven, CT*

Background: ATP release from dying cancer cells in response to platinum-based chemotherapy increases extracellular immunosuppressive adenosine, which binds and activates the A_{2a} and A_{2b} receptors on immune cells. Adenosine-mediated signaling impairs activation, proliferation, and cytotoxic activity of effector T cells, resulting in inhibition of antitumor activity. Concomitant adenosine receptor blockade may therefore enhance the therapeutic efficacy of chemo/immunotherapy regimens. Etrumadenant (AB928), the first clinical-stage, small-molecule, dual adenosine receptor antagonist, is highly potent, pharmacodynamically active, and has been well tolerated in dose escalation studies as monotherapy or combined with chemo/immunotherapy. Recently, results were reported for the ARC-3 phase 1/1b study of etrumadenant + modified 5-fluorouracil + oxaliplatin (mFOLFOX-6) in patients (pts) with mCRC. In this study, etrumadenant + mFOLFOX-6 was well tolerated without significant additive toxicity. Disease control was observed in patients with *RAS/BRAF* mutated mCRC, as well as 3L+ disease previously treated with FOLFOX and/or FOLFIRI (PR and/or SD >4 mo). Due to deep responses in 1L-3L+ pts, 6 pts had the opportunity to pursue surgery and radiotherapy with curative intent. The encouraging results from ARC-3 warrant further evaluation of etrumadenant-based combination therapy for mCRC. **Methods:** ARC-9 is a phase 1b/2, multicohort, open-label, randomized platform study designed to evaluate safety and clinical activity of etrumadenant (150 mg orally once daily [QD]) in combination with standard-of-care (SOC) regimens or novel therapeutics in pts with mCRC (Table). Cohort eligibility is based on prior anticancer treatment history. Pts enrolled in Cohorts A and B will be randomized (2:1) into the experimental vs SOC arms. Cohort C consists of a single arm to allow inclusion of novel agents as they become available with built in early stopping rules for futility. Pts who progress on the SOC arm of Cohort A can enroll in Cohort B; pts who progress on the SOC arm of Cohort B can crossover to the experimental arm. Primary endpoints across cohorts are shown in Table. Safety monitoring will occur throughout the trial, disease assessments will occur every 8 weeks, and correlative study pre- and on-treatment biopsies will be performed. Research Sponsor: Arcus Biosciences, Inc.

ARC-9 study design.

Cohort	Line of Therapy	Arms	1º Endpoints
A	2L, post-FOLFOX or FOLFIRI	Experimental: Etruma + mFOLFOX-6 + Zim ± Bev[a] SOC: FOLFOX + Bev[a]	PFS
B	3L, post-FOLFOX and/or FOLFIRI	Experimental: Etruma + mFOLFOX-6 + Zim ± Bev[a] SOC: Regorafenib	PFS, OS
C	> 3L	Experimental: Etruma + Zim + novel agent	ORR

[a] Administered if Bev is not contraindicated. Bev, bevacizumab; Etruma, etrumadenant; IRI, irinotecan; L, line; ORR, objective response rate; OS, overall survival; PFS, progression-free survival

TPS151 Trials in Progress Poster Session

A phase Ⅰ/Ⅱa clinical study of cetuximab combined with fruquintinib in the third-line treatment of RAS/BRAF wild-type colorectal cancer. *First Author: Yong Li, Traditional Chinese Medicine Hospital of Guangdong Province, Guangzhou, China*

Background: The standard third-line treatment of mCRC is regofenib, fruquintinib or TAS-102. However, the efficacy was not satisfied. Because VEGF and EGFR share the downstream signal pathway, targeting these two pathways may have synergistic efficacy. Preclinical studies have confirmed the effect of the combination of regorafenib and cetuximab. The subsequent phase Ⅰb study in advanced cancer showed the combination is effective. Fruquintinib is the same anti-VEGF drugs and was approved in China. Our department has treated one patient of advanced colorectal cancer, no standard regimen after third-line treatment. The efficacy is SD and PFS time exceeded 6 months. Therefore this study explores the safety and efficacy of fruquintinib combined with cetuximab. **Methods:** This is a single-center, non-random, prospective, open exploratory study. Eligible pts were diagnosed as advanced RAS/BRAF wild-type colorectal cancer and had received at least two prior regimens of standard therapies. The purpose of phase Ⅰ is to confirm the safety and the appropriate dose of fruquintinib combined with cetuximab. The phase Ⅱa investigate the safety and the efficacy of fruquintinib combined with cetuximab. Phase Ⅰ: The dose of cetuximab is 500mg/m2 every two weeks which is clinically tolerable, so the dose need not be adjusted. fruquintinib is taken once daily for the first 21 days of each 28-day cycle and the dose adjustment is required due to the side effects. The standard dose of fruquintinib is 5mg/d, but the side effects are serious. The dose of 3mg/d is the minimum effective dose, therefore the initial dose of fruquintinib starts from 4mg, and three patients are enrolled. If DLT appeared in less than three patients, the dose elevated to 5mg/d. Three patients were enrolled in the 5mg/d dose group. If DLT appeared in less than three patients, the right dose of fruquintinib was 5mg/d. If DLT appeared in all three patients of the 5mg/d, fruquintinib was declined to 4mg/d combined with cetuximab to carry out a phase Ⅱa study. Fruquintinib initial dose is 4mg/d. If DLT was present in all three patients, the dose was reduced to 3mg/d. The standard dose of fruquintinib (3mg/d) was determined to be MDT, and the subsequent phase Ⅱa study was conducted by giving fruquintinib 3mg/d. The phase Ⅱa study is cetuximab 500mg/m2 biweekly combined with fruquintinib according to the confirmed dose in phase Ⅰ, taking it once daily for the first 21 days of each 28-day cycle. The number of cases is 20.Response assessment via CT/MRI is to be done q8 wks (RECIST 1.1). Continue until disease progression or unacceptable toxicity. The primary objective is to estimate safety, grade 3/4 adverse, and DLT. Secondary objectives include ORR, PFS, and OS. Final analysis to be done 6 mo after enrollment of the final pt. Clinical trial information: ChiCTR2000038227. Research Sponsor: None.

TPS152 Trials in Progress Poster Session

Platform trial of BI 754091, an anti-PD-1 antibody, in patients with previously treated advanced solid tumors: Combination with BI 836880, a VEGF/Ang2-blocking nanobody. *First Author: Maen A. Hussein, Florida Cancer Specialists, Lady Lake, FL and Sarah Cannon Research Institute, Nashville, TN*

Background: Combining anti-programmed cell death protein 1 (PD-1) antibodies with other immuno-modulatory or targeted therapies may improve outcomes. NCT03697304 is an open-label, Phase II, platform trial assessing BI 754091, an anti-PD-1 antibody, combined with other agents. Here, we describe Module C in which BI 754091 will be combined with BI 836880, a humanized bispecific nanobody, that targets vascular endothelial growth factor (VEGF) and angiopoietin2 (Ang2). VEGF and Ang2 play key roles in tumor angiogenesis and have an immunosuppressive effect in the tumor microenvironment. Combining anti-VEGF/Ang2 with an anti-PD-1 therapy promotes an immunopermissive state supportive of T-cell-mediated tumor cell death. **Methods:** Patients are being enrolled in 5 cohorts: 1) locally advanced/metastatic gastric or gastroesophageal adenocarcinoma with ≥1 prior treatment (anti-PD-[L]1 naïve); 2) any advanced/metastatic solid tumor (excluding NSCLC and melanoma) with prior anti-PD-(L)1 treatment, which progressed after achieving at least stable disease (SD) for 4 months; 3) advanced/metastatic solid tumors with no benefit from prior anti-PD-(L)1 treatment (SD <4 months); 4) locally advanced/metastatic microsatellite stable (MSS) colorectal cancer with ≥1 prior treatment (anti-PD-[L]1 naïve); 5) advanced MSS and mismatch-repair proficient endometrial carcinoma which progressed following 1 line of chemotherapy (anti-PD-[L]1 naïve). Patients will receive BI 836880 (720 mg every 3 weeks [Q3W] intravenously [IV]) and BI 754091 (240 mg Q3W IV). Treatment will continue until progressive disease, unacceptable toxicity, consent withdrawal, or for a maximum of 1 year (treatment may be extended in case of clinical benefit). The primary endpoint is objective response (OR; complete or partial response per RECIST v1.1 as assessed by the investigator). Secondary endpoints are duration of OR, disease control and progression-free survival. Safety will also be assessed. Approximately 30 patients will be enrolled per cohort at sites in North America and the United Kingdom. Clinical trial information: NCT03697304. Research Sponsor: Boehringer Ingelheim.

TPS153 Trials in Progress Poster Session

MOUNTAINEER: open-label, phase II study of tucatinib combined with trastuzumab for HER2-positive metastatic colorectal cancer (SGNTUC-017, trial in progress). *First Author: John H. Strickler, Duke University Medical Center, Durham, NC*

Background: The clinical benefit of approved therapies in patients (pts) with metastatic colorectal cancer (mCRC) who progress on first- and second-line chemotherapy (FOLFOX and FOLFIRI) is limited. In pts with chemotherapy-refractory RAS wild type mCRC, antibodies targeting EGFR offer a monotherapy response rate of approximately 20% and a progression-free survival (PFS) of 4 months (Price 2014). HER2 is a validated target in gastric and breast cancers, with HER2 amplification occurring in ~3–5% of pts with mCRC. Tucatinib (TUC), recently approved for HER2+ metastatic breast cancer, is a tyrosine kinase inhibitor (TKI) highly selective for HER2 with minimal inhibition of EGFR. In pt-derived xenograft models of HER2+ mCRC, the combination of TUC + trastuzumab (TRAS) showed significantly greater antitumor activity compared with either agent alone (Kulukian 2020). The MOUNTAINEER trial was initiated to evaluate the efficacy and safety of TUC in combination with TRAS in pts with HER2+ RAS wild-type mCRC. Interim analysis of the initial 26 pts enrolled in MOUNTAINEER demonstrated an objective response rate (ORR) of 52.2% (12 partial responses [PRs] in 23 evaluable pts), median duration of response of 10.4 months, with a median PFS of 8.1 months and a median overall survival (OS) of 18.7 months (Strickler 2019). Based on these results, the trial was expanded to enable better estimation of ORR and safety. **Methods:** MOUNTAINEER (NCT03043313) is an open-label, pivotal phase 2 trial that initially consisted of a single cohort of up to 45 pts (Cohort A) treated with TUC (300 mg BID) and TRAS (8 mg/kg IV followed by 6 mg/kg IV every 3 weeks). The trial was expanded to include an additional 70 pts randomized 4:3 into 2 cohorts: Cohort B (N = 40) who will receive TUC + TRAS, and Cohort C (N = 30) who will receive TUC monotherapy. Pts in Cohort C will be treated with TUC (300 mg orally twice daily) with the option to crossover to TUC + TRAS if an objective response is not achieved by 12 weeks, or if progressive disease develops at any time. Eligible pts have RAS wild-type and HER2+ mCRC, and must have previously received regimens that include fluoropyrimidines, oxaliplatin, irinotecan, anti-VEGF therapy, and an anti-PD-1 if the tumor has dMMR proteins or is MSI-H. Pts who have received prior HER2-directed therapies are not eligible. Additionally, pts must have measurable disease and ECOG PS of 0 to 2. The primary endpoint of this trial is confirmed ORR (per RECIST v1.1) in Cohorts A + B as assessed by blinded independent central review. Secondary endpoints include duration of response, PFS, OS, and safety and tolerability. Enrollment is ongoing in the US and planned for the EU. Clinical trial information: NCT03043313. Research Sponsor: Seattle Genetics, Inc.

TPS154 Trials in Progress Poster Session

FRESCO-2: A global phase III study of the efficacy and safety of fruquintinib in patients (pts) with metastatic colorectal cancer (mCRC). *First Author: Arvind Dasari, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Pts with mCRC have limited treatment options following progression on standard therapies. Current standard of care (SOC) after pts progress on trifluridine/tipiracil (TAS-102) or regorafenib is re-challenge with previous systemic treatments, enrollment in a clinical trial, or best supportive care (BSC). Fruquintinib (Elunate) is a novel, highly selective, vascular endothelial growth factor (VEGF) receptor (VEGFR)-1, -2, and -3 tyrosine kinase inhibitor (TKI) (*Cancer Biol Ther* 2014;15:1635-1645). Fruquintinib is approved in China to treat pts with mCRC who received or are intolerant to fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, anti-VEGF therapy, and, if *RAS* wild type, anti-epidermal growth factor receptor (EGFR) therapy. Approval was based on results of the phase 3 FRESCO study (2013-013-00CH1; NCT02314819; *JAMA* 2018;319:2486-2496), in which fruquintinib 5 mg daily (QD), 3 weeks on, 1 week off (3 on/1 off), significantly improved overall survival (OS) in pts with mCRC in the 3rd-line+ setting when compared to placebo (median OS 9.3 months [mo] versus 6.6 mo; hazard ratio [HR] 0.65; $p < .001$). Progression-free survival (PFS) was also superior (median PFS 3.7 mo versus 1.8 mo; HR 0.26; $p < .001$). The toxicities of fruquintinib were consistent with those of other VEGF TKIs and were manageable. At the time FRESCO was conducted in China, SOC for pts with mCRC differed from that in the US, EU, and Japan. We describe here a global phase 3 study (FRESCO-2; 2019-013-GLOB1; NCT04322539) being conducted to investigate fruquintinib's efficacy and safety in pts with refractory mCRC and a treatment profile representative of the global SOC. **Methods:** FRESCO-2 is a randomized, double-blind, placebo-controlled study to compare fruquintinib + BSC to placebo + BSC. Key inclusion criteria are progression on or intolerance to treatment with TAS-102 and/or regorafenib; previous treatment with standard approved therapies including chemotherapy, anti-VEGF therapy, and, if *RAS* wild type, anti-EGFR therapy. Prior therapy with immune checkpoint or BRAF inhibitors is required for pts with corresponding tumor alterations. Pts (~522) will be randomized 2:1 to receive either fruquintinib 5 mg orally (PO) QD + BSC or placebo 5 mg PO QD + BSC, with a 3 on/1 off schedule. Randomization will be stratified by prior therapy, *RAS* status, and duration of metastatic disease. The primary endpoint is OS; secondary endpoints include PFS, disease control rate, objective response rate, duration of response, and safety. Final OS analyses will be performed when 364 OS events are observed; futility analysis will be conducted with 1/3 (121) OS events. If enrichment of post-regorafenib pts occurs, enrollment to that strata will be capped at approximately 262. FRESCO-2 will be activated in the US, EU, and Japan; global enrollment is anticipated over 13 mo. Clinical trial information: NCT04322539. Research Sponsor: Hutchison MediPharma Limited.

TPS155 Trials in Progress Poster Session

A phase Ib/II study of the polo-like kinase 1 (PLK1) inhibitor, onvansertib, in combination with FOLFIRI and bevacizumab for second-line treatment of patients with KRAS-mutated metastatic colorectal Cancer (mCRC). *First Author: Daniel H. Ahn, Ohio State University Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, Columbus, OH*

Background: Chemotherapy in combination with targeted agents are standard-of-care options for patients for mCRC with response rates > 50% in first line. In the second line setting, efficacy of chemotherapy and targeted agents are much lower with response rates of 5% for FOLFIRI (5-fluorouracil, leucovorin, irinotecan) + bevacizumab (anti-VEGF). New treatment options are urgently needed in particular for the 50 % of patients harboring a KRAS mutation. PLK1 is a serine/threonine kinase, master regulator of the mitotic checkpoint and cell division. PLK1 is over-expressed in CRC and its overexpression is associated with poor prognostic. A genome wide RNAi screen identified PLK1 as a synthetic lethal target in KRAS mutant CRC cells, inducing cell cycle arrest and apoptosis upon inhibition. Onvansertib is an oral, highly selective PLK1 inhibitor that demonstrates single agent and synergistic activity with irinotecan and 5-FU in preclinical CRC models. Additionally, KRAS mutated versus wild-type cells showed higher sensitivity to onvansertib. PLK1 inhibition is a potential target in KRAS-mutated mCRC, and the combination of onvansertib + FOLFIRI + bevacizumab may provide a new second-line treatment option. **Methods:** The primary objective of this single-arm Phase 1b/2 study is to assess the safety and preliminary efficacy of onvansertib in combination with FOLFIRI and bevacizumab in the second line setting for KRAS-mutated mCRC patients. For the Phase 1b segment, a standard 3 + 3 dose-escalation design is used to determine the maximum tolerated dose or recommended phase 2 dose (RP2D) of onvansertib. As of September 15th 2020, the first two dose levels have been cleared for safety and the third is enrolling. Efficacy will be determined by objective response rate (ORR) according to RECIST v1.1 (primary endpoint), progression-free survival and reduction in KRAS allelic burden in liquid biopsies (secondary endpoints). Biomarker analyses include genomic profiling of circulating tumor DNA genomic to evaluate altered pathways that correlate with patient clinical response. Based on a one-sided one sample log-rank test with 10% Type I error, there will be at least 90% power to detect an improvement in ORR from 5% to 20% with 32 patients. Clinical trial information: NCT03829410. Research Sponsor: Cardiff Oncology.

TPS156 Trials in Progress Poster Session

Olaparib ± bevacizumab versus bevacizumab + fluorouracil in patients with unresectable or metastatic colorectal cancer not progressing on first-line FOLFOX + bevacizumab: Phase III LYNK-003 study. *First Author: Carlos Alberto Mayo, Merck & Co., Inc., Kenilworth, NJ*

Background: Patients with metastatic colorectal cancer (CRC) often receive intensive platinum-based regimens, such as FOLFOX (fluorouracil [5-FU], leucovorin, oxaliplatin), as first-line (1L) therapy. For patients who do not progress during 1L platinum-based induction therapy, maintenance with a less intensive regimen can enhance clinical benefit and reduce toxicity. The CAIRO3 study showed a progression-free survival (PFS) benefit and a trend toward overall survival (OS) benefit in patients who received maintenance treatment with a fluoropyrimidine and bevacizumab versus observation following induction treatment of six cycles of platinum-based therapy. Olaparib is an oral PARP inhibitor that has efficacy in platinum-sensitive cancers. The randomized, open-label, phase 3 LYNK-003 trial will investigate the efficacy and safety of olaparib, alone or with bevacizumab, compared with bevacizumab plus 5-FU in advanced CRC that has not progressed during 1L induction treatment with FOLFOX plus bevacizumab. **Methods:** Patients aged ≥18 years with histologically confirmed metastatic or unresectable CRC that has not progressed after 1L induction of ≥6 cycles of FOLFOX plus bevacizumab and who can no longer tolerate oxaliplatin are eligible. Patients must have an ECOG performance status of 0-1, adequate organ function, and provide tumor tissue for biomarker analysis. Patients will be randomly assigned 1:1:1 to olaparib 300 mg twice-daily (BID), olaparib 300 mg BID plus bevacizumab 5 mg/kg every 2 weeks (Q2W), or bevacizumab 5 mg/kg Q2W plus 5-FU 2400 mg/m^2 over 46–48 hours Q2W. Randomization will be stratified by response to prior FOLFOX plus bevacizumab (stable disease vs partial response/complete response), mutation status ($BRAF_{mut}$ and/or Ras_{mut} vs $BRAF_{wt}$ plus Ras_{wt}), and number of prior FOLFOX plus bevacizumab cycles (6-8 vs > 8 cycles). Response will be assessed by computed tomography or contrast-enhanced magnetic resonance imaging per RECIST 1.1 by blinded independent central review (BICR) every 8 weeks for the first 12 months and every 12 weeks thereafter. Treatment will continue until documented disease progression, unacceptable toxicity, investigator's decision to discontinue, or patient withdrawal. The primary endpoint is PFS per RECIST 1.1 by BICR. Secondary endpoints are OS, objective response rate, duration of response, and safety. Approximately 525 patients will be enrolled. Currently, patients are being enrolled at 18 locations in 4 countries. Clinical trial information: NCT04456699. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

TPS157 Trials in Progress Poster Session

An open-label, phase II study of patritumab deruxtecan (HER3-DXd, U3-1402) in patients (pts) with previously treated advanced/metastatic colorectal cancer (CRC). *First Author: Kanwal Pratap Singh Raghav, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Patritumab deruxtecan (HER3-DXd; U3-1402) is a novel, investigational antibody drug conjugate comprising an anti-HER3 monoclonal antibody, a tetrapeptide-based linker, and a topoisomerase I inhibitor payload. Ongoing clinical trials of HER3-DXd in pts with metastatic breast cancer or non-small cell lung cancer have shown promising clinical activity and acceptable safety. HER3 (human epidermal growth receptor 3), a member of the tyrosine kinase receptor family, is overexpressed in most CRC tumors and associated with an adverse prognosis. Significant tumor regression with HER3-DXd has been observed in CRC murine xenograft models, regardless of *KRAS* mutation status. Here we introduce the design of a phase 2 study (U31402-A-U202) that is evaluating HER3-DXd in previously treated pts with advanced/metastatic CRC. **Methods:** U31402-A-U202 (NCT04479436) is an open-label, multicenter phase 2 study that will enroll 80 pts in the USA, Europe and Asia. Pts are enrolled who are aged ≥ 18 years with advanced/metastatic colorectal adenocarcinoma that is resistant/refractory/intolerant to ≥ 2 prior lines of therapy including a fluoropyrimidine, irinotecan, a platinum agent, an anti-EGFR agent (if clinically indicated), an anti-VEGF agent (unless contraindicated [CI]), and an immune checkpoint inhibitor (unless CI) for microsatellite instability-high CRC. Pts with current/previous interstitial lung disease or clinically severe pulmonary compromise are excluded. Archival tumor biopsy and pre-treatment tumor biopsy are collected from all pts at screening, with HER3 protein expression measured by immunohistochemistry (IHC). In part 1, results of the HER3 IHC assay from the pre-treatment tumor biopsy are used to assign pts into 1 of 2 cohorts (C). C1: HER3 high (IHC 3+, 2+), n = 24; C2: HER3 low/negative (IHC 1+, 0), n = 12. Pts receive 5.6 mg/kg HER3-DXd IV every 3 weeks. An interim futility analysis will be conducted separately for C1 and C2 and will determine enrollment in part 2, with 2 potential scenarios: enrollment continues irrespective of HER3 IHC status, or enrollment continues in HER3 high pts only. The primary objective is the evaluation of the antitumor activity of HER3-DXd as measured by objective response rate (ORR) (assessed by BICR according to RECIST v1.1). ORR will be summarized with the 2-sided 95% confidence interval. Secondary objectives include the evaluation of efficacy as measured by ORR (assessed by investigator according to RECIST v1.1), duration of response, time to tumor response, disease control rate, progression-free survival (assessed by investigator and BICR according to RECIST v1.1), overall survival, safety and tolerability, HER3 protein expression in tumor tissue and relationship with efficacy, and pharmacokinetic properties. Clinical trial information: NCT04479436. Research Sponsor: Daiichi Sankyo.

TPS158 Trials in Progress Poster Session

NRG-GI004/SWOG-S1610: Colorectal Cancer Metastatic dMMR Immuno-Therapy (COMMIT) Study—A randomized phase III study of atezolizumab (atezo) monotherapy versus mFOLFOX6/bevacizumab/atezo in the first-line treatment of patients (pts) with deficient DNA mismatch repair (dMMR) or microsatellite instability high (MSI-H) metastatic colorectal cancer (mCRC). *First Author: Michael J. Overman, University of Texas MD Anderson Cancer Center, and SWOG, Houston, TX*

Background: Despite activity of programmed cell death-1 (PD-1) pathway inhibition in dMMR/MSI-H mCRC, approximately one-third of patients demonstrate progressive disease as best response to anti-PD1 monotherapy. Preclinical models have demonstrated synergistic interactions between FOLFOX, anti-VEGF, and anti-PD-1. We hypothesize that the dMMR/MSI-H mCRC subset may be more effectively targeted by the combination of PD-1 pathway blockade and mFOLFOX6/bevacizumab (bev) rather than with anti-PD-1 therapy (atezo) alone. **Methods:** Initially a three-arm study, the mFOLFOX6/bev arm was closed to new enrollment on 6-4-20 due to emerging data; the redesigned COMMIT is a prospective phase III open-label trial that will randomize (1:1) mCRC dMMR/MSI-H pts (N=211) to either atezo monotherapy or mFOLFOX6/bev+atezo combination. Stratification factors include BRAFV600E status, metastatic site, and prior adjuvant CRC therapy. Primary endpoint is progression-free survival (PFS) as assessed by site investigator. Secondary endpoints include OS, objective response rate, safety profile, disease control rate, duration of response, and centrally-reviewed PFS. Health-related quality of life is an exploratory objective. Archived tumor tissue and blood samples will be collected for correlative studies. Key inclusion criteria are: mCRC without prior chemotherapy for advanced disease; dMMR tumor determined by local CLIA-certified IHC assay (MLH1/MSH2/MSH6/PMS2) or MSI-H by local CLIA-certified PCR or NGS panel; and measurable disease per RECIST. Support: U10CA180868, -180822, -180888, -180819, UG1CA189867, U24CA196067; Genentech, Inc. Clinical trial information: NCT02997228. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

159 Oral Abstract Session

Confirmed three-year RFS and OS of the randomized trial of adjuvant S-1 versus S-1 plus docetaxel after curative resection of pStage III gastric cancer (JACCRO GC-07). *First Author: Kazuhiro Yoshida, Department of Surgical Oncology, Gifu University Graduate School of Medicine, Gifu, Japan*

Background: JACCRO GC-07 is a randomized controlled trial to explore postoperative S-1/docetaxel compared to S-1 alone after D2 gastrectomy for pStage III gastric cancer (GC) patients. The second interim analysis demonstrated that the significant improvement of RFS was obtained by S-1/docetaxel compared to S-1 alone. The study was terminated by the recommendation of independent data and safety monitoring committee and the results were reported at ASCO 2018 and published in the Journal of Clinical Oncology (Yoshida K et al. 2019; 37:1296-1304). As 3 years have passed after completion of the enrollment, preplanned analysis was performed with the updated information of the patients. **Methods:** Patients with pStage III GC were randomly assigned to receive either S-1/docetaxel (S-1 80-120mg/body on days 1-14 with a 7-day rest followed by docetaxel 40mg/m^2 on day 1 and S-1 80-120mg/body on days 1-14 every 21 days for 6 cycles followed by S-1 80-120mg/body on days 1-28 every 42 days for 4 cycles) or S-1 (80-120mg/body on days 1-28 every 42 days for 8 cycles) after D2 gastrectomy. Block randomization was performed by a central interactive computerized system stratified by the stage (IIIA, IIIB, IIIC) and histological type (differentiated or undifferentiated). The sample size of 1,100 was necessary to detect a 7% increase in the 3-year RFS. The primary endpoint was 3y RFS and the secondary endpoints were OS, TTF and safety. **Results:** In the present analysis, 400 recurrences and 324 deaths were confirmed among 912 patients during the median follow-up period of 42.5 months (0.3-85.16). The 3y RFS of 67.7% in the S-1/docetaxel group was significantly superior to 57.4% in the S-1 group (HR 0.715, 95% CI: 0.587-0.871, p = 0.0008) and the 3y OS was 77.7% in the S-1/docetaxel group and that of S-1 group was 71.2%, respectively (HR 0.742, 95% CI: 0.596-0.925, p = 0.0076), confirming the significant improving effect on the survival of the patient. **Conclusions:** Adjuvant S-1 plus docetaxel is recommended for patients with pStage III gastric cancer who underwent D2 gastrectomy without neoadjuvant chemotherapy. Clinical trial information: UMIN 000010337. Research Sponsor: Japan Clinical Cancer Research Organization.

160 Oral Abstract Session

Randomized double-blind placebo-controlled phase 2 study of bemarituzumab combined with modified FOLFOX6 (mFOLFOX6) in first-line (1L) treatment of advanced gastric/gastroesophageal junction adenocarcinoma (FIGHT). *First Author: Zev A. Wainberg, UCLA Medical Center - Cancer Care - Santa Monica, Los Angeles, CA*

Background: Bemarituzumab (bema), a first-in-class humanized IgG1 monoclonal antibody, selectively binds to FGFR2b, inhibits ligand binding and mediates antibody-dependent cell-mediated cytotoxicity. A phase 1 study of bema monotherapy in solid tumors had no dose-limiting toxicities and a confirmed objective response rate (ORR) of 18% in patients (pts) with refractory FGFR2b+ gastric cancer (GC). **Methods:** The FIGHT study (NCT03343301) is a global, randomized, double-blind, placebo-controlled phase 2 trial. Pts with unresectable locally advanced or metastatic GC that was not HER2+ were eligible if their tumor was positive for FGFR2b overexpression by centrally performed immunohistochemistry (IHC) or for *FGFR2* amplification by circulating tumor DNA (ctDNA). Pts were treated with mFOLFOX6 and randomized 1:1 to bema 15mg/kg or placebo (pbo) every 2 weeks with 1 additional 7.5mg/kg bema/pbo dose on day 8. Treatment was continued until disease progression, intolerable toxicity, or death. The primary endpoint was investigator-assessed progression-free survival (PFS) and key secondary endpoints include overall survival (OS), overall response rate (ORR), and frequency of adverse events. Statistical significance (2-sided a of 0.2) was tested sequentially for PFS, OS and ORR. **Results:** Of 910 1L GC pts whose tumors were evaluated 275 (30%) were FGFR2b+. Of 155 pts randomized, 77 to bema+mFOLFOX6 and 78 to pbo+mFOLFOX6, 149 were FGFR2b+ by IHC and 26 by ctDNA. The primary endpoint was met with an improvement in median PFS of 9.5 mo (bema) vs 7.4 mo (pbo) (hazard ratio [HR], 0.68; 95% confidence interval [CI], 0.44-1.04; p=0.07). The secondary endpoint of OS was met; median not reached in the bema arm vs 12.9 mo for pbo (HR, 0.58, 95% CI, 0.35-0.95; p=0.03). Among patients with measurable disease, ORR improved from 40% (pbo) to 53% (bema). Improved efficacy was observed across all 3 endpoints (PFS, OS, ORR) with increasing levels of overexpression of FGFR2b on tumor cells. Grade ≥3 AEs were reported in 83% of pts in the bema arm vs 74% pts in the pbo arm with serious AEs in 32% and 36% respectively. Stomatitis was higher in the bema arm (31.6% vs 13.0%) and corneal AEs were more common in the bema arm (67% vs 10%). There were no reported AEs of retinal detachment or hyperphosphatemia in the bema arm. **Conclusion:** Approximately 30% of 1L pts with advanced GC not HER2+, were identified to be FGFR2b+, primarily by IHC. In this randomized, placebo controlled, double-blind phase 2 study, the addition of bema to mFOLFOX6 led to clinically meaningful and statistically significant improvements in PFS, OS and ORR. An increase in corneal AEs and stomatitis was associated with bema. These results support a prospective randomized phase 3 study in GC and the evaluation of bema in other FGFR2b+ tumor types. Clinical trial information: NCT03694522. Research Sponsor: Five Prime Therapeutics.

161 Oral Abstract Session

Genomic pathway of gut microbiome to predict efficacy of nivolumab in advanced gastric cancer: DELIVER trial (JACCRO GC-08). *First Author: Yu Sunakawa, Department of Clinical Oncology, St. Marianna University School of Medicine, Kawasaki, Japan*

Background: Nivolumab (Nivo) monotherapy demonstrated survival benefit in previously treated gastric cancer (GC) patients (pts) (Kang YK, et al. *Lancet* 2017). About 60% of the pts did not respond to Nivo in late-lines, and its predictive markers are needed in GC. Several studies revealed that the efficacy of anti-PD-1-based immunotherapy was associated with composition of gut microbiome in various types of cancers, but little is known about GC. We therefore investigated whether genomic information in gut microbiome will serve as predictors for Nivo in advanced GC. **Methods:** The observational/translational study (DELIVER trial: UMIN000030850) has enrolled 501 pts with advanced GC treated with Nivo alone from March 2018 to August 2019 to discover gut microbiome biomarkers using fecal samples which were collected before treatment with Nivo. Primary endpoint was the relationship between genomic pathway in gut microbiome and efficacy of Nivo, whether progressive disease (PD) or not at the first evaluation according to RECIST criteria. Secondary endpoints included several relationships between markers of microbiome and clinical outcomes. Genomic data were measured by genome shotgun sequence at central lab. Biomarkers were analyzed by Wilcoxon rank sum test in the first 200 pts (training cohort). The top 30 candidates in an ascending order of *p*-value were validated in the last 300 pts (validation cohort) using Bonferroni method. **Results:** One hundred eighty of 200 pts and 257 of 301 pts were available for massive metagenomic and clinical data in the training cohort and validation cohort, respectively. The PD was 62.2% (95%CI 54.7-69.3) in the training cohort and 53.2% (95%CI 47.0-59.4) in the validation cohort. More diverse microbiome was observed in pts with non-PD compared to pts with PD. Although there was no statistically significant pathway to be validated for a primary endpoint under Bonferroni method, we found that bacterial invasion of epithelial cells pathway in the KEGG pathway was associated with clinical outcome of Nivo in both training cohort (p= 0.057) and validation cohort (p= 0.014). Upregulation of the pathway was related to PD at the first evaluation for Nivo treatment. An exploratory analysis of genus showed that *Odoribacter* and *Veillonella* were associated with tumor response to Nivo in both cohorts. **Conclusions:** Our translational study indicated for the first time that bacterial invasion of epithelial cells pathway in gut microbiome may potentially become a novel biomarker for treatment with Nivo in advanced GC. In addition, we found gastric cancer-specific gut microbiome to predict response to immune checkpoint inhibitors. Clinical trial information: UMIN000030850. Research Sponsor: Ono Pharmaceutical and Bristol-Myers Squibb.

162 Oral Abstract Session

Impact of preoperative therapy for locally advanced thoracic esophageal cancer on the risk of perioperative complications: Results from multicenter phase III trial JCOG 1109. *First Author: Kazuo Koyanagi, Department of Gastroenterological Surgery, Tokai University School of Medicine, Isehara, Japan*

Background: We have conducted randomized three-arm phase III trial comparing cisplatin plus 5-FU (CF) versus docetaxel plus CF (DCF) versus radiation with CF (CF-RT) as preoperative therapy for locally advanced esophageal cancer, which is on-follow-up for primary analysis planned in 2023 (JCOG 1109). This study aimed to evaluate the influence of preoperative therapies on perioperative complications and risk factors for perioperative complications after three-arm preoperative therapies. **Methods:** Patients with potentially resectable advanced thoracic esophageal cancer were randomly assigned to three preoperative therapies and followed by open or thoracoscopic esophagectomy with regional lymphadenectomy. Clinical data, surgical results, and perioperative complications in the patients received DCF and CF-RT were compared with those in the patients received CF. Univariate and multivariate analyses were performed to explore the risk factors of perioperative complications. **Results:** Between December 2012 and July 2018, 601 patients were randomized (CF/DCF/CF-RT; 199/202/200). Of 589 eligible patients, 546 patients underwent surgery (185/183/178). Patients` characteristics were not different between arms. Median number of harvested lymph node in patients received CF-RT was significantly lower than that in patients received CF (49 vs. 58; $P < 0.0001$). Incidence of ≥ Grade 2 perioperative complications in patients received DCF was lower than that in patients received CF (44.8% vs. 56.2%; $P = 0.036$). Incidence of ≥ Grade 2 chylothorax in patients received CF-RT was higher than that in patients received CF (5.1% vs. 1.1%; $P = 0.032$). Incidence of reoperation and intra-hospital death in patients received DCF and CF-RT did not differ from that in patients received CF. Multivariate analysis showed that operation time (≥ median) and open esophagectomy were independently associated with an increase in ≥ Grade 2 perioperative complications. CF-RT was associated with an increase in occurrence of ≥ Grade 2 chylothorax (Relative Risk 4.84; $P = 0.043$). **Conclusions:** Preoperative DCF and CF-RT does not increase the risk of perioperative complications and mortality when compared with standard preoperative CF therapy, but CF-RT increases the risk of chylothorax after esophagectomy for advanced thoracic esophageal cancer. Research Sponsor: None.

163 Rapid Abstract Session

A randomized clinical trial evaluating the efficacy and safety of the addition of oral metronomic chemotherapy after completion of standard chemoradiation versus observation in patients with locally advanced esophageal and gastroesophageal junction squamous cell carcinoma. *First Author: Vanita Noronha, Tata Memorial Centre, Mumbai, India*

Background: In RTOG 85-01, patients with locally advanced esophageal and gastroesophageal junction (GEJ) cancer treated with concurrent chemoradiotherapy (CRT) had a median overall survival (OS) of 14 months and 5-year OS of 27%. Improving outcomes in these patients is an unmet need. We investigated the addition of oral metronomic chemotherapy (OMC) following definitive CRT. **Methods:** A randomized integrated phase II/III clinical trial (CTRI/2015/09/006204) in patients with squamous cell carcinoma of the esophagus or the GEJ who had completed definitive radical CRT within the past 12 weeks, had an ECOG PS 0-2 and no clinical or radiologic evidence of progressive disease. Patients were stratified based on whether or not they had received induction chemotherapy followed by CRT, and then randomized 1:1 to receive OMC (celecoxib 200 mg twice daily and methotrexate 15 mg/m^2 weekly) for 12 months or observation. The primary efficacy endpoint for the phase II portion was progression free survival (PFS). The secondary endpoints were OS and toxicity. With a power of 70% and an alpha of 10%, we hypothesized a hazard ratio of 1.5, with a median follow-up of 6 months. The planned sample size for the phase II portion was 151 patients. The p-value for stopping the trial after the phase II part of the study was set at 0.2 for the PFS. **Results:** Between Jan 2016 and Dec 2019, we enrolled 151 patients, 75 to the OMC arm and 76 to observation. The median age was 57 years, 59% were male. The tumor originated in the upper thoracic esophagus in 79% patients, with median tumor length 6 cm. Induction chemotherapy was received by 14% of the patients. Concurrent CRT consisted of median 63 Gy in median 35 fractions; 91% patients received concurrent weekly paclitaxel and carboplatin with radiation. OMC was started at a median of 11 weeks (IQR, 9 to 12) from the start of CRT. Grade 3 or higher toxicities (regardless of relatedness to study intervention) were noted in 27 patients (17.9%), 18 in the OMC arm and 9 in the observation arm; P=0.071. The median time to disease progression or death was 23 months (95% CI, 7.9-38.1) in the OMC arm and not reached in the observation arm; HR, 1.33, 95% CI, 0.83-2.14; P=0.23. The 1-year PFS was 67% in both the arms; the 2-year PFS were 48% and 61% in the OMC and observation arms respectively. The median OS was 36 months (95% CI, 17.9-54) in the OMC arm and not reached in the observation arm; HR, 1.75; 95% CI, 1.02-2.99; P, 0.037. The 1-year OS was 74.7% in the OMC arm and 88% in the observation arm; the 2-year OS was 53.9% in the OMC arm and 75% in the observation arm. **Conclusion:** Adjuvant oral metronomic chemotherapy after radical CRT does not improve outcomes in patients with locally advanced esophageal or GEJ squamous cell carcinoma. Clinical trial information: CTRI/2015/09/006204. Research Sponsor: Tata Memorial Center Research Administration Council.

164 Rapid Abstract Session

Zanidatamab (ZW25) in HER2-expressing gastroesophageal adenocarcinoma (GEA): Results from a phase I study. *First Author: Funda Meric-Bernstam, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: For patients with human epidermal growth factor receptor 2 (HER2)-overexpressing GEA, trastuzumab in combination with chemotherapy is the only approved HER2-targeted therapy, and they have limited treatment options after progression. Zanidatamab, a HER2-targeted bispecific antibody, has shown durable antitumor activity with good tolerability in a range of HER2-expressing cancers. **Methods:** In this 3-part Phase 1 study (NCT02892123), zanidatamab (10 mg/kg QW, 20 mg/kg Q2W, or 30 mg/kg Q3W) is administered as a single agent (Parts 1 & 2; QW or Q2W) or in combination with chemotherapy (Part 3; Q2W or Q3W). Eligibility criteria includes GEA with HER2 expression as assessed by immunohistochemistry (IHC) 3+ or IHC 2+, progression after standard of care therapy, and measurable disease per RECIST 1.1 (Part 2 requirement only). **Results:** In Parts 1 and 2, 36 GEA patients have been treated with zanidatamab (QW [n = 5]; Q2W [n = 31]). In Part 3, 26 GEA patients have been treated (zanidatamab Q2W + (paclitaxel [n = 11] or capecitabine [n = 6]); zanidatamab Q3W + capecitabine [n = 9]). **Conclusions:** Zanidatamab, both as a single agent and in combination with chemotherapy, is well tolerated with promising and durable anti-tumor activity in heavily pretreated GEA patients (including prior HER2-targeted therapy). These data support further investigation of zanidatamab as a novel therapeutic for patients with HER2-expressing GEA. Clinical trial information: NCT02892123. Research Sponsor: Zymeworks Inc.

	Zanidatamab Single-Agent (Parts 1 & 2) (N = 36)	Zanidatamab + Chemo combination (Part 3) (N = 26)
Median prior systemic therapies, n (range)	3 (1-7)*	2 (1-7)
Patients with prior HER2 therapies, n (%)	34 (94)	24 (92)
Patients with zanidatamab-related adverse events (AEs) (Any), n (%)	26 (72)	21 (81)
Grade 1/2	22 (61)	17 (65)
Grade 3+**	4 (11)	4 (15)
Response evaluable, n	34	20
Objective response, n (%)	13 (38)	12[R] (60)
Disease control rate, n (%)	21 (62)	17 (85)
Median duration of response, months (95% CI)‡	6.0 (1.9, 9.2)	8.9 (3.5, Not estimable)

Note: Data cutoff: Jul 28, 2020. *, 35 patients had prior systemic therapy; **, all were Grade 3 except for one Grade 4 neutropenia event in Part 3; #, includes one patient with complete response; ‡, in response evaluable patients who had a confirmed complete or partial response followed by ≥1 response assessment The most common (occurring in ≥ 20%) zanidatamab-related AEs were: diarrhea (44%) and infusion-related reaction (36%) in Parts 1 & 2 (all Grade 1/2 except one Grade 3 diarrhea event); and diarrhea (58%) and fatigue (27%) in Part 3 (all Grade 1/2 except one Grade 3 fatigue event).

165 Rapid Abstract Session

Outcomes of a phase II study of intraperitoneal paclitaxel plus systemic capecitabine and oxaliplatin (XELOX) for gastric cancer with peritoneal metastases. *First Author: Daryl Chia, Department of Surgery, University Surgical Cluster, National University Health System, Singapore, Singapore*

Background: The addition of intraperitoneal (IP) paclitaxel (PTX) to systemic chemotherapy comprising taxane/fluoropyrimidine doublet has shown promising results for patients with gastric cancer (GC) and peritoneal metastases (PM). However, this has not been studied in combination with platinum/fluoropyrimidine doublet which is the current standard-of-care for metastatic GC. We conducted a prospective phase 2 trial of IP PTX with capecitabine and oxaliplatin (XELOX) in patients with GCPM. **Methods:** The trial enrolled 44 patients with GCPM who received treatment comprising IP PTX (40mg/m^2 on day 1,8), PO capecitabine (1000mg/m^2 twice daily from day 1-14) and IV oxaliplatin (100mg/m^2 on day 1) in 21-day cycles. Patients with synchronous GCPM were eligible for conversion surgery comprising radical gastrectomy if they had good response after chemotherapy, negative cytology on 2 consecutive peritoneal fluid assessments, no extraperitoneal metastasis and no peritoneal disease during surgery. The primary endpoint was overall survival and secondary endpoints were progression-free survival and safety. Outcomes from the trial were also compared with a retrospective cohort of 39 patients with GCPM who received identical systemic chemotherapy (SC) comprising platinum/fluoropyrimidine agents alone. **Results:** The median OS for the IP and SC groups was 14.6 and 10.6 months (HR 0.44; 95% CI, 0.26-0.74; P=0.002). The 1-year OS was 67.8% in the IP group and 32.3% in the SC group (Logrank p<0.001). The median PFS for the IP and SC group was 9.5 and 4.4 months respectively (HR 0.39; 95% CI, 0.25-0.66; P<0.001). Patients in the SC group were younger (IP vs. SC, 61 vs. 56 years, p=0.021) and had better baseline performance status (ECOG 0, IP vs. SC, 47.7% vs. 76.9%, p=0.007) compared to the IP cohort. In the IP group, conversion surgery was performed in 36.1% (13/36) of patients, with a median OS of 24.2 (95%CI 13.1 - 35.3) months and 1-year OS of 84.6%. Wound-related complications requiring the port to be explanted or re-sited occurred in 9% (4/44) of patients. **Conclusions:** IP PTX with XELOX is a promising treatment option for GCPM patients. For patients with good response, conversion surgery was feasible with favourable outcomes. Clinical trial information: NCT01739894. Research Sponsor: National Medical Research Council Translational and Clinical Flagship Programme, Singapore (NMRC/TCR/009-NUHS/2013).

Median overall survival (OS) between groups.

Group (n)	Median OS, months (95% CI)	1-year OS (%)	HR (95% CI) *	P-value
IP group (n=44)	14.6 (12.6 - 16.6)	67.8%	0.44 (0.26 - 0.74)	0.002
IP group with conversion surgery (n=13)	24.2 (13.1 - 35.3)	84.6%	0.20 (0.08 - 0.45)	0.000
IP group without conversion surgery (n=23)	12.5 (9.4 - 15.6)	55.7%	0.76 (0.43 - 1.33)	0.366
Systemic chemotherapy group (n=39)	10.6 (2.4 - 18.8)	32.3%	-	-

* Cox proportion hazard with reference to systemic chemotherapy group.

166 Rapid Abstract Session

Esophagectomies for malignancy among general and thoracic surgeons: A propensity score-matched NSQIP analysis stratified by surgical approach. *First Author: Shravan Leonard-Murali, Henry Ford Hospital, Department of Surgery, Detroit, MI*

Background: Training of general and thoracic surgeons continues to diverge, especially with the increasing role for minimally invasive surgical (MIS) approaches. Previous studies of esophagectomy outcomes by specialty do not adequately address malignancy or surgical approach. We sought to evaluate perioperative outcomes of esophagectomy for malignancy stratified by surgical specialty and approach using a national database. **Methods:** The National Surgical Quality Improvement Program (NSQIP) Targeted Esophagectomy Dataset was queried for esophagectomies for malignancy and grouped by surgeon specialty: thoracic surgery (TS) or general surgery (GS). Those with missing data were excluded (n = 6). To account for confounding due to specialty selection bias, we performed propensity score matching (PSM) by age, body mass index, ethnicity, American Society of Anesthesiologists class ^{3} 3, and surgical approach in a 1:1 ratio. An absolute standardized difference of ≤ 0.1 was considered an appropriate balance. The primary outcome was mortality and secondary outcomes were anastomotic leak, Clavien-Dindo grade ≥ 3 and positive margin rate. Univariate logistic regression analysis was performed for these outcomes on the matched cohort, with stratification by surgical approach (open vs. MIS). **Results:** A total of 1463 patients met inclusion criteria (512 GS, 951 TS). After PSM each group was comprised of 512 patients with similar demographics, neoadjuvant chemotherapy and radiation rates, and preoperative stage. The TS group consisted of 169 (33.0%) open and 343 (67.0%) MIS cases, while the GS group consisted of 177 (34.6%) open and 335 (65.4%) MIS cases. Postoperative complications, including surgical site infection, pneumonia, pulmonary embolism, stroke, and myocardial infarction were similar between matched groups, and remained similar when stratified by surgical approach. Mortality rates were similar between the TS and GS groups, both overall (14 (2.7%) vs. 10 (2.0%)) and when stratified by surgical approach (MIS: 11 (3.2%) vs. 10 (3.0%), open: 3 (1.8%) vs. 0 (0%)). By univariate analysis of the matched cohort stratified by surgical approach, TS patients had similar odds as GS patients of anastomotic leak (open: adjusted odds ratio (AOR) = 1.11, 95% confidence interval (95%CI) = 0.58 - 2.15, p = 0.75; MIS: AOR = 0.70, 95%CI = 0.47 - 1.04, p = 0.08), Clavien-Dindo grade ≥ 3 (open: AOR = 1.27, 95%CI = 0.79 - 2.06, p = 0.32; MIS: AOR = 1.01, 95%CI = 0.73 - 1.39, p = 0.97), positive surgical margins (open: AOR = 0.75, 95%CI = 0.33 - 1.68, p = 0.49; MIS: AOR = 0.62, 95%CI = 0.35 - 1.07, p = 0.09), and mortality (open: unable to be calculated due to 0 deaths in the GS group; MIS: AOR = 1.08, 95%CI = 0.45 - 2.62, p = 0.87). **Conclusions:** Esophagectomy for malignancy had a similar perioperative safety profile and positive margin rate among general and thoracic surgeons, regardless of surgical approach. Research Sponsor: None.

167 Rapid Abstract Session

Checkmate 577: Health-related quality of life (HRQoL) in a randomized, double-blind phase III study of nivolumab (NIVO) versus placebo (PBO) as adjuvant treatment in patients (pts) with resected esophageal or gastro-esophageal junction cancer (EC/GEJC). *First Author: Eric Van Cutsem, University Hospitals Gasthuisberg Leuven and KU Leuven, Leuven, Belgium*

Background: NIVO is the first adjuvant therapy to provide a statistically significant and clinically meaningful improvement in disease-free survival (DFS) versus PBO in resected EC/GEJC following neoadjuvant chemo-radiotherapy as demonstrated by CheckMate 577. NIVO was well tolerated with an acceptable safety profile. This analysis provides additional information on the exploratory HRQoL endpoints in this clinical trial. **Methods:** The effect of NIVO versus PBO on HRQoL, including general and disease-related symptoms, functioning, disease burden, and overall QoL, was assessed using FACT-E and EQ-5D-3L patient-reported outcome (PRO) questionnaires administered at baseline (BL), every 4 weeks during the 12-month treatment period, and at post-treatment follow-up visits (up to 2 years after last dose). Longitudinal change from BL in PRO scores over 12 months was assessed using descriptive statistics. Additionally, mixed model for repeated measures and time to deterioration analyses evaluated the difference between treatment with NIVO and PBO (data not shown). **Results:** 794 pts with EC/GEJC were randomized 2:1 to NIVO (n = 532) or PBO (n = 262). PRO completion rates were ≥ 95% at BL and ~ 90% at 12 months on treatment. Mean (SD) BL HRQoL scores were similar between treatment arms for the FACT-E total score (NIVO: 133.40 [20.97]; PBO: 134.03 [20.40]); esophageal cancer subscale (ECS; NIVO: 50.2 [9.3]; PBO: 50.1 [8.9]); EQ-5D Visual Analogue Scale (NIVO: 70.4 [22.3]; PBO: 69.1 [24.1]); and EQ-5D Utility Index (NIVO: 0.820 [0.179]; PBO: 0.831 [0.163]) based on the UK value set. Descriptive analyses showed a trend for increases from baseline at most time points through week 49 for both NIVO and PBO treatment groups for FACT-E total score, ECS, and EQ-5D Visual Analogue Scale and Utility Index. **Conclusions:** Preliminary results from CheckMate 577 demonstrated that pts on NIVO treatment showed trends of improvement in both esophageal-specific and general HRQoL. Similar trends were also observed in pts treated with PBO over 1 year. Pts treated with NIVO did not experience a reduction in HRQoL, further supporting clinical data to demonstrate treatment benefit and tolerability for adjuvant NIVO in pts with resected EC/GEJC. Clinical trial information: NCT02743494. Research Sponsor: Bristol Myers Squibb.

168 Rapid Abstract Session

Health-related quality of life (HRQoL) of pembrolizumab plus chemotherapy versus chemotherapy as first-line therapy in patients with advanced esophageal cancer: The phase III KEYNOTE-590 study. *First Author: Wasat Mansoor, The Christie NHS Foundation Trust, Manchester, United Kingdom*

Background: In the randomized, international, double-blind, placebo-controlled KEYNOTE-590 (NCT03189719) study, pembrolizumab (pembro) + chemotherapy (chemo) provided statistically significant and clinically meaningful improvement in OS, PFS, and ORR vs placebo + chemo as first-line therapy for patients (pts) with locally advanced/unresectable or metastatic adenocarcinoma or esophageal squamous cell carcinoma (ESCC) or Siewert type 1 esophagogastric junction adenocarcinoma (EGJ). Here we report HRQoL outcomes in KEYNOTE-590. **Methods:** 749 pts were randomized 1:1 to pembro 200 mg or placebo Q3W for up to 2y + chemo (cisplatin 80 mg/m^2 Q3W [d1; 6 doses] + 5-FU 800 mg/m^2 on d1-5 Q3W). EORTC QLQ-C30, EORTC QLQ-OES18, and EQ-5D-5L questionnaires were administered at baseline, every 3 weeks (Q3W) up to week 24, and then Q9W up to 1 year or end of treatment, and at the 30-d safety follow-up visit. HRQoL was assessed in all treated patients who completed ≥1 HRQoL assessment (N = 711: 356 for pembro + chemo; 355 for chemo). Change from baseline to week 18 in EORTC-QLQ-C30 global health status (GHS)/QoL and physical functioning, and in QLQ-OES18 scores were prespecified secondary endpoints. Change from baseline to week 18 in EQ-5D scores was an exploratory endpoint. Time to deterioration (TTD) was evaluated for all endpoints. Least square mean (LSM) change from baseline (95% CI) was compared using a constrained longitudinal data analysis model. TTD was compared using a stratified log rank test and Cox proportional hazards model. *P*-values are nominal and two-sided. **Results:** QLQ-C30, QLQ-OES18 and EQ-5D-5L compliance was ≥90% in both arms at baseline and at week 18. There was no significant difference in least squares mean (LSM) change from baseline to week 18 in GHS/QoL status between arms (LSM difference [95% CI] -0.10 [-3.40-3.20]; *P* = 0.9530). Median TTD in GHS/QoL was similar between arms (HR, 0.86 [95% CI, 0.66-1.13]; *P* = 0.2864). Outcomes were similar in ESCC PD-L1 CPS ≥10, ESCC, and PD-L1 CPS ≥10 patient populations. LSM change from baseline to week 18 for QLQ-OES18 pain subscale was better for pembro + chemo (-4.78) vs chemo (-1.85) (-2.94, -5.86 to -0.02; *P* = 0.0487). There was no significant difference in LSM change from baseline to week 18 between arms for reflux (-1.19; -4.49-2.10; *P* = 0.4781) or dysphagia (-2.35; -7.78-3.07; *P* = 0.3945). VAS LSM change from baseline to week 18 was similar between arms (1.20, -1.61-4.01; *P* = 0.4016). **Conclusions:** HRQoL was stable and similar over 18 weeks in the pembro + chemo and chemo arms. Together with superior OS, PFS, and ORR and a manageable safety profile with pembro + chemo, these results support the clinically meaningful benefit of pembro + chemo in patients with advanced esophageal cancer including EGJ adenocarcinoma. Clinical trial information: NCT03189719. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

169 Poster Session

Double disparities in patients with gastric cancer: Clinicopathology and survival of older adults in a Hispanic-rich population. *First Author: Madison H. Williams, University of Texas Health San Antonio, San Antonio, TX*

Background: Gastric cancer incidence increases with advancing age with a median age at diagnosis of 68. However, older adults (age ≥65) are underrepresented in clinical trials. Additionally, Hispanic populations have a higher incidence of gastric cancer compared with non-Hispanic patients and there is evidence that this population has worse outcomes. Given this double disparity in older Hispanic adults, we evaluated the differences in disease characteristics at diagnosis and survival outcomes in older adults compared to younger adults with gastric cancer at our South Texas cancer center serving a predominantly Hispanic population. **Methods:** We performed a retrospective analysis of patients with a diagnosis of gastric cancer from 2000 – 2018, who had follow-up at Mays Cancer Center, San Antonio, TX. Older patients were defined as ≥65 years and younger patients were defined as <65 years. Median overall survival (mOS) was estimated from Kaplan-Meier curves and groups were compared using the log-rank test. **Results:** A total of 190 patients met criteria for analysis. Patients were predominantly younger (age <65), with 128 (67.4%) young and 62 (32.6%) older. Most patients were Hispanic (66.4% of younger and 64.5% of older) and male (51.6% of younger and 66.1% of older). The majority of patients had an ECOG performance status of 0-2, including 61.7% and 64.5% (p = 0.55) of younger and older patients, respectively. At baseline, there was no significant difference in location of primary tumor, grade, stage at diagnosis, or histologic classification between younger and older patients (Table). There was also no significant difference between the two groups in H. pylori status, location of metastases, or HER2 status. Of the 109 patients with follow-up for survival, the mOS was 17 months (95% CI: 15-55) for younger patients versus 14 months (95% CI: 13-NR) for older patients (p = 0.19). **Conclusions:** In this retrospective analysis of predominantly Hispanic patients with gastric cancer, we found that there were no statistically significant differences in clinicopathologic features at diagnosis or in survival between younger versus older adults. Our study was approximately 2/3 Hispanic, a population for which there is a paucity of data, especially in older adults. Given the limited published research available to guide the management of older patients with gastric cancer, including Hispanics, further prospective real-world studies are needed to evaluate toxicity and quality of life in order to improve the care of older adults with gastric cancer. Research Sponsor: None.

	Younger	Older	P-value
Gastric body	33.6%	37.1%	0.29
Antrum	28.9%	21%	
GEJ	17.2%	17.7%	
Fundus	5.5%	3.2%	
Cardia	3.9%	11.3%	
Poorly differentiated	56.3%	48.4%	0.3
Stage IV	49.2%	33.9%	0.49
Diffuse-type	35.9%	22.6%	0.17
Intestinal-type	11.7%	21%	

170 Poster Session

The effect of gender on outcomes in esophageal cancer. *First Author: Jordan McDonald, USF Health Morsani College of Medicine, Tampa, FL*

Background: Few epidemiological studies address differences in outcomes by gender in locoregional esophageal cancer (LEC) for which the current standard of care is chemoradiation followed by surgical resection. Although male gender is associated with the majority of LEC cases, we sought to determine if gender could impact clinical presentation as well as surgical and oncologic outcomes in our single institution 20 year experience. **Methods:** A retrospective query of our institution's IRB-approved database of patients that had surgical therapy between 2008 and 2019 for esophageal cancer (EC) was performed. Patients were stratified by gender and analyzed based on characteristics such as tumor histology, tumor location, clinical stage at presentation, age at diagnosis, receipt of neoadjuvant therapy, surgical intent, surgical complications, length of post-operative hospital stay, response to neoadjuvant therapy, final pathology, and recurrence. Chi-square, ANOVA and Kaplan Meier survival analysis were performed on the previously defined groups. **Results:** The cohort studied included 1180 patients with resection for EC. Of those, 1005 (85.2%) had adenocarcinoma, 145 (12.3%) had squamous cell cancer (SCC), 10 (0.8%) had adenosquamous carcinoma, and 20 (1.7%) had other histological variants. There were 985 (83.5%) male patients and 195 (16.5%) female patients. SCC was more common in females (29.2% in females vs. 8.9% in males, p = 0.000) and females tended to have tumor location in the upper thoracic esophagus more often (4.7% in females vs. 0.9% of males, p = 0.000). Additionally, females developed surgical complications more often than males (72.2% vs. 64.7%, p = 0.045). Staging at diagnosis (p = 0.508), receipt of neoadjuvant treatment (p = 0.676), and age at diagnosis (65.3 years in males vs. 66.3 years in females, p = 0.934) had no association with gender. Response to neoadjuvant therapy (p = 0.157) and cancer recurrence (p = 0.434) did not have significant associations with gender. The median overall survival was not statistically significantly different but trended to be longer for females (73.4 months in females [95% CI: 51.5-95.4] vs. 47.0 months in males [95% CI: 39.6-54.5], p = 0.160). **Conclusions:** Based on our high-volume cancer center study, female patients were more likely to have SCC, upper thoracic esophageal lesions, and surgical complications following resection. While univariate analysis did not demonstrate significant differences in overall survival between genders, there are plans to report additional data after controlling for other variables. Further studies are warranted to validate these findings, given the potential for higher prioritization of an organ preservation approach for this patient population. Research Sponsor: None.

171 Poster Session

Incidence of early-onset gastric and esophagus cancers has changed over time with disproportionate impact on Black and Hispanic patients. *First Author: Nataly Valeria Torrejon, Cleveland Clinic, Cleveland, OH*

Background: The increased incidence of gastro-esophageal junction adenocarcinoma has been well-described, but how the proportion of early versus older onset cancer has changed over time remains incompletely understood. This study characterized the socioeconomic and pathologic characteristics of early-onset gastro-esophageal malignancies. **Methods:** All patients with gastric cancer (GC) and esophageal cancer (EC) from 2004-2015 in the National Cancer Database were included and categorized by age under or over 60 years. Differences in demographics, disease stage, treatment characteristics and socioeconomic factors between young and older patients were assessed by Chi-square test. The effect of age, race, insurance status, community median income and community educational attainment on overall survival (OS) were assessed using uni- and multivariable Cox models with Bonferonni correction when indicated. **Results:** The study population comprised 158,599 patients with GC and 139,210 patients with EC. For GC, 43,146 patients (27.2%) were under age 60. The proportion of patients diagnosed under 60 increased over time: 26.7% in 2004-2006, 26.9% in 2007-2009, 27.6% in 2010-2012 and 27.5% in 2013-2015. Compared to older patients, young patients were more likely to be Black (16.7% vs. 13.2%), Asian (7.6% vs. 6.1%) or Hispanic (15.5% vs. 7.7%), diagnosed with stage 4 disease (43.5% vs. 31.3%) and to have poorly differentiated grade (61% vs. 51.7%), p value $<$ 0.0001 for all. For EC, 38,801 patients (27.8%) were under age 60. The proportion of patients diagnosed under 60, decreased over time: 29.6% in 2004-2006, 28.3% in 2007-2009, 27.6% in 2010-2012 and 26.2 % in 2013-2015. Compared to older patients, young patients were more likely to be Black (12.6% vs. 8.2%) or Hispanic (4.2% vs. 3.1%), diagnosed with stage 4 disease (34.3% vs. 26.1%), p value $<$ 0.0001 for all. There was no difference in histologic grade between younger and older patients (41.1% vs. 40.3%, p = 0.85). Age $<$ 60 years was associated with improved OS in both GC and EC. After adjusting for other demographic, socioeconomic, disease stage and treatment-related factors, Black patients had the worst median OS compared to other races in both malignancies as shown in the Table. **Conclusions:** Early-onset GC has increased over time while early-onset EC has decreased. Patients with early-onset gastric and esophageal cancer are more likely to be Black or Hispanic and to present with stage 4 cancer. Younger patients with GC are also more likely to have poorly differentiated histology. Most concerning, Black patients have the worst OS compared to other races for both GC and EC. Research Sponsor: None.

Race	GC Median OS (months)	EC Median OS (months)
Black	11.7	9.3
Asian	22.4	14.8
White	12.4	13.5
Hispanic	15.2	13.4
P value	$<$ 0.0001	$<$ 0.0001

172 Poster Session

The impact of sociodemographic characteristics on gastric cancer outcomes: A retrospective review of a large single center study. *First Author: Dawood Findakly, Creighton University School of Medicine, Phoenix, AZ*

Background: Gastric cancer (GC) remains a pervasive condition in the US with high morbidity and mortality. Race/ethnicity, lack of insurance, and poverty may all be contributing to this burden, especially in select populations. We evaluated the impact of these sociodemographic factors on GC outcomes at a hospital with high immigrant-patient populations. **Methods:** We conducted a retrospective study to identify patients diagnosed with GC between year 2010 and 2019. Data obtained from our institution database regarding patients' sociodemographic factors, including age, gender, race/ethnicity, insurance status and type, and neighborhood socioeconomic status. Likewise, information on tumor histology, anatomic location, and stage were also obtained. Kaplan-Meier analysis was used to plot survival curves and analyze the impact of insurance on survival outcome. **Results:** One hundred eleven patients were analyzed in this study, with a male-to-female ratio of 1.26:1. The median age at the time of GC diagnosis was 52.9 (range 27-87) years, with median survival time ($\pm$SD, range) of 12.7 ($\pm$17.7, 0.25-84) months. Most patients (69.4%) were uninsured—out of which 76.7% presented with advanced-stage disease. Among those, the majority (70.3%) were Hispanic, and 60.4% were non-U.S. citizens. The most common tumor histology was diffuse-type adenocarcinoma in 55% of patients. Patients insured were on public coverage (Medicaid), private insurance, and Medicare at 11.7%, 9.9%, and 9.0%, respectively. In terms of survival, lack of insurance (p = 0.012) and Medicaid insurance (p = 0.046) were associated with the worst survival outcomes in GC patients. **Conclusions:** Our study reflects the trends in GC outcomes distinctly linked to significant sociodemographic disparities. Patients who lack insurance coverage had the worst survival outcomes. Therefore, efforts such as increasing healthcare access for this population-type at risk of sociodemographic incongruities may enhance outcomes and are crucial in fighting GC. Research Sponsor: None.

173 Poster Session

Impact of gender on treatment and survival of patients with esophageal cancer in the United States. *First Author: Camille Baumrucker, Sylvester Comprehensive Cancer Center, University of Miami School of Medicine, Miami, FL*

Background: Esophageal cancer (EC) is historically a male-predominant disease. Current available evidence on the impact of gender on clinical presentation and survival outcomes of EC is limited by small sample size or single institutional series. **Methods:** Patients with EC (stage I-III) were identified in the National Cancer Data Base (NCDB, 2004-2016). Clinicopathologic and treatment characteristics of male and female patients were compared using Chi-square analysis. Overall survival (OS) was estimated using Kaplan-Meier method and Cox proportional hazards regression. **Results:** Of 62,893 patients included, male gender was predominant (77.7% vs 22.3%). Adenocarcinoma was the most common subtype (66.7%); however, squamous cell carcinoma was more predominant in females (57.1% vs. 26.5%, p$<$0.001). Females were significantly older (68.5 vs. 66.1 years; p$<$0.001) and more likely African American (AA) (14% vs. 8.1%; p$<$0.001). Females were more likely to present with local disease (stage I, 19.6% vs. 18.2%; p$<$0.001), while males presented more likely with locoregional disease (LRD, stage II/III, 80.4% vs 81.8%, p$<$0.001). Females had worse OS compared to males (18.1 vs. 19.7 mo; p=0.001; cI: 23.5 vs. 31.9mo, p$<$0.001; cII/III: 17.2 vs 18.3mo, p=0.473). White females had worse OS than white males (18.6 vs. 20.4mo, p$<$0.001), while AA females had better OS (13.5 vs. 12.6mo, p=0.001). Among patients with LRD, females less frequently received chemotherapy (CT, 75.4% vs. 82.9%, p$<$0.001), radiation therapy (RT, 78.9% vs. 82.6%, p$<$0.001), and esophagectomy (28% vs. 40.5%, p$<$0.001). Females who underwent esophagectomy had improved OS over males (40.3 vs. 32.7mo; p$<$0.001). More specifically, white females who underwent esophagectomy had improved OS over white males (47.6 vs 38mo, p$<$0.001); however, AA males and females who underwent esophagectomy had similar OS (33.8 vs 32.6mo, p=0.452). Female gender, advanced age, AA race, high comorbidity score and clinical stage, and lack of access to CT, RT, and esophagectomy were independent predictors of mortality (Table). **Conclusions:** Females with EC seem to have less access to CT, RT and esophagectomy, which is associated with worse OS compared to males. Healthcare policies should be implemented to increase access to standard of care treatment for female patients with EC. Research Sponsor: None.

		HR	95% CI	p-value
Age		1.012	1.011-1.013	$<$0.001*
Gender	Male	1.126	1.099-1.154	$<$0.001*
Race	White (Ref)			
	AA	1.11	1.072-1.149	$<$0.001*
Insurance	Uninsured (Ref)			
	Private	0.727	0.686-0.77	$<$0.001*
	Medicaid/Medicare	0.804	0.759-0.851	$<$0.001*
	Other	0.719	0.658-0.785	$<$0.001*
Comorbidity Score	0 (Ref)			
	1	1.141	1.114-1.168	$<$0.001*
	2	1.288	1.244-1.334	$<$0.001*
Area	Rural (Ref)			
	Metro	0.975	0.912-1.043	0.466
	Urban	1.047	0.976-1.123	0.199
Clinical Stage	LRD	1.678	1.63-1.727	$<$0.001*
Histology	SCC	1.03	1.006-1.054	0.013
RT		0.885	0.858-0.913	$<$0.001*
CT		0.698	0.677-0.719	$<$0.001*
Esophagectomy		0.442	0.432-0.452	$<$0.001*

174 Poster Session

Racial differences in tumor biology and treatment of gastric cancer in the United States. *First Author: Joshua Tseng, Cedars-Sinai Medical Center, Los Angeles, CA*

Background: Racial disparities for gastric cancer are often identified in the literature. Although patients in Asia consistently demonstrate a survival benefit compared to those in the West, Asian patients in the US still retain this advantage, which suggests that tumor biology may be a major factor. The goal of our study is to identify racial differences in patient demographics, tumor biology and treatment for gastric cancer in the United States. **Methods:** The National Cancer Database was queried from 2006-2016 for patients with a diagnosis of gastric adenocarcinoma. Patient demographics, tumor characteristics, and treatment patterns were compared by patient ethnicity (White, Black, Hispanic, and Asian) with Kruskal-Wallis test and Pearson's chi-squared test. Kaplan-Meier survival curves used to assess overall survival, and cox regression used to identify independent prognostic factors for survival. **Results:** 116,717 patients with gastric cancer identified; 78,066 were White, 17,486 were Black, 8,494 were Asian, and 12,671 were Hispanic. White patients were most likely to be older than 70 and have proximal tumors, and least likely to have diffuse type adenocarcinoma. Hispanic and Black patients were most likely to present with metastases. Asian patients were most likely to receive surgery and least likely to receive chemotherapy or radiotherapy. Stage for stage, Asians had the longest median survival, followed by Hispanic, Black, and White patients. Prognostic factors associated with a survival benefit include Asian ethnicity (HR 0.72, 95% CI 0.68-0.74), Hispanic ethnicity (HR 0.76, 95% CI 0.73-0.79), Black ethnicity (HR 0.95, 95% CI 0.93-0.98), private insurance (HR 0.91, 95% CI 0.87-0.96), higher income (HR 0.85, 95% CI 0.82-0.88), treatment at academic center (HR 0.87, 95% CI 0.83-0.91), higher-volume centers (HR 0.90, 95% CI 0.87-0.93), receiving surgery (HR 0.42, 95% CI 0.41-0.43), chemotherapy (HR 0.56, 95% CI 0.55-0.57), and radiation (HR 0.96, 95% CI 0.93-0.98). **Conclusions:** Treatment differences between Eastern and Western countries for gastric cancer persist between ethnic groups within the United States, with Asian patients retaining a survival benefit. Black and Hispanic patients present with aggressive disease and unfavorable socioeconomic factors that are detrimental to overall survival. Research Sponsor: None.

175 Poster Session

Using breath analysis as a screening tool to detect gastric cancer: A systematic review. *First Author: Ghazal Haddad, Faculty of Medicine, University of Toronto, Toronto, ON, Canada*

Background: In its early stages, gastric cancer symptoms are frequently lacking, resulting in an often late and incurable diagnosis. A non-invasive, cheap, and reliable screening method for gastric cancer could improve outcomes and increase the number of surgically resectable gastric cancers. Breath analysis has emerged as an experimental method of non-invasive screening of gastric cancer and identification of individuals suitable for confirmatory, diagnostic upper gastrointestinal endoscopy. We aimed to evaluate the accuracy and applicability of breath analysis for gastric cancer detection in adults. **Methods:** This systematic review searched MEDLINE, EMBASE, BIOSIS, CENTRAL, and Compendex until 11 July 2019 for original studies analyzing exhaled breath to detect gastric cancer in patients. Two authors then independently screened the abstracts, titles, and full texts. Summary sensitivity and specificity analyses were obtained using a hierarchical bivariate method. Positive predictive value and number needed to screen (NNS) of breath analysis methods for gastric cancer detection were calculated for each country using gastric cancer prevalence by country obtained from the Global Cancer Observatory. Non-quantitative results were descriptively summarized. Risk of bias was assessed using the QUADAS-2 tool. This study protocol was pre-registered in PROSPERO (CRD42020139422). **Results:** Twenty studies were included. Together, the studies included 2,976 subjects. The pooled mean age of the subjects in the gastric cancer groups was 60.5 ± 11 years while the pooled mean age for control groups was 55.4 ± 12 years. Within these twenty studies, breath analysis technologies most commonly used were mass spectrometry (MS)-based methods; other methods included volatile organic compound sensors, thermal desorption tubes, and silicon nanowire field effect transistors. Across all included studies, we found and summarized the characteristics of 131 chemical compounds found in the exhaled breath of study subjects. Eleven studies (total n = 1905) involving all technologies reported quantitative results, with sensitivities ranging from 67-100% and specificities from 71-98%. The summary sensitivity across six studies utilizing MS-based breath analysis methods was 85.3% (95% CI: 82-96%); summary specificity was 81.7%. (95% CI: 78-85%). Based on the MS-based values, we estimated that screening with MS-based breath tests could lower the NNS by more than four-fold in the 15 countries with the highest prevalence of gastric cancer. **Conclusions:** Breath analysis is a promising method for gastric cancer detection with good diagnostic performance and potential to decrease the NNS for endoscopy-based gastric cancer detection. However, due to the heterogeneity of breath analysis technologies, rigorous studies with standardized, reproducible methods are needed to evaluate the clinical applicability of these technologies. Research Sponsor: McLaughlin Scholarship at the University of Toronto.

176 Poster Session

Localized diffuse-type gastric adenocarcinoma: Influence of baseline positron emission tomography on survival and therapy response. *First Author: Ahmed Abdelhakeem, The University of Texas - MD Anderson Cancer Center, Houston, TX*

Background: Diffuse type of gastric adenocarcinoma (dGAC) confers a poor but variable prognosis compared to intestinal type of GAC. The value of baseline uptake of FDG-PET in localized dGAC is unclear and ~40% are not FDG-PET avid. We analyzed outcomes based on the avidity (high with SUV > 3.5 or low with SUV ≤3.5) of the primary on baseline FDG-PET. **Methods:** We retrospectively selected 111 localized dGAC cases who had baseline FDG-PET for staging. We compared the FDG-PET avidity with overall survival (OS) and response to preoperative therapy. Standard statistical methods were utilized. **Results:** The mean age was 59.4 years and with many female patients (47.7%). All patients had dGAC. The high-SUV group (58 [52.3%] patients) and the low-SUV group (53 [47.7%] patients) were equally divided. While the median OS for all patients was 49.5 months (95% CI: 38.5 – 98.8 months), it was 98.0 months for the low-SUV group and 36.0 months for the high-SUV (*p* value = 0.003). While the median PFS for all patients was 38.2 months (95%CI: 27.7 – 97.6 months), it was 98.0 months for the low-SUV group was and 27.0 months for the high-SUV group (*p* value = 0.005). Clinical responses before surgery were more common in the low-SUV group but there were only 4 patients with pathologic complete response in the entire cohort. **Conclusions:** Our unique data suggest that localized dGAC patients with low SUV fare better than those with high SUV meaning highly metabolic GACs consuming glucose confer poor prognosis and overall all dGACs seem resistant to therapy. Research Sponsor: None.

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Factors associated with treatment duration from start of second-line ramucirumab plus paclitaxel or nab-PTX for advanced gastric cancer: real-world evidence from Japanese Claim Database. *First Author: Shuichi Hironaka, Department of Medical Oncology and Hematology, Oita University Faculty of Medicine, Yufu, Japan*

Background: Recently, the value of RWE has been recognized to be important. We investigated the first line(1L)-2L therapy(Tx) sequence for AGC and factors associated with whole treatment period after RAM plus(+) (nab-)PTX therapy using RWE in Japan. **Methods:** This study used a hospital-based claims database in Japan. Patients who were diagnosed with GC and started 1L Tx between Jun 2015 and Jul 2019 were selected. The 1L Tx was defined as fluoropyrimidine(FP)+platinum (with or without trastuzumab[Tmab]), and defined to be discontinued when it was suspended for >90 days or switched to different antitumor drugs (2L Tx). In patients who started RAM+(nab-)PTX as 2L Tx, factors associated with overall Tx duration (from start of 2L Tx to the last dose of chemotherapy including subsequent Tx) were explored by Cox regression analysis. **Results:** 10581 patients (mean age 67.9 years, male 73.9%) received 1L Tx (9024 patients without Tmab and 1557 patients with Tmab). In patients who discontinued 1L Tx, the proportion of 1L-2L Tx transition was 61% (4509/7443) without Tmab and 68% (849/1245) with Tmab. Among 5358 patients who received 2L Tx, 3650 patients (68%) received RAM+(nab-)PTX. The median overall Tx duration was 6.7 months after initiation of 2L Tx with RAM+(nab-)PTX. Factors positively associated with the overall Tx duration from initiation of 2L Tx with RAM+(nab-)PTX were Tmab use before data cutoff (Sep 2019; hazard ratio [95% CI] 0.9 [0.79-1.00]), previous oral FP (0.7 [0.54-0.89]), duration of 1L Tx >150 days (0.8 [0.74-0.87]). Factors negatively associated were peritoneal metastasis or ascites (1.3 [1.17-1.40]), comorbidities e.g., edema (1.3 [1.07-1.45]), renal disease (1.1 [1.01-1.30]), diabetes (1.1 [1.01-1.22]), previous oxaliplatin (1.2 [1.09-1.30]), and rehabilitation (1.9 [1.67-2.24]) or nutritional intervention (1.5 [1.34-1.68]) within 1 month before and after starting 2L Tx. **Conclusions:** Many of the patients received RAM+(nab-)PTX as 2L Tx regardless of Tmab. This large-scale RWE demonstrated that Tmab use, oral FP, and long 1L Tx duration were associated with longer treatment course from start of 2L RAM+(nab-)PTX therapy. Research Sponsor: Eli Lilly Japan K.K.

178 Poster Session

Real-world outcomes of esophagectomy versus chemoradiotherapy for clinical stage I esophageal squamous cell carcinoma. *First Author: Hiroki Yukami, National Cancer Center Hospital East, Kashiwa, Japan*

Background: Recently, JCOG0502 trial have shown a comparable efficacy with chemoradiotherapy (CRT) and esophagectomy as standard treatment in patients with clinical stage (cStage) I esophageal squamous cell carcinoma (ESCC), showing the standard treatment option of CRT. However, there is few reports for comparison of clinical outcomes with these treatments in real-world. The aim of this study was to clarify the real-world outcomes in cStage I ESCC who performed with CRT or esophagectomy. **Methods:** This retrospective study included patients with clinical stage I ESCC who received thoracoscopic or open esophagectomy with three-field lymph node dissection or CRT mainly consisted of 5-fluorouracil and platinum with concurrent radiotherapy (50.4 Gy/28Fr or 60 Gy/30Fr) between 2009 and 2017 at National Cancer Center Hospital East. Survival outcomes were calculated using the Kaplan-Meier method, and the differences were evaluated using the log-rank test. **Results:** Among a total of 156 patients, 128 were male and median age was 68 years old. 120 and 36 patients underwent esophagectomy and CRT, respectively. ECOG performance status 0/1/2 were 138/12/6 patients. Tumor location was Ut/Mt/Lt in 16/87/53 patients. Clinical tumor depth (MM-SM1/SM2-SM3) were 33/123 patients. Patients' characteristics were similar among treatment groups, except clinical tumor depth (SM2-3; 84.2% in esophagectomy group vs. 61.1% in CRT group, p = 0.005). All patients underwent radical surgery in esophagectomy group, while three patients (8.3%) in CRT group were received additional esophagectomy or endoscopic resection due to residual disease. With a median follow-up of 72 months, 5-year overall survival (OS) and progression-free survival rate were 81.5%/77.0% in esophagectomy group and 82.6/74.4% in CRT group (p = 0.89 and p = 0.48). In safety profile, grade 3 or higher stenosis was observed in 21.7% of esophagectomy group. There was no treatment-related death in both groups. In subgroup analysis for OS, elderly patients (75 years and older) tended to have better 5-year OS rate in CRT group (76.9% in esophagectomy group vs. 81.8% in CRT group), while younger patients (< 75 years) showed comparable 5-year OS rate in both groups (82.4% in esophagectomy group vs. 82.9% in CRT group). **Conclusions:** Real-world data reproduced the results of clinical trial, supporting CRT as one of the standard treatment options in patients with cStage I ESCC. Research Sponsor: None.

179 Poster Session

Retrospective study of nivolumab monotherapy for advanced esophageal squamous cell carcinoma. *First Author: Hayato Mikuni, National Cancer Center Hospital, Tokyo, Japan*

Background: Based on the results of the ATTRACTION-1 and ATTRACTION-3 trials, nivolumab monotherapy has used for the treatment of metastatic or recurrence esophageal cancer patients who were refractory or intolerant to fluoropyrimidine and platinum since February 2020 in Japan. However, the ATTRACTION-1 trial mainly included patients who received nivolumab monotherapy as third or later-line treatments, which was different from the ATTRACTION-3 trial which mainly included patients as second-line treatment. Therefore, it is still unclear whether the treatment lines affect the efficacy of nivolumab in clinical practice. **Methods:** Medical records were retrospectively reviewed for patients diagnosed with metastatic or recurrence esophageal squamous cell carcinoma (ESCC) who received nivolumab monotherapy as second- or third or later-line treatments in our hospital. We evaluated progression-free survival (PFS), overall survival (OS), objective response rate (ORR), disease control rate (DCR) based on the RECIST ver1.1, and the incidences of adverse events (AEs) based on the CTCAE ver5.0. **Results:** Sixty-two patients were identified as the subject of this study. Thirty patients received nivolumab as second-line treatment (48.4%) and 32 patients as third or later-line treatments (51.6%). The median age (range) were 67 (33-80)/61 (52-84), PS 0 were 40.0/21.9%, prior taxane treatment rate were 6.7/93.8%, respectively. The ORR/DCR were 22.7/45.5% in second-line treatment, and 24.1/44.8% in third or later-line treatments (p=1.00). The median PFS (95% CI) was 2.3 (1.4-6.2)/2.3 (1.2-3.6) months in the second-/third or later-line treatments (HR=0.86, p=0.58). AEs of grade 3 or higher were observed in 6.7/6.3% of the second-/third or later-line treatments. **Conclusions:** There was no clear difference between second -line and third or later-line treatments in the short-term efficacy of nivolumab monotherapy in advanced ESCC patients. Research Sponsor: None.

180 Poster Session

Treatment patterns, healthcare resource use, economic, and survival outcomes associated with nonresectable advanced esophageal cancers in Taiwan. *First Author: Yiling Tsai, Chang Gung University, Taoyuan City, Taiwan*

Background: In Taiwan, limited real-world data indicate that initial EC diagnosis tends to occur at an advanced stage with limited therapeutic options and poor prognosis. **Methods:** This was a retrospective 'real world' observational study using the Taiwan National Health Insurance Research Database (NHIRD). Patients having at least one hospital record with a primary ICD-9 or ICD-10 code of EC were selected from Jan 1st, 2013 through Dec 31st, 2018. The first date of EC diagnosis was defined as the index date. Patients were followed for a minimum ± 30 days from the index date and were stratified by staging, clinical presentation (i.e. resectable vs. non-resectable advanced) and tumor histotype (squamous cell carcinoma, adenocarcinoma, unknown). Key characteristics such as demographics, clinical parameters, medication utilization, health care resource utilization, costs incurred, and survival were tracked for the overall population, resectable and non-resectable, advanced cohorts. **Results:** Patients identified with non-resectable advanced EC (N = 4,340) had a mean (SD) age of 59.7 (12.3) years and the vast majority were male (n = 4,044, 93.2%). Approximately half (50.4%) had Stage 3 disease and an additional 36.2% with stage 4, with the remainder Stage 1, 2 or Unknown. The majority (91.8%) were diagnosed with squamous cell carcinoma. 71.3% of patients received first line (1L) chemotherapy, most commonly with fluorouracil + cisplatin (69.9% of 1L) or platinum monotherapy (13.8% of 1L). 36.3% of patients survived one year with mean (SD) annualized post-index EC-related costs of New Taiwan (NT) $791,827.4 (NT$ 582,663.8). **Conclusions:** In Taiwan, the most common 1L chemotherapeutic treatment modality for Taiwanese patients with EC were fluorouracil + cisplatin. The EC-related costs for these patients appear to be a substantial financial burden in Taiwan. Research Sponsor: Bristol, Myers, Squibb Pharmaceutical Corporation.

181 Poster Session

Update results of paclitaxel and cisplatin in combination with anlotinib as first-line regimen for advanced esophageal squamous cell carcinoma (ESCC): A multicenter, single-arm, open-label phase II **clinical trial.** *First Author: Junsheng Wang, AnYang Tumor Hospital, Anyang, China*

Background: The prognosis of pts with advanced ESCC remains dismal clinically. Paclitaxel and cisplatin were used as the standard first-line regimen in ESCC for almost two decades. As a novel multitarget tyrosine kinase inhibitor mainly targeting anti-angiogenic single pathway, anlotinib was demonstrated to be an effective second-line monotherapy for pts with advanced or recurrent ESCC in China. Consequently, the aim of this study was to investigate the efficacy and toxicity of paclitaxel and cisplatin combined with anlotinib as first-line therapy for advanced ESCC. **Methods:** Pts with previously untreated metastatic or unresectable, locally advanced ESCC, who had not received (neo) adjuvant therapy/radical surgery within 6 months were recruited in this study. Eligible subjects were given paclitaxel (135mg/m^2, iv, q3w) and cisplatin (60~75mg/m^2, iv, d1~3, q3w) plus anlotinib (10mg, po, d1~14, q3w) for 4~6 cycles during initial therapy. For those without progressive disease, maintenance treatment was administrated with anlotinib monotherapy (10mg, po, d1~14, q3w) until progression or unacceptable toxicity. The tumor response was assessed by investigator according to RECIST version 1.1 using CT scans every two cycles. And the calculated sample size of this study was 47. The primary endpoint was PFS, secondary endpoints were safety, objective response rate (ORR), disease control rate (DCR) and duration of response (DOR). **Results:** From Oct 2019 to Aug 2020, 27 pts were available for efficacy and safety evaluation. In best overall response assessment, there were 7.4% CR (2/27), 66.7% PR (18/27) and 25.9% SD (7/27). ORR was 74.1% (95%CI: 53.7. ~ 88.9), and DCR was 100.0% (95%CI: 87.2~100.0). The median PFS of the 27 pts was not yet available. The safety profile indicated that the most common drug-related adverse events were myelosuppression, gastrointestinal reaction, fatigue, hypertension, constipation, hypokalemia and hepatotoxicity. The common grade 3-4 treatment-related adverse events were myelosuppression (18.5%), hypertension (7.4%). **Conclusions:** The current results indicated that paclitaxel and cisplatin combined with anlotinib as first line therapy for advanced ESCC exhibited encouraging efficacy and manageable adverse events. The conclusion should be validated in more pts consecutively. Clinical trial information: NCT04063683. Research Sponsor: Chia Tai Tianqing Pharmaceutical Group Co., Ltd.

Overall response	Paclitaxel and cisplatin + anlotinib (n = 27)
CR	2
PR	18
SD	7
PD	0
ORR, n (%, 95%CI)	20 (74.1, 53.7 ~88.9)
DCR, n (%, 95%CI)	27 (100, 87.2~100.0)

182 Poster Session

Efficacy and safety of apatinib in treatment of gastric cancer: A real-world study. *First Author: Yijie Ma, Department of Medical Oncology, Henan Cancer Hospital, Zhengzhou, China*

Background: Apatinib is a small molecule TKI inhibitor, which had been approved in China for treatment of advanced gastric cancer refractory to two or more lines of prior chemotherapy. Its efficacy and safety have been demonstrated in previous randomized controlled clinical studies. However, the efficacy and safety of apatinib in real world is lacking. This study aimed to evaluate the anti-tumor activity and toxicity of apatinib in real world. **Methods:** Patients older than 18 years with histologically diagnosed with gastric cancer were enrolled and treated with either apatinib alone or in combination with other drugs. The primary endpoint was progression-free survival (PFS), and secondary endpoints were overall survival (OS), overall response rate (ORR) and disease control rate (DCR). The adverse events were also recorded. **Results:** From March 2018 to March 2019, a total of 1000 patients were enrolled. Among them, 48(0.48%), 13(0.13%), 225 (22.5%), 389 (38.9%), and 325 (32.5%) patients received apatinib as postoperative auxiliary-, neo-adjuvant-, first-, second-, and third- or higher line therapy, respectively. Efficacy evaluation was performed in 901 patients. Thirty-five patients achieved complete response (CR), 116 patients achieved partial response (PR), 596 patients achieved stable disease (SD), and 154 patients had progressive disease (PD), illustrating an ORR of 16.76% and a DCR of 82.91%. The mPFS was 5.32 months (95% CI, 4.93-5.75), and mOS was 9.76 months (95% CI, 8.97-10.81). In addition, the mOS of apatinib in first-line, second-line, and third-line treatments were 12.68 months, 9.49 months, and 7.62 months, respectively. Patients received apatinib in combination with other drugs had longer survival than apatinib alone, with mPFS 5.62 months vs 4.47 months and mOS 10.81 months vs 7.95 months. Such phenomenon was also observed in ORR (18.21% vs 13.04% , $P< 0.001$) and DCR (84.88% vs 77.87% , $P< 0.001$). The main adverse events (AE) were anemia (67.2%), thrombocytopenia (36.2%), leukopenia (34.5%)and anorexia (37.6%). The most common grade 3-4 adverse events included neutropenia, anemia and thrombocytopenia. **Conclusions:** In the real world, apatinib showed promising efficacy and manageable toxicities in patients with gastric cancer. Patients benefit more when received apatinib combination therapy. Clinical trial information: NCT03478943. Research Sponsor: Jiangsu Hengrui Pharmaceutical Co. LTD.

183 Poster Session

Patient-reported symptom burden and functioning in patients with advanced esophageal, gastroesophageal junction (GEJ), and gastric cancer undergoing chemotherapy. *First Author: Xin Shelley Wang, Department of Symptom Research, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: For advanced upper gastrointestinal (GI) cancers, patient-reported symptoms are driven by both disease and treatment toxicities. This real-world longitudinal study was designed to evaluate patient-reported outcomes (PROs) of symptom burden and functioning among patients (pts) treated with anti-cancer therapy. **Methods:** Adult pts with advanced esophageal, gastroesophageal junction (GEJ), or gastric cancer were invited to participate in a prospective, longitudinal study. PRO assessment included pre-treatment and weekly completion of the M.D. Anderson Symptom Inventory GI module (MDASI-GI) as pts initiated a new line of therapy. Clinical and disease characteristics and treatment details were obtained from electronic health records. Up to 12 weeks longitudinal PRO data were analyzed using mixed-effect modeling with random intercept. Pts were classified into high or low symptom groups by group-based trajectory modeling. Time to deterioration in functioning (defined as a ≥2-point increase from baseline on 0-10 scale) was examined with Kaplan-Meier method. **Results:** At the interim analysis, 76 pts had enrolled: 33 (43%) were chemotherapy naïve for advanced disease, 18 (24%) had received 1 line of therapy, 14 (18%) had received >1 line of therapy, and 11 (14%) were excluded from this analysis due to study discontinuation without follow-up assessment. Among the 65 eligible pts in this analysis, 46 (70.8%) were male, most were white (n = 56, 86.2%), and 44 (67.7%) had an ECOG performance status score of 0-1. Pain, fatigue, disturbed sleep, lack of appetite and inability to eat were the most common severe symptoms reported prior to and during therapy. Pts who had received one line of therapy reported worsening symptoms of pain, fatigue, lack of appetite, difficulty swallowing, and reduced general activity, work, and enjoyment of life over time (group and time interaction $P<.05$). Pts with >1 line of prior therapy had increased neuropathy symptoms (numbness/tingling) than those who were treatment-naïve ($P= 0.022$). The median time to functioning deterioration of ≥2 points from baseline on the MDASI-"General activity" was 7 weeks. Up to 57% of pts were classified into high symptom trajectory group of pain, fatigue, disturbed sleep, and drowsiness with moderate to severe symptoms (≥4 points out of possible 10) over time; group membership was related to moderate to severe symptoms at baseline, after adjusting for age, sex, ECOG performance status, cancer site and prior therapies. **Conclusions:** This real-world observational study suggests that pts with advanced stage upper GI cancer undergoing standard therapy report high symptom burden. These preliminary findings support the use of a targeted symptom monitoring using well-defined PROs during active therapy, thereby adding the knowledge obtained from PROs to improve routine patient care. Research Sponsor: U.S. National Institutes of HealthEli Lilly and Company.

184 Poster Session

A multicountry chart review of treatment patterns and outcomes for patients with resected esophageal or gastroesophageal junction cancer. *First Author: Prianka Singh, Bristol Myers Squibb, Princeton, NJ*

Background: Global neoadjuvant and adjuvant treatment patterns among patients with resected Esophageal Cancer (EC) and Gastroesophageal Junction cancer (GEJC) remain unclear. This study describes real-world treatment patterns and outcomes for patients receiving surgery for Stage II or III EC or GEJC. **Methods:** Physicians in North America (US, Canada), Asia (China, Japan, Taiwan), and Europe (UK, France, Germany, Italy, Spain) provided clinical and treatment data in this retrospective, non-interventional chart review conducted from April-June 2020. Included patients were adults (Japan ≥20 years; elsewhere, ≥18 years), who underwent resection of Stage II or III EC or GEJC between October 2017 and October 2018 and were followed until death, loss to follow up, or end of data collection. **Results:** Physicians (N = 609) provided data on 1693 patients of mean age of 62.4 years, who received surgery for Stage II or III esophageal squamous cell carcinoma (ESCC) (33.3%), esophageal adenocarcinoma (EAC) (31.5%), or GEJC (35.2%) and were followed a mean (median) of 17.7 (17) months (to death or end of study period). At diagnosis, 85.6% of patients had performance status of 0/1. The majority of patients received an R0 resection (overall, 70.6%; ESCC, 76.6%, EAC, 67.4%, GEJC, 68.0%; $p < 0.05$); of these, 32.0% had a complete pathological response and 64.1% had a partial pathological response. Neoadjuvant therapy use differed among the treatment groups (ESCC 56.5%; EAC, 65.9%; GEJC, 62.6%, $p < 0.05$), as did adjuvant therapy (ESCC: 39.8%; EAC, 40.3%; GEJC, 44.5%; p = 0.023). Recurrence rate following surgery did not differ between groups for any recurrence (overall, 21.0%; ESCC 18.5%, EAC 23.6%, GEJC 21.1%); for local or regional recurrence (overall, 11.6%; ESCC, 10.3%; EAC, 12.7%; GEJC, 11.7%); or for metastatic recurrence (overall, 9.5%; ESCC, 8.2%; EAC, 10.9%; GEJC, 9.4%). The median time to local or regional recurrence (for those who progressed during the reporting period) was 8 months from date of initial surgery (overall, 8 mo; ESCC, 8 mo; EAC, 7 mo; GEJC, 8.5 mo; $p > 0.05$). The frequency of 1L systemic therapy for advanced disease at the time of survey completion was 16.1% overall and differed among patients with ESCC (14.6%); EAC (17.8%); and GEJC (15.9%); $p > 0.05$. **Conclusions:** This large multi-country real world data study shows that over half of all patients received neoadjuvant therapy, and over a third received adjuvant treatment. The high unmet need in this population is evident from the post-resection recurrence rate of 21.1% at median 8 months and the high proportion of patients who went on to require advanced disease treatment. Research Sponsor: Bristol Myers Squibb.

185 Poster Session

A retrospective multicenter study: Clinicopathological factors affecting recurrence-free survival in operable gastric cancer patients. *First Author: Emre Yekeduz, Ankara University Faculty of Medicine, Medical Oncology Department, Ankara, Turkey*

Background: Gastric cancer is one of the most common cancers in Asian countries, particularly. However, according to the American Cancer Society, 27,600 new gastric cancer cases and 11,010 deaths due to gastric cancer will be observed in the US in 2020. The rates of 5-year overall survival (OS) are 69.5% and 32% in the localized and regional diseases. Despite surgery and adjuvant treatment, gastric cancer's recurrence rate is still not reasonable. In this multicenter study, we aimed to identify the clinicopathological factors that affect gastric cancer recurrence. **Methods:** Clinical and pathological data of the patients performed surgery between the 2009-2018 in the two university hospitals in Turkey was collected retrospectively. Recurrence-free survival (RFS) was estimated using Kaplan-Meier and categorical variables were compared using a log-rank test. After identifying clinicopathological factors affecting RFS, a multivariate analysis was performed using Cox regression analysis. All statistical analyses were performed using IBM SPSS Statistics software, version 27 (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27 Armonk, NY: IBM Corp.). **Results:** Three hundred fifty-four patients were included in this study. Two out of three of all patients were male and the median age at diagnosis was 56 years old (Interquartile Range (IQR):48-64). The median follow-up was 25 months (IQR:15-50). The median RFS was 53.2 months (95% Confidence Interval (CI) could not calculated). 5-year survival rate was 64% and the median overall survival (OS) was 136 months (95% CI: 98-173). According to results of multivariate analysis, there was an increased risk for recurrence in patients with preoperative hypoalbuminemia (albumin < 3.5 gr/dl) [Hazard Ratio (HR): 5.3 (95% CI: 1.2-23.4]; p=0.005), and performed R1 resection [HR:5.7 (95% CI:1.2-25.3), p=0.02]. Additionally, patients administered chemoradiotherapy (CRT) had a lower risk for recurrence compared to those administered chemotherapy (CT) alone [HR:0.15 (95% CI:0.04-0.57), p=0.005]. **Conclusions:** Hypoalbuminemia in the preoperative setting and R1 resection were independent factors that affected gastric cancer recurrence. However, postoperative CRT decreased the recurrence rate of gastric cancer compared to CT alone. Low albumin level is an indicator of a systemic inflammatory response and according to previous studies, hypoalbuminemia was a poor prognostic factor in gastric cancer patients. Although CT alone is considered efficient for patients undergone D2 lymph node dissection, our study showed that CRT decreased the recurrence rates compared to CT alone. This result might be related to the higher number of patients undergone D1 dissection in our study. Research Sponsor: None.

186 Poster Session

Treatment patterns and overall survival for recurrent esophageal or gastroesophageal junctional cancer: A nationwide European population-based study. *First Author: Marieke Pape, Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, Netherlands*

Background: Esophageal cancer has a high risk for recurrence after treatment with curative intent. This study describes the characteristics of patients with esophageal or gastroesophageal junctional cancer at the time of recurrence, treatment patterns and overall survival (OS) after recurrence. **Methods:** Patients selected from the nationwide Netherlands cancer registry had received a primary diagnosis of non-metastatic squamous cell carcinoma or adenocarcinoma of esophagus or gastroesophageal junction in 2015 or 2016 and experienced recurrence after primary treatment with curative intent. Curative intent was defined as receiving resection (with or without [neo]adjuvant therapy) or definitive chemoradiotherapy (dCRT) without surgery. Recurrence within or after six months was calculated from resection date or end of dCRT. OS was calculated from recurrence and analysed using Kaplan-Meier curves with Log-Rank test. **Results:** We identified 856 patients who presented with disease recurrence after potentially curative treatment with resection (75%) or dCRT (25%). At recurrence, the majority of patients were male (78%),the median age was 68 years and 77% of patients had adenocarcinoma. Twenty-six percent of patients had disease recurrence within six months after curative treatment. Eighteen percent of patients had locoregional recurrence only, 48% distant recurrence only and 33% both locoregional and distant recurrence. Among patients with a distant recurrence, 37% had metastases in non-regional lymph nodes, 31% in the liver and 30% in the lung. After disease recurrence, 29% of patients received systemic therapy (chemo- or targeted therapy), 5% chemoradiotherapy, 1% surgery and 66% best supportive care only. The most common systemic treatment regimen was CapOx/FOLFOX (54%) and13% of patients received a targeted agent: trastuzumab containing regimen (n = 26) or paclitaxel and ramucirumab (n = 5). Among all patients, the median OS from date of recurrence was 4.4 months. Patients with recurrence within six months had a poorer median survival (2.1 months) compared to patients with recurrence after six months (5.7 months; $p < 0.001$). Median OS in patients with locoregional recurrence only was 7.4 months, distant recurrence only was 4.0 months, and both locoregional and distant recurrence was 3.4 months ($p < 0.001$). Patients with prior primary treatment with resection had median OS of 4.2 months and patients with prior dCRT of 5.1 months (p = 0.605). **Conclusions:** The majority of patients had distant metastases at disease recurrence and a small proportion received systemic therapy after recurrence. Overall prognosis was poor, and survival outcomes were poorest among patients with recurrence within six months of initial curative treatment suggesting a worse biological tumor behaviour. Research Sponsor: Bristol Myers Squibb.

187 Poster Session

Gastric cancer burden: Evidence from a safety-net hospital. *First Author: Arnold Forlemu, Creighton University School of Medicine, Phoenix, AZ*

Background: Gastric cancer is a leading cause of cancer-related deaths worldwide, with more than eleven thousand estimated gastric cancer deaths expected to occur this 2020 in the United States (US). Understanding the burden and trends in gastric cancer across demographics and different locations in the US is crucial to develop effective preventive strategies. This study describes, characterizes, and identifies high risk group gastric cancer patients, who may benefit the most from preventive and management strategies. **Methods:** A retrospective study was conducted between 2010 to 2019 at our institution to identify patients diagnosed with gastric cancer during that period. Data on demographics, risk factors, mode of presentation, pathology, site, type, and stage of gastric cancer were obtained. Chi-square was used to compare categorical variables. Regression analysis was used to evaluate factors associated with late-stage disease and cancer type. **Results:** A total of 111 patients were analyzed in this study. The median age of gastric cancer patients was 52 years (range 27 to 87 years). Most of the patients were Hispanic (70.3%), non-citizens (59.5%), were uninsured (69.4%), and 67.6% were living below the federal poverty level (FPL). Also, 31.5% of the patients had a family history of cancer, had diffuse-type adenocarcinoma (61%), late-stage disease (76.6%), 52.4% of the cancers were in the distal portion of the stomach. Uninsured patients were more likely to die compared to insured patients, however, this difference was not statistically significant (64.9% vs 47.1%, p = 0.077). Age below 40, Hispanic ethnicity, being uninsured, and living below FPL were associated with higher rates of late-stage disease and diffuse-type cancer ($p < 0.05$). **Conclusions:** Our data suggest a younger age at gastric cancer diagnosis than the national average. Moreover young, and uninsured Hispanics presented with advanced gastric cancer and may represent a high-risk target population for preventive strategies. Research Sponsor: None.

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Serum pepsinogen as a biomarker for gastric cancer: A nested case-control study using the prostate, lung, colorectal, and ovarian (PLCO) cancer screening trial data. *First Author: Haejin In, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY*

Background: Gastric cancer (GC) lacks specific symptoms, resulting in diagnosis at later stages and high mortality. Serum pepsinogen is a biomarker for atrophic gastritis, which is an intermittent phase in the development of GC. A serum based biomarker that indicates increased risk of GC would be useful for targeted prevention strategies. **Methods:** The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial is a large randomized trial conducted over 10 centers in the US between 1993 and 2001. Serum samples were collected at baseline and participants were followed for development of incident GC. ELISA-based pepsinogen tests were conducted on pre-diagnostic serum samples of patients who developed GC and age, sex, and race-matched controls. Pepsinogen negative (PG-) and positive (PG+) status was determined using pepsinogen I (PGI) and pepsinogen I to II ratio (PGR). Those with PGR $\geq$ 3 and PGI $>$ 70μg/L were considered PG- while those with lower levels on either or both were considered PG+. Cox proportional hazard models were used to determine the hazard ratio (HR) and 95% confidence intervals (95%CI) of PG+ for GC. To examine the association of PG with non-cardia and cardia GC separately, propensity matching was used to create control subsets matched on age, sex, and race. **Results:** Pepsinogen test results were available on 105 GC cases (70 non-cardia and 35 cardia) and 220 matched controls. Median and range of time from pepsinogen measurement to incident GC diagnosis was 78.6 and 3.0-152.2 months, respectively. GC patients were more likely to be PG+ (31.4% vs 5.5%, $p < 0.001$) and current smokers (20.0% vs 7.7%, p = 0.004) at baseline than controls. Compared to PG-, PG+ were at an increased risk of any GC (HR = 3.77; 95%CI = 2.50-5.71). After adjusting for family history of GC, smoking, and BMI, PG+ were still at a significantly increased risk of GC compared to PG- (adjusted HR = 4.42; 95%CI = 3.14-6.21). For 138 controls matched to 70 non-cardia cancers, PG+ were at an increased risk of non-cardia GC compared to PG- (HR = 5.65, 95%CI = 3.67-8.70; adjusted HR = 7.26, 95%CI = 4.84-10.90). For 70 controls matched to 35 cardia cancers, PG+ were not at greater risk of cardia GC compared to PG- (HR = 1.79, 95%CI = 0.72-4.44; adjusted HR = 1.95, 95%CI = 0.81-5.37). **Conclusions:** Pre-diagnostic serum pepsinogen levels from a large prospective cohort study predicted development of non-cardia GC but not cardia GC. PG could be considered as a potential risk biomarker to identify individuals at higher risk of non-cardia GC for targeted screening or interventions. Research Sponsor: U.S. National Institutes of Health.

189 Poster Session

Risk factors for gastric cancers in the United States: Variation by anatomic site and race/ethnicity. *First Author: Haejin In, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY*

Background: Gastric cancer (GC) is a high mortality cancer in the US. Differences in risk factors by anatomic location and race/ethnicity have been suggested but remain understudied in the US population. **Methods:** The Multiethnic Cohort (MEC) is a prospective cohort study that collected data on 5 racial/ethnic groups [Whites (W), Blacks (B), Latino (L), Japanese-American (JA), and Hawaiian (HA)] from Hawaii and Los Angeles in 1993-1996. Participants completed a detailed baseline survey and were followed for development of incident cancer. Cox regression models were used to calculate hazard ratios (HR) and 95% confidence intervals (CI) to identify GC risk factors by anatomic location (cardia, non-cardia) and by race/ethnicity. **Results:** Data from 192,626 participants was available. The cohort was 25% W, 17% B, 23% L, 28% JA, and 7% HA. During a median follow up of 20.3 years, 1,109 non-cardia and 201 cardia incident GCs were diagnosed. Older age (per year, non-cardia HR 1.08, 95% CI 1.07-1.92; cardia HR 1.06, 95% CI 1.05-1.09), male sex (non-cardia HR 1.6, 95% CI 1.4-1.8; cardia HR 3.0, 95% CI 2.1-4.4), and current (non-cardia HR 1.7, 95% CI 1.5-2.2, cardia HR 3.4, 95% CI 2.2-5.3) or former (non-cardia HR 1.3, 95% CI 1.1-1.5; cardia HR 2.0, 95% CI 1.3-2.9) smoking were associated with both cancer types. Notably, race/ethnicity (ref W: B HR 3.0, 95% CI 2.2-4.0; L HR 2.5, 95% CI 1.8-3.3; JA HR 3.9, 95% CI 3.0-5.1; HA HR 3.9, 95% CI 2.8-5.5), foreign-born (ref: self & parents US born: HR 1.3 95% CI 1.1-1.7), and family history of GC (OR 1.9, 95% CI 1.5-2.3) were associated with non-cardia GC. BMI $\geq$30 (HR 1.6, 95% CI 1.1-2.3), having $\geq$1 drink/week (HR 1.6, 95% CI 1.1-2.3), and being JA (ref W: HR 1.9, 95% CI 1.2-2.9) were associated with cardia GC. Risk factors other than age differed by race/ethnicity for non-cardia GC. Male sex was a risk factor for B, L and JA only. Having less than a high school education was a risk factor for B and JA only, smoking a risk factor for L and JA only, and having diabetes a risk factor for B only. Being in the highest sodium intake quartile was a risk factor among W and HA. A family history of GC was a risk factor for W, L, and JA. Having foreign-born parents was a risk factor for W and being foreign-born was a risk factor for JA. **Conclusions:** GC risk factors differ between subtypes and, for non-cardia, between race/ethnic groups. These differences provide an insight into the etiology of GC and the disproportionate incidence rates in high-risk groups, potentially aiding in the design of targeted intervention strategies. Research Sponsor: U.S. National Institutes of Health.

190 Poster Session

Is shift-work associated with increased risk of esophageal cancer for males? A meta-analysis. *First Author: Chenyu Sun, AMITA Health Saint Joseph Hospital Chicago, Chicago, IL*

Background: Globally, more than 570,000 people are diagnosed of esophageal cancer each year. Shift-work involving circadian disruption was designated as a probable cause of cancer by The International Agency for Research on Cancer. Previous studies investigating the relationship between shift-work and esophageal cancer among showed controversial results. Thus, this meta-analysis was conducted. **Methods:** A comprehensive literature search on PubMed was conducted to identify all relevant studies published prior to September 2020 according to the established inclusion criteria. The quality assessment was performed by the Newcastle-Ottawa Scale (NOS). The pooled odds risk (OR) and 95% confidence intervals (CI) were calculated to estimate the association between the shift-work and esophageal cancer risk. Random-effect or fixed-effect model was used to calculate the pooled OR, based on heterogeneity significance. Subgroup analyses were conducted based on night-shift versus rotating-shift. Sensitivity analysis and publication bias detection were also performed. All statistical analyses were performed using RevMan software (version 5.3; Cochrane library) and STATA 12.0 statistical software (Stata Corp., College Station, TX), and all P values were two-tailed, the test level was 0.05. **Results:** 21 articles were obtained from database searching, and 9 articles were obtained from other sources. 3 articles involving 52,098 participants were included. All studies were considered moderate to high quality. All included studies investigated only males on the association between shift-work and esophageal cancer risk. A statistically significant association between shift-work and increased esophageal cancer risk among males was found (OR 2.09, 95%CI: 1.48, 2.94, $P < 0.0001$, $I^2 = 29\%$). In subgroup analyses, night-shift work was associated with a non-statistically significant increased risk of esophageal cancer (OR 1.56, 95%CI: 0.96, 2.53, $P = 0.07$, $I^2 = 0\%$). In contrast, Rotating-shift was associated with increased esophageal cancer risk (OR 2.80, 95%CI: 1.72, 4.57, $P < 0.0001$, $I^2 = 0\%$). Sensitivity analysis confirmed the stability of the result. Funnel plot, Egger's test, and Begg's test found no publication bias of analysis (P = 0.572). **Conclusions:** The current meta-analysis demonstrates that shift-work is associated with increased esophageal cancer risk for males. However, no association between night-shift work and esophageal cancer risk was found. In contrast, association between rotating-shift work and increased esophageal cancer risk was found. Original studies on females regarding shift-work and esophageal cancer risk are lacking. More original studies on this topic for both male and female are needed to further explore shift-work impacts on esophageal cancer risk. Research Sponsor: None.

191 Poster Session

Evaluating the clinical impact of a shortened infusion duration for ramucirumab: A population pharmacokinetic model-based approach. *First Author: Paolo Abada, Eli Lilly and Company, Indianapolis, IN*

Background: Ramucirumab is a human recombinant immunoglobin G1 monoclonal antibody (mAb) antagonist of vascular endothelial growth factor receptor-2. Ramucirumab dosed at 8 mg/kg every 2 weeks or 10 mg/kg every 3 weeks, either as monotherapy or in combination with chemotherapy, was initially studied with as an intravenous infusion over 60 minutes following premedication with a histamine-1 receptor antagonist. Lengthy intravenous infusions are inconvenient for patients and increase the workloads of nursing and administrative staff. Shortening the infusion duration of ramucirumab could therefore benefit both patients and healthcare professionals. The current analysis determined the impact such a change could have on the pharmacokinetic (PK) profile of ramucirumab. Additionally, the relationship between infusion rate and incidence of immediate infusion-related reactions (IRRs; occurring on the day of administration), common adverse events associated with mAb infusions, was assessed. **Methods:** A population pharmacokinetic model was established using concentration–time data collected from 2522 patients who received one of five different ramucirumab regimens involving an intravenous infusion over ~60 minutes in 17 clinical studies. The final PK model was used to simulate concentration–time profiles and exposure parameters following ramucirumab infusion durations of 30 vs 60 min. Phase II/III clinical study data from patients receiving ramucirumab were pooled to assess the association between ramucirumab infusion rate and incidence of immediate IRRs using multivariate logistic regression analysis. **Results:** Ramucirumab infusions of 30- and 60-min durations resulted in equivalent concentration–time profiles and, hence, equivalent systemic exposure to ramucirumab. Among 3216 patients receiving ramucirumab in phase II/III studies, 254 (7.9%) had at least one immediate any-grade IRR; 17 (0.5%) experienced grade ≥3 immediate IRRs. The incidence of immediate IRRs (any grade or grade ≥3) was similar across infusion rate quartiles. Under multivariate logistic analysis, infusion rate was not significantly associated with an increased risk of an immediate IRR (odds ratio per 1 mg/min increase 1.014, 95% confidence interval 0.999, 1.030; p=0.071). **Conclusions:** Administering ramucirumab using different infusion durations (30 vs 60 min) did not affect ramucirumab exposure. Analysis of clinical study data showed a faster infusion rate was not associated with an increased risk of immediate IRRs. It is considered unlikely that shortening the infusion duration of ramucirumab will impact its clinical efficacy or overall safety profile, and is now an option for administration in the U.S. Research Sponsor: Eli Lilly and Company.

192 Poster Session

Lymph node mapping in gastric cancer: A pilot study in Western patients. *First Author: Akie Watanabe, University of British Columbia (UBC), Vancouver, BC, Canada*

Background: Adequate surgical lymphadenectomy is integral to the staging and treatment of gastric cancer. A number of Asian studies have explored the utility of lymph node (LN) mapping in gastric cancer but this in not commonly performed in Western countries. We sought to evaluate the utility and safety of LN mapping in Western patients. **Methods:** We conducted a pilot study of 13 patients with histologically proven non-metastatic gastric adenocarcinoma that received endoscopic peri-tumoral indocyanine green fluorescence (ICG) injections immediately prior to surgical resection to facilitate LN mapping. Illumination with ICG around the primary tumor, in lymphatic basins, tracts, and lymph nodes were confirmed by the PINPOINT system on recorded videos. Descriptive statistical analysis was performed. **Results:** Among the 13 patients enrolled, median age was 75 years and 7 were men. On pathologic review, 15% were T1, 54% were T2, and 69% had were node negative. Tumours were located in the proximal third in 1 patient, middle third in 2 patients and distal third in 10 patients. All patients had a laparoscopic subtotal gastrectomy and 10 patients had a D2 lymphadenectomy. 5 patients received preoperative and 7 received postoperative chemotherapy. The median number of LNs harvested was 26 [IQR 24-34]. Video confirmation of ICG mapping of the primary tumor, lymphatic basins, tracts, and LNs were obtained in all patients. All LNs identified with ICG uptake were removed with surgical lymphadenectomy. ICG mapped LNs fell outside the D1 distribution in 100% and outside the D1-plus distribution in 54% of cases. ICG mapped LNs were within the D2 distribution in all cases. No ICG related allergic reactions or procedural complications were observed. Postoperative complications included 2 grade A pancreatic fistulas, 1 gastrointestinal bleed, and 1 NSTEMI. Peri-operative morality was zero. **Conclusions:** We demonstrate ICG lymph node mapping as a safe and useful technique for identifying regional draining lymph nodes and for primary tumor localization in Western patients. The majority of cases found LNs draining outside the D1 and D1+ distributions, highlighting the importance of appropriate lymphadenectomies in gastric cancer. Research Sponsor: None.

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Impact of age on outcomes and symptoms in patients with advanced gastroesophageal cancer (GEC). *First Author: Fahad Almugbel, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia*

Background: Although age is a non-modifiable risk factor for most cancers, alone it is not very helpful in deciding on the best treatment for patients. Insufficient data exist in the oldest old (> 75 years) compared to young-old (65-75 years) and to younger (< 65 years) patients with de novo metastatic GEC regarding which factors influence response and outcomes. **Methods:** We retrospectively assessed all patients with de novo metastatic GEC seen from 2006-2015 at the Princess Margaret Cancer Center in Toronto-Ontario, Canada. We used Kaplan-Meier plots and Cox proportional hazards analyses to examine factors associated with progression-free survival (PFS) and overall survival (OS). To examine patient-reported outcomes we used the Edmonton Symptom Assessment System (ESAS) in the first six months of therapy using cross-sectional and longitudinal analyses. **Results:** A total of 580 de novo metastatic GEC patients were seen between 2006 and 2015. Of these (14%) were oldest old, (31%) were young-old (age 65-75) and 54% were younger (< 65 years). Most patients (67-80%) were male. Median OS for the entire cohort was 9.1 mo. (95% confidence interval (CI) 8.0 – 10.1); the shortest OS was in the oldest old group at 4.5 mo. compared to 8.7 mo. in young-old and 9.8 mo. in younger group, p < 0.001. PFS was also significantly different among the age groups (4.4 mo., 6.1 mo., and 6.5 mo., respectively), p = 0.0145. In a multivariate model predictors for OS were age (young-old group), number of metastasis, and Eastern Cooperative Oncology Group (ECOG) performance scale (PS). Similar predictors were found for PFS; however, age was not a significant factor. Of the 55 patients who provided ESAS data, 58% were < 65 and 42% were age≥ 65. The most common symptoms at presentation were fatigue, appetite, and well-being. There were no differences by age group (all p > 0.05). **Conclusions:** Patients age > 75 have poorer OS compared to younger age groups but PFS does not differ, suggesting similar benefits with treatment in appropriately selected older adults with advanced GEC. Symptom profiles were similar with age. Further comprehensive care is needed for older patients with advanced GEC to improve their survival. Research Sponsor: None.

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Laparoscopic versus open esophagectomy for patients with esophageal cancer: Systematic review and meta-analyses of randomized controlled trials. *First Author: Usama Waqar, Aga Khan University, Karachi, Pakistan*

Background: There has been an increase in the use of minimally invasive approaches for complex cancer operations. However, its benefit has not been clearly demonstrated for esophageal cancers when compared to open procedures. The purpose of this meta-analysis was to compare operative and postoperative outcomes for partial minimally invasive esophagectomy (MIE) versus open esophagectomy (OE) for patients with esophageal carcinoma. **Methods:** We conducted a systematic review using CENTRAL, PubMed, Global Index Medicus, ClinicalTrials.gov, EU Clinical Trials Register, and WHO ICTRP until August 30, 2020 without restrictions on publication date, language, or publication status. We included randomized controlled trials evaluating MIEs and partial MIEs including laparoscopic approach with OE for esophageal cancer. All trials including any one of our primary outcome measures -mortality and morbidity- were included. Two authors assessed trials for inclusion. Meta-analyses were conducted for categorical outcomes when heterogeneity was low (I^2< 50%). We reported risk ratios with 95% confidence intervals and GRADE quality of evidence based on our risk of bias assessment. **Results:** Of 5638 retrieved studies, 10 studies representing 6 trials consisting of 951 patients were included. 347 underwent partial MIE, 106 total MIE, and 498 OE. These were categorized into four cohorts: Co-A: Partial MIE versus OE (4 trials); Co-B: Partial MIE with thoracotomy versus OE (2 trials); Co-C: Partial MIE with cervical incision versus OE (2 trials); Co-D: Complete MIE versus OE (2 trials). Co-A revealed that partial MIE was associated with lower risk of serious adverse events (0.54[0.36-0.83]; 3 trials; 471 participants; I^2= 48%), with specifically lower rates of delayed gastric emptying (0.32[0.13-0.80]; 3 trials; 666 participants; I^2= 0%), pulmonary complications (0.49[0.29-0.84]; 3 trials; 471 participants; I^2= 27%), and mortality (0.67[0.54-0.83]; 4 trials; 692 participants; I^2= 0%). Co-B revealed that partial MIE with thoracotomy was associated with lower risk of pulmonary complications (0.61[0.38-0.99]; 2 trials; 231 participants; I^2= 0%) and mortality (0.66[0.50-0.87]; 2 trials; 231 participants; I^2= 0%). Co-C revealed that partial MIE with cervical incisions were associated with lower risk of serious adverse events (0.38 [0.22-0.64]; 1 trial; 240 participants), including pulmonary complications (0.29 [0.13-0.65]); 1 trial; 240 participants) and mortality (0.68[0.50-0.94]; 2 trials; 461 participants). Co-D revealed no significant differences between MIE and OE. All significant findings reported originated from high-quality evidence. **Conclusions:** When compared with completely open esophagectomy, partial MIE is associated with lower risk of mortality and serious adverse events, especially delayed gastric emptying and pulmonary complications. Research Sponsor: None.

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Duloxetine (DL) in treatment of oxaliplatin-induced peripheral neuropathy (PN). *First Author: Jeffrey Chi, Northwell Health Cancer Institute, Lake Success, NY*

Background: Oxaliplatin is commonly used to treat many GI cancers, especially colorectal (CRC), pancreatic (PC), and gastric (GC); however, peripheral neuropathy (PN) is the dose-limiting toxicity. Duloxetine (DL) is a second-generation selective serotonin and norepinephrine reuptake inhibitor (SNRI) used for the treatment of depression, anxiety, PN-associated with diabetes or ongoing pain due to medical conditions such as fibromyalgia. In this retrospective study, we evaluated the role of DL in reduction of oxaliplatin-induced neuropathy. **Methods:** Patients with GI cancers receiving oxaliplatin-based chemotherapy regimens from Nov 2016 to Nov 2019 were included. Patients with pre-existing PN from other etiologies such as diabetes, alcoholism, autoimmune disease, infections, hereditary, etc. were excluded. Neurological evaluations were performed serially before initiating DL and every 4 weeks thereafter according to Common Terminology Criteria for Adverse Events (CTCAE) v5.0. DL was given at 30 mg by mouth (PO) once daily and if tolerated after 3 days, was escalated to 60 mg once daily. Response was calculated to include number of patients with stable PN, improved PN, or no benefit. Adverse toxicities were graded. **Results:** 53 patients with median age of 53 years (range: 38 – 72) received DL for oxaliplatin-induced PN during treatment of GI cancers (CRC: 40%, PC:30%, GC: 10%, others: 10%). Improvement in PN from higher to lower grades was witnessed at 2 weeks in only 4 patients. At 4 week of DL, 3/53 (6%) patients improved from G3 PN to G2, 6/53 (11%) from G3 to G1, and 28/53 (52.8%) from G2 to G1, 14/53 (26%) and 2/53 (4%) had stable G3 and G2 PN respectively. At 8 week of DL, 10/53 (19%) of patients improved from G3 to G2, 3/53 (6%) from G2 to G1, 23/53 (43%) from G1 to G0, while 11/53 (21%), 2/53 (4%) and 4/53 (8%) remained stable at G1, G2 and G3 respectively. Overall DL resulted in a response rate of 89% and stable PN in 11%. 5 patients had to stop DL due to G3 drowsiness, insomnia, dry mouth and headache. Overall, DL was well-tolerated with majority of toxicities in G1-2 grade: dizziness (15%), drowsiness (11%), sexual side effects (11%), dry mouth (11%), insomnia (8%), headache (8%). In addition to PN, DL helped in improving depression in 50% of these patients and decreased the pain score in an additional 23%. **Conclusions:** DL resulted in a clinically significant improvement in PN-induced by oxaliplatin with manageable toxicity profile. Additionally, DL also improved depression and pain score. DL may be considered as an option in ameliorating PN in these patients, however, caution must be taken about DL and other drugs interaction. Our study warrants a prospective randomized trial to study the effectiveness of DL in treating oxaliplatin-induced PN. Moreover, cost effectiveness of DL in concurrently improving PN, depression and pain needs to be studied as well. Research Sponsor: None.

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Risk factors for the continuation of S-1 adjuvant chemotherapy for gastric cancer analyzed from the JCOG1104 phase III trial. *First Author: Takanobu Yamada, Kanagawa Cancer Center, Yokohama, Japan*

Background: The phase III trial (JCOG1104), comparing between 4- (6 months) and 8-course (1 year) of S-1 as the adjuvant chemotherapy for pathological stage II gastric cancer, registered a total of 590 patients between Feb. 2012 and Mar. 2017 until the study was terminated due to futility at the interim analysis (relapse-free survival at 3 years: 93.1% in the 8-course group and 89.8% in the 4-course group). Non-inferiority of the 4-course to the 8-course was not shown, highlighting a continuation of S-1 adjuvant chemotherapy for one year. This preplanned exploratory study investigated the risk factors for time to treatment failure (TTF). **Methods:** TTF was defined as the time from randomization to the date of termination of S-1 before the planned treatment period, relapse, or any cause of death, whichever came first, and censored on the last date of contact for a surviving patient after completing the planned treatment or the last date of S-1 in the patients under the protocol treatment when the trial was closed. The risk factor of TTF was analyzed by Cox proportional hazard model using the variables of the planned treatment period, PS, age, sex, body weight loss (percentile of the body weight loss at the registration compared with that before surgery: BWL), albumin, lymphocyte count, creatinine clearance (Ccr), extent of gastrectomy (total gastrectomy vs. others), surgical approach (open vs. laparoscopic approach), and blood loss during surgery. As TTF did not reach 50%, proportion of treatment completion was compared. **Results:** Among 590 registered patients, this study included 530 patients (273 in the 8-course group and 257 in the 4-course group) by excluding 24 ineligible patients, 7 patients who did not start the protocol treatment, and 29 patients with unavailable data for variables. Proportion of treatment completion at 6 months estimated by Kaplan-Meier method were 89.2% in the 4-course group and 84.6% in the 8-course group (P=0.1204), and that at 1 year was 73.6% in the 8-course group. Risk factors of TTF before 6M identified by multivariable analysis with stepwise selection method including both groups, in which all patients completed treatment were censored at 6 months, were the planned treatment period (4-courses vs. 8-course, HR 0.611, 95% Confidence interval (CI) 0.375-0.996, P=0.0482), age (continuous value, HR 1.039, 95% CI 1.004-1.074, P=0.0266), and Ccr (<80 vs. >80 ml/min, HR 1.943, 95% CI 1.105-3.415, P=0.0211). As for the TTF in the 8-course group, BWL (>10% vs <10%, HR 2.167, 95% CI 1.269-3.703, P=0.0046) and Ccr (<80 vs. >80 ml/min, HR 1.900, 95% CI 1.186-3.045, P=0.0076) were independent risk factors. **Conclusions:** Compared to 8-course, 4-course of S-1 adjuvant chemotherapy was associated with a higher 6-month proportion of treatment completion. When planning the adjuvant chemotherapy with S-1 for one year, BWL (>10%) and low Ccr (<80 ml/min) were risk factors for treatment failure. Clinical trial information: UMIN000007306. Research Sponsor: None.

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The association of renal function with safety and efficacy of cisplatin plus S-1 (CS) therapy and docetaxel plus cisplatin plus S-1 (DCS) therapy in patients with advanced gastric cancer (AGC): An exploratory analysis of JCOG1013. *First Author: Shuichi Hironaka, Division of Medical Oncology and Hematology, Oita University Faculty of Medicine, Yufu, Japan*

Background: JCOG1013, a phase III study comparing CS therapy with DCS therapy for AGC, failed to demonstrate the superiority of DCS to CS in overall survival (OS) (Yamada Y, Lancet GH 2019). Because cisplatin and gimeracil (an inhibitor of dihydropyrimidine dehydrogenase contained in S-1) are excreted in urine, it is speculated that renal dysfunction may affect the safety and efficacy of CS and DCS in patients (pts) with AGC. **Methods:** Among 741 all randomized pts, pts with serum creatinine level < 1.2 mg/dL were included in this study. Pts were categorized by creatinine clearance (CrCl) and treatment into A1 (CrCl ≥ 80 mL/min, CS), A2 (60 < CrCl < 80, CS), A3 (CrCl < 60, CS), B1 (CrCl ≥ 80, DCS), B2 (60 < CrCl < 80, DCS), and B3 (CrCl < 60, DCS). Adverse events, OS, progression-free survival (PFS), objective response rate (ORR) were compared by CrCl in group A (A1 vs. A2 vs. A3) and group B (B1 vs B2 vs B3), respectively, and between the treatment groups according to CrCl (A1 vs. B1, A2 vs. B2, A3 vs. B3). **Results:** Of 723 pts (169/136/57 in A1/A2/A3 and 170/138/53 in B1/B2/B3), the median CrCl was 94.1/71.9/53.4 mL/min in A1/A2/A3 and 98.2/70.0/55.6 mL/min in B1/B2/B3 group. The incidence of Grade (G) 4 hematological toxicity was 7.8/16.3/25.9% in A1/A2/A3 (P < 0.01), and 29.1/29.3/22.0% in B1/B2/B3 (P = 0.44), and that of G3-4 non-hematological toxicity was 46.1/64.4/64.3% in A1/A2/A3 (P < 0.01) and 54.6/64.7/74.5% in B1/B2/B3 (P < 0.01), respectively. The median OS was 15.4/15.5/15.4 months in A1/A2/A3 (P = 0.89) and 15.3/13.7/13.7 months in B1/B2/B3 (P = 0.72). The median PFS was comparable in A1/A2/A3 (7.1/6.8/6.2 months, P = 0.88) and B1/B2/B3 groups (7.5/7.2/7.8 months, P = 0.85). ORR showed no significant difference in A1/A2/A3 (58.9/57.8/46.9%, P = 0.31) and B1/B2/B3 groups (62.0/61.5/51.5%, P = 0.36). Comparisons between treatment arms according to CrCl (A1 vs. B1, A2 vs. B2, A3 vs. B3) did not show any significant difference in OS (P = 0.88, 0.65, 0.83) and PFS (P = 0.91, 0.63, 0.46). **Conclusions:** In this exploratory analysis of JCOG1013, CrCl might be associated with safety (G4 hematological toxicity for CS, and G3-4 non-hematological toxicity for CS and DCS), but not with efficacy in either group. Clinical trial information: 000007652. Research Sponsor: Ministry of Health, Labour and Welfare and Japan Agency for Medical Research and Development.

198 Poster Session

Selecting the optimal neoadjuvant treatment approach based on the risk of an involved surgical margin in locally advanced adenocarcinoma of the esophagus and esophagogastric junction. *First Author: Tim Spencer, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, United Kingdom*

Background: Optimal neoadjuvant (NA) treatment for adenocarcinoma of the esophagus and esophagogastric junction is unknown. This study aims to evaluate an approach of offering NA chemoradiotherapy (CRT) to T3/T4 tumours with a threatened circumferential resection margin (CRM) on staging imaging (computerized tomography/endoscopic ultrasound/positron emission tomography) and NA chemotherapy (CT) to T3/T4 tumours with a non-threatened CRM. **Methods:** Cases with clinically staged T3/T4 tumours who underwent a radical esophagectomy at a single tertiary referral centre between 2013 and 2019 were retrospectively reviewed. NA CRT was given as 41.4Gqy in 23 fractions with weekly carboplatin/paclitaxel and NA CT was given as a platinum based combination. Survival outcomes are described using the Kaplan-Meier method and calculated from NA treatment start. **Results:** 81 patients were identified - 18 (22%) received CRT and 63 (78%) received CT. More cases had Stage IVA disease in the CRT group (28% vs. 8%). CT consisted of a platinum/fluoropyrimidine doublet (43%), triplet with epirubicin (51%) or FLOT (6%). Median follow up was 68 months. Median length of post-operative stay (11 days for both) and rate of death within 90 days of surgery (6% vs. 3%) were similar. Rates of R0 resection (100% vs. 67%) and tumour regression grade 1/2 (55% vs. 14%) favoured CRT. There was no difference in overall survival (HR 0.92 (95%CI: 0.45-1.87), p=0.81). Estimated 3 year relapse-free survival was 39% (95%CI: 14-64) for CRT and 45% (95%CI: 33-58) for CT. Location of first relapse was local, distant or both in 0%, 75% and 25% for CRT and 6%, 50% and 44% for CT. In the CT group, overall survival was inferior for patients with an R1 resection (HR: 6.30 (95%CI 3-14), p<0.001). **Conclusions:** Neoadjuvant chemoradiotherapy for CRM-threatened cases of locally advanced adenocarcinoma of the esophagus and esophagogastric junction resulted in a very low rate of R1 resection and similar survival outcomes to non-CRM-threatened cases treated with neoadjuvant chemotherapy. Tailoring the neoadjuvant approach based on risk to CRM involvement appears feasible and warrants further investigation. Research Sponsor: None.

Summary of key stage, pathology and survival data.

	Neoadjuvant Chemotherapy	Neoadjuvant Chemoradiotherapy
N	63 (77.8%)	18 (22.2%)
Stage III / Stage IVA	58 (92%) / 5 (8%)	13 (72%) / 5 (28%)
Positive Resection Margin (R1)	21 (33%)	0 (0%)
Tumour Regression Grade 1-2	9 (14.3%)	10 (55%)
90 day post-operative Mortality	2 (3%)	1 (6%)
Median Survival (months)	34 (18.3-64.2)	34 (21.4-37.3)
Est. 3yr Overall Survival	49.6% (37.0-62.2)	45.3% (17.3-73.3)
Est. 3yr Relapse-free Survival	45.2% (32.7-57.7)	39.1% (13.6-64.6)

199 Poster Session

RAINBOW-Asia: A randomized, multicenter, double-blind, phase III study of ramucirumab plus paclitaxel versus placebo plus paclitaxel in the treatment of advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma following disease progression on first-line chemotherapy with platinum and fluoropyrimidine. *First Author: Rui-hua Xu, Sun Yat-sen University Cancer Centre, Guangzhou, China*

Background: Ramucirumab (RAM), a fully human IgG1 monoclonal antibody targeting vascular endothelial growth factor receptor 2, has been approved in combination with paclitaxel (PTX) in patients with advanced gastric cancer in the second-line setting outside of China in around 80 countries based on the significant overall survival (OS) benefit in the global phase 3 RAINBOW study. RAINBOW-Asia was a bridging study of RAINBOW to evaluate the efficacy and safety of RAM in a predominantly Chinese population. **Methods:** Patients with advanced gastric or gastro-esophageal junction (GEJ) adenocarcinoma who experienced disease progression on first-line chemotherapy (platinum plus fluoropyrimidine with or without an anthracycline) were randomized at a 2:1 ratio to receive RAM (8 mg/kg) on day 1 and 15 plus PTX (80 mg/m^2) on day 1, 8, and 15 of a 28-day cycle or placebo (PL) plus PTX. Randomization was stratified by ECOG Performance Status (0 versus 1) and peritoneal metastases (yes versus no). The co-primary endpoints were PFS and OS. **Results:** From Mar 2017 to Jun 2020, 440 pts were randomized (RAM+PTX: 294; PL+PTX: 146). Median PFS was significantly improved with RAM+PTX compared to PL+PTX (4.14m *vs*. 3.15m; HR = 0.765 [95% CI: 0.613 to 0.955]; p = 0.0184). Median OS was 8.71m with RAM+PTX and 7.92m with PL+PTX (HR = 0.963 [95% CI: 0.771 to 1.203]; p = 0.7426). Grade ≥ 3 treatment-emergent adverse events (TEAEs) occurring in > 5% of patients with RAM+PTX were: neutrophil count decreased (54.3% RAM+PTX; 38.6% PL+PTX), white blood cell count decreased (43.3% *vs*. 29.0%), anaemia (15.7% *vs*. 16.6%), hypertension (7.2% *vs*. 6.2%), and febrile neutropenia (6.1% *vs*. 0.7%). **Conclusions:** The combination of RAM+PTX as 2nd-line therapy demonstrated a statistically significant PFS benefit, and OS benefit consistent with RAINBOW study in a predominantly Chinese population with advanced gastric and GEJ cancer. The safety profile of RAM was consistent with previous studies. No new safety signal was observed. Clinical trial information: NCT02898077. Research Sponsor: Eli Lilly and Company.

200 Poster Session

A phase I study to evaluate the safety of multiantigen stimulated tumor specific cell therapy (MASCT-I) in subjects with advanced gastric cancer. *First Author: Zhaode Bu, Department of Gastrointestinal Surgery, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Peking University Cancer Hospital & Institute, Beijing, China*

Background: Gastric cancer was the fifth cancer world wide and the third leading cause of cancer-related death. PD-1 antibody has been approved for treatment in gastric cancer patients with positive expression of PD-L1 and microsatellite instability. MASCT-I (Multi-Antigen Stimulated Cell Therapy-I Injection) is an autologous non-engineered immune cell therapy for solid tumor, it is composed of multiple-antigen peptides(15 tumor associated antigens) loaded mature dendritic cells (DCs) and in vitro DC stimulated and proliferated effector T cells, the combination of MASCT-I and PD1 antibody could have a synergistic anti-tumor effect. **Methods:** This is a single center, phase I trial to explore the safety and tolerance of the combination of MASCT-I and PD-1 antibody in advanced gastric cancer (NCT03393416). 15 patients with PD-L1 expression or microsatellite instability were enrolled between April 2018, and June 2019. Camrelizumab was administered once every two weeks, DC and T cells were sequential administered once a month. Therapy continued until the disease progresses. **Results:** Only adverse reaction below grade 2 was observed related to MASCT-I , such as fever, fatigue etc. Abnormal liver function and reactive capillary hyperplasia may be related to Camrelizumab. Among the 15 patients, the longest treatment duration was 18.9 months, and the median progression-free survival (mPFS) was 3.93 months, among which, mPFS of patients with microsatellite instability is 10.23 months, mPFS of patients expressing PD-L1 is 2.35 months, which is slightly higher than the historical data of Camrelizumab alone in the treatment of advanced gastric cancer (8 weeks for mPFS). The patient 1002 always had high content of CD8+ cells and NK cells and the positive immune response in their bodies, which may plays a role in killing the tumor cells. **Conclusions:** The combination of MASCT-I and Camrelizumab in the treatment of advanced gastric cancer or gastroesophageal junction cancer is a safe treatment regimen, and its efficacy deserves further study. Clinical trial information: NCT03393416. Research Sponsor: HRYZ BIO Co., Ltd.

201 Poster Session

Perioperative FLOT plus anti-PD-L1 avelumab (FLOT-A) in resectable oesophagogastric adenocarcinoma (OGA): Interim safety analysis results from the ICONIC trial. *First Author: Avani Athauda, The Royal Marsden Hospital, Surrey, United Kingdom*

Background: ICONIC is a single-arm phase II trial investigating the safety and efficacy of perioperative FLOT-A in resectable OGA. Following a 3+3 design safety run-in phase, standard dose FLOT with 10mg/kg IV avelumab (dose level 0) q2weeks was taken forward into the main study. The aims of this pre-planned interim analysis were to assess perioperative safety and R0 resection rates. **Methods:** The interim analysis occurred once the 15th patient treated at dose level 0 reached 30 days post-surgery. **Results:** At data cut-off, 15 patients had received at least one cycle of FLOT-A and had undergone resection. The median age of patients was 63y (range: 25 – 73). 71% had an ECOG PS of 0. 60% of tumours were staged as T3 at baseline and 40% T2; 67% were N0, 7% N1 and 27% N2. Due to 5-FU related cardiac toxicity, two patients switched to alternative chemotherapy without 5-FU and avelumab. 13/15 patients (87%) completed 4 cycles of pre-operative FLOT-A; of these, five patients had avelumab omitted for one cycle for toxicity evaluation and management. 9/15 patients (60%) experienced a G3/4 adverse event (AE). These were FLOT-A-related in 8/15 patients (53.3%). The commonest G3/4 AEs were febrile neutropenia, neutropenia and diarrhoea. Median time from last chemotherapy to surgery was 6.4 weeks. No delays or failure to proceed to surgery occurred due to avelumab-related complications. 7% of patients had an American Society of Anaesthesiologists (ASA) preoperative risk score of I, 47% a score of II and 47% a score of III. 73% of patients had operations involving a thoracic approach (10 minimally invasive Ivor-Lewis oesophagogastrectomy with two field radical lymphadenectomy, 1 left thoracoabdominal oesophagogastrectomy and 4 gastrectomy with D2 lymphadenectomy). Median time to extubation was 6h (IQR: 4-24). The median Acute Physiology and Chronic Health Evaluation (APACHE) score at day 1 post-op was 12 (IQR: 10-15) with a median of 3 days (IQR: 2-4) of CCU care. No unexpected complications were reported intra-operatively or during post-operative recovery in FLOT-A treated patients. 5/14 evaluable patients at data cut-off (35.7%) had Clavien-Dindo grade II post-operative complications and 3/14 (21.4%) grade IIIa complications; of these 1 patient had an anastomotic leak that was treated endoscopically. There were no emergency re-operations. All 15 patients achieved R0 resections and were discharged home after a median of 13d (IQR: 11-16) in hospital. **Conclusions:** To date, FLOT-A has not led to unexpected or unusually severe perioperative complications in the context of major complex upper GI surgery for resectable OGA. Clinical trial information: NCT03399071. Research Sponsor: Merck.

202 Poster Session

FRONTiER: A feasibility trial of nivolumab with neoadjuvant CF or DCF therapy for locally advanced esophageal carcinoma (JCOG1804E)—The short-term results of cohort A and B. *First Author: Shun Yamamoto, Division of Gastrointestinal Medical Oncology, National Cancer Center Hospital, Tokyo, Japan*

Background: The standard neoadjuvant chemotherapy (NAC) in Japan for locally advanced esophageal squamous cell cancer (ESCC) is CDDP + 5-FU (CF). Immune checkpoint inhibitors (ICI) such as nivolumab provide a survival benefit in ESCC, and have potential as NAC agents in lung, skin, and breast cancers, amongst others. However, whether ICI are efficacious in combination with cytotoxic agents, and whether ICI impact the safety of subsequent surgery after they are used as NAC for ESCC patients (pts) is currently unclear. **Methods:** FRONTiER is a multi-cohort phase I study designed to evaluate the safety and efficacy of ICI combined with NAC in ESCC. Histologically proven ESCC pts with cT1N1-3M0 or cT2-3N0-3M0 (8th-UICC TNM classification), 20–75 years old, PS ≤ 1, no prior therapies against any cancer were eligible. The primary endpoint was the incidence of dose-limiting toxicities (DLT) from the initial dose to the 30th postoperative day. This study contained 4 experimental cohorts, the NAC regimen of cohort A consisted of 2 courses of CDDP at 80 mg/m^2, nivolumab at 360 mg/body on day 1 and 5-FU at 800 mg/m^2 on days 1–5, q3wks. The regimen of cohort B consisted of one administration of nivolumab at 240 mg/body 2 weeks before chemotherapy, followed by the same treatments as cohort A. **Results:** Thirteen pts were enrolled to cohort A (n = 6) and B (n = 7). Characteristics were follows; median age: 62 (range: 34–75), PS 0/1: 9/4 pts, clinical stage I/II/III: 2/1/10 pts. One pt in cohort B was excluded from safety evaluation due to R2 resection, no DLTs were observed in 12 pts. The most frequent adverse events (≥ grade 3) were neutropenia in 6 pts during NAC, lung infection in 1, hyperglycemia in 1, pleural effusion in 1, infection (right neck) in 1, anemia in 1, abdominal pain in 1, and anatomic leakage in 1 during the postoperative period. Within 30 days post-operation, grade 2 adrenal insufficiency was observed in 1 pt of cohort B. No grade 4 adverse events or treatment-related deaths were seen. All pts received two courses of NAC + nivolumab and R0 resection was achieved in 12 pts (92.3%) without interruption of treatment. A pathological complete response was achieved in 2 pts (33.3%) in cohort A. **Conclusions:** Neoadjuvant CF + nivolumab with/without prior administration of nivolumab followed by surgery for locally advanced ESCC was well tolerated and showed promising efficacy. Clinical trial information: NCT03914443. Research Sponsor: ONO Pharmaceuticals.

203 Poster Session

A phase II study of perioperative capecitabine plus oxaliplatin for clinical SS/SE N1-3 M0 gastric cancer (OGSG1601). *First Author: Atsushi Yasuda, Surgery, Kindai University School of Medicine, Osakasayama, Japan*

Background: D2 gastrectomy followed by adjuvant S-1 is one of the standard therapy for the patients (pts) with stage III gastric cancer (GC) in Japan; however, the outcome is not satisfactory. We examined the efficacy of perioperative capecitabine and oxaliplatin (CapeOx) in pts with clinical SS/SE N1-3 M0 GC. **Methods:** The eligibility criteria included histopathologically confirmed clinical T3(SS)/T4a(SE) N1-3 M0 GC according to the Japanese Classification of GC (JCGC; 3rd English Edition). Three cycles of neoadjuvant CapeOx (NAC; capecitabine, 2,000 mg/m^2 for 14 days; oxaliplatin, 130 mg/m^2 on day 1, every 3 weeks) were administered, followed by five cycles of adjuvant CapeOx after D2 gastrectomy. The primary endpoint was the pathological response rate (pRR) according to JCGC (≥Grade 1b). **Results:** Thirty-seven pts were enrolled from April 2016 to May 2017, and fully evaluated for efficacy and toxicity. Thirty-three pts (89.2%) completed the planned three cycles of NAC and underwent gastrectomy, with an R0 resection rate of 78.4% (n = 29) and a pRR of 54.1% (n = 20, p = .058; 90% confidence interval [CI], 39.4-68.2) were demonstrated. The relative dose intensity (RDI) of capecitabine and oxaliplatin were 90.5% and 91.9%, respectively. Among 27 pts who initiated AC, 21 (63.6%) completed the treatment, and the RDI of capecitabine and oxaliplatin were 80.9% and 65.1%, respectively. Grade 3-4 toxicities during NAC included neutropenia (8%), thrombocytopenia (8%), and anorexia (8%) and during AC included neutropenia (37%), diarrhea (4%), and anorexia (4%), but no treatment-related death was reported. The overall survival (OS) rate and relapse free survival (RFS) rate at 3 years was 83.8% (95% CI, 72.7-96.5%) and 73.0% (95% CI, 60.0-88.8%), respectively. Subgroup analyses according to residual tumor after surgery (R status) showed a 3-year OS and RFS rate of 86.2% (95% CI, 74.5-99.7%) and 75.7% (95% CI, 63.0-90.8%) for R0. **Conclusions:** Perioperative CapeOx showed good feasibility and favorable prognosis with sufficient pathological response, although statistical significance at .058 did not reach the commonly accepted cutoff of .05. The data obtained using this novel approach warrant further investigations. Clinical trial information: 000021641. Research Sponsor: Yakult Honsha Co., Ltd.

204 Poster Session

Three-year follow-up of ATTRACTION-3: A phase III study of nivolumab (Nivo) in patients with advanced esophageal squamous cell carcinoma (ESCC) that is refractory or intolerant to previous chemotherapy. *First Author: Keisho Chin, Department of Gastroenterology, The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan*

Background: Previous results from the ATTRACTION-3 phase 3 trial demonstrated a significant improvement in overall survival and a favorable safety profile compared with taxane chemotherapy (CT) in previously-treated ESCC patients. To our knowledge, no long-term efficacy and safety data of this immune checkpoint inhibitor has been reported in ESCC. Herein, we report the three-year survival data of Nivo in ESCC. **Methods:** In ATTRACTION-3, 419 patients with unresectable advanced or recurrent ESCC refractory or intolerant to 1 prior fluoropyrimidine/platinum-based CT were randomized in a 1:1 ratio to receive Nivo (N = 210) or the investigator's choice of CT (paclitaxel or docetaxel) (N = 209) until disease progression or unacceptable toxicity. The primary endpoint was overall survival (OS). A subgroup analysis of OS according to the best overall response (BOR) was performed. The onset of treatment-related adverse events of special interest over time in the Nivo arm was also evaluated. **Results:** As of data cut-off on 25 May 2020, 3 years after the last patient was enrolled, the median OS (mOS) was 10.91 months with Nivo versus 8.51 months with CT [hazard ratio (HR) 0.79; 95% confidence interval (CI) 0.64-0.97]. The OS rates of patients with Nivo and CT were 20.2 % and 13.5 % at 24 months, and 15.3% and 8.7% at 36 months, respectively. In the subgroup analysis of OS by BOR, mOS in CR/PR patients were 19.91 and 15.41 months (HR 0.84, 95%CI 0.46-1.54) and that in SD patients were 17.38 and 9.36 months (HR 0.45, 95%CI 0.26-0.78) in the Nivo and CT arm, respectively. Furthermore, mOS in PD patients were 10.91 and 6.18 months (HR 0.56, 95%CI 0.33-0.95) in the Nivo and CT arm, respectively. No new safety signals were detected during the three-year follow-up. Time to onset of the event of special interest was within the range of events previously observed in other indications. **Conclusions:** At three-year follow up, Nivo continued to show improved OS over CT in pretreated patients with advanced ESCC patients. Nivo showed a longer mOS than CT regardless of BOR. During the three-year follow-up, no new safety signals were observed. Clinical trial information: NCT02569242. Research Sponsor: Ono pharmaceutical company, Bristol Myers Squibb.

205 Poster Session

Feasibility study of TAS-118 plus oxaliplatin as perioperative chemotherapy for patients with locally advanced gastric cancer (APOLLO-11). *First Author: Daisuke Takahari, The Cancer Institute Hospital of the Japanese Foundation for Cancer Research, Tokyo, Japan*

Background: TAS-118 (S-1 and leucovorin) + oxaliplatin (L-OHP) improved overall survival (OS) compared to S-1 + cisplatin for patients (pts) with advanced gastric cancer (GC) (Kang, Lancet Oncol. 2020). This study investigated the feasibility of peri (pre and post)-operative (op) chemotherapy (chemo) with TAS-118 ± L-OHP in pts with locally advanced resectable GC. While it was reported that pre-op TAS-118 + L-OHP followed by D2 gastrectomy was well tolerated and showed promising efficay (Takahari, ASCO-GI. 2020), the recommended post-op chemo regimen, TAS-118 or TAS-118 + L-OHP, has yet to be determined. **Methods:** Eligible pts with GC of clinical T3-4N1-3M0 were enrolled. The protocol treatment consisted of pre-op chemo with 4 courses of TAS-118 (40-60 mg/body, orally, twice daily, 7 days) + L-OHP (85 mg/m^2, intravenously, day 1) in a 2-week cycle, and gastrectomy with D2 lymphadenectomy, followed by post-op chemo with 12 courses of TAS-118 (step 1) and 8 courses of TAS-118 + L-OHP (step 2). Step 2 was started if the dose-limiting toxicity (DLT) occurred in < 6 of 10 pts in step 1. Up to 20 pts were included in the analysis of feasibility after a recommended regimen was determined. **Results:** Between December 2016 and February 2019, 45 pts were enrolled. The numbers of pts with cT3/4a and cN1/2/3 were 13/32 and 25/17/3, respectively. Excluding 14 pts (4 achieving pathological complete response, 4 not satisfying the criteria for post-op chemo, 3 physician judgement or pt withdrawal, 2 progressive disease, 1 adverse event [AE]), 31 pts (11/20 in step 1/2) received the post-op chemo. No DLT was observed in either step. The post-op chemo completion rate was 90.9% (95% CI, 63.6-99.5) in step 1 and 80.0% (95% CI, 59.9-92.9) in step 2. The median relative dose intensity of TAS-118 in step 1 was 83.3%, and those of TAS-118 and L-OHP in step 2 were 69.9% and 74.3%, respectively. One pt in step 2 discontinued post-op chemo due to AE. Grade ^{3} 3 AEs observed in ≥ 10% of pts were weight loss in both step 1 and step 2 (2 in each), and hypokalemia (n = 3) and neutropenia (n = 2) in step 2. At 1-year follow-up after the last pt was enrolled, recurrence-free survival and OS rates were 91.1% (95% CI, 78.0-96.6) and 100%, respectively at 12 months, and 69.1% (95% CI, 49.6-82.3) and 95.5% (95% CI, 71.9-99.3), respectively at 24 months. **Conclusions:** Taken together with the feasibility and efficacy of pre-op chemo, peri-op chemo with TAS-118 + L-OHP with D2 gastrectomy was well tolerated and showed promising efficacy. Clinical trial information: UMIN000024688. Research Sponsor: Taiho and Yakult.

206 Poster Session

Final results of a phase III trial to evaluate bursectomy for patients with subserosal/serosal gastric cancer (JCOG1001). *First Author: Hitoshi Katai, National Cancer Center Hospital, Tokyo, Japan*

Background: We previously reported that the superiority of bursectomy was not demonstrated for subserosal(SS)/serosal(SE) gastric cancer by the second interim analysis performed with 54% of the expected events observed. We report the final 5-year follow-up data. **Methods:** Eligibility criteria included histologically proven adenocarcinoma of the stomach, cT3(SS) or cT4a(SE). Patients were intraoperatively randomized to non-bursectomy arm or bursectomy arm. Primary endpoint was overall survival (OS), and secondary endpoint was relapse-free survival (RFS). A total of 1,200 patients were required to detect a hazard ratio of 0.77 with a one-sided alpha of 5% and 80% power. **Results:** A total of 1204 eligible patients with cT3 / cT4a gastric cancer were randomized (602 in non-bursectomy arm, 602 in bursectomy arm, respectively). Patients' background and operative procedures were well balanced between the arms. The 5y-OS were 76.5% (95% CI, 72.8 to 79.7) in non-bursectomy arm and 74.9% (71.2 to 78.2) in bursectomy arm. Hazard ratio (HR) for bursectomy was 1.03 (0.83-1.27, one-sided p = 0.598). The 5y-RFS were 70.7% (66.9 to 74.2) in non-bursectomy arm and 66.8% (62.9 to 70.5) in bursectomy arm [HR: 1.131 (0.93-1.38)]. HR for death was almost similar in all sub-categories (0.73-1.29) except cN2 (13th edition of Japanese Classification of Gastric Carcinoma); HR classified by cN was 1.06 (95% CI: 0.75-1.49) for cN0 (n = 521), 1.25 (0.92-1.71) for cN1 (n = 525), and 0.59 (0.32-1.06) for cN2 (n = 158) (p = 0.048 for interaction). The most frequent site of recurrence was the peritoneum [74 (12.3%) in non-bursectomy arm, 73 (12.1%) in bursectomy arm], and bursectomy arm showed a trend of increasing liver metastasis (n = 45, 7.5%) as compared with non-bursectomy arm (n = 33, 5.5%). Six independent poor prognostic factors were identified by multivariable analysis for OS: age ≥ 66 (vs. ≤ 65) (HR, 1.30; 95% CI, 1.04-1.62), macroscopic type 3/5 (vs. type 0/1/2) (1.43; 1.15-1.79), total gastrectomy (vs. distal gastrectomy) (1.44; 1.03-2.02), pT3 (vs. pT1-2) (1.77; 1.17-2.676), pT4 (vs. pT1-2) (3.00; 1.99-4.53), pN1 (vs. pN0) (2.34; 1.52-3.59), pN2-3b (vs. pN0)(4.02; 2.82-5.74) and adjuvant chemotherapy (vs. without chemotherapy) (0.53; 0.42-0.67), but bursectomy was not significant (1.10 0.89-1.36). **Conclusions:** In the final analysis as well as in the interim analysis, bursectomy was not recommended as a standard treatment for cT3 or cT4 gastric cancer. Clinical trial information: UMIN000003688. Research Sponsor: Japan Agency for Medical Research and Development.

207 Poster Session

Nivolumab in advanced esophageal squamous cell carcinoma (ATTRACTION-1/ONO-4538-07): Minimum of five-year follow-up. *First Author: Ken Kato, National Cancer Center Hospital, Tokyo, Japan*

Background: ATTRACTION-1/ONO-4538-07 (AT-1), an open-label, single-arm, multicenter phase 2 clinical trial conducted in Japan, evaluated the clinical activity and safety of nivolumab in patients with advanced esophageal squamous cell carcinoma (ESCC) refractory/intolerant to fluoropyrimidine-, platinum-, and taxane-based chemotherapy. We previously reported the 2-year follow-up findings of AT-1, in which nivolumab demonstrated antitumor activity with a manageable safety profile for these patients. Here we report the final findings from AT-1 at a minimum follow-up of 5 years. **Methods:** Patients aged ≥20 years with an Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0-1 received 3 mg/kg nivolumab intravenously every 2 weeks in 6-week cycles until disease progression or unacceptable toxicity. The primary endpoint was centrally-assessed objective response rate (ORR), defined as the proportion of patients whose best overall response was either a complete or partial response. Secondary endpoints included overall survival (OS), investigator-assessed ORR, progression-free survival (PFS), change in tumor burden, time to response, time to disease progression, and duration of response. **Results:** Between February 25 and November 14, 2014, a total of 65 patients were enrolled. Sixty-four patients were evaluated for the efficacy, and all patients were evaluated for the safety. At the final database lock on August 6, 2020, 11 (17.2%, 95% confidence interval [CI] 9.9-28.2) of 64 patients had an objective response by central assessment. The median OS was 10.8 months (95% CI, 7.4-13.9), and the estimated 5-year OS rate was 6.3% (95% CI, 2.0-14.0). The median PFS was 1.5 months (95% CI, 1.4-2.8), and the estimated 5-year PFS rate was 6.8% (95% CI, 2.2-15.1). Treatment-related adverse events that occurred with a frequency of > 10% were diarrhea and rash. The presentation will include characteristics of long-term survivors as well as detailed efficacy and safety data of nivolumab. **Conclusions:** This final assessment represents the longest follow-up of patients with advanced ESCC treated with nivolumab. Nivolumab demonstrated continued long-term efficacy in these patients based on a minimum of 5-year long-term survival update of AT-1. Furthermore, no new safety signals with nivolumab were identified during long-term follow-up. These findings are consistent with those of nivolumab monotherapy for various types of cancer. Clinical trial information: No.142422. Research Sponsor: Ono Pharmaceutical, Bristol-Myers Squibb.

208 Poster Session

The impact of nutrition support in advanced gastric adenocarcinoma patients treated with chemotherapy. *First Author: Keiji Sugiyama, Department of Medical Oncology, Nagoya Medical Center, Nagoya, Japan*

Background: Numerous studies have demonstrated how malnutrition and cachexia are associated with poor survival in advanced gastric cancer (AGC). The impact of nutrition support involving multidisciplinary specialists is unclear, particularly among patients with AGC being treated with chemotherapy. This study aimed to clarify the differences in patient characteristics and survival outcomes between patients receiving nutrition support (NS) and routine care (RC). **Methods:** We retrospectively analyzed 212 consecutive patients with AGC at a single institution between January 2015 and June 2020. Inclusion criteria were: histologically confirmed metastatic or recurrent gastric and adenocarcinoma and gastroesophageal junction patients treated with chemotherapy, ECOG performance status (PS) 0-2, and adequate organ function. Time to treatment failure (TTF) in the entire cohort, patients with a positive Glasgow prognostic score (GPS) (graded as 1 and 2), and hypoalbuminemia (cutoff was 3.5 g/dl) were evaluated. Univariate and multivariate analyses were conducted to identify whether NS was an independent prognostic factor of time to treatment failure (TTF). Multivariate analysis included variables with p-values ≤0.1 in univariate analyses. **Results:** A total of 97 patients met the inclusion criteria with 67 (69%) and 30 (31%) patients classified into the RC or NS group, respectively. The median age was 71 years (range, 26-92). The median follow-up time was 8.4 months (range, 0.5-66). Patient characteristics revealed that NS was offered to patients with poorer prognostic nutritional index (PNI) (cutoff was 45, p=0.02), GPS positivity (p=0.01), and high neutrophil-lymphocyte ratio (NLR) (cutoff was 3, p=0.01). In the entire cohort, TTF in the RC and NS groups was 4.3 and 5.3 months (p=0.15), respectively. Among the patients with GPS positivity (graded as 1 and 2) and hypoalbuminemia, TTF in the RC and NS group were 2.3 and 5.0 months (p=0.05), and 2.3 and 5.3 months (p=0.02), respectively (Table). Variables with p-values ≤0.1 in univariate analyses for TTF were PS, NS, and prior gastrectomy. As per multivariate analyses, PS and NS were significant positive prognostic factors for TTF. **Conclusions:** NS was provided to patients with unfavorable clinical features. Among the AGC patients treated with chemotherapy, having GPS positivity or hypoalbuminemia seems to be a good indication for NS. Research Sponsor: None.

Median time to treatment failure within the entire cohort and sub-groups of the routine care group and the nutrition support group.

	Entire cohort (months, 95% CI)	GPS 1 and 2 (months, 95% CI)	Hypoalbuminemia (months, 95% CI)
Routine care group	4.3 (2.6-6.0)	2.3 (1.8-3.7)	2.3 (1.8-3.9)
Nutrition support group	5.3 (3.3-6.4)	5.0 (3.2-6.4)	5.3 (3.3-6.4)
P value	0.15	0.05	0.02

209 Poster Session

Preoperative docetaxel, cisplatin, and 5-fluorouracil for resectable esophagogastric junction adenocarcinoma: A retrospective study. *First Author: Toshiharu Hirose, Division of Gastrointestinal Medical Oncology, National Cancer Center Hospital, Tokyo, Japan*

Background: In Western countries, 5-FU plus leucovorin, oxaliplatin, docetaxel (DTX) (FLOT) is the standard perioperative treatment for resectable gastric adenocarcinoma and esophagogastric junction adenocarcinoma (EGJ-AC). Preoperative chemotherapy with DTX plus cisplatin and 5-FU (DCF) has been developed for esophageal squamous cell carcinoma in Japan. However, there have been few reports on the safety and efficacy of preoperative triple therapy for resectable EGJ-AC. **Methods:** The subjects of this retrospective study were patients (pts) with histologically confirmed resectable EGJ-AC who received preoperative DCF chemotherapy (DTX 70 mg/m² and cisplatin 70 mg/m² on day 1, and continuous infusion of 5-FU 750 mg/m²/day on days 1–5, every 3 weeks with a maximum of three cycles) at our hospital from Jan 2015 to Apr 2020. We evaluated the completion rate of >2 courses of DCF and R0 resection in all cases, and also examined histological response, progression-free survival (PFS), overall survival (OS), and adverse events during preoperative chemotherapy. **Results:** Thirty-two pts were included in this study, and the median observation period was 13.1 months (3.9–57.2). Characteristics were median age (range) 63 (42–80) years, PS 0/1 66/34%, clinical stage I/IIA/IIB/III/IVA/IVB (supraclavicular lymph node) 3/13/3/10/22/32/13%. Treatment completion rate was 84%. Histological response (grade 1a/1b/2/3) was obtained in 18/8/4/1 (58/26/13/3%) pts. Median PFS (95%CI) was 16.8 months (15.0–18.5), and median OS was not reached (3-year OS rate 73.8%). Grade >3 adverse events were observed in 20(63%) pts (neutropenia in 14 [44%], febrile neutropenia in 4 [13%]). No treatment-related deaths occurred. **Conclusions:** Preoperative DCF chemotherapy for resectable EGJ-AC was well tolerated. Further investigation is required to evaluate the long-term efficacy of this treatment strategy. Research Sponsor: None.

210 Poster Session

A phase I/II trial of trifluridine/tipiracil in combination with irinotecan in patients with advanced gastric cancer refractory to fluoropyrimidine, platinum, and taxane. *First Author: Hiroki Hara, Saitama Cancer Center, Saitama, Japan*

Background: Trifluridine/tipiracil (FTD/TPI) or irinotecan is a treatment option in the heavily pretreated patients with advanced gastric cancer (AGC) with the limited efficacy. Thus, we investigated the recommended dose of trifluridine/tipiracil (FTD/TPI) and irinotecan for these patients. **Methods:** Patients who refractory to fluoropyrimidine, platinum and taxane were enrolled into four cohorts (Level 1A/1B/2A/2B) used a escalated dose of irinotecan [100 (Level 1) or 125 mg/m^2 (Level 2) on Days 1 and 15 of a 28-day schedule] with 2 dosage schedules of FTD/TPI: 35 mg/m^2/dose, twice daily (bid), on days 1-5 and 8-12 of a 28-day cycle (Level A) or on days 1-5 and days 15-19 of a 28-day cycle (Level B). The primary objectives were the determination of the maximum tolerated dose, dose-limiting toxicities (DLTs), and recommended phase II dose (RP2D) for phase I part and the evaluation of disease control rate (DCR) targeting > 55% in all enrolled patients for phase II part. **Results:** Eleven patients were enrolled from 4 institutions in Japan; 2 at Level 1A, 3 at Level 1B and 6 at Level 2B. DLTs occurred in 2/2 patient at Level 1A (Grade 3 gum infection and Grade 3 febrile neutropenia on Day 29, outside the 28-day DLT assessment period, determined equivalent to DLT), and 2/6 patients at Level 2B (Grade 3 mucositis oral and Grade 3 febrile neutropenia). Grade 3 or higher treatment-related adverse events were neutropenia (90.9%), leukopenia (54.5%), anemia (45.5%) and febrile neutropenia (18.2%). One patient at Level 2B achieved partial response and the DCR was 72.7% (95% CI 39.0- 94.0%). The median progression-free survival and overall survival was 3.0 months (95% CI 0.92- not reached) and 10.2 months (95% CI 2.2- not reached), respectively. **Conclusions:** The RP2D was determined to be Level 1B although further investigation to explore optimal regimen is needed. Clinical trial information: UMIN000031346. Research Sponsor: Taiho Pharmaceutical.

211 Poster Session

Sintilimab plus oxaliplatin/capecitabine (CapeOx) as neoadjuvant therapy in patients with locally advanced, resectable gastric (G)/esophagogastric junction (GEJ) adenocarcinoma. *First Author: Haiping Jiang, Department of Medical Oncology, First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China*

Background: The application of anti-programmed death 1 (PD-1) antibodies in neoadjuvant setting has not been well established. This phase 2 study (NCT04065282) was conducted to evaluate the efficacy and safety of sintilimab plus CapeOx as neoadjuvant therapy for resectable G/GEJ adenocarcinoma. **Methods:** Patients with histologically confirmed resectable G/GEJ adenocarcinoma (stage cT3-4NxM0) were enrolled to receive neoadjuvant therapy with sintilimab (3mg/kg for wt $<$ 60kg, 200mg for wt $\geq$60kg, Q3W) plus CapeOx (oxaliplatin 130mg/m^2 iv D1, capecitabine 1000mg/m^2 bid po D1-14, Q3W) for 3 cycles. Gastrectomy was scheduled within 4 weeks after last dose of neoadjuvant treatment. Tumor imaging evaluation was performed at baseline and within 1 week before gastrectomy. The primary endpoint was pathological complete response (pCR) per Becker criteria. **Results:** As of August 4, 2020, 36 pts were enrolled. Patients who had received gastrectomy after neoadjuvant treatment (n = 26) were included in this analysis. 25 (96.2%) pts completed 3 cycles of neoadjuvant treatment, except one completed 2 cycles due to grade 3 AST increased. All pts received complete resection (R0). 6 (23.1%) pts achieved pCR (TRG1a) and 14 (53.8%) pts achieved major pathologic response (MPR, TRG1a/b). 3 pts had partial response (ORR was 3/5 among pts with target lesions) and no patients progressed per RECIST 1.1 before surgery. Among 18 pts who received PET-CT evaluation per PERCIST, 11 (61.1%) achieved partial metabolic response (PMR). Neoadjuvant treatment-related AEs (neoTRAEs) to any drug were reported in 25 (96.2%) pts. Mostly TRAEs were grade 1-2, and only 6 (23.1%) pts experienced grade 3 TRAEs (Neutropenia in 4 pts, Leukopenia, Thrombocytopenia, AST increased, and GGT increased in 1 pt each). One patient experienced grade 1 hypothyroidism which is considered to be immune-related AE. There is no serious peri-operative complication and mortality. **Conclusions:** Sintilimab plus oxaliplatin/capecitabine showed promising efficacy with high pCR and MPR rate and well-tolerated safety profile in neoadjuvant settings. This combination regimen might present a new option for patients with locally advanced, resectable G/GEJ adenocarcinoma. Clinical trial information: NCT04065282. Research Sponsor: None.

212 Poster Session

Phase I study of BI 754091 plus BI 754111 in Asian patients with gastric/gastroesophageal junction or esophageal cancer. *First Author: Kensei Yamaguchi, Japanese Foundation for Cancer Research, Tokyo, Japan*

Background: Dual blockade of immune checkpoint molecules, PD-1 and LAG-3, has been proposed to restore T-cell function and thus enhance antitumor responses. This Phase I trial evaluated BI 754091 (anti-PD-1) with BI 754111 (anti-LAG-3) antibodies in Asian pts with advanced solid tumors (NCT03433898). Here, we present results from pts with anti-PD-(L)1 inhibitor-naïve gastric/gastroesophageal junction or esophageal cancer (Cohorts A and B). **Methods:** In Parts 1 and 2 (dose escalation), the recommended dose for the combination was determined as BI 754091 240 mg + BI 754111 600 mg IV Q3W. In Part 3, the combination was assessed in expansion cohorts including pts with gastric/gastroesophageal junction cancer (Cohort A) and esophageal cancer (Cohort B). Eligible pts had received $\geq$1 line of prior systemic therapy but no prior anti-PD-(L)1 therapy. The primary endpoint in Part 3 was objective response (OR; confirmed complete response or partial response [PR]) per RECIST 1.1. **Results:** In Cohort A/B, 36/37 pts were treated: 26/31 (72/84%) male, median age 60/63 years. Patients were enrolled in Taiwan (1/7 pts, 3/19%), Japan (12/27 pts, 33/73%) or Korea (23/3 pts, 64/8%). The median number of regimens of prior systemic therapy was 2/2 (Cohorts A/B, range: 16/14). All pts in Cohort B had squamous cell carcinoma. At the time of analysis, pts in Cohort A/B had undergone a median of 84/73 days on treatment (range: 31346/8325), from the start of treatment until the date of snapshot, death or discontinuation. Confirmed OR (PR) was observed in 4/7 pts in Cohorts A/B; overall response rate (ORR) was 11% and 19%. Stable disease (SD) was observed in 10/8 (28/22%) pts in Cohorts A/B and overall disease control rate was 39/41%. In Cohorts A/B, adverse events (AEs) and treatment-related AEs were experienced by 30/34 (83/92%) and 12/22 (33/59%) pts, respectively. The most commonly reported AEs were pyrexia (25/19%), decreased appetite (17/19%), increased aspartate aminotransferase (11/14%), anemia (11/11%) and nausea (6/14%). In Cohort A/B, 9/15 (25/41%) pts experienced immune-related AEs, most commonly rash in Cohort A (4 pts; 11%) and hyperthyroidism in Cohort B (4 pts; 11%). In Cohorts A/B, 2/6 (6/16%) patients experienced AEs leading to discontinuation of treatment. **Conclusions:** Treatment was well tolerated and preliminary antitumor activity was seen. Addition of LAG3 did not improve ORR beyond that expected for an anti-PD-1 monotherapy in gastric and esophageal cancer without patient selection. Clinical trial information: NCT03433898. Research Sponsor: Boehringer Ingelheim.

Patients, n (%)	Cohort A n = 36	Cohort B n = 37
Efficacy		
PR	4 (11)	7 (19)
SD	10 (28)	8 (22)
Progressive disease	17 (47)	17 (46)
Safety		
AEs, worst CTCAE Grade:		
≤3	29 (81)	32 (86)
4	0	2 (5)*
5	1 (3)	0

*Grade 4 AEs include one patient with liver disorder (not drug-related), and one patient with pneumonia (drug-related) and hypotension (not drug-related). Grade 5 AE was acute kidney injury (not drug-related).

214 Poster Session

Phase II study of systemic chemotherapy with S-1 plus oxaliplatin followed by surgery in patients with cT3-T4a and/or node-positive advanced adenocarcinoma of the esophagogastric junction: Primary endpoint results of the ESOX trial. *First Author: Yu Imamura, Department of Gastroenterological Surgery, Cancer Institute Hospital of the Japanese Foundation for Cancer Research, Koto-Ku, Tokyo, Japan*

Background: Perioperative chemotherapy has been suggested to be beneficial in patients with advanced gastric cancer. Based on the German FLOT-4 study, the FLOT regimen is considered as the new standard perioperative chemotherapy regimen for resectable gastric cancer in Europe. However, most clinical trials have included few or no cases of esophagogastric junction (EGJ) cancer, because of the difference in surgical procedures. The benefit of neoadjuvant chemotherapy in patients with advanced adenocarcinoma of the EGJ thus remains controversial in Japan. **Methods:** We conducted a phase II study in 13 Japanese institutions. Eligible patients had histopathologically confirmed adenocarcinoma of the EGJ (Siewert type I or II with invasion of the esophagus $\geq$30 mm) with clinical T3/4a and/or node-positive on imaging findings, who required thoracic surgery to achieve R0 resection. Patients received three cycles of S-1 (80 mg/m^2) twice a day on days 1–14 and oxaliplatin (130 mg/m^2) (SOX) on day 1 of a 21-day cycle before surgery. The primary endpoint was R0 resection rate and the secondary endpoints were overall response rate, pathological complete response (pCR) rate, 2-year and 3-year disease-free survival, overall survival, and toxicity. The planned sample size was 50 patients based on an expected R0 resection rate of 85% and the threshold was 70%, with a one-sided alpha of 0.1 and power of 80%. **Results:** Fifty patients were enrolled in this study between June 2016 and April 2020. Totals of 21/29 and 7/4/22/8/8/1 had Siewert type I/II and clinical stage IIA/IIB/IIIA/IIIB/IIIC/IV disease, respectively. The completion rates for preoperative chemotherapy and surgery were 92% and 88%, respectively. Neoadjuvant therapy resulted in downstaging in 46% of patients (95% confidence interval (CI) 31.8%-60.7%). The pCR rate was 18% (95% CI 8.6%-31.4%) and the R0 resection rate was 82.0% (95% CI 68.6%-91.4%, 80% CI 73.1%-88.9%). Adverse events $\geq$ grade 3 during chemotherapy included thrombocytopenia (10%), neutropenia (8%), anemia (4%), anorexia (4%), nausea(2%), hypocalcemia(2%), hyponatremia(2%) and diarrhea (2%). Surgical morbidity was acceptable (Clavien-Dindo Grade IIIa surgical complications included anastomotic leakage (6.3%), pleural effusion (4.2%), thromboembolism (2.1%), and anastomotic infection (2.1%)). **Conclusions:** Neoadjuvant SOX met the primary endpoint of R0 resection rate 82% ($>$ 70%), with acceptable adverse effects and no impression on surgeries, suggesting that neoadjuvant SOX might be a new treatment strategy for patients with EGJ adenocarcinoma in Japan. Clinical trial information: 000020815. Research Sponsor: None.

215 Poster Session

Camrelizumab in combination with apatinib as second-line treatment for advanced esophageal squamous cell carcinoma: A single-arm, open-label, phase II study. *First Author: Feng Wang, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China*

Background: Esophageal squamous cell carcinoma (ESCC) is a lethal cancer with a high unmet medical need. Camrelizumab, an anti-PD-1 monoclonal antibody, significantly improved overall survival (OS) and objective response rate (ORR) in Chinese patients (pts) with advanced ESCC compared with chemotherapy, with a manageable safety profile in phase III randomized trial (ESCORT). However, the absolute long-term survival benefiting from PD-1 inhibitors is limited, and new effective treatments are needed. Here, our study aimed to assess the efficacy and safety of combination with camrelizumab and apatinib (VEGFR2 inhibitor) as second-line treatment for advanced ESCC. **Methods:** This ongoing phase II trial (NCT03736863) in six sites in China enrolled pts aged 18-75 with unresectable locally advanced, locally recurrent, or metastatic ESCC that progressed or were intolerant after first-line chemotherapy, and an ECOG performance status of 0-1. Pts received 200 mg intravenous camrelizumab every two weeks plus 250 mg oral apatinib daily in 4-week cycles until disease progression, unacceptable adverse events (AEs) or withdrawal of consent. The primary endpoint was investigator-assessed ORR. Secondary endpoints included disease control rate (DCR), progression-free survival (PFS) and OS. **Results:** At data cutoff (Sept 11, 2020), 36 pts were enrolled, 7 females and 29 males, and 25 pts had lymph node metastases. Twelve pts received radiotherapy and 25 underwent surgery. Twenty-five pts were included in the efficacy analysis with median follow-up time of 5.0 months and 36 pts in the safety analysis with median follow-up time of 4.6 months. The primary endpoint ORR without confirmation was 40 % with complete response in two pts (8%) and partial response in eight pts (32%). Thirteen pts (52%) had stable disease, and the DCR was 92%. The median PFS and OS were not reached. A total of 72.2% of pts had AEs, and 30.6% of pts experienced grade 3 AEs. The most common AEs (all grade, grade$\geq$3) were elevated aspartate aminotransferase (30.6%, 19.4%), elevated alanine aminotransferase (30.6%, 13.9%), hypertension (25%, 2.8%) , neutrophil (25%, 5.6%), thrombocytopenia (25%, 0%), leukopenia (22.2%, 2.8%), anemia (11.1%, 0%), proteinuria (11.1%, 0%), hematochezia (8.3%, 0%), reactive cutaneous capillary endothelial proliferation (5.6%, 2.8%), pruritus (5.6%, 0%), esophageal fistula (5.6%, 0%), fatigue (2.8%, 0%) and hypothyroidism (2.8%, 0%). **Conclusions:** This is the first study to explore the combination of PD-1 inhibitor and anti-angiogenesis inhibitor as a second-line treatment for advanced ESCC. Camrelizumab plus apatinib demonstrated encouraging clinical efficacy and acceptable safety as second-line treatment, and might be a favorable option for pts with advanced ESCC. Further phase III randomized trials are warranted. Clinical trial information: NCT03736863. Research Sponsor: Jiangsu Hengrui Medicine Co., Ltd.

216 Poster Session

Phase II study of sintilimab combined with FLOT regimen for neoadjuvant treatment of gastric or gastroesophageal junction (GEJ) adenocarcinoma. *First Author: Ning Li, Department of Medical Oncology, Henan Cancer Hospital, The Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, China*

Background: Perioperative treatments have significantly improved survival in patients with resectable gastric cancer, increasing 5-year overall survival from 23% with surgery alone to 45% with FLOT, Although FLOT has been recognized as the first choice for neoadjuvant chemotherapy in gastric or GEJ adenocarcinoma, its efficacy needs to be improved. Sintilimab, a fully human IgG4 monoclonal antibody that binds to programmed cell death receptor-1 (PD-1), has shown remarkable clinical efficacy in various cancers. We aimed to assess the activity and safety profile of the combination of FLOT and sintilimab for neoadjuvant treatment of gastric or GEJ adenocarcinoma. **Methods:** In this ongoing, single-arm, phase II study, we recruited patients from Henan Cancer Hospital in China with histopathologically diagnosed resectable gastric or GEJ adenocarcinoma who had clinical T3/N+ or higher stage. Patients were given 4 cycles of FLOT (docetaxel 50 mg/m2, oxaliplatin 80 mg/m2, leucovorin 200 mg/m2, fluorouracil 2600 mg/m2, 24-h infusion on day 1, q2w) in combination with 3 cycles of sintilimab (200mg, iv, d1, q3w), followed by D2 surgery and 4 postoperative cycles of FLOT. The primary endpoint was pathological complete response (pCR). The secondary endpoints included major pathological remission (MPR) and R0 resection rate and adverse events . **Results:** A total of 20 patients were enrolled in the study between Aug 10 2019 and Sep 15 2020. One patient refused surgery, one person's disease progressed. Two patients have not yet completed neoadjuvant treatment . 16 pts who experienced D2 resection, 10 (62.5%) achieved major pathologic response (MPR), including 3 (18.8%) with a pathologic complete response (pCR) in primary tumor. The R0 resection rate was up to 93.8%, The grade 3 or 4 treatment-related adverse events (TRAE) included lymphopenia(25%), anaemia (20%),fatigue (20%),leucopenia (15%), neutropenia (5%), diarrhea(5%), Alanine aminotransferase increased(5%),There was no surgical delays or unexpected surgical complications related to drug toxicity. **Conclusions:** Neoadjuvant combination of sintilimab and FOLT is a safe and efficacious treatment option for patients with gastric or GEJ adenocarcinoma, 18.8% pCR rate and 62.5%MPR rate is encouraging. Our clinical study is still enrolling, and the survival effects are under follow up. Clinical trial information: NCT04341857. Research Sponsor: None.

217 Poster Session

Results of a phase II trial of ramucirumab plus irinotecan as second-line treatment for patients with advanced gastric cancer (HGCSG 1603). *First Author: Yasuyuki Kawamoto, Division of Cancer Center, Hokkaido University Hospital, Sapporo, Japan*

Background: Ramucirumab (RAM) is a fully human IgG1 monoclonal vascular endothelial growth factor receptor-2 (VEGFR-2) antibody. The RAINBOW trial showed RAM plus paclitaxel (PTX) increased overall survival (OS) compared with PTX alone for advanced gastric cancer (AGC) in second-line treatment. WJOG 4007 trial demonstrated equivalent efficacy between irinotecan (IRI) and PTX. We conducted this trial to examine the efficacy and safety of RAM plus IRI combination therapy in the second-line treatment for AGC. **Methods:** This non-randomized, single arm, phase 2 trial was carried out at 22 institutes in Japan. AGC patients with refractory or intolerance to primary chemotherapy were eligible. RAM 8 mg/kg and IRI 150 mg/m^2 combination therapy administered every two weeks were continued until progression or emergence of adverse events requiring discontinuation. The primary endpoint was progression-free survival (PFS) rate at six-month, the target was set as 16% with an expected threshold of 39%. A total of 35 cases are planned for registration. The secondary endpoints were OS, PFS, response rate (RR) and safety. This trial was registered with Japan Registry of Clinical Trials, number jRCTs011180029. **Results:** Between Jan 2018 and Sept 2019, 35 patients were enrolled. Median age was 70 (range, 47-80); female/male were 10/25; ECOG PS 0/1, 22/13. PFS rate at six months was 26.5% (95%C.I., 13.2-41.8%, p = 0.1353). Median PFS and OS were 4.2 (95%C.I., 2.5-5.4 months) and 9.6 months (95%C.I., 6.5-16.6 months), respectively. RR was 26% and disease control rate was 85%. Grade 3 or higher adverse events that occurred in more than 5% of patients were neutropenia (51%), leucopenia (43%), anemia (20%), anorexia (14%), febrile neutropenia (11%), diarrhea (9%), hypertension (9%), proteinuria (9%), hypokalemia (9%), hypoalbuminemia (9%), thrombocytopenia (6%), and hyponatremia (6%). No death and new safety signals with a causal relation to study treatment were observed. **Conclusions:** Although the primary endpoint was not achieved statistically, the results are clinically encouraging, especially take into account that more elderly patients enrolled in this trial. The combination of RAM plus IRI has anti-cancer activity and manageable safety profile in second-line treatment for patients with AGC. Clinical trial information: jRCTs011180029. Research Sponsor: Eli Lilly Japan K.K.

218 Poster Session

A multi-institutional phase Ib/II trial of first-line triplet regimen (Pembrolizumab, Trastuzumab, Chemotherapy) for HER2-positive advanced gastric and gastroesophageal junction cancer (PANTHERA Trial): Molecular profiling and clinical update. *First Author: Sun Young Rha, Yonsei Cancer Center, Yonsei University Health System, Seoul, South Korea*

Background: We report the updated clinical data and molecular profiling results of a multi-institutional phase Ib/II trial of triple combination (pembrolizumab, trastuzumab, and chempotherapy) as first line therapy for HER2 positive advanced gastric and gastroesophageal junction (AGC/GEJ) cancer. (PANTHERA trial; NCT02901301). **Methods:** Pembrolizumab 200mg IV D1, Trastuzumab 6mg/kg (after 8mg/kg load) D1, Capecitabine 1000mg/m^2 bid D1-14, and Cisplatin 80mg/m^2 D1 every 3 weeks was selected as recommended phase II dose. The primary endpoint for phase II was ORR per RECIST v1.1. Secondary endpoints included PFS, OS, DOR, safety, and predictive biomarker analysis by targeted NGS. **Results:** At the time of data lock on Aug 31, 2020, total of 43 patients were treated with median follow up of 18.2 months, and 3 patients remained on the treatment, and 6 patients finished 2-year treatment without progression. ORR was 76.7% (CR 16.3%, PR 60.5%, conversion surgery 4.6%) with 26 pts (56.6%) showing more than 50% of tumor burden reduction. Median PFS was 8.6 months (95% CI 7.2-16.5) and median OS was 19.3 months (95% CI 16.5-NR). There were no MSI-H/dMMR or EBV-positive pts. No patient discontinued pembrolizumab because of immune-related adverse events. Clinical features including PD-L1 status (55.3% of pts ≥ CPS 1 and 13.2% of pts ≥ CPS 10 among available 38 pts), metastatic organ or baseline tumor burden was not related to the survival. Ninety-eight tumor tissues from 39 pts (paired tumor tissues from 22 pts) were analyzed with targeted NGS. Although every pts were HER2 IHC-positive, baseline *HER2* amplification by NGS was related to the survival (*HER2* amp (n=8) vs *HER2* non-amp (n=23); mPFS, not reached vs 7.7 months, *P*=0.0178; mOS, not reached vs 17.9 months, *P*=0.044) but no other signaling pathways predicted pts' survival. *HER2* mutations including L869R or D769H were related to the acquired resistance. High TMB showed a tendency toward better survival (mPFS; High (n=7) vs Low (n=24) TMB, 22.0 vs 8.2, *P*=0.2835) due to small number of patients. Updated immune markers and serial NGS analyses will be presented. **Conclusions:** First-line triplet regimen (Pembrolizumab, Trastuzumab, and Chemotherapy) showed promising efficacy based on HER2 amplification by NGS regardless of PD-L1 status in AGC/GEJ cancer. Correlative biomarkers found from NGS study need to be validated through on-going phase III Keynote-811 study. Clinical trial information: NCT02901301. Research Sponsor: None.

ORR (95% CI)	DCR (95% CI)	PFS (95% CI)	OS (95% CI)	DOR (95% CI)	6-months PFS (95% CI)
76.7% (61.4-88.2)	97.7% (87.7-99.9)	8.6 months (7.2-16.4)	19.3 months (16.5-NR)	10.8 months (7.2-21.8)	79.1% (64.0-90.0)

Response and Survival of PANTHERA Trial (cut-off date: Aug-31-2020).

219 Poster Session

Palliative endoscopic spray cryotherapy to prevent worsening of dysphagia and improve quality of life in esophageal cancer. *First Author: Swathi Eluri, University of North Carolina School of Medicine, Chapel Hill, NC*

Background: Patients with locally advanced esophageal cancer can have progressive dysphagia and associated worsening quality of life (QOL). Maintenance of esophageal patency by reducing intraluminal tumor burden can improve QOL by palliating dysphagia and delay or prevent the need for feeding tubes and esophageal stents. We aimed to assess the effect of endoscopic palliative cryoablation with trūFreeze Spray Cryotherapy (SCT) on dysphagia burden, QOL, and survival in patients with esophageal cancer. **Methods:** This is a multi-center prospective study of esophageal cancer patients at 10 sites in the United States. Subjects are 18-89 years old with luminal esophageal cancer, non-surgical candidates, not receiving systemic therapy, without esophageal stents, or history of prior SCT for esophageal cancer. SCT is an endoluminal ablation modality using non-contact medical grade liquid nitrogen (LN2) reaching a temperature of -196^0 C delivered by a catheter. SCT was performed at 6 week intervals or as clinically indicated at a dose of 2x30 or 3x30 seconds per every 2-3 cm treatment site. Dysphagia and QOL were assessed with the 5-point Dysphagia score and EORTC QLQ 30 and OES18 esophageal module. **Results:** Of 49 subjects, mean age is 74.2 ± 11.8, 88% are men, 92% have esophageal adenocarcinoma and 19% have prior esophageal surgery or esophagectomy. 75% had a history of chemotherapy and/or radiation, and 58% (n=21) had a tumor stage >2. Subjects had a total of 258 treatment sessions over a mean follow-up of 329.7 ± 219.1 days, and received a median of 4 (IQR:2-7) SCT sessions with an average dose of 90 (3x30 sec) seconds/treatment site. There were 19 procedure related adverse events (20.4% of patients and 7.4% of procedures), all of which were mild (n=13) or moderate (n=6) in severity. Mean baseline dysphagia score was 1.7 ± 0.9 and 89% maintained (72%) or improved (17%) their baseline dysphagia score after initial SCT, p<0.05, and maintained this degree of symptom burden with ongoing SCT for a mean 239 ± 198 days. 28.6% (n=14) needed an esophageal stent after a mean 168 ± 169 days and 8% (n=4) had a feeding tube placed after a mean 145 ± 76 days after initial treatment. There was improvement in global health status (61.9 ± 23.3 vs 67.7 ± 19.7) and social functioning (73.9 ± 24.7 vs 81.2 ± 28.0) with decreased dysphagia (OES18: 21.5 vs. 16.7) and eating problems (26.1 vs. 20.6), p<0.05 for all. During the follow-up period, 49% of this palliative group survived and median survival was 386 days. Factors associated with survival with SCT were earlier cancer stage (69% stage 1 or 2 were survivors vs. 20% non-survivors; p=0.03) and ≤25% of luminal obstruction by tumor (62% vs. 36%; p=0.06). **Conclusions:** Liquid nitrogen SCT is an effective option to curb dysphagia progression in palliation of esophageal cancer and improves overall quality of life. Degree of luminal obstruction and tumor stage predicted survival. Clinical trial information: NCT03243734. Research Sponsor: STERISU.S. National Institutes of Health.

220 Poster Session

Neoadjuvant PD-1 blockade in combination with chemotherapy for patients with resectable esophageal squamous cell carcinoma. *First Author: Chao Cheng, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China*

Background: Programmed death-1 (PD-1) blockade may induce tumor regression in patients with advanced esophageal squamous cell carcinoma (ESCC), but little is known about the efficacy of PD-1 blockade in neoadjuvant therapy of resectable ESCC. **Methods:** Under an approved clinical trial protocol, a pilot study was conducted by enrolling patients with untreated, resectable (stage II or IIIA) ESCC. After written informed consent, each patient received two 21-day cycles of neoadjuvant treatment with camrelizumab (200mg), albumin-paclitaxel (260mg/m^2) and carboplatin (area under the curve = 5) followed by surgical resection about 6 weeks after the first dose. The primary end points were safety and feasibility. We also reported the objective response rate (ORR), disease control rate (DCR) and tumor pathological response. **Results:** Between January 19, 2020, and July 21, 2020, we assessed 35 patients for screening, of whom 20 patients were enrolled. Neoadjuvant combination of camrelizumab, carboplatin and albumin-paclitaxel had an acceptable side-effect profile, and was not associated with delays in surgery. The ORR was 85%, and the DCR was 100%. Eighteen (90%) patients were taken into the surgery, and all of them successfully underwent R0 resection. Five (5/18 = 27.8%) patients had a pathological complete response (pCR), and eight (44.4%) patients had major pathological responses (MPR).The most common treatment-related grade 1–2 adverse events were leukopenia (12, 60%), neutropenia (11, 55%) and nausea (8, 40%). Two (10%) patients suffered grade 3 neutropenia. There was no grade 4 adverse events and treatment-related deaths. **Conclusions:** Neoadjuvant camrelizumab plus carboplatin and albumin-paclitaxel had manageable treatment-related toxic effects, did not delay surgery. This regimen induced pCR or MPR in 72.2% of resected tumor, demonstrating its antitumor efficacy in resectable ESCC. Clinical trial information: ChiCTR2000028900. Research Sponsor: None.

221 Poster Session

Clinical implication of using up both fluoropyrimidine (FU) and paclitaxel (PTX) in patients with severe peritoneal metastases (SPM) of gastric cancer (GC). *First Author: Hiroyuki Arai, Department of Clinical Oncology, St. Marianna University School of Medicine, Kawasaki, Japan*

Background: JCOG1108/WJOG7312G trial showed favorable but not significantly better outcomes of 5-FU/*l*-leucovorin (*l*-LV) /PTX combination (FLTAX) compared to 5-FU/*l*-LV (FL) in untreated patients with SPM of GC. However, a half of patients treated with FL could not sequentially use PTX which is a key drug for peritoneal metastasis. We conducted a post hoc analysis to investigate the clinical implication of using up both FU and PTX in either combination or sequential strategy for GC patients with SPM. **Methods:** Among 101 patients enrolled in the trial (FL: *N* = 51; FLTAX: *N* = 50), overall survival (OS) was compared between three subgroups: patients treated with FL followed by PTX (FL/PTX: *N* = 25), those treated with FL followed by best supportive care (BSC) (FL/BSC: *N* = 21), and those treated with FLTAX (per protocol population, *N* = 48). To identify the factors affecting the likelihood of using sequential PTX (LUSP), we compared baseline characteristics between the FL/PTX and FL/BSC subgroups. Each baseline covariate was tested for the impact on LUSP by logistic regression model. The difference of treatment efficacy between FL and FLTAX was assessed in subgroups stratified by the factors identified to affect LUSP. **Results:** Patients in the FL/PTX subgroup showed significantly better OS than those in the FL/BSC subgroup (median OS, 7.8 vs 2.0 months; hazard ratio [HR] 0.24, 95% confidence interval [CI] 0.12-0.48, $p < 0.01$) and equivalent OS compared to those in the FLTAX subgroup (median OS, 7.8 vs 8.0 months; HR 0.83, 95% CI 0.50-1.39, $p = 0.49$). Compared with patients in the FL/BSC subgroup, those in the FL/PTX subgroup had a trend for lower frequency of Glasgow prognostic score (GPS) 2 (40.0% vs 66.7%, $p = 0.17$) and unresectable type (76.0% vs 95.2%, $p = 0.07$). GPS 2 and unresectable type were identified as factors with a worse impact on LUSP compared to GPS 0 and recurrent type, with odds ratio (OR) of 0.29 (95% CI 0.05-1.78, $p = 0.18$) and that of 0.16 (95% CI 0.02-1.44, $p = 0.10$), respectively. Among all patients enrolled in the trial, 43 patients had both GPS2 and unresectable type (score 2), 45 had either (score 1), 11 had neither (score 0), and two lacked the data of GPS. Median OS in the patients with score 2, 1, and 0 was 4.7, 7.8, and 18.8 months, respectively (score 2 vs 0, HR 4.37, 95% CI 1.84-10.42; score 1 vs 0, HR = 2.80, 95% CI 1.19-6.64). Compared to FL, FLTAX showed better OS in patients with score 2 (HR = 0.60, 95% CI 0.32-1.13) and in those with score 1 (HR = 0.77, 95% CI 0.42-1.42), but worse OS in those with score 0 (HR = 4.74, 95% CI 0.49-45.85). **Conclusions:** Combination or sequential use of active two drugs, 5-FU and PTX, might contribute to better OS of GC patients with SPM. However, because selection of patients suitable to sequential use is difficult, the combination strategy FLTAX is a favorable treatment option. Research Sponsor: The study was supported in part by the National Cancer Research and Development Fund (26-A-4, 29-A-3), a Grant-in-Aid for Clinical Cancer Research (H26-144) from the Ministry of Health, Labour and Welfare of Japan, and by the Japan Agency for Medical Rese.

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Camrelizumab in combination with preoperative chemotherapy for locally advanced esophageal squamous cell carcinoma: A single-arm, open-label, phase II study. *First Author: Feng Wang, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China*

Background: At present, esophageal cell carcinoma (ESCC) has a dismal prognosis with huge unmet clinical needs. With the potential benefit of combining PD-1 inhibitor with neoadjuvant chemotherapy (nCT), we conducted a phase II trial to assess the efficacy and safety of Camrelizumab (anti-PD-1 antibody) plus nCT for locally advanced ESCC. **Methods:** 26 patients (pts) with histologically confirmed stage II/III/IVa (cT2-4aN0-3M0) ESCC were enrolled from February 2020 to September 2020.The study was divided into two stages, stage1: we administered 1 cycle of Camrelizumab for induction therapy (200 mg q2 weeks); stage2: pts received 2 cycles of Camrelizumab (200 mg every 3 weeks) plus docetaxel and nedaplatin, followed by surgery within 4~6 weeks after neoadjuvant therapy completion. Primary endpoint was major pathologic response (MPR). Secondary endpoints included pathologic complete response (pCR), R0 resection rate, disease-free survival (DFS) and overall survival (OS). In total 40 pts will be enrolled. **Results:** At the cutoff date of Sep 22, 2020, 26 eligible pts were enrolled (65% males, median age 63), neoadjuvant treatment was completed in 17 pts and is ongoing in 7 pts. Thus far 12 out of 17 pts were resected, 5 pts are planned to undergo surgery, 1 pt had interval metastases preoperatively, 1 pt declined surgery. All patients underwent an R0 resection. Postoperative pathology showed that T stage decreased in 10 pts with 83% reduction rate. 5 pts (42%) reached major pathologic response, 3 pts (25%) reached pathologic complete response, the others maintained stable disease (33%). No grade 3 immunotherapy related AEs were observed, no surgery related mortality. The most common AEs (all grade, grade≥3) were anemia (31%, 3%), leukopenia (7%, 0%), neutrophil (3%,0%), hypoalbuminemia (21%, 0%), hematochezia (14%, 0%), fatigue (10%, 0%) and thyroid dysfunction (24%, 0%). Date for median PFS and OS were not matured. **Conclusions:** Camrelizumab in combination with preoperative chemotherapy followed by surgery for locally advanced ESCC showed promising downstaging effect and MPR with good tolerance, and its efficacy and safety could be further studied in later trials. Clinical trial information: NCT03917966. Research Sponsor: Jiangsu HengRui Medicine Co., Ltd.

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The preliminary efficacy and safety of KN046 plus concurrent chemoradiation therapy in recurrent and metastatic esophageal squamous cell carcinoma. *First Author: Bing Song Qin, Department of Tumor Radiotherapy, The First Affiliated Hospital of Soochow University, Soochow, China*

Background: Definitive or palliative chemoradiation therapy has been employed in the management of esophageal squamous cell carcinoma (ESCC). Immune checkpoint inhibitor has improved outcomes in metastatic stage IV pts. Here we report the addition of KN046, a PD-L1/CTLA-4 bispecific antibody, to concurrent chemoradiation (CRT) therapy to determine the safety and efficacy of this approach (ChiCTR2000031544). **Methods:** Pts with recurrent or metastatic ESCC, not been treated by CRT or other systemic treatment within 6 months, were recruited and received palliative CRT consisting of cisplatin (75 mg/m^2 IV Q3W for 4~6 cycles), paclitaxel (135~175 mg/m^2 IV Q3W for 4-6 cycles) and radiation (SBRT or conventional and dose are determined at the investigator's discretion according to institutional standard). KN046 at ascending doses of 1, 3 and 5 mg/kg Q3W was added within 7-14 days after the completion of radiation therapy (RT) and concurrently with chemotherapy, followed by KN046 Q2W maintenance. Dose limiting toxicities (DLTs) were assessed for the first treatment cycle of KN046. Anti-tumor activity was assessed according to RECIST 1.1 every 6 weeks within the first year, and every 12 weeks thereafter. **Results:** As of June 30, 2020, 18 subjects were enrolled and received KN046 treatment (1mg/kg, n = 3; 3mg/kg, n = 11; 5mg/kg, n = 4). The median KN046 exposure was 11.5 weeks. No DLT was reported. 3 (16.7%) subjects experienced Grade 3, KN046 related adverse events (1 Grade 3 pneumonitis and 2 Grade 3 colitis recovered after steroid and antibiotic Tx). For 18 evaluable subjects, the disease control rate and objective response rate were 94.4% and 44.4%, respectively. DOR and PFS were not matured yet as of cutoff date. At 3 mg/kg, objective response was observed in 5 out of 9 subjects (55.6%) with measurable disease and disease control rate was 100%; 7/9 (77.8%) subjects experienced further tumor reduction after initiation of KN046 treatment. It is worth to note that, 2 subjects at 3mg/kg achieved complete response after receiving KN046 treatment. **Conclusions:** The addition of KN046 to CRT was well tolerated and showed promising efficacy signal in recurrent or metastatic ESCC. This pilot study enables further investigation of a new treatment modality of KN046 with CRT in this detrimental disease with poor prognosis. Clinical trial information: 2000031544. Research Sponsor: Alphamab.

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Gastric and gastroesophageal adenocarcinoma survival outcomes relative to completion of perioperative fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT): A single-center retrospective analysis. *First Author: Michael J Allen, Princess Margaret Cancer Center, University Health Network, Toronto, ON, Canada*

Background: Perioperative FLOT is standard-of-care for locally advanced resectable gastric and gastroesophageal (GEJ) adenocarcinoma. Completion of perioperative chemotherapy (8 cycles) is potentially jeopardised by significant toxicity and intolerance. Only 46% of patients completed all cycles in the initial phase 2/3 trial (FLOT-AIO). We sought to determine the rate of treatment completion in a real-world population and any subsequent impact on survival of incomplete treatment. **Methods:** A retrospective analysis of gastric and GEJ adenocarcinoma patients treated with perioperative FLOT at Princess Margaret Cancer Centre, Toronto between September 2017 and July 2020 was performed. The rate of perioperative FLOT administration, disease-free survival (DFS) and overall survival (OS) was analysed, with outcomes compared between patients that completed perioperative FLOT and those that didn't. **Results:** 32 patients were identified as receiving neoadjuvant FLOT. Mean age was 61.5y, 26 (81%) were male and 29 (91%) were non-Asian. All patients were ECOG 0-1. The median number of neoadjuvant cycles was 4. 29 (91%) had surgery (2 = disease progression; 1 = declined surgery). 10 (34%) patients had minimal/nil response upon resection (College of American Pathologists Tumour Regression Grading (TRG) Score 3), 5 of whom received adjuvant FLOT whilst 5 did not (p0.28). 10 (34%) patients did not receive adjuvant FLOT, 18 (62%) did and 1 received 8 cycles of neoadjuvant chemotherapy. Nil demographic differences were observed between 'yes' and 'no' adjuvant FLOT groups. The reasons for not having adjuvant chemotherapy were: metastatic disease diagnosed post-operatively (n = 2), TRG Score 3 (n = 4), patient declined further chemotherapy (n = 1), reduced performance status and/or toxicity (n = 2), and the patient requiring treatment for a second malignancy (n = 2). 10 (34%) patients completed perioperative chemotherapy. Median DFS was 12.5m (95% CI 7.9-12.5) for 'no' FLOT' and was not-reached for 'yes' FLOT (p = 0.29). 18m DFS was 50% (95% CI 27-93) v 81% (95% CI 64-100) respectively. The median OS for 'no' adjuvant FLOT was 16.7m (95% CI 11.5-16.7) with 5 deaths. Zero deaths due to malignancy had occurred at 23.3m in those who received adjuvant FLOT (p0.00164). 1 death in the 'yes' group occurred due to interstitial lung disease. **Conclusions:** In our small population size 34% of patients completed perioperative FLOT. Whilst nil statistically significant difference was observed in mDFS, an improved mOS was observed in those that received adjuvant FLOT suggesting an importance in receiving the maximum number of cycles of chemotherapy. Given the challenges of administering adjuvant FLOT future trials into the feasibility and efficacy of 8 cycles of neoadjuvant FLOT should be considered. Research Sponsor: None.

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Durvalumab (D) and PET-directed chemoradiation (CRT) after induction FOLFOX for esophageal adenocarcinoma. *First Author: Geoffrey Yuyat Ku, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Based on the positive results of the CALGB 80803 study (J Clin Oncol 2017;35:1 [abstr]), we have added D to induction FOLFOX and pre-op CRT. **Methods:** Patients (Pts) had $T_{any}N+$ or $T3\text{-}4N_{any}M0$ esophageal and Siewert Type I-III GEJ adenocarcinoma staged by EUS, PET/CT and CT. Pts received mFOLFOX6 $\times 2$ prior to repeat PET/CT. PET responders (PETr) received 5-FU or capecitabine and oxaliplatin with RT to 50.4Gy, while induction PET non-responders (PETnr) received carboplatin/paclitaxel with RT. All Pts received D 1,500 mg q4W $\times 2$ starting 2 wks prior to and during CRT. Esophagectomy was planned 6-8 weeks after CRT. Pts who had R0 resections received adjuvant D 1,500mg q4W $\times 6$. **Results:** 36 Pts have been enrolled: 25 GEJ, 11 esophageal; 23 N+ and 32 T3/4. 26 of 36 Pts (72%) are PETr. 2 Pts developed metastatic disease after CRT and 9 Pts remain on preop treatment. 25 Pts have had surgery (Table). Pathologic complete response (pCR) was seen in 6 (24%); 5 Pts (20%) had ypT1N0 tumors with 99% response and 2 Pts (8%) had ypT0N1 with 99% response. 20 Pts (80%) had >90% response. 3 Pts had MSI tumors (2 PETr; 1 pCR, 1 T1aN0 99% response, 1 ypT2N0 90% response). Notable grade (gd) 3/4 adverse events (AEs) observed were neutropenia in 8 Pts (22%), diarrhea and vomiting in 2 Pts each (6%). Notable gd 1/2 AEs in ≥20%: anemia (31 Pts), thrombocytopenia (29 Pts), nausea (21 Pts), fatigue (25 Pts), increased AST (20 Pts), constipation and diarrhea (9 Pts), diarrhea (8 Pts). Immune-related AEs noted were gd 2 dermatitis (2 Pts), gd 3 hepatitis and gd 1 hypothyroidism in 1 Pt each. Median length of post-op stay was 8 days, with 12% anastomotic complication rate, including 1 Pt who died of hematemesis 16 days after discharge from 55-day hospitalization. **Conclusions:** The addition of D to induction FOLFOX and PET-directed CRT is safe and feasible. pCR and near-pCR in $^1/_2$ of operated Pts is encouraging and compares favorably to the pCR rate of 31% in CALGB 80803 Pts who received induction FOLFOX. The final pCR rate and correlatives for the fully accrued study will be presented. Clinical trial information: NCT02962063. Research Sponsor: AstraZeneca, Other Foundation.

	Pathologic response			
Operated patients (n=25)	**100%**	**99%**	**>90%**	**<90%**
PET responder (n=19)	5	5	4	3
MSS tumor	1	1	-	-
MSI tumor				
PET non-responder (n=6)	-	2	1	2
MSS tumor	-	-	1	-
MSI tumor				
TOTAL	6 (24%)	8 (32%)	6 (24%)	5 (20%)

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Phase Ib trial of varlitinib plus weekly paclitaxel in EGFR/HER2 co-expressing advanced gastric cancer (AGC). *First Author: Yunbeom Sang, Division of Medical Oncology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea*

Background: EGFR and HER2 are over-expressed in gastric cancer, and activation of EGFR signaling in HER2-overexpressing gastric cancer can confer resistance to HER2-directed treatment like trastuzumab. Varlitinib (also known as ASLAN001) is a small-molecule, adenosine triphosphate competitive inhibitor of the tyrosine kinases - EGFR, HER2, and HER4. We present phase 1b results of the phase1b/2 study to evaluate the safety and efficacy of varlitinib in combination with weekly paclitaxel in EGFR/HER2 co-expressing AGC patients as a second-line treatment. (KCT0003583). **Methods:** An open-label phase Ib trial was conducted using a 3+3 design. AGC patients who had failed first-line fluoropyrimidine-containing chemotherapy, with evidence of both EGFR and HER2 overexpression by IHC (≥1+), were enrolled. The primary objective was to assess the dose limiting toxicity (DLT) and recommended phase 2 dose (RP2D) of varlitinib [Dose 1: 300 mg BID, Dose -1: 300mg intermittent dose] and weekly paclitaxel (80 mg/m^2 D1,8,15) every 4 weeks along with evaluation of anti-tumor activity. **Results:** From July 2019 to May 2020, 9 patients were enrolled at Dose 1 level of varlitinib 300mg bid and 6 patients were evaluable for safety per protocol. Two patients did not finish DLT period: one patient withdrew after 1 week and one patient received palliative surgery for panperitonitis caused by gastric cancer metastasis. One patient had major violation in IP administration as the patient took varlitinib intermittently. Among the 6 evaluable patients, there was 1 DLT of G4 AST/ALT elevation and G3 hyperbilirubinemia, which resolved after 3 weeks. The most common treatment related adverse events (TRAEs) were neutropenia (n=5), all of which were grade ≥ 3, but no lasting more than 7 days. Grade 2 TRAEs included rash (n=2), mucositis (n=2) and peripheral sensory neuropathy (n=2). After a median follow-up of 3.0 (range, 1.9~ 6.2) months, the best responses were stable disease in 4 patients. Currently, 4 patients are ongoing. **Conclusions:** The combination of varlitinib 300mg bid and weekly paclitaxel 80mg showed manageable safety profiles and determined as RP2D. Currently, multi-site phase 2 part is now underway. Clinical trial information: KCT0003583. Research Sponsor: None.

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KEYlargo: A phase II study of first-line pembrolizumab (P), capecitabine (C), and oxaliplatin (O) in HER2-negative gastroesophageal (GE) adenocarcinoma. *First Author: Hope Elizabeth Uronis, Duke University Medical Center, Durham, NC*

Background: Gastric and esophageal adenocarcinomas are a leading cause of cancer death worldwide. Many of these patients (pts) present with locally advanced unresectable or metastatic disease and are treated with combination cytotoxic chemotherapy. Single agent P is FDA approved for patients with recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma (GEJ) whose tumors have a combined positive score (CPS) ≥ 1 after disease progression on or after two lines of therapy including fluoropyrimidine and platinum and her2/neu-targeted therapy (if indicated). More effective therapy is needed earlier in the disease trajectory. We conducted a single-arm phase II trial to establish the safety and efficacy of first-line C and O + P. **Methods:** Pts with previously untreated metastatic GE adenocarcinoma regardless of PDL-1 status received intravenous (IV) P 200mg with IV O 130mg/m^2 every three weeks and oral C 850mg/m^2 twice daily for 14 days on/7 days off. After the 6 patient safety cohort, pts first completed a biomarker cycle that included fresh tumor biopsy before P and one week after P before chemotherapy started. Archived FFPE tumor samples were also obtained from all pts with available tissue. The primary endpoint was progression free survival (PFS); secondary endpoints included response rate (RR) and overall survival (OS). **Results:** 36 pts were enrolled and 34 pts were evaluable for efficacy (1 pt withdrew for personal reasons before end of cycle 1 and 1 pt had immune-related toxicity during cycle 1 and was taken off study before any efficacy assessment). 9 pts (26%) had an esophageal primary, 18 pts (53%) had a GEJ primary and 7 pts (21%) had a gastric primary. Median PFS was 7.6 months [95% CI: 5.8 to 12.2], RR was 72.7% [95% CI: 57% to 88%], and median OS was 15.8 months [95% CI: 11.6 to NE]. 27 patients (81.8%) had decrease in disease burden (ranging from -19% to -100%). After > 18 months of follow-up, 5 patients remained in durable complete response (CR). Immune-mediated treatment related adverse events (TRAEs) included thyroid disorders (n=5; 14%), colitis (n=4; 11%), adrenal insufficiency (n=2; 5%), and type 1 diabetes (n=1). Sixteen patients (44%) experienced grade 3 or 4 TRAEs. There were no grade 5 TRAEs. **Conclusions:** The combination of C and O + P had acceptable safety and significant clinical activity. These promising results indicate that C and O + P merits further study as a first line option for patients with unresectable locally advanced or metastatic GE adenocarcinoma. Updated survival and correlative data will be presented. Clinical trial information: NCT03342937. Research Sponsor: Merck.

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Trifluridine/tipiracil outcomes in third- or later lines versus placebo in metastatic gastric cancer treatment: An exploratory subgroup analyses from the TAGS study. *First Author: Josep Tabernero, Vall d'Hebron University Hospital and Institute of Oncology (VIHO), Barcelona, Spain*

Background: Metastatic gastroesophageal cancer (GC/GEJC) is an aggressive disease with poor prognosis and a median overall survival (mOS) of around 1 year. While new treatments have emerged, the need for better understanding of the biology and patient profiling is essential given the heterogeneity of the disease. Previously, the TAGS study showed an improved OS with trifluridine/tipiracil (FTD/TPI) vs placebo in heavily pretreated metastatic GC/GEJC patients with a 31% risk reduction in death. This exploratory subgroup analysis of TAGS aims to assess the efficacy, safety, and quality of life (QoL) results observed in patients who received FTD/TPI or placebo in third line (3L) and those who received FTD/TPI beyond the third line (4L+). This analysis will help provide physicians a clearer view of what is expected in the third-line setting in terms of outcomes and to confirm the efficacy of FTD/TPI in later lines. **Methods:** Patients were divided into two groups: (i) patients who had received FTD/TPI or placebo after two lines of previous systemic therapy (3L) (n = 126 vs 64); and (ii) patients who had received FTD/TPI or placebo (n = 211 vs 106) after three or more lines of previous systemic therapy (4L+). Patient demographics/baseline characteristics, efficacy (OS, progression-free survival [PFS], and time to ECOG deterioration to 2 or more), safety, and QoL were assessed accordingly in these two groups. **Results:** Patient baseline characteristics in both groups were well balanced between FTD/TPI and placebo. The mOS for FTD/TPI vs placebo in 3L was 6.8 vs 3.2 months (HR, 0.67; 95% CI, 0.47-0.97; *P*= 0.0318); whereas, in 4L+, it was 5.2 vs 3.7 months (HR, 0.72; 95% CI, 0.55-0.95; *P*= 0.0192). The mPFS for FTD/TPI vs placebo in 3L was 3.1 vs 1.9 months (HR, 0.54; 95% CI, 0.38-0.77; *P*= 0.0004); whereas, in 4L+, it was 1.9 vs 1.8 months (HR, 0.57; 95% CI, 0.44-0.74; *P*< 0.0001). Time to deterioration of ECOG to 2 or more for FTD/TPI vs placebo in 3L was 4.8 vs 2.0 months (HR, 0.60; 95% CI, 0.42-0.86; *P*= 0.0049); whereas, in 4L+, it was 4.0 vs 2.5 months (HR, 0.75; 95% CI, 0.57-0.98; *P*= 0.0329). No relevant clinical differences were found in the impact on QoL in the overall study population. The safety profile of FTD/TPI remained consistent through all subgroup analyses. **Conclusions:** This analysis confirms the efficacy and safety of using FTD/TPI vs placebo in GC/GEJC patients in third and later lines with a survival benefit that seems to be slightly superior in 3L. Results of QoL in both 3L and 4L+ were consistent with previously published subgroup analyses and with the overall TAGS study population. When FTD/TPI is taken in 3L as recommended in the international guidelines, physicians can expect to provide their patients with a mOS of 6.8 and mPFS of 3.1 months. Clinical trial information: NCT02500043. Research Sponsor: Taiho Oncology and Taiho Pharmaceutical.

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LEAP-005: A phase II multicohort study of lenvatinib plus pembrolizumab in patients with previously treated selected solid tumors—Results from the gastric cancer cohort. *First Author: Hyun Cheol Chung, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea*

Background: Lenvatinib, an anti-angiogenic multiple receptor tyrosine kinase inhibitor, in combination with the anti–PD-1 antibody pembrolizumab, has demonstrated promising antitumor activity with manageable safety in the first- or second-line in a phase 2 trial of patients with advanced gastric cancer. LEAP-005 (NCT03797326) is a phase 2, multicohort, nonrandomized, open-label study evaluating efficacy and safety of lenvatinib plus pembrolizumab in patients with previously treated advanced solid tumors; here, we present findings from the gastric cancer cohort of LEAP-005. **Methods:** Eligible patients were aged ≥18 years with histologically or cytologically confirmed metastatic and/or unresectable gastric cancer, received at least 2 prior lines of therapy, had measurable disease per RECIST v1.1, ECOG PS of 0–1, and provided a tissue sample evaluable for PD-L1 expression. Patients received lenvatinib 20 mg once daily plus pembrolizumab 200 mg Q3W for up to 35 cycles of pembrolizumab (approximately 2 years) or until confirmed disease progression, unacceptable toxicity, or withdrawal of consent. Treatment with lenvatinib could continue beyond 2 years in patients experiencing clinical benefit. Primary endpoints were ORR (per RECIST v1.1 by blinded independent central review) and safety. Secondary endpoints included disease control rate (DCR; comprising CR, PR, and SD), duration of response (DOR), PFS, and OS. Tumor imaging was performed Q9W from treatment initiation for 54 weeks, then Q12W to week 102, and Q24W thereafter. **Results:** 31 patients were enrolled in the gastric cancer cohort; 87% were male, 58% were aged < 65 years, and 71% had PD-L1 combined positive score (CPS) ≥1. Median time from first dose to data cutoff (April 10, 2020) was 7.0 months (range, 1.9–11.9); 19 patients (61%) had discontinued treatment. ORR was 10% (95% CI, 2–26); 1 patient had CR (3%), and 2 had a PR (6%). 12 patients (39%) had SD. Median DOR was not reached (range, 2.1+ to 2.3+ months). DCR was 48% (95% CI, 30–67). Median PFS was 2.5 months (95% CI, 1.8–4.2). Median OS was 5.9 months (95% CI, 2.6–8.7). 28 patients (90%) had treatment-related AEs, including 13 patients (42%) with grade 3–5 AEs. 1 patient had a treatment-related AE that led to death (hemorrhage). 8 patients (26%) had immune-mediated AEs: hypothyroidism (n = 5), hyperthyroidism (n = 2), and pneumonitis (n = 1). There were no infusion-related reactions. **Conclusions:** In patients with advanced gastric cancer who received 2 prior lines of therapy, lenvatinib plus pembrolizumab demonstrated promising antitumor activity and a manageable safety profile. Based on these data, enrollment in the gastric cancer cohort has been expanded to 100 patients. Clinical trial information: NCT03797326. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

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Association of total neoadjuvant therapy with favorable clinical outcomes in patients with locally advanced esophageal and gastroesophageal junction adenocarcinomas (LA-GEJ CA). *First Author: Lauren Jurkowski, Medical College of Wisconsin, Milwaukee, WI*

Background: Both peri-operative chemotherapy and neoadjuvant chemoradiation have been shown to improve outcomes in patients (pts) with LA-GEJ CA compared to surgery alone. Rates of post-operative chemotherapy delivery remain suboptimal. Total neo-adjuvant therapy (TNT) in LA-GEJ CA - induction chemotherapy (IC) followed by concurrent chemoradiation (CRT) - may improve systematic delivery of neoadjuvant therapy and result in favorable clinical outcomes. **Methods:** We retrospectively reviewed medical records of 135 pts with LA-GEJ CA at our institution between 2/2007 and 11/2019; pertinent clinical data were abstracted with Institutional Review Board approval. Patients treated with IC and curative-intent CRT with ≥40 Gy dose of radiation for adenocarcinoma were included in this analysis (N = 59). Doublet or triplet IC regimens utilizing 5-Flurouracil(5-FU), Cisplatin/Oxaliplatin and Docetaxel were commonly administered while combinations of Carboplatin +Paclitaxel or 5-FU + Oxaliplatin were used in CRT. Clinical complete response (CCR) was defined as metabolic imaging and endoscopic biopsies negative for residual malignancy after completion of TNT. Patients were followed from diagnosis to recurrence and overall survival. Survival probabilities were estimated using the Kaplan-Meier method and compared between groups using a log-rank test. **Results:** Out of 59 evaluable pts, 69% were clinical stage T3, 71% were node positive. 37 pts (63%) underwent surgery, R0 resection rate was 89% (33/37), pathologic complete response (pCR) rate was 19% (7/37). Among the pts who did not undergo surgery, 41% (9/22) opted to forego surgery since they attained a CCR. For the entire cohort, median Disease-Free Survival (mDFS), median Overall Survival (mOS), and 3-yr OS were 2.4 yrs, 4.7 yrs, and 67% respectively. Pts who did not undergo surgery had a mDFS, mOS, and 3-yr OS of 1.5 yrs, 4.2 yrs, and 59% respectively. Median DFS, mOS, and 3-yr OS of patients who underwent surgery were 3.5 yrs, 5.8 yrs and 72% respectively. Patients who achieved a CCR and opted to forego surgery (N = 9) had a 3 -yr DFS of 42% vs 83% for pts (N = 7) who demonstrated a pCR after curative intent tri-modality therapy. (P = 0.0099) Interestingly, the same group that achieved CCR and opted out of surgery had 3yr OS of 89% vs 83% of those who demonstrated a pCR (p = 0.0042). **Conclusions:** TNT for pts with LA-GEJ CA is associated with high rates of R0 resection as well as excellent DFS and OS compared to historical controls, warranting prospective evaluation. The remarkable DFS and OS in patients who opted to forego surgery due to achieving CCR is reflective of the local and systemic control rendered by this approach. Careful characterization and close longitudinal follow-up of patients who achieve CCR may help identify a subgroup of LA-GEJ CA pts who may benefit from surgery sparing approaches. Research Sponsor: None.

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AK104 (PD-1/CTLA-4 bispecific) combined with chemotherapy as first-line therapy for advanced gastric (G) or gastroesophageal junction (GEJ) cancer: Updated results from a phase Ib study. *First Author: Jiafu Ji, Peking University Cancer Hospital and Institute, Beijing, China*

Background: OS and PFS benfits have been observed in combination of anti-PD-1 agent plus chemotherapy compared to chemotherapy alone as first-line advanced G/GEJ cancer (Checkmate-649). It uncovers the significant treatment prospects of immune checkpoint inhibitors combination therapies. The PD-1/CTLA-4 dual blockade has consistently demonstrated higher response rate compared to PD-1 monotherapy but higher toxicity. AK104, a PD-1/CTLA-4 bispecific antibody, is designed as a novel tetrameric form. It could preferentially binds to tumor-infiltrating lymphocytes (TILs) co-expressing PD-1 and CTLA-4 with higher avidity in the tumor micro-environment than peripheral sites. Therefore, AK104 is designed to retain the efficacy benefit derived from the combination of anti-PD-1 and anti-CTLA-4 while conferring superior safety compared to the co-administration of these individual agents. This Phase Ib study evaluates the safety and efficacy of AK104 and mXELOX in the first-setting of G/GEJ cancer cohorts (NCT03852251). **Methods:** Pts with untreated, inoperable advanced G/GEJ adenocarcinoma regardless of PD-L1 status were enrolled to cohorts of 3-6 pts at AK104 doses of 4, 6 and 10 mg/kg q2w + mXELOX [oxaliplatin 85 mg/m^2 and capecitabine 1000 mg/m^2] during dose escalation. Selected cohorts were expanded up to 18 pts to further establish the recommended Phase II dose. Tumor tissue for determination of PD-L1 status with combined positive score (CPS) must be provided from ≤ 6 months before study treatment. Antitumor activity was assessed by RECIST v1.1. **Results:** As of Sep 9, 2020, 34 pts (73.5% male, median age 63.1 yrs [29-75], 76.5% G and 23.5% GEJ) have received AK104 at doses of 4 mg/kg (n = 18), 6 mg/kg (n = 14) and 10 mg/kg (n = 2) + mXELOX. AK104-related adverse events (TRAEs) occurred in 79.4% of pts. G3 TRAEs occurred in 29.4% (10/34) and no G4 or G5 TRAE was reported. Most frequent TRAEs (incidence ≥ 15%) were neutrophil count decreased (26.5%), platelet count decreased (20.6%), white blood cell count decreased (17.6%), anaemia (17.6%) and infusion related reaction(17.6%). Grade ≥3 TRAEs reported in ≥2 pts were neutrophil count decreased (8.8%). Grade ≥3 immune-related AEs were reported in 8.8% of pts (hepatitis, pneumonitis, hyponatraemia). Of 24 pts evaluable for antitumor activity, ORR was 66.7% (95% CI 44.7, 84.4) including 2 CRs and 14 PRs . The disease control rate (DCR) was 95.8% (95% CI 78.9, 99.9). Response was seen regardless of PD-L1 status. At a median follow-up of 8.6 mons for the 4mg/kg cohort, 6-mons PFS rate was 69.5% (95%CI 41.3, 86.1). **Conclusions:** AK104 in combination with mXELOX had a manageable safety profile and encouraging antitumor activities in pts with advanced G/GEJ adenocarcinoma regardless of PD-L1 status. Enrollment is currently ongoing for 6 mg/kg and 10 mg/kg cohort. Clinical trial information: NCT03852251. Research Sponsor: Akeso Pharmaceuticals, Inc.

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Genomic characterization of a comprehensive collection of esophagogastric cancer patient-derived xenografts. *First Author: Ryan H. Moy, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Large-scale sequencing has identified multiple oncogenic drivers and molecularly defined subsets in esophagogastric cancer. However, besides therapies for HER2-positive and microsatellite instability-high disease, few genomic biomarker-driven treatments are currently approved. Patient-derived xenografts (PDXs) have emerged as promising preclinical models that capture the heterogeneity and biology of human tumors. Therefore, we established a comprehensive collection of esophagogastric cancer PDXs and performed next-generation sequencing (NGS) to genomically characterize these models. **Methods:** Starting in 2010, we developed an ongoing program for generating esophagogastric cancer PDXs from fresh tumor specimens that are acquired from surgical resections or biopsies and implanted into NOD scid gamma (NSG) mice either subcutaneously into flanks or orthotopically into the gastric wall. We reviewed clinical and pathologic characteristics of patients from whom established PDXs were derived, including stage, histology, HER2 status and treatment history. To identify oncogenic DNA alterations, NGS was performed on PDX material using MSK-IMPACT, a capture-based NGS platform. **Results:** From April 2010 to August 2018, we implanted 270 tumor samples, of which 112 were successfully engrafted (41.4%) including 57 gastric adenocarcinomas, 25 gastroesophageal junction adenocarcinomas, 23 esophageal adenocarcinomas, 4 squamous cell carcinomas and 3 small cell/high-grade neuroendocrine tumors. PDXs were generated from both primary tumors (n = 67, 59.8%) and metastases (n = 45, 40.2%), with many PDXs established from patients with metastatic disease who had progressed on standard therapy (n = 50, 44.6%). In addition, a large number of PDXs were derived from patients initially diagnosed with HER2-positive esophagogastric adenocarcinoma (n = 68, 60.7%). NGS of these PDXs demonstrated frequent alterations in *TP53*, receptor tyrosine kinases (*ERBB2*, *EGFR*), cell-cycle mediators (*CDK12, CCNE1, CCND3*) and histone methyltransferases (*KMT2C, KMT2D*), consistent with clinical sequencing. **Conclusions:** Comprehensive molecular profiling demonstrates that esophagogastric cancer PDXs recapitulate the genomic heterogeneity and tumor biology of patients. This panel represents one of the largest described collections of esophagogastric cancer PDXs and serves as a powerful platform to investigate mechanisms driving tumor growth and metastasis, identify predictive biomarkers for treatment responsiveness and develop novel genomically-driven therapeutic strategies. Research Sponsor: Department of DefenseConquer Cancer Foundation of the American Society of Clinical OncologyMSK Society.

234 Poster Session

Angiogenesis-related factors associated with nivolumab efficacy in patients with advanced gastric cancer after refractory or intolerant to ramucirumab-based therapy. *First Author: Yuki Matsubara, Department of Clinical Oncology, Aichi Cancer Center Hospital, Nagoya, Japan*

Background: Nivolumab (Nivo) is a standard therapy after ramucirumab (RAM)-based second-line chemotherapy in patients (pts) with advanced gastric cancer (AGC). However, the relationship between angiogenesis-related factors and the efficacies of immune-checkpoint inhibitors after anti-angiogenic chemotherapy is unclear. **Methods:** We retrospectively evaluated pts with AGCs who received Nivo after RAM-based second-line chemotherapy at a single institution from Nov 2017 to Aug 2019. Clinical benefit of Nivo was defined as CR, PR, or >4 months of SD and non-CR/non-PD. In addition, preserved serum samples at time points of pre-RAM, pre-Nivo, and post-Nivo (within 12 weeks from the start of Nivo) were analyzed by using the designated panel, containing vascular endothelial growth factor-A/D (VEGF-A/D), placental growth factor (PlGF), soluble vascular endothelial growth factor receptor-1/2/3 (sVEGFR-1/2/3), Interleukin-6/8 (IL-6/8), soluble intercellular adhesion molecule-1 (sICAM-1), soluble vascular cell adhesion molecule-1 (sVCAM-1), tissue inhibitor of metalloproteinase-1 (TIMP-1), angiopoietin-2, hepatocyte growth factor (HGF), interferon gamma (INF-γ), osteopontin (OPN), soluble neuropilin-1, and thrombospondin-2 (TSP-2). We investigated the association between angiogenesis-related factors and clinical outcomes with Nivo. **Results:** We evaluated 167 samples from 58 pts, including 10 pts (17.2%) exhibiting clinical benefit. Characteristics of pts were as follows: median age, 68; male, 74%; PS, 0/1-2, 17/83%; HER2 positive, 16%; prior gastrectomy, 40%; histology, intestinal/diffuse, 16/84%; disease status, metastatic/recurrent, 69/31%; lung metasstasis, 14%; liver metasstasis, 26%; peritoneum metastasis, 67%; lymph node metastasis, 31%. The median progression-free survival (PFS) and overall survival (OS) of Nivo were 1.7 and 6.2 months, respectively, with a median follow-up of 5.0 months. There were no correlations between pre-Nivo levels of angiogenesis-related factors and clinical benefit; however, the median post-Nivo/pre-Nivo VEGF-A ratio was significantly lower in pts with clinical benefit than in those without clinical benefit (0.44 versus 0.94, p = 0.008). By multivariate analysis using characteristics of pts and data from pre-Nivo samples, VEGF-A above the median level of 1400 pg/mL and sVCAM-1 below the median level of 1640000 pg/mL were independent prognostic factors for poor PFS (hazard ratio, 1.90, p = 0.033) and OS (hazard ratio, 2.02, p = 0.037), respectively. **Conclusions:** Our study suggests that rapid decline of serum VEGF-A level after Nivo and higher VEGF-A before Nivo were respectively associated with the clinical benefit of Nivo and poor survival in pts with AGC treated with Nivo after RAM-based second-line chemotherapy. Research Sponsor: None.

235 Poster Session

The immune checkpoint CD73 (NT5E) in gastric adenocarcinoma (GAC): Biological characterization and clinical implications. *First Author: Massimiliano Salati, Division of Oncology, Department of Oncology and Hematology, University Hospital of Modena, Modena, Italy*

Background: CD73, an ecto-5'-nucleotidase (NT5E), serves as an immune checkpoint by generating adenosine, which in turn leads to immune-suppression and immune-escape. Elevated tissue levels of CD73 have been linked to poor patient survival across several cancer types and CD73 blockade is currently being tested in clinical trials. The biological role of CD73 and its translational relevance is largely unexplored in gastric adenocarcinoma (GAC). **Methods:** Data mining from transcriptomics big data sources including GEPIA2, HPA and Coexpedia platforms was performed to extract relevant information regarding CD73 expression profile, co-expressed network, association with clinico-pathologic features and survival of GAC. Difference between groups were evaluated by Student's t-test, while correlation analysis was performed through Pearson's coefficient. Kaplan-Meier methods was used to estimate survival and log-rank test to make comparison between curves. **Results:** RNA sequencing expression data of 9,736 tumors and 8,587 normal tissue samples from the TCGA and the GTEx projects were analyzed. CD73 mRNA was significantly more expressed in tumour (n = 408) compared to paired normal samples (n = 211) (16.19 vs 3.5 transcripts/million; $p < 0.001$) and its expression level increased with pathologic stage (from stage I to III). CD73 gene was listed among the top-ten survival-associated genes (p = 4.74e-5) in GAC and together with FGF1 it displayed the greatest survival contribution in this disease among clinically validated genes. Regarding its impact on survival, GAC patients with high CD73 expression (n = 192) experienced a poorer overall survival (OS) compared to the low CD73 group (n = 192) (HR 1.9; log-rank $p < 0.001$), while regarding relapse-free survival (RFS), the unfavourable value of CD73 expression emerged after 20 months (HR 1.3; log-rank p = 0.23). The prognostic role on OS was validated in a cohort of 354 GAC, where high CD73 expression resulted in 5-year OS of 19% vs 46% (p = 0.00010). When inquiring for context-associated co-expression networks, Caveolin 1 (score = 10.939), FOS-like antigen 1 (score = 7.525) and plasminogen activator urokinase receptor (score = 7.422) were top-ranked co-expressed genes. **Conclusions:** In this hypothesis-generating analysis, we provided insights into CD73 expression pattern, co-expression networking and prognostic significance in GAC. Future studies in clinically annotated populations are warranted to confirm the value of CD73 in GAC. Research Sponsor: None.

236 Poster Session

The incidence of Epstein-Barr Virus-associated gastric cancer in an Irish population. *First Author: Catherine Weadick, Mater Misericordiae University Hospital, Dublin, Ireland*

Background: Gastric adenocarcinoma is the fourth most frequent cancer worldwide and the second leading cause of cancer deaths. According to The Cancer Genome Atlas (TCGA) 9% of gastric carcinomas are associated with Epstein-Barr Virus (EBV). EBV- associated gastric carcinoma (EBV-GC) has distinct clinicopathological features, with a marked lymphocytic infiltrate, a generally diffuse histological type and a better prognosis. The immune cell infiltration in EBV-GC suggests a role for immune checkpoint inhibition, which currently has modest activity in unselected gastric cancer. **Methods:** All cases of gastric or junctional adenocarcinoma diagnosed between Jan 2019 and March 2020 in Mater Misericordiae University Hospital (MMUH) and Jan 2017 and Jan 2019 in Cork University Hospital (CUH) were identified. Electronic medical records were retrospectively reviewed to collect demographic and clinicopathological data such as AJCC TNM stage, tumour subtype and grade, HER-2 status, MMR proficiency and EBV status as determined by EBV-encoded RNA in situ hybridization. **Results:** N = 103 cases of gastric or junctional adenocarcinoma were identified. 67 male, 36 female, median age 64.5 (range 34 – 95). 40/103 had undergone surgical resection. EBER-ISH was assessed in all patients. 8 of 103 (7.8%) patients showed EBV positivity. These cases were all male patients, median age 62 (range 51-73). The tumours were located as follows; 2 in the cardia, 5 in the body and 1 not documented. The specimens were graded as; 87.5% (7/8) tumours being poorly differentiated and 1/8 moderate to poorly differentiated. The tumour subtypes were specified as; 62.5% (5/8) diffuse, 12.5% (1/8) intestinal and 25% (2/8) mixed intestinal and diffuse. 5/8 patients were locally confined and underwent resection for N0 disease. 3/8 (37.5%) patients had metastatic disease. None of the 8 EBV-GC cases were identified as being HER-2 positive or MMR-deficient. **Conclusions:** EBV-GC accounted for 7.8% of all gastric cancers in two large tertiary referral centres in Ireland. 37.5% of these patients had metastatic disease. Given this frequency and a possible predictive role in selecting for immunotherapy we conclude that routine assessment of EBV status is feasible in advanced gastric cancer. Research Sponsor: None.

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Association of B cells in tumor microenvironment (TME) with clinical benefit to programmed cell death protein-1 (PD-1) blockade therapy in esophageal squamous cell carcinoma (ESCC). *First Author: Jhe-Cyuan Guo, National Taiwan University Cancer Center, Taipei City, Taiwan*

Background: Previous studies have indicated B cells as potential predictive markers for anti-PD-1 blockade therapy in several cancer types. The study explored whether B cells in TME and B cell related gene signatures are associated with clinical benefit (CB) for ESCC patients receiving anti-PD-1/PD-ligand 1 (PD-L1) therapy. **Methods:** Sixty-six ESCC patients treated with PD-1/PD-L1 blockade-based immunotherapy were enrolled. Tumor response was evaluated per RECIST 1.1, and CB was defined as complete response, partial response or stable disease at least 6 months. Transcriptome of formalin-fixed paraffin-embedded ESCC tissues were generated by NanoString nCounter platform with Human PanCancer Immune Profiling panel (n=25), Gene Set Enrichment Analysis (GSEA) was performed to identify the differential immune-related pathways, and CIBERSORT was applied to estimate the levels of infiltrating immune cells. The expression of CD20 was evaluated by immunohistochemistry (IHC) (n=66). **Results:** Of 66 enrolled patients (M: F= 65: 1, median age of 59), 44 and 22 were of recurrent and de novo metastatic ESCC. Forty and 26 received PD-1/PD-L1 blockade alone and PD-1/PD-L1-based combination immunotherapy, respectively. The response rate was 17%, and the CB rate was 24%. The median progression-free-survival (PFS) and overall survival are 1.8 and 5.5 months, respectively. B cell signature was significantly increased in patients with CB ($P < 0.05$) and associated with longer progression-free survival and overall survival (both $P < 0.05$). The genes related to B cells, B cell functions, and T cell functions were up-regulated in patients with CB compared to that with non-CB (all $P < 0.05$). Naïve B cells and plasma cells were significantly increased in patients with CB (both $P < 0.05$). The expression levels of stromal CD20 by IHC trended to increase in patients with CB ($P = 0.08$). **Conclusions:** B cells in tumor microenvironment may be associated with CB of anti-PD-1/PD-L1 therapy in patients with ESCC. (Funded by MOST 105-2314-B-002 -186 -MY3; MOHW107-TDU-B-211-114017; MOST 108-2314-B-002 -076 -MY3; MOST 107-2314-B-002-199 -). Research Sponsor: Ministry of Science and Technology, Taiwan; Ministry of Health and Welfare, Taiwan.

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Comprehensive evaluation of genomic alterations in patients with gastric and gastroesophageal adenocarcinoma stratified according to *TP53* mutation status. *First Author: Anthony Wood, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*

Background: Gastric (GC) and gastroesophageal adenocarcinomas (GEA) are molecularly diverse. Molecular biomarkers of clinical significance have been identified that impact treatment decision making. *TP53* is the most frequently altered gene with approximately 50% of patients harboring mutations. However, *TP53* mutations have not yet been confirmed as a target of therapeutic benefit. This study aimed to identify distinct genomic alterations that are dominant in *TP53* mutated (MUT) versus wild-type (WT) GC and GEA in order to elucidate alternative therapeutic targets within these subsets. **Methods:** De-identified data for 3741 patients with GC and GEA was obtained from Foundation Medicine. The data obtained were age, gender, tumor mutational burden (TMB), and the distinct genomic alterations noted on DNA sequencing. The dataset was sorted by *TP53* mutation status. Differences in mutation frequency were detected using the Fisher's exact test of independence with a p-value of < 0.01 designated as the cutoff value for statistical significance. **Results:** The dataset consisted of 2946 GCs and 795 GEAs. *TP53* mutations were present in 65.8% of specimens. 61.6% of GCs and 81.4% of GEAs were *TP53* MUT positive ($p = < .001$). Median TMB score and the frequency of tumors with a TMB score > 10 was similar in both *TP53* MUT and WT groups. 49 genes had statistically different mutation frequencies in *TP53* MUT vs. WT patients. Top co-occurring genetic alterations in *TP53* MUT patients included amplification and point mutations in *MYC, CCNE1, MET, ERBB2,* and *EGFR*. Amplification and point mutations in *MDM2, CDK4, ARID1A, PIK3CA,* and *ERBB3* were the top co-occurring genetic alterations in *TP53* WT patients. **Conclusions:** There was a high frequency of *TP53* mutations in this group of GC and GEA patients, with a higher incidence of *TP53* mutations identified in GEA samples. The mutational profiles of these tumors differed according to *TP53* mutation status. These differences may be able to serve as the foundation for future clinical investigations. Research Sponsor: University of South Florida Graduate Medical Education.

239 Poster Session

HER2-overexpression/amplification and survival in patients with resectable esophageal/gastroesophageal junction adenocarcinoma (E/GEJ-AC) treated with neoadjuvant carboplatin/paclitaxel-based chemoradiation. *First Author: Yening Feng, Mayo Clinic Rochester, Rochester, MN*

Background: After trastuzumab (T) approval for advanced HER2-positive E/GEJ-AC, HER2 testing has increased in patients (pts) with resectable disease. Neoadjuvant carboplatin/paclitaxel chemoradiation (nCP-CRT) is a common therapy approach. We performed the largest evaluation, to our knowledge, of the prognostic impact of HER2 in E/GEJ-AC pts treated with nCP-CRT. **Methods:** We retrospectively reviewed medical records of all trimodality-eligible (T_2^+ or N^+) pts with E/GEJ-AC who started nCP-CRT (usually 50.4 Gy) with planned surgery at Mayo Clinic (2014-2019). HER2 was tested using standard criteria for HER2 positivity (ie, immunohistochemistry 3+ or amplification by *in situ* hybridization). Clinicopathologic data and time to recurrence (TTR), disease free survival (DFS), overall survival (OS), survival after recurrence (SAR), and pathologic complete response (pCR – ie, no residual tumor in primary or nodes) were collected. Kaplan Meier and multivariate Cox analysis were used. **Results:** Of 161 consecutive eligible pts, HER2 status was available in 107 pts (HER2-positive n=26, HER2-negative n=81) of whom n=82 had surgery and n=19 had pCR. Most tumors were clinical T3 (80%) or N+ (81%), histologic grade 3 of 3 (62%). HER2 positivity was significantly associated with lower grade, but not with age, clinical T or N, or ECOG performance status (PS). A similar proportion of HER2-positive (*vs* negative) pts had surgery. Among pts who had surgery, pCR rates were lower in HER2-positive (*vs* negative) pts (11% [2/19] *vs* 27% [17/63]). After a median follow up of 23 mo, DFS and TTR were significantly shorter in HER2 positive (*vs* negative) pts, independent of other pretreatment covariables (Table). Yet OS was comparable. Lung recurrence was enriched in HER2 positive (*vs* negative) pts. Among pts with recurrence, SAR was longer in HER2-positive *vs* -negative pts. A total of 53% (10/19) of previously HER2-positive pts received T-based therapy after recurrence, and these pts were the drivers of favorable SAR (median 22 mo in n=10 HER2-positive pts who received T *vs* 11 mo in n=9 HER2-positive pts who did not receive T *vs* 11 mo in n=40 HER2-negative pts; *P* log-rank=.01). **Conclusions:** HER2 positivity (*vs* negativity) is independently associated with shorter TTR and DFS, but more comparable OS. The adverse association of HER2 on tumor response and TTR may have been largely overcome through enhanced survival after recurrence, although OS data are maturing. These data may have implications for the design of endpoints in future curative-intent anti-HER2 trials. Research Sponsor: None.

	HER2 positive *vs* negative.			
	No. events	2-yr event-free rate	Adj HR (95% CI)	Adj *P*
TTR	19 *vs* 40	19% *vs* 48%	1.9 (1.0, 3.6)	.04
DFS	21 *vs* 42	19% *vs* 42%	2.0 (1.1, 3.7)	.02
OS	9 *vs* 24	64% *vs* 67%	1.3 (.6, 2.9)	.56

Adjusted for age, grade, clinical T and N stage, ECOG PS

240 Poster Session

Impact of tumor location on effectiveness of first-line 5-FU-based palliative doublet chemotherapy in patients with metastatic gastroesophageal cancer. *First Author: Suleyman Yasin Goksu, University of Texas Southwestern Medical Center, Dallas, TX*

Background: While gastroesophageal cancers with different primary tumor locations can have distinct molecular characteristics and clinical outcomes, the efficacy of palliative chemotherapy in tumors with different locations is unknown. Using primary tumor location as a surrogate for molecular subtype, we investigated the differential efficacy of first-line doublet chemotherapy in metastatic gastroesophageal adenocarcinomas. **Methods:** We performed a retrospective review of patients with metastatic gastroesophageal adenocarcinoma who received first-line palliative chemotherapy at the University of Texas Southwestern Medical Center and the Dallas County Safety Net Parkland Hospital diagnosed between 2011-2019. Cases were identified using cancer registries. We categorized the tumor location as proximal or distal based on endoscopy and imaging studies. Disease response was assessed on the first staging scan and classified as 'disease shrinkage, stability, or progression.' Overall and progression-free survival were evaluated using Kaplan-Meier and Cox proportional hazards methods. **Results:** 99 patients were identified; 58.6% had proximal tumors. Patients with proximal tumors were more likely to be white (38% vs. 13%, p = 0.008) and older with age $\geq$ 50 years (71% vs. 51%, p = 0.04) and less likely to have peritoneal metastasis (48% vs. 78%, p = 0.003) than distal tumors. Patients with proximal tumors had a higher disease shrinkage than patients with distal tumors (53% vs. 21%, p = 0.004). Patients with proximal tumors also had better overall survival (median 12.5 vs. 8.7 months) and progression-free survival in response to 5-FU based chemotherapy (median 5 vs. 4 months) compared to patients with distal tumors, but this was not statistically significant. On multivariable analysis, tumor location was not independently predictive of progression-free survival after adjusting for age, gender, presence of signet rings, diffuse, intestinal histology, and peritoneal metastasis (HR 1.22 95% CI 0.74-2.00), but pretreatment albumin was (HR 0.63 95% CI 0.43-0.94). **Conclusions:** Proximal gastroesophageal cancers have a better clinical response to first-line 5FU containing chemotherapy than distal cancers. Currently, there is no platform to determine molecular subgroups that is commercially available. Until testing for this becomes available, differences in response rates to palliative chemotherapy in gastroesophageal cancers with different anatomical locations should be recognized and studied further. Research Sponsor: None.

ABSTRACT WITHDRAWN

242 Poster Session

Investigating chemopotentiation by low-dose fractionated radiation therapy for disseminated intra-abdominal gastric cancer. *First Author: France Carrier, University of Maryland, Baltimore, Baltimore, MD*

Background: Treatment options are rather limited for gastrointestinal cancer patients whose disease has disseminated into the intra-abdominal cavity. There is currently no modality that has been shown to prolong survival of this patient sub-population. Here, we designed pre-clinical studies to evaluate the potential application of chemopotentiation by Low Dose Fractionated Radiation Therapy (LDFRT) for disseminated gastric cancer and evaluate the role of a likely biomarker, the Dual Oxidase 2 (DUOX2) enzyme. **Methods:** Nude mice were injected orthotopically with human gastric cancer cells expressing endogenous or lower levels of DUOX2 and randomly assigned to four treatment groups: 1; vehicle alone, 2; chemotherapy consisting of a modified regimen of docetaxel, cisplatin and 5'-fluorouracil (mDCF) for three consecutive days, 3; Low Dose- Whole Abdomen Radiation Therapy (LD-WART) (5 fractions of 15 cGy in three days), 4; mDCF and LD-WART. Blood was harvested at day 14 and 45 and cancer progression was evaluated by fluorescence imaging (Xenogen). **Results:** The combined regimen was well tolerated in all animals and led to DUOX2 upregulation, increased serum protein oxidation and reduced cancer progression in the DUOX2 positive tumors. Tumors expressing lower DUOX2 levels were more sensitive to chemotherapy but no additional benefit was obtained with LD-WART. The potential clinical significance of these findings is exemplified by a tumor microarray demonstrating that only about 46% of human gastric tumors expressed DUOX2. The molecular mechanisms underlying DUOX2 effects in response to the combined regimen include NF-kB upregulation and VEGF down regulation. Moreover, the combined regimen of mDCF and LDFRT was also effective on a Cancer Stem Cell (CSC)-Like subpopulation of mouse gastric cancer cells. **Conclusions:** Taken together these data suggest that DUOX2 could be used as a potential biomarker for patient stratification for chemopotentiation by LD-WART for positive tumors while chemotherapy alone would be more effective for DUOX2 negative tumors. The absence of added toxicity suggests that these cycles could be repeated. Research Sponsor: VA merit award.

243 Poster Session

Regulation of p14ARF by Siva1 in *H. pylori*-infected gastric epithelial cells. *First Author: Manikandan Palrasu, University of Miami, Miami, FL*

Background: *Helicobacter pylori* (*H. pylori)* is the strongest known risk factor for gastric cancer. Bacterial degradation of tumor suppressor proteins affect the host microbe's interactions and host cellular response, which contribute to tumorigenesis. p14ARF, a crucial tumor suppressor protein that activates p53 protein under oncogenic stress plays a major role in oncogenic stress response (OSR) regulation. However, little is known about the mechanism of ARF and OSR regulation in *H. pylori*-infected gastric epithelial cells. **Methods:** The expression of p14ARF and cytotoxin-associated gene A (CagA) were analyzed in gastric cells co-cultured with *H. pylori* strains isolated from high-gastric risk and low-gastric risk areas by immunoblotting. To investigate the potential role of CagA in regulation of p14ARF, we employed isogenic *cagA*− and *cagE*− *H. pylori* mutants in gastric epithelial cells, and C57BL/6 mice (n = 10). We also analyzed the expression of Siva1 in human individual infected with *cagA*-positive (n = 13) and *cagA*-negative (n = 13) bacteria as well as uninfected human subjects (n = 6). siRNA was used to inhibit activity of Siva1 protein. **Results:** In this study, *H. pylori* strains expressing high levels of CagA virulence factor and associated with a higher gastric cancer risk more strongly suppress p14ARF compared with low-risk strains *in vivo* and *in vitro*. We found that degradation of p14ARF induced by CagA is mediated by E3 ubiquitin ligase Siva1, which works in concert with another E3 ubiquitin ligase TRIP12. Decreased expression of Siva1 protein and consequent up-regulation of p14ARF was also found in gastric mucosa of *H. pylori*-infected mice and human individuals. Tumorigenic strain 7.13 was more potent in upregulation of Siva1 and downregulation of p14ARF than non-tumorigenic strain B128. Inhibition of p14ARF protein by *H. pylori* causes inhibition of autophagy in infected cells. **Conclusions:** Our results provide first evidence that carcinogenic *H. pylori* strains significantly alter the host tumor suppressor protein p14ARF, leading to suppression of host OSR and autophagy, which may affect host-bacteria interactions and tumorigenic alteration in the stomach. Research Sponsor: NIH.

244 Poster Session

The interaction between microsatellite instability high (MSI-high) gastric cancer and chemotherapy on survival. *First Author: Elvira Lise Vos, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Subgroup analysis of trials data suggested a favorable prognostic role for microsatellite instability high (MSI-high) status in resectable gastric cancer, but a lack of survival benefit from neoadjuvant/adjuvant chemotherapy; questioning current standard of care for MSI-high locally advanced gastric cancer. To help guide treatment decision making, we retrospectively studied the interaction between MSI status and chemotherapy on survival in a single institution. **Methods:** All clinically advanced (tumor stage 3-4 or positive lymph nodes) gastric cancer patients that underwent gastrectomy between 2000-2018 with MSI status available from immunohistochemistry (IHC, deficient mismatch repair protein expression (dMMR) vs proficient (pMMR)) or DNA next generation sequencing testing (NGS, MSI-high vs low/stable (MSS)) were included. Clinicopathological characteristics and overall survival (OS) was compared between patients with neoadjuvant/adjuvant chemotherapy and without, stratified for MSI status, by Kaplan-Meier and Cox regression analysis. **Results:** From a total of 1,844 clinically advanced patients with resection, MSI status was available in 559 as determined by IHC in 420, NGS in 88, and both in 51 with a concordance rate of 50/51 (98%). Tumors were dMMR/MSI-high in 84 (15%) and pMMR/MSS in 475 (85%). Patients with dMMR/MSI-high tumors were more often older, female, and had distal tumors with intestinal subtype. Neoadjuvant and/or adjuvant chemotherapy was administered in 53 (63%) in the dMMR/MSI-high group and 367 (77%) in the pMMR/MSS (p = 0.006). Median (interquartile range) time of follow-up was 32 (19-57) months. In the total cohort, OS after 3 years was 82% in the dMMR/MSI-high and 59% in pMMR/MSS ($p < 0.001$). In the patients with neoadjuvant/adjuvant chemotherapy only, the dMMR/MSI-high had improved OS (3-years OS: 80% vs 60%, p = 0.001), and after adjustment for age and clinical tumor stage in multivariable analysis, dMMR/MSI-high status was associated with improved OS (HR 0.38 95%CI 0.22-0.68). In the dMMR/MSI-high group only, 3-year OS was 80% with chemotherapy vs 86% without (p = 0.374), and chemotherapy was not associated with a difference in OS after multivariable analysis (HR 1.03 95%CI 0.40-2.66). In case of neoadjuvant chemotherapy, grade 1 pathological response (> 90%) was observed in 1/41 (2.4%) of the dMMR/MSI-high tumors vs 43/278 (16%) of the pMMR/MSS tumors respectively (p = 0.026). **Conclusions:** The incidence of MSI-high tumors in our cohort of clinically locally advanced, resectable, gastric cancers was 15%. Patients with MSI-high tumors had worse pathological treatment response to neoadjuvant chemotherapy, but better OS, compared to microsatellite stable tumors. However, in patients with MSI-high tumors, OS was not altered by neoadjuvant/adjuvant chemotherapy. We recommend assessing MSI status in locally advanced gastric cancer. Research Sponsor: None.

245 Poster Session

Development and validation of a targeted sequencing panel for application to treatment-refractory solid tumor. *First Author: Woo Sun Kwon, Yonsei University College of Medicine, Seoul, South Korea*

Background: Next generation sequencing has revolutionised genomic studies of cancer, having facilitated the development of precision oncology treatments based on a tumour's molecular profile. We aimed to develop a targeted sequencing panel for application to treatment-refractory solid tumor types with particular focus on tumours of the stomach cancer, plus test for utility in FFPE, fluid sample and cancer cell lines. **Methods:** "CancerMaster" is custom RNA probes for target enrichment sequencing. It consists of all unions (7,811 regions, 2.5Mb) of reported exons of 524 tumor and immune related genes. The panel contains special RNA probes, which enables detection of microsatellite instability, Epstein-Barr virus and Human papillomavirus. Also, the CancerMaster panel analyzes 524 genes as well as genomic signatures including microsatellite instability (MSI), tumor mutational burden (TMB) and HLA allele. FFPE samples and 49 gastric cancer (GC) cell lines were collected for performance and application testing. Panel sensitivity and precision were measured using well-characterised DNA controls (n = 117), and specificity by Sanger sequencing, pyrosequencing, FoundationOne CDx. **Results:** We achieved a mean coverage of 1,032x, with sensitivity and specificity of >99% and precision of >97%. In this study, we evaluated 26 Yonsei Cancer Center (YCC) GC cell lines and 23 GC cell lines from other sources (ATCC, KCLB, and JCRB). Application to 49 gastric cancers cell lines resulted in detection of copy number variant (CNV), single number variant (SNV) and small InDel aligned to whole exome sequencing data. In addition to previous novel EBV infected cell line (YCCEL1/YCC-10, J Gen Virol. 2013), we observed amplification and overexpression of receptor tyrosine kinase (RTK) including HER2 (YCC-19, 32, 33, 38), EGFR (YCC-11, 21), Met (YCC-31, 34), and FGFR2 (YCC-28, 30) in YCC GC cell lines; confirming that protein was overexpression by Western blot or Flow cytometry in 19/49 (38.8%). Interestingly, amplification of RTKs was detected mutually exclusive pattern with other RTK amplification. **Conclusions:** We have developed and validated an analytically-validated panel for application to cancers of treatment-refractory types. Research Sponsor: None.

246 Poster Session

Disease-free and overall survival in nonmetastatic esophageal or gastroesophageal junctional cancer after treatment with curative intent: A nationwide population-based study. *First Author: Marieke Pape, Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, Netherlands*

Background: Among patients with potentially curable esophageal cancer (EC) or gastroesophageal junctional cancer (GEJC) treated with curative intent, survival remains poor and around half of these patients have disease recurrence within a few years. This study addresses the need for real-world data on disease-free survival (DFS) and overall survival (OS) in patients with EC or GEJC who underwent potentially curative treatment. **Methods:** Patients selected from the nationwide Netherlands cancer registry (NCR) had received a primary diagnosis of non-metastatic EC or GEJC (excluding patients with T4b tumors) in 2015 or 2016 and received treatment with curative intent. Curative intent was defined as receiving resection (with or without [neo]adjuvant therapy) or definitive chemoradiotherapy (dCRT) without surgery. DFS and OS were analysed using Kaplan-Meier curves with Log-Rank test from resection date or end of dCRT. A sub-analysis was performed for NCR patients selected to align with the population of the CheckMate-577 phase 3 study of adjuvant nivolumab, i.e. patients with non-cervical stage II/III disease, R0 resection and residual pathological disease after neoadjuvant CRT (nCRT) and surgery. **Results:** We identified 1916 patients of median age of 67 years and predominantly male (76%). The majority (79%) received surgery and 21% of patients received dCRT. In resected patients, 83% received nCRT, 10% neoadjuvant chemotherapy (with or without adjuvant CRT) and 7% received no (neo)adjuvant treatment. Compared to the resected group, the population receiving dCRT had significantly fewer males (65% vs 78%), a higher median age (72 vs 65 years) and worse performance status. Patients receiving dCRT significantly shorter median DFS (14.2 months) and OS (20.9 months) compared to resected patients (DFS: 26.4 months, $p < 0.001$; OS: 40.5 months, $p < 0.001$). The 1- and 3-year DFS probabilities were 68% and 44%, respectively, in resected patients, and 56% and 24%, respectively, in patients receiving dCRT. In patients receiving nCRT followed by surgery, the median DFS and OS were 25.2 and 38.0 months, respectively, and 1- and 3-year DFS probabilities were 67% and 43%, respectively. In the sub-analysis (n = 725) the median DFS and OS were 19.2 and 29.4 months, respectively, and the 1- and 3-year DFS rates were 62% and 36%, respectively. **Conclusions:** Although patients are treated with curative intent, a considerable amount of patients with non-metastatic EC or GEJC experienced recurrence within two years. Resected patients had a higher DFS and OS compared to patients receiving dCRT. Research Sponsor: Bristol Meyers Squibb.

247 Poster Session

The impact of prior therapies on outcomes with trifluridine/tipiracil (FTD/TPI) in the phase III TAGS trial. *First Author: Kohei Shitara, National Cancer Center Hospital East, Kashiwa, Japan*

Background: It is unclear whether prior treatment with ramucirumab (RAM) or RAM plus paclitaxel (PAC), standard second-line treatments for metastatic gastric or gastroesophageal junction cancer (mGC/GEJC), can influence outcomes with third-line chemotherapy in this patient (pt) population (pop). In the phase 3 TAGS trial, FTD/TPI showed a survival benefit vs placebo (PBO) in pts with mGC/GEJC who had received ≥2 prior chemotherapy regimens. Post hoc analyses were performed to assess the impact of prior RAM, PAC or RAM+PAC treatment on the efficacy and safety of FTD/TPI in TAGS. **Methods:** Pts in the TAGS trial were categorized into 5 subgroups based on prior treatment received as follows: A) RAM (alone or combined with other agents), B) no RAM, C) PAC (but no RAM), D) RAM+PAC (sequentially or in combination) and E) neither PAC nor RAM. While subgroups A and B were pre-specified, all other subgroups were identified post hoc. Efficacy (overall survival [OS] and progression-free survival [PFS]) and safety were assessed in these subgroups. **Results:** In the overall pop (N=507), 33% had received prior RAM (alone/combined); 30% prior RAM+PAC; 27% prior PAC but no RAM; and 40% had received neither PAC nor RAM. As only 3% of all pts received prior RAM but no PAC, that subgroup was not considered in this analysis. FTD/TPI treatment was consistently associated with benefits in OS and PFS vs placebo across all pt subgroups (Table). Among pts randomized to FTD/TPI, OS benefit was similar between pts who received RAM+PAC vs those who received neither (HR, 1.15; 95% CI, 0.84–1.58) and between pts who received PAC (but no RAM) vs those who received neither (HR, 0.91; 95% CI, 0.66–1.25). The FTD/TPI safety profile was consistent across all subgroups, with similar overall incidences of grade ≥3 adverse events (AEs). Minor variations in hematologic toxicities were noted (Table). **Conclusions:** In the phase 3 TAGS trial, FTD/TPI treatment in the third or later line provided efficacy benefits vs PBO and demonstrated a consistent safety profile in pts with mGC/GEJC regardless of prior treatments. Clinical trial information: NCT02500043. Research Sponsor: Taiho Oncology, Inc.

	All pts			Prior RAM			No prior RAM			Prior Pac (no RAM)			Prior RAM+PAC			No prior RAM or PAC		
	FTD/TPI	PBO	HR (95% CI)	FTD/TPI	PBO	HR (95% CI)	FTD/TPI	PBO	HR (95% CI)	FTD/TPI	PBO	HR (95% CI)	FTD/TPI	PBO	HR (95% CI)	FTD/TPI	PBO	HR (95% CI)
ITT pop, n	337	170		114	55		223*	115		99	37		106	48		124	78	
Median OS, mo	5.7	3.6	0.69 (0.56-0.85)	5.0	3.8	0.76 (0.53-1.08)	6.0	3.3	0.66 (0.51-0.85)	5.7	3.0	0.47 (0.31-0.73)	4.6	3.6	0.73 (0.50-1.05)	6.1	3.7	0.83 (0.60-1.16)
Median PFS, mo	2.0	1.8	0.57 (0.47-0.70)	1.9	1.7	0.54 (0.38-0.77)	2.2	1.8	0.58 (0.46-0.75)	1.9	1.8	0.57 (0.37-0.85)	1.9	1.7	0.51 (0.36-0.74)	2.3	1.8	0.62 (0.46-0.84)
Safety pop, n	335	168		109	55		226*	113		99	36		105	48		123	77	
Grade ≥3 AE, %																		
Any	80	58		76	56		81	58		80	61		76	60		83	56	
Neutropenia	34	0		38	0		32	0		32	0		37	0		32	0	
Anemia	19	8		19	11		19	6		26	8		17	10		15	5	

*Slightly different source parameters accounted for minor variations in pt numbers.

248 Poster Session

The interdisciplinary team: Education as a means to exemplify and optimize patient outcomes in gastric/GEJ cancers through collaborative discussions. *First Author: Kinjal Parikh, Medscape Oncology, New York, NY*

Background: Care of patients with gastric/GEJ cancer involves multimodality treatment including various systemic and supportive approaches and collaboration of interdisciplinary team members. Optimizing care requires not only adherence to the latest evidence-based and guideline-driven recommendations but also the management of underlying comorbidities or treatment-induced conditions. This complex interplay of factors in treatment planning requires timely education for oncologists and nurses/NPs in both clinically driven topics and interdisciplinary collaboration. **Methods:** A series of 2 CME/CE-certified activities were launched to educate oncologists and nurses/NPs on the changing paradigms in gastric cancer as well as the interdisciplinary collaboration needed to optimize patient eligibility for treatment. Effectiveness was analyzed using 3 multiple-choice questions measuring knowledge and competence and 1 confidence question were presented as pre-/post-repeated pairs for each of the activities. Oncologists and nurses/NPs who completed both the pre- and post-CME questions were included in the analysis and McNemar's tests were conducted to assess statistical significance of the results with $p < .05$ being considered significant. The CME activities launched in 2/2020 with data collected and reported as of 9/2020. **Results:** 8034 learners participated in the activities including 1163 oncologists and 3665 nurses/NPs. Analyses from the activities found improvement in knowledge, competence, and confidence. Data from oncologists (n = 94-302) and nurses/NPs (n = 169-510) are reported. Statistically significant changes were seen for oncologists in: Knowledge regarding the impact of nutrition and anemia can have on quality-of-life (QOL) and further treatments (50% pre, 72% post; $p < .001$); Competence related to implementing strategies to address nutrition and anemia to improve quality-of-life and to advance treatment (45% pre, 72% post; $p < .001$); Confidence regarding their ability to work together as an integrated, interdisciplinary team to enhance quality of life and treatment outcomes through a holistic treatment approach (68% pre, 83% post; $p < .001$). And for nurses/NPs in: Knowledge regarding the impact that nutrition and anemia can have on QOL and further treatments (34% pre, 50% post; $p < .01$). **Conclusions:** This online, interactive, expert-led, CME/CE-certified educational activity resulted in gains in oncologist and nurse/NP knowledge, competence, and confidence surrounding advanced gastric/GEJ cancer management and team collaboration. As patients with gastric cancer continue to present with poor performance status and require not only systemic interventions but also amelioration of underlying conditions, education remains essential for optimal outcomes to members of the interdisciplinary team. Research Sponsor: Eli Lilly.

249 Poster Session

Prognostic impact of chemoradiation-related lymphopenia in patients with gastric and gastroesophageal cancer. *First Author: Daniel W Kim, Massachusetts General Hospital, Boston, MA*

Background: Limited data exists on how chemoradiation (CRT)-induced lymphopenia affects survival outcomes in patients with gastric and gastroesophageal junction (GEJ) cancer. We evaluated the association between severe lymphopenia and its association with survival in gastric and GEJ cancer patients treated with CRT. We hypothesized that severe lymphopenia would be a poor prognostic factor. **Methods:** We performed a retrospective analysis of 154 patients with stage 1-3 gastric or GEJ cancer who underwent CRT at our institution. Patients underwent photon-based radiation therapy (RT) with a median dose of 50.4 Gy (IQR 45.0-50.4 Gy) over 28 fractions and concurrent chemotherapy (CTX) with carboplatin/paclitaxel, 5-fluorouracil based regimen, or capecitabine. 49% received CTX prior to RT. 84% underwent surgical resection, 57% pre-CRT and 26% post-CRT. Absolute lymphocyte count (ALC) at baseline and at 2 months since initiating RT were analyzed. Severe lymphopenia, defined as Grade 3 or worse lymphopenia (ALC $<$ 0.5 k/μl), was analyzed for any association with overall survival (OS). **Results:** Median time of follow up was 48 months. Median age was 65. 77% were male and 86% were Caucasian. ECOG PS was 0 or 1 in 90% and 2 in 10%. Tumor location was stomach in 38% and GEJ in 62%. Timing of CRT was preoperative among 68% and postoperative among 32%. The median ALC at baseline for the entire cohort was 1.6 k/ul (range 0.3-7.0 k/ul). At 2 months post-CRT, 49 (32%) patients had severe lymphopenia. Patients with severe lymphopenia post-CRT had a slightly lower baseline TLC compared to patients without severe lymphopenia (median TLC 1.4 k/ul vs. 1.6 k/ul; p = 0.005). There were no differences in disease and treatment characteristics between the two groups. On the multivariable Cox model, severe lymphopenia post-CRT was significantly associated with increased risk of death (HR = 3.99 [95% CI 1.55-10.28], p = 0.004). ECOG PS 2 (HR = 34.97 [95% CI 2.08-587.73], p = 0.014) and postoperative CRT (HR = 5.55 [95% CI 1.29-23.86], p = 0.021) also predicted worse OS. The 4-year OS among patients with severe lymphopenia was 41% vs. 61% among patients with vs. without severe lymphopenia (log-rank test p = 0.041). **Conclusions:** Severe lymphopenia significantly correlated with poorer OS in patients with gastric or GEJ cancer treated with CRT. CRT-induced lymphopenia may be an important prognostic factor for survival in this patient population. Closer observation in high-risk patients and treatment modifications may be potential approaches to mitigating CRT-induced lymphopenia. Research Sponsor: None.

250 Poster Session

Clinical and molecular characteristics of early-onset versus average-onset esophagogastric cancer. *First Author: Melissa Amy Lumish, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: While the rate of esophagogastric (EG) cancer is declining, early onset (EO) gastric cancer prior to age 50 is rising. It is unknown whether EO-EG cancer represents a distinct entity. This study investigates the clinical and molecular characteristics of EO compared with average onset (AO)-EG cancers. **Methods:** We reviewed clinical and molecular features of gastric (G), esophageal (E) and gastroesophageal junction (GEJ) cancer in patients treated at MSKCC between 2005 and 2018. We defined early onset as age $<$ 49, based on the age cutoff for urgent endoscopy referral. Clinical symptoms at diagnosis, primary tumor location, histology, HER2 and MSI status and molecular alterations were compared using Fisher's exact test. Benjamini-Hochberg method was used to decrease the false discovery rate. **Results:** We analyzed 738 pts with EG cancer (age $<$ 49 n=151; age $>$50 n=587). Race and sex were different with more Asian (19% vs. 9%), fewer Caucasian (62% vs. 81%) ($P<0.001$) and more female patients (40% vs. 29%, $P=0.014$) in the EO group. Time from symptom onset to diagnosis was longer in the EO group (median (IQR) 144 d (66-276) vs. 75 d (34-136), $P=0.009$), though stage did not differ ($P=0.49$). Patients with EO-EG cancer had less weight loss ($P<0.001$), but no other distinct presenting symptoms. Primary disease site was different with more gastric in the EO group (66% vs. 55%, $P=0.04$). Signet-ring histology was more common in the EO group (11% vs. 3%; $P=0.0009$). ERBB2 amp and MSI-H were similar, with a trend toward more MSI-H in the AO group (ERBB2 amp $P=0.88$, $Q=0.830$; MSI-H $P=0.0157$, $Q=0.056$). The most frequent somatic alterations were similar in EO vs. AO pts, including TP53 (68% vs. 70%, $P=0.370$, $Q=0.825$), CDH1 (15% vs. 11%, $P=0.139$, $Q=0.825$), RHOA (6% vs. 5%, $P=0.395$, $Q=0.825$). There was a trend toward more ARID1A (19% vs. 7%, $P<0.01$, $Q=0.250$) and FBWX7 (5% vs. 2%, $P=139$, $Q=0.825$) mutations in the AO group. **Conclusions:** Presenting symptoms, stage, histology, HER2 and MSI status are similar in patients with EO vs. AO-EG cancer. There is a trend in EO toward longer time to diagnosis, gastric primary site of disease, signet-ring histology and fewer ARID1A and FBWX7 mutations. Expanded clinical and molecular data will be presented. Research Sponsor: None.

Characteristics of EO- vs. AO-EG cancer.

	AO-EG N=587	EO-EG N=151	P-value
Primary Site			**0.042**
Esophageal (E, GEJ)	203 (35%)	38 (25%)	
Gastric (G)	244 (42%)	73 (48%)	
Not specified	140 (24%)	40 (26%)	
Histology			**0.005**
Adenocarcinoma	312 (53%)	76 (50%)	
Other	34 (6%)	6 (4%)	
Squamous Cell Carcinoma	11 (2%)	1 (1%)	
Signet-Ring	10 (2%)	11 (7%)	
Not specified	220 (37%)	56 (37%)	
Race			**0.0001**
Caucasian	476 (81%)	97 (64%)	
Asian	54 (9%)	28 (19%)	
Black or African American	25 (4%)	9 (6%)	
Other	13 (2%)	11 (7%)	
Unknown	19 (3%)	6 (4%)	
Stage			**0.49**
I	12 (2%)	4 (3%)	
II	27 (5%)	6 (4%)	
III	62 (11%)	12 (8%)	
IV	215 (37%)	59 (39%)	
Not specified	271 (46%)	70 (46%)	
Time to diagnosis (d)			**0.036**
Median (IQR)	66 (32 - 123)	97 (35 - 190)	
Not specified	256 (44%)	66 (44%)	

TPS251 Trials in Progress Poster Session

A phase Ib multicenter study of trifluridine/tipiracil (FTD/TPI) in combination with irinotecan (IRI) in patients with advanced recurrent or unresectable gastric and gastroesophageal adenocarcinoma (aGEC) after at least one line of treatment with a fluoropyrimidine and platinum containing regimen. *First Author: Farshid Dayyani, University of California Irvine, Division of Hematology/Oncology, Department of Medicine, Orange, CA*

Background: In 2L+ aGEC, taxanes +/- ramucirumab or IRI are recommended treatment options. IRI has been tested in multiple single arm and randomized trials in second line (2L)+ aGEC, with reported objective response rates (ORR) in the 15-29% range and median progression-free survival (PFS) of $<$3 months (mo). Outcomes for aGEC remain poor with a median overall survival (OS) of 9.6 mo and PFS at 6 mo (PFS6) of only 36%. The TAGS trial in third line (3L)+ aGEC showed a significant improvement in OS from 3.6 mo to 5.7 mo with FTD/TPI over placebo. A 2L treatment with taxanes after 1L platinum containing regimens is currently associated with worsening peripheral neuropathy, which often leads to dose reductions, treatment delays, and a reduced quality of life for patients. The feasibility of FTD/TPI combined with IRI (+/- bevacizumab) in a modified 14-day schedule has been published for advanced colon cancer (PMID: 31924737) with no new safety signals while also encouraging activity in a cohort of heavily pretreated patients. **Methods:** Hypothesis:The combination of FTD/TPI with IRI in 2L+ aGEC is feasible, clinically active, and provides a treatment option which is not associated with development of peripheral neuropathy. Trial Design: 2-center, prospective, open label, non-randomized phase 1b trial. Eligibility: Diagnosis of aGEC, 1+ line of treatment including a fluoropyrimidine/platinum, ECOG 0-2, adequate organ function. Treatment: FTD/TPI 25mg/m2 on days 1-5 and IRI 180mg/m2 on day 1 every 14 days. G-CSF in allowed as needed. Primary objective: Feasibility of the regimen and estimate of efficacy. Primary endpoint: PFS6. Secondary objectives: OS, ORR, adverse events. Total number of pts to be enrolled N=20. Current enrollment (September 2020) N=14. Clinical trial information: NCT04074343. Research Sponsor: Taiho Pharmaceutical Co., Ltd.

TPS252 Trials in Progress Poster Session

MOUNTAINEER-02: Phase II/III study of tucatinib, trastuzumab, ramucirumab, and paclitaxel in previously treated HER2+ gastric or gastroesophageal junction adenocarcinoma—Trial in Progress. *First Author: John H. Strickler, Duke University Medical Center, Durham, NC*

Background: Tucatinib (TUC), a highly selective HER2-directed TKI recently approved for HER2+ metastatic breast cancer (MBC), is being developed as a novel therapy for patients (pts) with metastatic colorectal cancer (mCRC) and other GI tumors. While trastuzumab (Tras) with chemotherapy is standard in the 1st-line setting for metastatic HER2+ gastric or gastroesophageal junction adenocarcinoma (GEC), no anti-HER2 therapy has demonstrated an OS benefit over chemotherapy in 2nd-line, possibly due to loss of HER2 expression following Tras-based therapy. In GEC xenograft models, dual targeting of HER2 with TUC and Tras showed superior activity to either agent alone. Interim results from the MOUNTAINEER study have shown promising activity for TUC and Tras in HER2+ mCRC. The MOUNTAINEER-02 study is evaluating the efficacy and safety of TUC in combination with Tras, ramucirumab (Ram), and paclitaxel (Pac) in pts with HER2+ GEC. **Methods:** MOUNTAINEER-02 (NCT04499924) is a phase 2/3 study evaluating TUC and Tras with the 2nd-line standard of care, Ram and Pac. Pts receive TUC 300 mg or placebo PO BID, Tras (6 then 4 mg/kg) or placebo (IV on Days 1 and 15 of each 28-day cycle), Pac (IV on Days 1, 8, 15), and Ram (IV on Days 1 and 15). Eligible pts have locally-advanced unresectable or metastatic HER2+ GEC, have received a HER2-directed antibody, and 1 prior line of therapy for advanced disease. Pts must be $\geq$18 years of age, with an ECOG $\leq$1, and have had no prior exposure to Ram, anti-HER2 or anti-EGFR TKI, HER2-directed antibody-drug conjugates, or taxanes $\leq$12 months before enrollment. Due to the potential impact of TUC on Pac metabolism, the study will include an initial Pac dose finding stage. The open-label phase 2 part will determine the recommended dose of Pac (60 or 80 mg/m^2) combined with TUC, Tras, and Ram in 6-12 patients, and evaluate the safety and activity of the regimen in Cohorts 2A and 2B (30 patients each). The randomized, double-blind, phase 3 part will compare the efficacy and safety of TUC and Tras (Arm 3A; ~235 patients) vs. placebo (Arm 3B; ~235 patients), both in combination with Ram and Pac, and also evaluate activity of TUC with Ram and Pac (Arm 3C; ~30 patients). The dual primary phase 3 endpoints are OS and PFS per investigator, with confirmed ORR as a key secondary endpoint. HER2 status is determined at baseline using a blood-based NGS assay, and IHC/ISH of fresh or archival tumor biopsies, if available. Pts must be HER2+ by blood-based NGS in Cohort 2A and phase 3; in Cohort 2B, pts must be HER2+ in a biopsy taken post-progression during/after 1st-line therapy, but HER2-negative by blood-based NGS. Disease assessments per RECISTv1.1 will occur q6 weeks for 36 weeks, then q9 weeks. The pharmacokinetics of TUC, Pac, and their metabolites will be evaluated in a subset of pts, including a cohort with gastrectomies. Enrollment is ongoing in the U.S. Clinical trial information: NCT04499924. Research Sponsor: Seattle Genetics, Inc.

TPS253 Trials in Progress Poster Session

Phase II study of cabozantinib (cabo) combined with pembrolizumab (pembro) in metastatic or recurrent gastric and gastroesophageal adenocarcinoma (GEC) to overcome resistance to checkpoint inhibitors. *First Author: Farshid Dayyani, University of California Irvine, Division of Hematology/Oncology, Department of Medicine, Orange, CA*

Background: GEC is the third leading cause of cancer mortality and the fifth most common malignancy worldwide. Fluoropyrimidine and platinum-based combinations are the most commonly used 1L treatment regimens. There are few standard treatment options after 1st line regimens. In the 3L+ GEC Keynote-059 trial, objective response rate (ORR) with Pembro was 15.5% in PD-L1(+) vs. 6.4% in PD-L1(-) tumors. While the responses were durable, the 6-months PFS (6-PFS) was only 14.1% and the median PFS was 2.0 mo. This highlights the remaining unmet need for the majority of patients who either are refractory or develop disease progression following treatment with PD-1 inhibitors in GEC. Cabo plus checkpoint inhibitors have shown clinical benefit in various cancers including hepatocellular, renal cell (RCC), urothelial and castration-resistant prostate cancers. In the CheckMate-9ER trial, Cabo+Nivolumab improved both OS and PFS vs sunitinib in 1L RCC. In patients with RCC who had progression on anti-PD1 inhibitor treatment, Cabo showed promising activity with an ORR of 33% and DCR of 79% (ESMO 2018, abstract 3793). Hypothesis: Based on preclinical and clinical observations, Cabo might contribute to overcoming primary or secondary resistance to PD-1 blockade in GEC. **Methods:** Prospective, open label, non-randomized phase 2 trial. Eligibility: Diagnosis of GEC, 2+ line of treatment including previous fluoropyrimidine/platinum, ECOG 0-2, adequate organ function, prior checkpoint inhibitor if tumor PD-L1 CPS≥10%. Treatment: Cabozantinib 40mg PO daily, Pembrolizumab 200 mg IV on day 1 of 21d cycle. Primary objective: Feasibility of the combination and estimate of efficacy. Primary endpoint: PFS-6. Secondary objectives: OS, ORR, adverse events. Total number of patients to be enrolled N = 27. Current enrollment (Sep 2020) N = 10. Statistics: If the PFS-6 is $>$ 25%, the study would be regarded as positive, in which case it is planned to expand patient enrollment into a larger single arm phase 2 trial with additional sites to establish the efficacy of the regimen. Clinical trial information: NCT04164979. Research Sponsor: Exelixis.

TPS254 Trials in Progress Poster Session

Randomized controlled phase III trial to investigate superiority of robot-assisted gastrectomy over laparoscopic gastrectomy for clinical stage T1-2N0-2 gastric cancer patients: Japan Clinical Oncology Group study JCOG1907 (MONA LISA study). *First Author: Rie Makuuchi, Gastric Surgery Department, Cancer Institute Hospital of JFCR, Tokyo, Japan*

Background: Postoperative complications reportedly affect oncological outcomes in various cancers according to the timing of adjuvant chemotherapy and by influencing the immune function. Particularly, postoperative intra-abdominal infectious complications, including intra-abdominal abscess, pancreatic fistula, and anastomotic leakage, have been identified as prognostic factors for gastric cancer. Given the negative impact of such complications on patient survival, considering the short- and long-term outcomes, it is important to develop surgical procedures with fewer complications. In Japan, laparoscopic gastrectomy is a standard treatment modality for early gastric cancer. Randomized controlled trials have shown that laparoscopic gastrectomy is relatively less invasive and has similar postoperative complications and non-inferior patient survival rates when compared with open gastrectomy. However, several challenges associated with the procedure need to be overcome, such as the limited movement of the forceps. Robot-assisted gastrectomy allows surgeons to perform more meticulous surgical interventions with articulated devices; therefore, reducing the possibility of postoperative complications, as demonstrated by a few prospective studies performed in Japan. However, a non-randomized controlled trial conducted in Korea reported that there were no benefits of robot-assisted gastrectomy in terms of postoperative complications. Furthermore, no randomized controlled trials have directly compared robot-assisted and laparoscopic gastrectomy to provide solid evidence regarding the merits of the former. **Methods:** To confirm the superiority of robot-assisted gastrectomy over laparoscopic gastrectomy for patients with cT1-2N0-2M0 gastric cancer, we designed JCOG1907 (UMIN000039825) as a multicenter randomized phase III trial. In the standard arm, we performed laparoscopic gastrectomy with lymphadenectomy, while in the experimental arm, we performed robot-assisted gastrectomy with lymphadenectomy. The primary endpoint is the incidence of postoperative intra-abdominal infectious complications of Clavien-Dindo classification grade ≥II. Major secondary endpoints are relapse-free survival, overall survival, overall postoperative complications, and short-term clinical outcomes after gastrectomy. The planned sample size is 1040 participants, with a one-sided alpha of 5% and a power of 70%, with an expected 3% decrease in postoperative intra-abdominal infectious complications (6% vs. 3%). Over the period of 5 years, patients will be enrolled from 35 Japanese institutions. Enrollment has started in March 2020, and as of August 2020, 30 patients have already been enrolled. Clinical trial information: UMIN000039825. Research Sponsor: None.

TPS255 Trials in Progress Poster Session

CS1001-304: A phase III study of fluorouracil and cisplatin (FP) with CS1001, an anti-PD-L1 antibody, or placebo in unresectable locally advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC). *First Author: Jin Li, East Hospital Affiliated to Tongji University, Shanghai, China*

Background: ESCC is the predominant histological subtype of esophageal cancer, particularly in Asian countries. Platinum-based chemotherapy is the first-line standard therapy for patients with unresectable, locally advanced, recurrent or metastatic ESCC. The FP regimen is recommended as the preferred treatment by guidelines. However, the survival benefit conferred by this therapy leaves considerable space for improvement, with median OS being less than 1 year. Blockade of the immune checkpoint receptors has shown clinical benefits in multiple tumor types. Recent studies combining standard treatments with checkpoint inhibitors have shown encouraging efficacy and favorable safety profile in patients with unresectable, locally advanced, recurrent or metastatic ESCC. CS1001 (sugemalimab) is the first full-length, fully human immunoglobin G4 (IgG4, s228p) anti-programmed death-ligand 1 (PD-L1) monoclonal antibody developed by the OMT transgenic rat platform. In an ongoing Phase Ib trial, CS1001 in combination with FP regimen demonstrated an ORR of 67.6% (25/37) and an mPFS of 9.0 months with a manageable safety profile in unresectable, locally advanced or distantly metastatic ESCC (19 Feb 2020 data cutoff; Shen, L., et al, ESMO 2020). **Methods:** CS1001-304 is a randomized, double-blind Phase III study to compare the efficacy and safety of FP regimen with CS1001 or placebo as first-line treatment in ESCC. The study enrolls patients with histologically or cytologically confirmed unresectable locally advanced, recurrent or metastatic ESCC who have ECOG PS of 0-1, patients are not eligible for curative therapy (curative surgery or definitive chemoradiotherapy), and have not received any prior systemic anti-tumor therapy for locally advanced or metastatic disease. Approximately 540 patients will be randomized at 2:1 into CS1001 + FP and placebo + FP arms respectively, stratified by PD-L1 expression status (PD-L1 expression $<$ 1% vs $\geq$ 1% and $<$ 10% vs $\geq$10%), ECOG PS (0 vs 1) and distant metastasis (no vs yes). Patients randomized to either arm will receive FP regimen (fluorouracil: 800 mg/m^2/day, continuous intravenous infusion [IV], D1-4 of each cycle; cisplatin: 80 mg/m^2, IV, D1 of each cycle), Q3W for up to 6 cycles in combination with CS1001 1200 mg or placebo (IV, D1 of each cycle), Q3W for up to 24 months. AEs will be monitored throughout the study and graded per NCI CTCAE v5.0. Tumor response will be assessed by RECIST v1.1 every 6 weeks in the first 12 months, and every 12 weeks thereafter. The primary endpoints are blinded independent central review (BICR)-assessed PFS and OS. Secondary endpoints include investigator-assessed PFS, BICR and investigator-assessed ORR and DoR, safety, PK profile, and immunogenicity. The study is actively enrolling patients in over 60 sites in China. Clinical trial information: NCT04187352. Research Sponsor: CStone Pharmaceuticals.

TPS256 Trials in Progress Poster Session

Open-label, phase II study of ladiratuzumab vedotin (LV) for advanced gastric and gastroesophageal junction adenocarcinoma (SGNLVA-005, Trial-in-Progress). *First Author: Amna Falak Sher, Stony Brook University Hospital, Stony Brook, NY*

Background: LIV-1 is a transmembrane protein expressed in a variety of cancer types. SGN-LIV1A, or ladiratuzumab vedotin (LV), is a novel investigational humanized IgG1 antibody-drug conjugate (ADC) directed against LIV-1. LV mediates delivery of monomethyl auristatin E (MMAE), which drives antitumor activity through cytotoxic cell killing and induces immunogenic cell death. In a phase 1 study, LV was tolerable and active in heavily pretreated patients with metastatic breast cancer at a recommended dose of 2.5 mg/kg every 21 days (Modi 2017). More frequent, fractionated dosing has improved the activity and/or safety of other ADCs. Thus, this study is currently evaluating the safety and efficacy of weekly LV dosing (Days 1, 8, and 15 of every 3-week cycle) in different advanced solid tumors with various LIV-1 expression, including advanced gastric and gastroesophageal junction (GEJ) adenocarcinoma, esophageal squamous cell carcinoma, small cell lung cancer (SCLC), non-small cell lung cancer (squamous and nonsquamous), head and neck squamous cell carcinoma, castration resistant prostate cancer, and melanoma. **Methods:** SGNLVA-005 (NCT04032704) is an open-label, phase 2 study evaluating LV monotherapy in patients with 8 different advanced solid tumors in two parts (administered as a 30 minute intravenous infusion [IV]: Part A LV 2.5 mg/kg IV every 3 weeks [up to n = 72 total]; Part B LV 1.0 or 1.25 mg/kg every 1 week [up to n = 252 total]). The study is enrolling previously treated patients with unresectable locally advanced or metastatic disease. Patients must have measurable disease per RECIST v1.1, an Eastern Cooperative Oncology Group (ECOG) score of 0 or 1, and adequate organ function. Cohort specific inclusion criteria require that patients in the gastric and GEJ adenocarcinoma and esophageal squamous cell carcinoma cohorts must have received and progressed during or after no more than 1 prior line of platinum based cytotoxic chemotherapy. Patients in the gastric and GEJ adenocarcinoma cohort may have received prior anti-programmed cell death (ligand) 1 (anti-PD[L]1) therapy (unless contraindicated), and patients with known human epidermal growth factor receptor 2 (HER2) overexpression must have received prior HER2-targeted therapy. Patients are not preselected based on tumor LIV-1 expression. Tumor samples will be analyzed for correlation between LIV-1 expression and tumor response. Safety and efficacy will be monitored throughout the study. Study objectives include objective response rate (primary); safety and tolerability, disease control rate, duration of response, progression-free and overall survival, and pharmacokinetics and immunogenicity (all secondary); and pharmacodynamics. Study accrual is ongoing in the USA, Italy, South Korea, Taiwan, Australia, and the UK. Clinical trial information: NCT04032704. Research Sponsor: Seattle Genetics, Inc.

TPS257 Trials in Progress Poster Session

A randomized controlled phase III trial of comparing local field with additional prophylactic irradiation in chemoradiotherapy for clinical-T1bN0M0 esophageal cancer: JCOG1904/ARMADILLO study. *First Author: Motoo Nomura, Department of Medical Oncology, Kyoto University Hospital, Kyoto, Japan*

Background: Parallel-group controlled trial of esophagectomy versus chemoradiotherapy (JCOG0502) showed chemoradiotherapy (CRT) is considered as a standard treatment option for clinical-T1bN0M0 esophageal squamous cell carcinoma (ESCC) with organ preservation. However, locoregional recurrence after CRT occurs in 20% of patients and requires salvage treatment including salvage surgery, chemo(radio)therapy, and endoscopic resection. Salvage treatments can cause complications and treatment-related death. CRT with elective nodal irradiation (ENI) have been reported to reduce the locoregional recurrence of esophageal cancer. We conduct the clinical trial to evaluate the efficacy of modified CRT with ENI compared with CRT without ENI for the patients with cTbN0M0 ESCC. The primary purpose of this study is to investigate whether modified CRT with ENI reduces the locoregional recurrence that cannot be completely resected by salvage endoscopic resection and preserve esophagus without compromising overall survival. **Methods:** Eligibility criteria include the followings; thoracic ESCC, adenosquamous, or basaloid cell carcinoma with clinical-T1bN0M0, age 20 or older, performance status 0 or 1, adequate organ function, and patient who do not have a preference to receive a surgical resection as an initial therapy. Patients are randomly assigned to following two arms using the minimization method with a random component to balance institution, tumor length ($\leq$4cm versus $>$ 4cm), and age ($\leq$65 years old versus $>$ 65 years old). Patients in arm A receive CRT consisted of CDDP (70 mg/m^2/day, days 1 and 29) and 5-FU (700 mg/m^2/day, days 1-4 and 29-32, civ) with concurrent radiotherapy (60 Gy/30 fr without ENI). Patients in arm B receive CRT consisted of CDDP (75 mg/m^2/day, days 1 and 29) and 5-FU (1000 mg/m^2/day, days 1-4 and 29-32, civ) with concurrent radiotherapy (50.4 Gy/ 28 fr with ENI of 41.4 Gy/23 fr). Primary endpoint is major progression-free survival (MPFS), defined as the time from randomization to the date of death or disease progression except achieving curative resection by salvage endoscopic resection. We assumed 5-year MPFS with arm A to be 70% and expected a 10% improvement for arm B. The planned sample size was calculated as a total of 280 patients (140 patients per arm) with a one-sided alpha of 5%, power of 70%, an accrual period of 4 years, and a follow-up period of 5 years. This trial was activated in July 2020. The study was also registered at the Japan Registry of Clinical Trials (jRCT) as study number jRCTs031200067. Clinical trial information: jRCTs031200067. Research Sponsor: National Cancer Center Research and Development Fund (29-A-3) of Japan.

TPS258 Trials in Progress Poster Session

A phase I open-label study to investigate safety and tolerability, efficacy, pharmacokinetics, pharmacodynamics, and immunogenicity of MT-5111 in patients with HER2-positive tumors. *First Author: Zev A. Wainberg, UCLA Medical Center - Cancer Care - Santa Monica, Los Angeles, CA*

Background: Engineered toxin bodies (ETBs) are comprised of a proprietarily engineered form of Shiga-like Toxin A subunit genetically fused to antibody-like binding domains. ETBs work through novel mechanisms of action & are capable of forcing internalization, self-routing through intracellular compartments to the cytosol & inducing potent cell-kill via the enzymatic & permanent inactivation of ribosomes. MT-5111 is a de-immunized ETB targeting HER2+ solid tumors. Its novel mechanism of action, via enzymatic ribosome inactivation, may not be subject to resistance mechanisms that exist for tyrosine kinase inhibitors, antibody-drug conjugates, or antibody modalities. MT-5111 binds an epitope on HER2, distinct from trastuzumab or pertuzumab, that may provide for combination potential with other HER2-targeting agents. MT-5111 is a 55 kilodalton protein & may have improved tumor penetration capability. The objective of this trial will be to determine the safety, tolerability, & maximum tolerated dose (MTD) of MT-5111 in patients (pts) with advanced HER2+ solid tumors. **Methods:** This Phase 1, first-in-human, open-label, dose escalation & expansion study will evaluate MT-5111 monotherapy in pts with HER2-positive solid tumors. The primary objective is to determine the MTD; secondary objectives include pharmacokinetics, tumor response & immunogenicity. Part 1 consists of MT-5111 dose escalation (0.5, 1.0, 2.0, 3.0, 4.5, 6.75, 10μg/kg/dose) based on a modified 3+3 design (n$\leq$42 pts); Part 2 (dose expansion) will evaluate MT-5111 at the MTD in $\leq$98 pts. All pts will be administered MT-5111 over 30 min via IV infusion on Days 1, 8, & 15 of each 21-day cycle until disease progression, unacceptable toxicity, death, withdrawal of consent, or another reason for withdrawal. Part 1 will include pts with any HER2+ solid cancers. Part 2 will enroll 3 expansion cohorts: HER2+ breast (BC), HER2+ gastric or gastroesophageal junction adenocarcinomas (collectively referred as gastroesophageal adenocarcinomas [GEA]) & other HER2+ solid cancers. Immunohistochemistry (IHC) status must be 2+ or 3+, regardless of *in situ* hybridization (ISH) results; if no IHC is available for pts with BC or GEA, ISH criteria per the American Society of Clinical Oncology College of American Pathologists guidelines will be used. In metastatic cases, HER2 positivity must be demonstrated on metastatic lesions. Pts with HER2+ BC should have had $\geq$2 lines of HER2-directed therapy; pts with HER2+ GEA should have received or been intolerant to trastuzumab. Pts with evaluable disease may be included in Part 1; in Part 2, all pts must have $\geq$1 measurable lesion per Response Evaluation Criteria in Solid Tumors v1.1. Further details can be found on clinicaltrials.gov (NCT04029922). Enrollment, which began in September 2019, is ongoing. Clinical trial information: NCT04029922. Research Sponsor: Molecular Templates.

TPS259 Trials in Progress Poster Session

Phase II study of pembrolizumab after chemoradiotherapy (CRT) as adjuvant therapy for locally advanced esophageal squamous cell carcinoma (LA-ESCC) patients at high risk of recurrence following preoperative CRT plus surgery. *First Author: Chih-Hung Hsu, National Taiwan University Cancer Center, Taipei City, Taiwan*

Background: LA-ESCC is a potentially curable disease, for which preoperative CRT followed by esophagectomy is a standard-of-care. Previous studies have identified that close/involved margin and lymph node metastasis with extranodal invasion (ENI) in post-CRT surgical specimens are associated with increased risk of recurrence. In CheckMate-577 trial, adjuvant nivolumab significantly improved disease-free survival (DFS) in patients with esophageal cancer treated with preoperative CRT and surgery; in another trial (the "PACIFIC" trial), adjuvant durvalumab has significantly improved overall survival (OS) in stage III non-small cell lung cancer treated with definitive CRT. We hypothesize that adding pembrolizumab to CRT as an adjuvant therapy would improve the outcomes of LA-ESCC patients who are treated with preoperative CRT plus esophagectomy and with high-risk of recurrence. **Methods:** This single institution single-arm phase II study include patients with histologically confirmed LA-ESCC (AJCC 7th staging system: cT3-4aN0M0 or T1-4aN1-3M0) harboring at least one risk factor (closed/involved margin, ENI, or ypN2-3) in post-CRT surgical specimens. Patients with adenocarcinoma of esophagus or gastroesophageal junction or synchronously diagnosed with a squamous cell carcinoma of aero-digestive way other than ESCC are excluded. Patients enrolled will receive adjuvant weekly cisplatin–CRT (cisplatin, 30mg/m^2 for 2 cycles every week; radiotherapy, 180-200 cGy/fraction for 10-13 times) followed by pembrolizumab (200 mg, every 3 weeks, for 18 cycles). The primary endpoint of this study is 1-year relapse-free survival (RFS) rate; and the key secondary endpoints include RFS, 3-year RFS rate, OS, 3-yr OS rate, toxicity and safety. The study, registered with clinical trial ID of NCT03322267, started patient enrollment in Aug 2018. As of Aug of 2020, 11 of 46 planned patients have been enrolled. Clinical trial information: NCT03322267. Research Sponsor: Merck Sharp and Dohme.

TPS260 Trials in Progress Poster Session

Phase II study of zolbetuximab plus pembrolizumab in claudin 18.2: Positive locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma (G/GEJ)—ILUSTRO Cohort 3. *First Author: Samuel J Klempner, Massachusetts General Hospital, Boston, MA*

Background: Five-year survival with advanced G/GEJ is poor, and limited biomarkers exist to inform optimal treatment selection. Pembrolizumab, an anti-programmed death-1 receptor (PD-1) antibody, is approved for advanced/metastatic PD-ligand 1–positive (PD-L1$^+$) G/GEJ that progressed after $\geq$2 lines of therapy. The transmembrane tight junction protein claudin 18.2 (CLDN18.2) is normally confined to gastric mucosa but is often overexpressed in G/GEJ with roughly one-third of patients (pts) having high expression ($\geq$75%). Zolbetuximab, a chimeric IgG1 monoclonal antibody, binds to CLDN18.2 and mediates cancer cell death through antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity. Phase 2 (NCT01630083) results showed prolonged survival with zolbetuximab + epirubicin, oxaliplatin, and capecitabine (EOX) vs EOX alone in G/GEJ. Results of nonclinical studies showed enhanced antitumor activity with zolbetuximab + anti-murine PD-1 antibody, and it was hypothesized that a combination with pembrolizumab (new Cohort 3) might augment ADCC and antitumor immune response in CLDN18.2 overexpressing G/GEJ. **Methods:** This phase 2 open-label study (NCT03505320) will enroll ~112 adult pts from 22 sites in 5 countries into 3 cohorts; this abstract describes Cohort 3 (~62 pts). Key eligibility criteria are advanced/metastatic G/GEJ, measurable disease (RECIST v1.1), adequate organ function and performance status, and high/intermediate (Cohort 3A) or high (Cohort 3B) expression of CLDN18.2. Central testing of tumor tissue will determine CLDN18.2 expression; pts are considered CLDN18.2 positive (CLDN18.2$^+$) if $\geq$75% (high) or $\geq$50% to $<$ 75% (intermediate) of tumor cells demonstrate moderate-to-strong membranous IHC staining. Patients in Cohort 3B are required to be PD-L1$^+$, defined as a combined positive score $\geq$1 (IHC staining per the Dako 22C3 PD-L1 assay). Patients will receive zolbetuximab + pembrolizumab in the third/later line in Cohort 3A and third line in Cohort 3B. In Cohort 3A (safety cohort), zolbetuximab will be administered at a loading dose of 800 mg/m^2 IV on Day 1 Cycle 1 followed by 600 mg/m^2 IV every 3 weeks; a reduction from 600 mg/m^2 every 3 weeks is permitted. Pembrolizumab 200 mg IV will be administered on Day 1 of each 21-day cycle. Cohort 3B (expansion cohort) zolbetuximab dose is determined from results of Cohort 3A. Imaging will occur every 6 weeks for 24 weeks and every 12 weeks thereafter. The primary endpoint is objective response rate; additional endpoints include duration of response, disease control rate, and progression-free survival by independent review committee and investigator assessment. Pharmacokinetics, safety/tolerability, quality of life, and immunogenicity will be assessed. The study is currently recruiting pts. Clinical trial information: NCT03505320. Research Sponsor: Astellas Pharma, inc.

TPS261 Trials in Progress Poster Session

A phase Ib/II, multicenter, open-label, dose-escalation, and dose-expansion study evaluating trastuzumab deruxtecan (T-DXd, DS-8201) monotherapy and combinations in patients with HER2-overexpressing gastric cancer (DESTINY-Gastric03). *First Author: Yelena Y. Janjigian, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: For patients (pts) with HER2-overexpressing metastatic gastric cancer, trastuzumab + chemotherapy is a standard first-line option but provides only a modest overall survival (OS) benefit vs chemotherapy. T-DXd is an antibody-drug conjugate consisting of an anti-HER2 antibody, cleavable tetrapeptide-based linker, and a membrane-permeable topoisomerase I inhibitor payload. Results from a phase 1 trial showed promising antitumor activity (confirmed objective response rate [ORR], 43.2%) in pts with heavily pretreated HER2+ metastatic gastric cancer who received T-DXd (5.4 or 6.4 mg/kg; Shitara K, et al. *Lancet Oncol*. 2019;20:827-836). Here we describe the phase 1b/2 DESTINY-Gastric03 trial (NCT04379596) evaluating T-DXd monotherapy and combinations in pts with HER2-overexpressing gastric cancer. **Methods:** This is an open-label, multicenter, 2-part, phase 1b/2 study in pts with HER2-overexpressing (immunohistochemistry [IHC] 3+ or IHC 2+/in situ hybridization positive) locally advanced, unresectable or metastatic gastric or gastroesophageal junction cancer. In part 1 (dose escalation), pts who had received prior trastuzumab-containing therapy will be assigned to 1 of 5 arms: (1) T-DXd + 5-fluorouracil (5-FU); (2) T-DXd + capecitabine (C); (3) T-DXd + durvalumab; (4) T-DXd + 5-FU or C + oxaliplatin (Ox); or (5) T-DXd + 5-FU or C + durvalumab. In part 2 (dose expansion), pts with no prior treatment for metastatic disease will be randomized across 4 arms: (1) T-DXd; (2) trastuzumab + 5-FU or C + Ox or cisplatin; (3) T-DXd + 5-FU or C ± Ox; or (4) T-DXd + 5-FU or C + durvalumab. In part 2, pts will be stratified by HER2 status. Primary endpoints are safety, determination of recommended phase 2 doses (part 1), and investigator-assessed confirmed ORR per RECIST v1.1 (part 2). Secondary endpoints include confirmed ORR (part 1), disease control rate, duration of response, progression-free survival (all per investigator), OS, safety (part 2), pharmacokinetics, and immunogenicity. Clinical trial information: NCT04379596. Research Sponsor: AstraZeneca.

TPS262 Trials in Progress Poster Session

NRG Oncology NRG-GI007 trial-in-progress: Phase I study of OBP-301 (Telomelysin) and definitive chemoradiation (CRT) for patients with locally advanced esophageal and gastroesophageal adenocarcinoma who are not candidates for surgery. *First Author: Geoffrey Yuyat Ku, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Definitive CRT is a standard-of-care for patients with medically inoperable esophageal cancer (EC, NEJM 326:1593). The NRG/RTOG 0436 study of cisplatin/paclitaxel and RT (+/- cetuximab) as definitive therapy showed that about $^1/_2$ of patients have locally persistent disease (JAMA Oncol 3:1520). OBP-301 is a conditionally-restricted, replication-competent adenovirus derived from human adenovirus type 5 (Ad-5) that adds a human Telomerase Reverse Transcriptase (hTERT) gene promoter; it replicates only in tumor cells to cause lysis. It may enhance RT and may cause immunogenic cell death. A phase I study with RT in Japanese patients with inoperable EC showed tolerability and activity. **Methods:** In NRG-GI007, OBP-301 is added to weekly carboplatin/paclitaxel and RT to 50.4 Gy (1.8 Gy/fx ×28 fx) for patients with medically inoperable esophageal or gastroesophageal junction (GEJ) adenocarcinoma. Patients receive intratumoral OBP-301 1×10^{12} virus particles (vp)/ml via endoscopy (EGD) 3 days prior to CRT, then at days 12 and 26 of CRT, for a total of 3 doses. Restaging with PET and EGD occur 6-8 weeks later. Blood and tumor tissue are collected for immune- and viral-based correlative assays. Patients must be assessed to be medically inoperable and have ECOG performance status <1. The primary endpoint is safety, and clinical complete response (cCR) rate is a secondary endpoint. Initially, 6 patients are enrolled. If protocol-defined dose-limiting toxicity (DLT) occurs in <1 of 6 patients, the dose will be deemed to be safe and 9 more will be enrolled to further assess safety and obtain a preliminary assessment of cCR rate. If >2 of 6 patients have DLT, the dose of OBP-301 is reduced to 1×10^{11} vp/ml and another 6 patients will be treated. If <1 of 6 patients has a DLT at the lower dose, that dose will be deemed to be safe and 9 more will be enrolled. If >2 of 6 patients have DLT, then neither dose level will have met the safety rule and the trial will be ended. This trial opened to accrual on June 29, 2020. Clinicaltrials.gov NCT04391049. Funding: This project was supported by grants U10CA180868 (NRG Oncology Operations), U10CA180822 (NRG Oncology SDMC), U24CA180803 (IROC), from the National Cancer Institute (NCI) and Oncolys BioPharma. Clinical trial information: NCT04391049. Research Sponsor: U.S. National Institutes of HealthPharmaceutical/Biotech Company.

TPS263 Trials in Progress Poster Session

Pembrolizumab plus chemotherapy for previously untreated, HER2-negative unresectable or metastatic advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma: KEYNOTE-859. *First Author: Josep Tabernero, Vall d'Hebron University Hospital and Institute of Oncology (VIHO), Barcelona, Spain*

Background: For patients with unresectable, locally advanced recurrent or metastatic G/GEJ cancer, the standard of care includes a fluoropyrimidine plus a platinum-based agent as first-line therapy. The PD-1 inhibitor pembrolizumab has demonstrated durable antitumor activity in this patient population across lines of therapy. Herein, we describe the randomized, double-blind, phase 3 KEYNOTE-859 trial (NCT03675737) of first-line pembrolizumab plus chemotherapy in patients with advanced G/GEJ adenocarcinoma. **Methods:** Patients with histologically or cytologically confirmed, locally advanced unresectable or metastatic G/GEJ adenocarcinoma with known PD-L1 expression status, HER2-negative disease, measurable disease per RECIST v1.1, and ECOG performance status of 0 or 1 will be randomly assigned 1:1 to receive pembrolizumab plus chemotherapy or placebo plus chemotherapy. Randomization will be stratified by geographic region (Europe/Israel/North America/Australia vs Asia vs rest of world), PD-L1 tumor expression status (combined positive score < 1 vs ≥1), and combination chemotherapy (FP vs CAPOX). Pembrolizumab or placebo will be administered at 200 mg IV every 3 weeks (Q3W). The chemotherapy regimen will be investigator's choice of FP (continuous infusion of 5-fluorouracil [800 mg/m^2/day on days 1-5 of each cycle] plus IV cisplatin [80 mg/m^2] Q3W) or CAPOX (oral capecitabine [1000 mg/m^2 twice daily on days 1-14 of each cycle] plus IV oxaliplatin [130 mg/m^2 on day 1 of each cycle] Q3W). Duration of cisplatin or oxaliplatin may be capped at 6 cycles per local country guidelines; treatment with 5-fluorouracil or capecitabine may continue per protocol. Treatment with pembrolizumab or placebo will continue for ≤35 administrations (~2 years) or until disease progression, unacceptable toxicity, intercurrent illness that prevents further administration of treatment, investigator decision, or noncompliance. Imaging will be performed at screening and subsequently every 6 weeks until disease progression, start of new anticancer treatment, withdrawal of consent, or death. Adverse events will be monitored throughout the study from the time of randomization to 30 days after the last dose of study treatment (90 days for serious adverse events). The dual primary end points are OS and PFS per RECIST v1.1 as assessed by blinded independent central review (BICR). Secondary end points include ORR and DOR per RECIST v1.1 as assessed by BICR, safety, and tolerability. Enrollment is ongoing. Clinical trial information: NCT03675737. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

TPS264 Trials in Progress Poster Session

Margetuximab (M) combined with anti-PD-1 (retifanlimab) or anti-PD-1/LAG-3 (tebotelimab) +/- chemotherapy (CTX) in first-line therapy of advanced/metastatic HER2+ gastroesophageal junction (GEJ) or gastric cancer (GC). *First Author: Daniel V.T. Catenacci, Gastrointestinal Oncology Program, University of Chicago Medical Center, Chicago, IL*

Background: Trastuzumab (T), a monoclonal antibody (mAb) targeting HER2, is standard of care 1st-line therapy for advanced HER2+ GEJ/GC patients. M, an investigational Fc-engineered anti-HER2 mAb, targets the same HER2 epitope but with higher affinity for both 158V (high binding) and 158F (low binding) alleles of activating Fc receptor CD16A. Data suggest margetuximab coordinately enhances both innate and adaptive immunity, including antigen-specific T-cell responses to HER2. PD-1 and LAG-3 are T-cell checkpoint molecules that suppress T-cell function. Retifanlimab (also known as MGA012 or INCMGA00012) is a humanized, hinge-stabilized, IgG4 K anti-PD-1 mAb blocking binding of PD-L1 or PD-L2 to PD-1. Tebotelimab (also known as MGD013) is a humanized Fc-bearing bispecific tetravalent DART® protein that binds to both PD-1 and LAG-3, inhibiting their respective ligand binding. We previously reported that a CTX-free regimen of M+PD-1 blockade was well tolerated in GEJ/GC patients, and induced a 44% objective response rate (ORR) in a double-positive biomarker population. This was 2- to 3-fold greater than in historical controls with checkpoint inhibitors alone. This registration-directed trial assesses efficacy, safety, and tolerability of M+checkpoint inhibition ± CTX in metastatic/locally advanced, treatment-naïve, HER2+ GEJ/GC patients. **Methods:** This is a 2-cohort, adaptive open-label phase 2/3 study (NCT04082364). The first single arm, CTX-free cohort A, evaluates M+retifanlimab in HER2+ (immunohistochemistry [IHC] 3+) and PD-L1+ (excluding microsatellite instability high) patients. After 40 patients are evaluated for response/safety, additional patients will be enrolled if the threshold for continuation is met. In randomized cohort B, HER2+ (IHC 3+ or 2+/fluorescent in situ hybridization+) patients are enrolled irrespective of PD-L1 status. Part 1 of cohort B randomizes patients to 1 of 4 arms (50 patients each): control arm (T+CTX) or 1 of 3 experimental arms (M+CTX; M+CTX+retifanlimab; M+CTX+tebotelimab). CTX is investigator's choice XELOX or mFOLFOX-6. Part 2 of cohort B consists of control (T+CTX) vs 1 experimental arm (M+CTX) + either retifanlimab or tebotelimab, depending on results from part 1; with 250 patients each. The primary efficacy endpoint for cohort A (both parts) is ORR per RECIST 1.1; for cohort B part 2 it is overall survival. Clinical trial information: NCT04082364. Research Sponsor: MacroGenics, Inc.

265 Oral Abstract Session

Final results from a phase II study of infigratinib (BGJ398), an FGFR-selective tyrosine kinase inhibitor, in patients with previously treated advanced cholangiocarcinoma harboring an *FGFR2* gene fusion or rearrangement. *First Author: Milind M. Javle, MD Anderson Cancer Center, Houston, TX*

Background: Treatment options for cholangiocarcinoma (CCA) after progression on first-line gemcitabine-based therapy are limited. Fibroblast growth factor receptor 2 (*FGFR2*) gene fusions occur in 13–17% of intrahepatic CCA. A single-arm, phase II study (NCT02150967) evaluated infigratinib, an ATP-competitive FGFR1–3-selective oral tyrosine kinase inhibitor, in previously-treated advanced CCA with *FGFR* fusions/rearrangements. **Methods:** Adult patients with advanced/metastatic CCA with progression on ≥1 line of systemic therapy received infigratinib 125 mg orally for 21 days of each 28-day cycle until unacceptable toxicity or disease progression. All patients received prophylaxis with the oral phosphate binder sevelamer. Primary endpoint: objective response rate (ORR) by independent central review per RECIST v1.1, with duration of response (DOR). Secondary endpoints: progression-free survival (PFS), disease control rate, overall survival, safety, pharmacokinetics. Approximately 160 patients are planned (120/20/20 patients in Cohorts 1/2/3). This analysis focuses on Cohort 1 (patients with *FGFR2* gene fusions or rearrangements without receiving a prior FGFR inhibitor). **Results:** As of 31 March 2020, 108 patients, including 83 (77%) with *FGFR2* fusions, received infigratinib: median age 53 years (range 23–81 years); 54% had received ≥2 prior treatment lines. Median follow-up was 10.6 months (range 1.1–55.9 months). 96 patients (88.9%) discontinued treatment (12 ongoing). Centrally reviewed ORR was 23.1% (95% CI 15.6–32.2) including 1 CR and 24 PRs; median DOR was 5.0 months (range 0.9–19.1 months). Among responders, 8 (32.0%) patients had a DOR of ≥6 months. Median PFS was 7.3 months (95% CI 5.6–7.6 months). Prespecified subgroup analysis: ORR was 34% (17/50) in the second-line setting and 13.8% (8/58) in the third-/later-line setting (3–8 prior treatments). Most common treatment-emergent adverse events (TEAEs, any grade) were hyperphosphatemia (76.9%), eye disorders (67.6%, excluding central serous retinopathy/retinal pigment epithelium detachment [CSR/RPED]), stomatitis (54.6%), and fatigue (39.8%). CSR/RPED occurred in 16.7% of patients (including 1 G3 event; 0 G4). Other common grade 3/4 TEAEs were stomatitis (14.8%; all G3), hyponatremia (13.0%; all G3), and hypophosphatemia (13.0%; 13 G3, 1 G4). **Conclusions:** Infigratinib is associated with promising anticancer activity and a manageable AE profile in patients with advanced, refractory CCA with an *FGFR2* gene fusion or rearrangement. A phase III study of infigratinib versus gemcitabine/cisplatin is ongoing in the front-line setting (NCT03773302). Clinical trial information: NCT02150967. Research Sponsor: QED Therapeutics Inc.

266 Oral Abstract Session

Final results from ClarIDHy, a global, phase III, randomized, double-blind study of ivosidenib (IVO) versus placebo (PBO) in patients (pts) with previously treated cholangiocarcinoma (CCA) and an isocitrate dehydrogenase 1 (*IDH1*) mutation. *First Author: Andrew X. Zhu, Harvard Medical School/Massachusetts General Hospital Cancer Center, Boston, MA*

Background: CCA is a rare cancer for which there are limited effective therapies. *IDH1* mutations occur in ~20% of intrahepatic CCAs, resulting in production of the oncometabolite D-2-hydroxyglutarate, which promotes oncogenesis. IVO (AG-120) is a first-in-class, oral, small-molecule inhibitor of mutant *IDH1* (m*IDH1*). ClarIDHy aimed to demonstrate the efficacy of IVO vs PBO in pts with unresectable or metastatic m*IDH1* CCA. The primary endpoint was met with significant improvement in progression-free survival (PFS) by independent radiology center (IRC) with IVO vs PBO (hazard ratio [HR] = 0.37, $p < 0.0001$). Objective response rate (ORR) and stable disease for IVO were 2.4% (3 partial responses) and 50.8% (n = 63) vs 0% and 27.9% (n = 17) for PBO. IVO pts experienced significantly less decline in physical and emotional functioning domains of quality of life at cycle 2 day 1 vs PBO pts (nominal $p < 0.05$). **Methods:** Pts with m*IDH1* CCA were randomized 2:1 to IVO (500 mg PO QD) or matched PBO and stratified by prior systemic therapies (1 or 2). Key eligibility: unresectable or metastatic m*IDH1* CCA based on central testing; ECOG PS 0–1; measurable disease (RECIST v1.1). Crossover from PBO to IVO was permitted at radiographic progression. Primary endpoint: PFS by IRC. Secondary endpoints included overall survival (OS; by intent-to-treat), ORR, PFS (by investigator), safety, and quality of life. The planned crossover-adjusted OS was derived using the rank-preserving structural failure time (RPSFT) model. **Results:** As of 31 May 2020, ~780 pts were prescreened for an *IDH1* mutation and 187 were randomized to IVO (n = 126) or PBO (n = 61); 13 remain on IVO. Median age 62 y; M/F 68/119; 91% intrahepatic CCA; 93% metastatic disease; 47% had 2 prior therapies. 70% of PBO pts crossed over to IVO. OS data were mature, with 79% OS events in IVO arm and 82% in PBO. Median OS (mOS) was 10.3 months for IVO and 7.5 months for PBO (HR = 0.79; 95% CI 0.56–1.12; one-sided p = 0.093). The RPSFT-adjusted mOS was 5.1 months for PBO (HR = 0.49; 95% CI 0.34–0.70; $p < 0.0001$). Common all-grade treatment emergent adverse events (TEAEs, ≥ 15%) in the IVO arm: nausea 41%, diarrhea 35%, fatigue 31%, cough 25%, abdominal pain 24%, decreased appetite 24%, ascites 23%, vomiting 23%, anemia 18%, and constipation 15%. Grade ≥ 3 TEAEs were reported in 50% of IVO pts vs 37% of PBO pts, with grade ≥ 3 treatment-related AEs in 7% of IVO pts vs 0% in PBO. 7% of IVO pts experienced an AE leading to treatment discontinuation vs 9% of PBO pts. There were no treatment-related deaths. **Conclusions:** IVO was well tolerated and resulted in a favorable OS trend vs PBO despite a high rate of crossover. These data – coupled with statistical improvement in PFS, supportive quality of life data, and favorable safety profile – demonstrate the clinical benefit of IVO in advanced m*IDH1* CCA. Clinical trial information: NCT02989857. Research Sponsor: Agios Pharmaceuticals, Inc.

267 Rapid Abstract Session

IMbrave150: Updated overall survival (OS) data from a global, randomized, open-label phase III study of atezolizumab (atezo) + bevacizumab (bev) versus sorafenib (sor) in patients (pts) with unresectable hepatocellular carcinoma (HCC). *First Author: Richard S. Finn, Jonsson Comprehensive Cancer Center, Geffen School of Medicine at UCLA, Los Angeles, CA*

Background: Atezo + bev has been approved globally for pts with unresectable HCC who have not received prior systemic therapy, based on results from IMbrave150 (NCT03434379). At a median of 8.6 mo follow-up, both coprimary endpoints were met, with statistically significant and clinically meaningful improvements observed with atezo + bev vs sor for OS (HR, 0.58 [95% CI, 0.42, 0.79]; $P<0.001$) and independently-assessed progression-free survival (PFS; per RECIST 1.1; HR, 0.59 [95% CI, 0.47, 0.76]; $P<0.001$) (Finn, et al. *N Engl J Med* 2020). Here, we report an updated OS analysis for IMbrave150. **Methods:** The global, multicenter, randomized, open-label, Phase III study IMbrave150 enrolled 501 systemic treatment-naive pts with unresectable HCC, ≥1 measurable untreated lesion (RECIST 1.1), Child-Pugh class A liver function and ECOG PS 0/1. Pts were randomized 2:1 to receive either atezo 1200 mg IV q3w + bev 15 mg/kg IV q3w or sor 400 mg bid until unacceptable toxicity or loss of clinical benefit per investigator. This post hoc, descriptive OS analysis was conducted with 12 mo of additional follow up from the primary analysis. **Results:** 501 pts were enrolled, including 336 to atezo + bev and 165 to sor. At the clinical cut-off date of Aug 31, 2020, median follow-up was 15.6 mo and 280 OS events were observed. Median OS was 19.2 mo with atezo + bev vs 13.4 mo with sor (HR, 0.66 [95% CI, 0.52, 0.85]; $P=0.0009$). Survival at 18 mo was 52% with atezo + bev and 40% with sor. Survival benefit with atezo + bev over sor was generally consistent across subgroups and with the primary analysis. The updated objective response rate (ORR; 29.8% per RECIST 1.1) with atezo + bev was in line with the primary analysis, with more pts achieving complete response (CR; 7.7%) than previously reported. Additional response data are in Table. Safety was aligned with the primary analysis, with no new signals identified. **Conclusions:** IMbrave150 showed consistent clinically meaningful treatment benefit and safety with 12 mo of additional follow-up. The combination provides the longest survival seen in a front-line Phase III study in advanced HCC, confirming atezo + bev as a standard of care for previously untreated, unresectable HCC. Clinical trial information: NCT03434379. Research Sponsor: F. Hoffmann-La Roche, Ltd.

Updated ORR and DOR per independently-assessed RECIST 1.1 and HCC mRECIST.

	Atezo + Bev n = 326 RECIST 1.1	Sor n = 159 RECIST 1.1	Atezo + Bev n = 325 HCC mRECIST	Sor n = 158 HCC mRECIST
Confirmed ORR (95% CI), %	29.8 (24.8, 35.0)	11.3 (6.9, 17.3)	35.4 (30.2, 40.9)	13.9 (8.9, 20.3)
CR, n (%)	25 (7.7)	1 (0.6)	39 (12.0)	4 (2.5)
PR, n (%)	72 (22.1)	17 (10.7)	76 (23.4)	18 (11.4)
SD, n (%)	144 (44.2)	69 (43.4)	121 (37.2)	65 (41.1)
Median DOR (95% CI), mo	18.1 (14.6, NE)	14.9 (4.9, 17.0)	16.3 (13.1, 21.4)	12.6 (6.1, 17.7)

DOR, duration of response; HCC mRECIST, modified RECIST for HCC; NE, not estimable; PR, partial response; SD, stable disease.

268 Rapid Abstract Session

Pembrolizumab (pembro) vs placebo (pbo) in patients (pts) with advanced hepatocellular carcinoma (aHCC) previously treated with sorafenib: Updated data from the randomized, phase III KEYNOTE-240 study. *First Author: Philippe Merle, Hôpital de la Croix-Rousse, Hospices Civils de Lyon, Lyon, France*

Background: KEYNOTE-240 (NCT02702401) examined the anti-PD-1 antibody pembro and demonstrated improvement in OS and PFS vs pbo in pts with aHCC previously treated with sorafenib. However, the study did not meet prespecified statistical significance criteria for OS and PFS. Median OS (final analysis) was 13.9 mo for pembro vs 10.6 mo for pbo (HR 0.781; 95% CI 0.611-0.998). At the first interim analysis when PFS and ORR were prespecified to be tested, median PFS was 3.0 mo for pembro vs 2.8 mo for pbo (HR 0.775; 95% CI 0.609-0.987) and ORR was 16.9% (CR, n = 3) for pembro and 2.2% (CR, n = 0) for pbo. AEs were consistent with the known safety profile of pembro. Longer-term data from KEYNOTE-240 after ~1.5 years of additional follow-up are reported. **Methods:** Adults with confirmed aHCC who experienced failure (progression or intolerance) to sorafenib therapy were randomized 2:1 to pembro 200 mg IV Q3W + best supportive care (BSC) or pbo + BSC for ≤35 cycles or until confirmed progression/unacceptable toxicity, pt withdrawal of consent, or investigator decision. Dual primary end points were OS and PFS, assessed by blinded independent central review (BICR) per RECIST v1.1. Secondary end points included ORR, DOR, DCR, TTP (all assessed by BICR per RECIST v1.1), and safety. **Results:** Of 413 pts, 278 were randomized to pembro and 135 to pbo. As of July 13, 2020, median time from randomization to data cutoff was 39.6 mo (range 31.7-48.8) for pembro and 39.8 mo (31.7-47.8) for pbo. Median OS was 13.9 mo (95% CI 11.6-16.0) for pembro and 10.6 mo (8.3-13.5) for pbo (HR 0.771; 95% CI 0.617-0.964). Estimated OS rates at 24 and 36 mo for pembro and pbo were 28.8% and 20.4% and 17.7% and 11.7%, respectively. Median PFS was 3.3 mo (95% CI 2.8-4.1) for pembro and 2.8 mo (1.6-3.0) for pbo (HR 0.703; 95% CI 0.559-0.885). Estimated PFS rate at 24 mo was 11.8% for pembro and 4.8% for pbo. ORR was 18.3% (95% CI 14.0-23.4) for pembro and 4.4% (1.6-9.4) for pbo. Median time to response was 2.7 mo (95% CI 1.2-16.9) for pembro and 2.9 mo (1.1-6.9) for pbo. Median DOR was 13.9 mo (range 1.5+ to 41.9+) for pembro and 15.2 mo (2.8-21.9) for pbo; 45.1% of responders in pembro arm and 33.3% of responders in pbo arm had DOR ≥12 mo. DCR was 61.9% for pembro and 53.3% for pbo. Best overall responses were 10 CR, 41 PR, 121 SD, and 85 PD for pembro and 0 CR, 6 PR, 66 SD, and 54 PD for pbo. The median TTP was 4.0 mo (95% CI 2.8-5.3) for pembro and 2.8 mo (1.6-3.0) for pbo. No new or unexpected AEs occurred. The frequency of sponsor-assessed immune-mediated hepatitis events did not increase with additional follow-up. There continued to be no HBV or HCV viral flare events. **Conclusions:** In previously treated pts with aHCC, improvement in OS and PFS was maintained over time with pembro vs pbo, and the safety profile remained consistent over time. These data support the benefit:risk profile of pembro. Clinical trial information: NCT02702401. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

269 Rapid Abstract Session

Nivolumab (NIVO) plus ipilimumab (IPI) combination therapy in patients (Pts) with advanced hepatocellular carcinoma (aHCC): Long-term results from CheckMate 040. *First Author: Anthony B. El-Khoueiry, USC Norris Comprehensive Cancer Center, Los Angeles, CA*

Background: NIVO 1 mg/kg + IPI 3 mg/kg Q3W (4 doses) followed by NIVO 240 mg Q2W is approved in the US for sorafenib-treated pts with aHCC based on initial results from CheckMate 040 (NCT01658878), which reported objective response rate (ORR) of 32% and median overall survival (mOS) of 22.8 months (mo).[1] We present 44-mo long-term follow-up results from the CheckMate 040 NIVO+IPI cohort. **Methods:** Pts were randomized to 3 arms: [A] NIVO 1 mg/kg + IPI 3 mg/kg Q3W (4 doses) or [B] NIVO 3 mg/kg + IPI 1 mg/kg Q3W (4 doses), each followed by NIVO 240 mg Q2W, or [C] NIVO 3 mg/kg Q2W + IPI 1 mg/kg Q6W. Treatment continued until intolerable toxicity or disease progression. Safety and tolerability, ORR (blinded independent central review per RECIST v1.1), duration of response (DOR), disease control rate (DCR), and OS were assessed. Data cutoff was May 26, 2020. **Results:** 148 pts were randomized. Minimum follow-up was 44 mo. mOS remained at 22.2 mo in arm A, 12.5 mo in arm B, and 12.7 mo in arm C; 36-mo OS rates were 42%, 26%, and 30%, respectively. Durable responses were achieved across treatment arms, with DOR approaching 4 years in some cases. DCR was higher in arm A than arms B and C. In all arms, responses were observed regardless of baseline programmed death ligand 1 expression ($<1\%$ or $\geq 1\%$) or baseline alpha-fetoprotein level (<400 μg/L or ≥ 400 μg/L). Pts with hepatitis B or C virus (HBV or HCV) etiology had higher ORR than uninfected pts in arms B (29% vs 43% vs 9%) and C (31% vs 42% vs 0%). ORR was independent of etiology in arm A (HBV, 32%; HCV, 29%; uninfected, 31%). Additional efficacy data are in the table. There were no additional discontinuations due to treatment-related adverse events or immune-mediated adverse events (IMAEs) since the primary analysis. IMAEs were reported more frequently in arm A than arms B and C; the most common were rash, hepatitis, and adrenal insufficiency. Most IMAEs were reversible and resolved when treated using established algorithms. **Conclusions:** At a minimum follow-up of 44 mo, second-line NIVO1+IPI3 continued to demonstrate clinically meaningful responses and long-term survival benefit in aHCC. The safety profile was manageable and no new safety signals were identified with longer follow-up. Clinical trial information: NCT01658878. Research Sponsor: Bristol Myers Squibb and ONO Pharmaceutical Company Ltd.

	[A] NIVO1+IPI3 Q3W (n = 50)	[B] NIVO3+IPI1 Q3W (n = 49)	[C] NIVO3 Q2+IPI1 Q6W (n = 49)
ORR, n (%)	16 (32)	15 (31)	15 (31)
Complete response	4 (8)	3 (6)	1 (2)
Partial response	12 (24)	12 (24)	14 (29)
Stable disease	9 (18)	5 (10)	9 (18)
Progressive disease	20 (40)	24 (49)	21 (43)
DCR, % (95% CI)	54 (39-68)	43 (29-58)	49 (34-64)
Median DOR, mo (range)	17.5 (5-47+)	22.2 (4-44+)	16.6 (4-49+)
mOS, mo (95% CI)	22.2 (9.4-NE)	12.5 (7.6-16.4)	12.7 (7.4-30.5)
12-mo OS rate, % (95% CI)	61 (46-73)	56 (41-69)	51 (36-64)
24-mo OS rate, % (95% CI)	46 (32-59)	30 (18-44)	42 (28-56)
36-mo OS rate, % (95% CI)	42 (28-55)	26 (14-39)	30 (18-43)

NE, not evaluable.

1. Yau T, et al. *JAMA Oncology*. 2020; epub ahead of print.

270 Rapid Abstract Session

TACTICS: Final overall survival (OS) data from a randomized, open label, multicenter, phase II trial of transcatheter arterial chemoembolization (TACE) therapy in combination with sorafenib as compared with TACE alone in patients (pts) with hepatocellular carcinoma (HCC). *First Author: Masatoshi Kudo, Kindai University Faculty of Medicine, Osaka, Japan*

Background: To date many trials have been conducted to compare the efficacy and toxicity between TACE plus molecular targeted agents and TACE alone; all of them failed to show its clinical benefit in terms of progression free survival (PFS) or OS. In TACTICS trial (NCT01217034) TACE plus sorafenib significantly improved PFS over TACE alone in patients with unresectable HCC. (*Gut 2020;69:1374-1376*). Here we will report a final OS analysis from TACTICS trial with predefined mature OS events. **Methods:** Patients with unresectable HCC were randomized to TACE plus sorafenib (n=80) or TACE alone (n=76). Patients in the combination group received sorafenib 400 mg once daily for 2–3 weeks before TACE, followed by 800 mg twice daily during on-demand conventional TACE sessions until time to untreatable (unTACEable) progression (TTUP), defined as untreatable tumor progression, transient deterioration to Child-Pugh C or appearance of vascular invasion/extrahepatic spread. Co-primary endpoints were progression-free survival (PFS), which is defined as TTUP, or time to any cause of death and OS. Multiplicity was adjusted by gatekeeping hierarchical testing. **Results:** At the cut-off date of July 31, 2020, 131 OS events were observed. Median OS was 36.2 mo with TACE plus sorafenib vs 30.8 mo with TACE alone (HR, 0.861 [95%CI, 0.607, 1.223]; *P*=0.40). ΔOS was 5.4 mo. Updated PFS was 22.8 mo with TACE plus sorafenib vs 13.5 mo with TACE alone (HR, 0.661[95%CI, 0.466, 0.938]; *P*=0.02). Post-trial treatments with active procedures/agents were observed in 47 (58.8%) in TACE plus sorafenib and in 58 (76.3%) with TACE alone. Anticancer procedures in TACE alone group include resection/ablation in 14, transarterial therapy in 53 and radiation in 7. Anticancer medications in TACE alone include targeted agents in 40 (29 sorafenib, 5 regorafenib, 3 lenvatinib, 3 ramucirumab), other systemic chemotherapy in 5 and immunotherapy in 5. Safety was consistent with the primary analysis, with no new signals identified. **Conclusion:** In TACTICS, TACE plus sorafenib did not show OS benefit as compared with TACE alone although significantly better PFS was consistently observed. OS in TACE plus sorafenib in TACTICS trial showed the longest OS (36.2 mo) with the longest ΔOS (5.4 mo) as compared with the previous 5 TACE combination trials. The major reason for negative OS result was speculated that many post-trial active treatments were performed in control arm (76.3%), which implies that OS endpoint in TACE combination trial may not be feasible anymore in current era of sequential therapy with many active locoregional and systemic treatments. Clinical trial information: NCT01217034. Research Sponsor: Japan Liver Oncology Group.

271 Poster Session

Second-line tyrosine kinase inhibitors (TKIs) versus immunotherapy (IO) for advanced hepatocellular carcinoma (HCC): Real-world efficacy and safety analysis in patients with varying liver dysfunction. *First Author: Jeffrey Xia, University of Texas Health Science Center at San Antonio, San Antonio, TX*

Background: Within the last 4 years, the FDA approved five drugs as second-line therapies for advanced HCC. At our cancer center, the majority of our patients are Hispanic with varying liver dysfunction, and this real world population is not represented in registration trials of TKIs and IOs. Therefore, we analyzed survival and toxicities among second-line therapies for HCC at our Hispanic-majority NCI-designated cancer center. **Methods:** Retrospective analysis of patients with advanced HCC diagnosed at Mays Cancer Center from 1/2015-3/2019 who received second-line therapies, including IO (i.e. nivolumab), TKIs (i.e. cabozantinib, regorafenib), or hospice/best supportive care (BSC). Progression-free survival (PFS) was determined using Kaplan-Meier method, and hazard ratios estimated with Cox proportional hazards model. AEs according to Common Terminology Criteria for AEs v5.0 were analyzed with Fisher's exact test. **Results:** Of the patients receiving first-line therapy, the median age was 60 years (n=65), and patients were 75% (n=49) Hispanics. 58 (89%) patients went onto receive second-line therapy. Child-Pugh (CP) score: A 17%, B 55%, C 28%. Median PFS was 3.1 months with TKI (n=6), 3.3 months with IO (n=27), and 1.3 months with BSC (n=25) (Table). There was improved survival with IO when compared to BSC (HR=3.26; 95% CI: 1.58-6.72; p=0.00136). There was no significant difference when comparing IO to TKI (HR=0.94; 95% CI: 0.31-2.86; p=0.92), but a trend to improved PFS with TKI when compared to BSC (HR=3.08; 95% CI: 0.96-9.84; p=0.06). TKI group had significantly more rash (p=0.01) and hand-foot syndrome (HFS) (p<0.001) compared to IO and BSC. All other AEs demonstrated no significant difference between groups (Table). **Conclusions:** In our Hispanic-majority cohort, patients with varying liver dysfunction, including CP B & C cirrhosis, were more likely to receive IO or BSC. Both second-line treatment groups (IO or TKI) had increased mPFS compared to BSC. Both IO and TKI groups were tolerable compared to BSC, with expected toxicity per class of drug. More prospective studies comparing second-line agents should be done in patients with varying liver dysfunction to understand survival, tolerability, and quality of life. Research Sponsor: None.

	IO	TKI	BSC
Number of patients	27	6	25
Hispanics	78%	83%	72%
ECOG 0-1	96%	100%	36%
Etiology Cirrhosis:	70%	83%	25%
HCV	56%	83%	52%
EtOH	30%	17%	16%
Fatty liver/NASH			
CP score:	19%	67%	4%
A	59%	33%	56%
B	22%	0%	40%
C			
mPFS (months)	3.3 months	3.1 months	1.3 months
HR (95% CI)	Reference	1.06 (0.35-3.21)	3.26 (1.58-6.72)
p-value	–	0.91	0.0014
Most common AEs n (%):			
Nausea	2 (33)	10 (37)	13 (52)
Fatigue	5 (83)	22 (81)	24 (96)
Diarrhea	1 (17)	6 (22)	5 (20)
Hand-foot syndrome (HFS)	4 (67)	0 (0)	0 (0)
Rash (excluding HFS)	3 (50)	10 (37)	0 (0)
Immune-mediated reaction	1 (17)	8 (30)	0 (0)
Cytopenias	1 (17)	2 (7)	1 (4)

272 Poster Session

Clinical outcomes with multikinase inhibitors after progression on first-line atezolizumab plus bevacizumab in patients with advanced hepatocellular carcinoma: A multinational, multicenter retrospective study. *First Author: Changhoon Yoo, Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea*

Background: Atezolizumab-bevacizumab is the new standard of care for first-line treatment of advanced hepatocellular carcinoma (HCC). However, the optimal sequence of therapy after disease progression on atezolizumab-bevacizumab is unclear. **Methods:** This multinational, multicenter, retrospective study assessed clinical outcomes of patients with advanced HCC who received subsequent systemic therapy after progression on atezolizumab-bevacizumab in Korea, Hong Kong and Singapore between July 2016 and April 2019. **Results:** A total of 49 patients were included; the median age was 60 years (range, 3780) and 73.5% were male. All patients were classified as Child-Pugh A and Barcelona-Clinic Liver Cancer stage C. Multikinase inhibitors (MKIs), including sorafenib (n = 29), lenvatinib (n = 19), and cabozantinib (n = 1), were used as second-line therapy for all patients. The objective response rate (ORR) and disease control rate (DCR) were 6.1% and 63.3%, respectively, in all patients. With a median follow-up duration of 11.0 months, median progression-free survival (PFS) and overall survival (OS) were 3.4 months (95% confidence interval [CI] 1.84.9) and 14.7 months (95% CI 8.121.2) in all patients. Median PFS with lenvatinib was significantly longer than that with sorafenib (6.1 months vs. 2.5 months; *P*= 0.004), although there was no significant difference in median OS (16.6 months vs. 11.2 months; *P*= 0.347). Treatment-related adverse events (TRAEs) of any grade and grade 3 occurred in 42 (85.7%) and 8 (16.3%) of patients. Common TRAEs included hand-foot syndrome (HFS) (n = 26, 53.1%), fatigue (n = 14, 28.6%), hypertension (n = 14, 28.6%), and diarrhea (n = 12, 24.5%). **Conclusions:** Second-line treatment with MKIs, mostly sorafenib and lenvatinib, showed comparable efficacy and manageable toxicities in patients with advanced HCC after disease progression on atezolizumab-bevacizumab. Research Sponsor: None.

273 Poster Session

Real-world effectiveness of lenvatinib monotherapy among unresectable hepatocellular carcinoma patients treated in United States clinical practices. *First Author: Amit G. Singal, University of Texas Southwestern, Dallas, TX*

Background: In the United States (U.S.), lenvatinib monotherapy was approved in August 2018 for first-line treatment of patients with unresectable hepatocellular carcinoma (uHCC) based on the pivotal trial, REFLECT. Real-world data are essential to assess if this efficacy translates into effectiveness in clinical practice. The main objective of our real-world data (RWD) study was to assess clinical characteristics and effectiveness of lenvatinib among patients treated in U.S. clinical practices. **Methods:** A retrospective patient chart review study was conducted among adult patients (≥18 years) in the U.S. initiating lenvatinib monotherapy as first-line (1L) systemic therapy for uHCC between Aug 2018 and Sept 2019 and with ECOG status of 0 or 1. Data were extracted from individual patients' electronic health records and captured in electronic case report forms. Clinical outcomes assessed include provider-reported best response, progression-free survival (PFS) and overall survival (OS). PFS and OS were estimated using Kaplan-Meier methods. For PFS, patients were censored at end of treatment or end of follow-up in case of ongoing treatment, while censoring occurred at end of follow-up for OS. **Results:** Among 233 patients treated with 1L lenvatinib monotherapy, majority were male (68%) and most were Caucasian (52%) or African American (25%). Median age was 63 years and median body weight was 76 kg. The most common etiologies of liver disease were hepatitis C (36%), alcohol-related liver disease (28%), hepatitis B (16%) and non-alcoholic steatohepatitis (14%). Most patients had compensated cirrhosis, with 49% Child Pugh A and 43% Child Pugh B. All patients had uHCC, with most having Barcelona Clinic Liver Cancer stage B (29%) or C (44%) disease. Portal vein invasion was reported in 19%, of whom7% had main portal vein involvement. The median starting dose of lenvatinib was 12 mg daily. Over a median follow-up period of 9 months from HCC diagnosis, median PFS and OS were not reached. At 6 and 12 months landmark PFS was 85% and 65%, respectively and landmark OS was 92% and 73%, respectively. In the overall cohort, provider-reported best response was complete response (CR): 21%, partial response (PR):44% and stable disease (SD): 26%. Based on RECIST 1.1 (n = 125) CR:16%, PR:54%, SD:26% and mRECIST (n = 11) CR:73%, PR:0% and SD:18% were reported. Average duration of lenvatinib treatment was 7.4 months (median: 6.7 months) with 61% of patients remaining on lenvatinib at end of follow-up. Second-line (2L) treatment was initiated in 32 patients, with immunotherapy (50%), sorafenib (31%) and regorafenib (9%) being most common. Median time to 2L treatment from initiation of lenvatinib was about 8 months. **Conclusions:** Results from this retrospective real-world study in an U.S. population affirm the clinical effectiveness of 1L lenvatinib monotherapy among patients with uHCC. Research Sponsor: Eisai.

274 Poster Session

Efficacy and safety of nab-paclitaxel plus gemcitabine-cisplatin (GemCis/nab-P) in Korean patients with advanced biliary tract cancers (aBTC): Multicenter retrospective analysis. *First Author: Jaekyung Cheon, Division of Hematology and Oncology, Department of Internal Medicine, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, South Korea*

Background: A recent phase II trial (NCT02392637) demonstrated prolonged survival by treatment with GemCis/nab-P in patients (pts) with aBTC. Further evaluation in real-world setting is necessary to measure the clinical outcomes of GemCis/nab-P in daily practice in Asian pts. **Methods:** This is a multicenter retrospective analysis of data from 3 institutes in Korea. Between September 2019 and August 2020, a total of 104 pts who received GemCis/nab-P for the management of aBTC were included in this analysis. **Results:** Median age was 64 years (range, 34-84), and 60 pts (57.7%) were male. GemCis/nab-P was used as the starting regimen in 60 pts (57.7%), 16 pts (15.4%) received GemCis/nab-P after failure of GemCis ± investigational drug (mainly immune checkpoint inhibitors), and 28 pts (26.9%) added nab-P to initial Gem/Cis without progressive disease. Baseline characteristics were as follows: Intrahepatic cholangiocarcinoma (CCC)/extrahepatic CCC/gallbladder cancer in 42 (40.4%)/33 (31.7%)/29 (27.9%); metastatic or recurred/locally advanced in 82 (78.8%)/22 (21.2%) pts. According to RECIST v 1.1, objective response rates (ORR) and disease control rate (DCR) were 30.8% and 81.8% of all pts, 33.4% and 88.4% in initial GemCis/nab-P, 28.6% and 73.8% in intrahepatic CCC, 36.3% and 96.9% in extrahepatic CCC, and 27.6% and 75.9% in gallbladder cancer groups, respectively. In nab-P addition group, while the ORR and DCR of pts without GemCis failure were 39.3% and 85.7%, those with GemCis failure were 6.3%, 50.0%, respectively. Median overall survival and progression-free survival were not reached, with a median follow-up duration of 3.3 months (95% confidence interval [CI], 2.9-6.7). The most common grade 3-4 toxicities were neutropenia (n=36, 34.6%), anemia (n=17, 16.4%), thrombocytopenia (n=10, 9.6%), and febrile neutropenia (n=9, 8.1%). In patients with locally advanced BTC (n=22), 5 patients (22.7%) were converted to resectable disease and underwent surgery. **Conclusions:** GemCis/nab-P showed consistent real-life efficacy and safety outcomes for Korean aBTC pts compared with those from the phase 2 trial. Research Sponsor: None.

Treatment response.

			Nab-P addition group (n=44)*				
	Overall (n=104)	Initial GemCis/nab-P group (n=60)	After GemCis# failure (n=16)	Without GemCis #failure (n=28)	Intrahepatic (n=42)	Extrahepatic (n=33)	Gallbladder (n=29)
Best response							
CR	1 (1.0%)	1 (1.7%)	0	0	0	1 (3.0%)	0
PR	31 (29.8%)	19 (31.7%)	1 (6.3%)	11 (39.3%)	12 (28.6%)	11 (33.3%)	8 (27.6%)
SD	53 (51.0%)	33 (55.0%)	7 (43.8%)	13 (46.4%)	19 (45.2%)	20 (60.6%)	14 (48.3%)
PD	19 (18.3%)	7 (11.7%)	8 (50.0%)	4 (14.3%)	11 (26.2%)	1 (3.0%)	7 (24.1%)
Objective response rate	30.8%	33.4%	6.3%	39.3%	28.6%	36.3%	27.6%
Disease control rate	81.8%	88.4%	50.0%	85.7%	73.8%	96.9%	75.9%

* Response after addition of nab-P

GemCis ± investivational drug (mainly immune checkpoint inhibitors)

275 Poster Session

Efficacy and safety of lenvatinib in the real-world treatment of hepatocellular carcinoma: Results from a Canadian multicenter database (HCC CHORD). *First Author: Carla Pires Amaro, Tom Baker Cancer Center, University of Calgary, Calgary, AB, Canada*

Background: The REFLECT trial establishedlenvatinib (LEN) as a first-line treatment option for hepatocellular carcinoma (HCC). Compared to sorafenib (S), LEN has a higher objective response rate (ORR) and progression-free survival (PFS) with a slightly different toxicity profile. The aim of this study was to gather data regarding the efficacy and safety of LEN when used in the real-world treatment of HCC. To our knowledge, this is the first study to examine LEN use in HCC patients treated outside of Asia. **Methods:** HCC patients treated with LEN from 10 cancer centers in the Canadian provinces of British Columbia, Alberta, Ontario and Nova Scotia between July 2018 to July 2020 were included. Overall survival (OS), PFS, disease control rate (DCR) and ORR were retrospectively analyzed and compared across first- and second-to-fourth line use of LEN. ORR was determined radiographically according to the treating physician´s opinion in clinical notes and not RECIST 1.1 or mRECIST. Toxicities were also examined. **Results:** A total of 220 patients were included in this analysis. Median age was 67 years, 80% were men and 25.5% East Asian. The most frequent causes of liver disease were hepatitis C (37%) and B (26%). 62% of patients received any localized treatment before LEN, of those 26% had TACE, 15% TARE and 7.7% had liver transplant. Before starting LEN 29% of patients were ECOG 0 and 59% were ECOG 1. Most patients were Child-Pugh A (81%) and BCLC stage C (75.5%). Main portal vein invasion was present in 14% of the patients. Median follow-up was 4.5 months. A total of 173 patients (79%) received LEN as first line therapy and 47 patients (21%) were treated in second-to-fourth line. Of patients receiving LEN in first line, 22 (13%) started treatment with S, but switched to LEN before progression due to poor tolerance of S. ORR, DCR, PFS and OS are shown in the table. Toxicities occurred in 86% of patients and led to dose reductions in 76 (35%) patients and drug discontinuation in 53 (24%) patients. The most common side effects were fatigue (59%), hypertension (41%), decreased appetite (25%) and diarrhea (22%). **Conclusions:** Outcomes of HCC patients treated in Canada with LEN in the first line are comparable to those demonstrated in the REFLECT trial, despite the inclusion of Child-Pugh B and ECOG >1 patients. LEN use in second or later lines also showed similar outcomes, although more conclusions are difficult to draw due to the small numbers. LEN appears to be effective and safe in real world practice outside of Asia in first- and second-to-fourth line treatment of HCC. Research Sponsor: Tom Baker Cancer Centre Clinical Research Unit Grant.

	Overall n=220	LEN first line n=173	LEN second-to-fourth lines n=47	P value	REFLECT – LEN arm n=478
ORR	22%	23%	19%	*0.234	24%
DCR	66%	70%	54%	0.057	75.5%
PFS (95% CI), months	7.0 (5.4 - 8.6)	8.0 (6.4 - 9.6)	5.0 (1.3 - 8.7)	0.182	7.4 (6.9 - 8.8)
OS (95% CI), months	13.0 (9.4 - 16.6)	13.0 (9.0 - 17)	15.0 (7.7 - 22.3)	0.891	13.6 (12.1-14.9)

276 Poster Session

Longitudinal evaluation of quality of life (QoL) in patients (Pts) with FGFR2-driven cholangiocarcinoma (CCA) treated with pemigatinib. *First Author: Juan W. Valle, University of Manchester and Christie Hospital NHS Foundation Trust, Manchester, United Kingdom*

Background: CCA is associated with poor prognosis and reduced QoL. In the phase 2 FIGHT-202 study (NCT02924376) of the selective oral FGFR1–3 inhibitor pemigatinib, 35.5% and 46.7% of pts with previously treated advanced CCA and *FGFR2* fusions/rearrangements (RE) had a complete or partial response (CR/PR) and stable disease (SD), respectively; 14.9% had progressive disease (PD) [Abou-Alfa et al., *Lancet Oncology* 2020; 21:671-684]. QoL was an exploratory endpoint. **Methods:** Pts received pemigatinib 13.5 mg once daily (21-day cycle; 2 weeks on, 1 week off). QoL was assessed longitudinally by best overall response (BOR) per RECIST with the EORTC-QLQ-C30 and the biliary tract cancer-specific EORTC-QLQ-BIL21 questionnaires. QoL scores and longitudinal changes from baseline (BL) were analyzed using descriptive statistics. Treatment-related changes in QoL were a priori expected to be evident by cycle 6 day 1 (week 16). **Results:** Of 107 pts with *FGFR2* RE, 100 (93%) were evaluable for QoL, including36, 48, and 15 with CR/PR, SD, and PD, respectively. From BL to week 16, QLQ-C30 overall health status was maintained in pts with CR/PR and SD and worsened in pts with PD (Table). Emotional functioning remained stable and similar in pts with CR/PR and SD but worsened in pts with PD. All subgroups showed decline in role and social functioning. Pts with CR/PR and SD experienced decreases in QLQ-BIL21 pain and anxiety; all subgroups showed increases in QLQ-BIL21 treatment side effects. **Conclusions:** In these pts with advanced CCA, those with an SD as BOR had a similar pattern of changes in QoL as those with CR/PR to pemigatinib. Changes in QoL were directionally more favorable in pts with CR/PR or SD than pts with PD. Clinical trial information: NCT02924376. Research Sponsor: Incyte Corporation Inc.

Changes from BL to week 16 in QoL by BOR.

Mean (SD) score change	CR/PR	n	SD	n	PD	n
QLQ-C30						
Overall health status	-0.3 (1.3)	34	-0.3 (1.1)	35	-1.2 (0.8)	5
Emotional functioning	2.2 (17.0)	34	-0.6 (16.6)	36	-11.7 (9.5)	5
Role functioning	-4.0 (24.0)	33	-12.0 (26.3)	36	-20.0 (29.8)	5
Social functioning	-5.9 (25.6)	34	-11.1 (27.9)	36	-6.7 (14.9)	5
QLQ-BIL21						
Pain	-5.7 (20.0)	28	-3.5 (11.4)	27	8.3 (5.9)	5
Anxiety	-2.9 (13.4)	28	-5.4 (19.1)	26	8.3 (11.8)	5
Treatment side effects	19.0 (36.8)	28	13.9 (33.9)	24	6.7 (49.4)	5

277 Poster Session

Exploring the diagnostic journey and life impact of patients with cholangiocarcinoma (CCA): Results from a large patient survey in the United States. *First Author: Kristen Bibeau, Incyte Corporation, Wilmington, DE*

Background: Patients (pts) with CCA typically present with advanced disease and face a poor prognosis and impaired quality of life (QoL). Despite improvements in therapies, the impact of CCA on pts' daily lives has been rarely studied. This pt-focused survey explored the diagnostic journey, life impact including work status, QoL and psychosocial impacts of CCA. **Methods:** Pts with CCA were recruited in partnership with the Cholangiocarcinoma Foundation from Aug 23 through Sept 20, 2019, and were categorized by AJCC stage. Pts participated in a 30-min online survey to assess disease staging, symptoms, demographics, diagnosis journey, daily life impact, mental health, and sexual function. The survey included the validated disease specific European Organization for Research and Treatment of Cancer (EORTC) QLQ-BIL21, the Patient Health Questionnaire-9 (PHQ-9), and the Work Productivity and Activity Impairment (WPAI) questionnaire. **Results:** Of 1,286 pts invited, 707 (55%) completed the survey (male, 77%; age ≥55 y, 13%; currently employed, 78%; perihilar CCA, 47%; intrahepatic CCA, 41%; distal CCA, 12%; stage 1–2, 22%, stage 3a, 51%, stage 3b–4, 20%, in remission, 4%, unknown stage, 2%). Median duration from symptom onset to CCA diagnosis was 19 months (range, 1–241), and median duration from diagnosis to completing survey was 24 months (0–744). Initial misdiagnosis occurred in 35% of pts (n=247); among whom the most common misdiagnosis was gall bladder cancer (52% [n=129]); misdiagnosis of cancer of unknown origin occurred in 9% of pts (n=21). CCA was most frequently first suspected and diagnosed by oncologists (38% [n=269] and 70% [n=492]); among non-specialty physicians, more first suspected than diagnosed CCA (eg, primary care physicians, 22% [n=156] vs 3% [n=22]). Pts' primary considerations in treatment decisions were physician judgment (38% [n=272]), QoL (16% [n=111]), time spent in hospital (11% [n=75]), laboratory results (11% [n=79]), other pt experiences (6% [n=42]). On the EORTC QLQ-BIL21, pts reported negative life impact from anxiety (mean [SD], 52.9 [19.2]), tiredness (52.3 [19.3]), and treatment (51.3 [28.8]). On the WPAI, 61% of pts (n=429) reported some, and 28% (n=200) reported considerable impact on work status. On the PHQ-9, 58% (n=408) of pts reported significant impact of depression on daily life, with 72% (n=506) and 25% (n=177) reporting that depression makes daily life somewhat, or very difficult, respectively. Pts also reported considerable or some impact on sexual desire (51% [n=362]; 36% [n=255]) and intimacy (47% [n=332]; 39% [n=273]). **Conclusions:** Pts with CCA who participated in this survey were mostly <55 y of age and had experienced CCA symptoms for an extended time (2 y) before diagnosis, at which time CCA was often initially misdiagnosed. The burden of CCA symptoms on daily lives, work productivity, and mental health is immense. Research Sponsor: Incyte Corporation Inc.

278 Poster Session

Posttreatment after lenvatinib in patients with advanced hepatocellular carcinoma. *First Author: Keisuke Koroki, Department of Gastroenterology, Graduate School of Medicine, Chiba University, Chiba, Japan*

Background: In clinical practice, the major disadvantage of lenvatinib to treat advanced hepatocellular carcinoma (HCC) is the lack of a posttreatment agent that has shown clear effectiveness. Thus, the establishment of second-line treatment after lenvatinib treatment failure is an urgent clinical issue to be addressed in systemic therapy in patients with advanced HCC. The study used real-world clinical data to explore candidate drugs that might be appropriate as second-line treatment after lenvatinib. **Methods:** We retrospectively reviewed the medical records of all patients with advanced HCC who received lenvatinib as the first-line agent in seven institutions in Japan between 23 March 2018 and 31 September 2019. **Results:** During the study period, 178 patients with advanced HCC received lenvatinib as first-line systemic therapy. At the time of lenvatinib administration, most patients were Eastern Cooperative Oncology Group Performance Status grade 0 or 1 (94.9%) and Child–Pugh class A (84.3%). According to the baseline radiological assessments, 25.3% and 36.0% of patients had macrovascular invasion and extrahepatic metastasis, respectively. Overall survival and progression-free survival (PFS) for lenvatinib treatment were 13.3 months (95% CI: 11.5–15.2) and 6.7 months (95% CI: 5.1–8.3), respectively. Of the 151 patients who discontinued lenvatinib, 71 (47.0%) converted to posttreatment. The conversion rates from lenvatinib to a second-line agent and from a second-line agent to a third-line agent were 41.4% and 42.4%, respectively. Based on multivariate analysis, lenvatinib response was defined as complete or partial according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST). Lenvatinib discontinuation due to radiological progression, according to mRECIST, was associated with a significantly higher probability of conversion to posttreatment after lenvatinib. Of the 63 patients who received second-line systemic therapy, 53 (84.1%) were administered sorafenib, with a PFS, response rate (RR), and disease control rate (DCR) of 1.8 months (95% CI: 0.6–3.0), 1.8%, and 20.8%, respectively. According to the Cox proportional hazards regression model, lenvatinib discontinuation due to radiological progression, Child–Pugh class B, and intrahepatic tumor volume > 50% at the time of sorafenib administration significantly contributed to a shorter PFS. Of the 22 patients who received regorafenib after lenvatinib discontinuation, five cases were as second-line therapy, and 17 were as third-line therapy. PFS, RR, and DCR for regorafenib treatment were 3.2 months (range, 1.5–4.9 months), 13.6%, and 36.3%, respectively. **Conclusions:** Sorafenib was not considered a candidate posttreatment agent after lenvatinib, except in a limited number of patients who discontinued lenvatinib without radiological progression. Regorafenib is a potential posttreatment agent after lenvatinib. Research Sponsor: None.

279 Poster Session

Contemporary real-world treatment patterns and outcomes of patients with advanced/metastatic hepatocellular carcinoma receiving second-line systemic therapy in the United States. *First Author: Arjun Gupta, Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD*

Background: Several therapies have recently gained regulatory approval in the United States (US) as second-line (2L) treatment options for patients with advanced unresectable or metastatic hepatocellular carcinoma (HCC). Treatment patterns and associated outcomes in a real-world population, especially in the contemporary era, remain understudied. **Methods:** This retrospective study utilized electronic health record data collected during routine patient care in outpatient oncology practices in the US. Adult patients diagnosed with advanced/ metastatic HCC between April 2017 and January 2020 were identified from the Concerto HealthAI database. Patients who survived at least one month from the end of first-line (1L) systemic therapy but did not initiate 2L therapy were classified as having received supportive care alone (SCA). Demographics, patient and disease characteristics, treatment patterns, and outcomes were described descriptively. Median overall survival (OS) from initiation of 2L therapy or end of 1L therapy for patients receiving SCA until death was estimated by the Kaplan-Meier method. **Results:** A total of 586 patients with advanced/ metastatic HCC were identified in the database. 330 patients received 1L therapy, and of those patients 63% (N= 207) received systemic 2L therapy (n= 105) or SCA (n= 102). At first diagnosis of advanced/ metastatic HCC, the median age was 64 years, and 86% were male. Of patients with ECOG status available at diagnosis (67%), 45% had ECOG status 0-1. The most common 1L agents prescribed were sorafenib (n= 126, 61%), lenvatinib (n= 28,14%) and sorafenib + nivolumab (n= 13, 6%) The most frequent agents prescribed in 2L were nivolumab (n= 44, 42%), sorafenib (n=18,17%), and lenvatinib (n=9, 9%). The median OS of patients receiving any systemic 2L therapy was 7.7 months (95% confidence interval 5.7-11.1) from time of receiving 2L therapy, whereas the median OS of patients receiving SCA was 5.0 months (95% confidence interval 3.3-7.1) from time of end of 1L therapy. **Conclusions:** In this contemporary national real-world cohort of patients with advanced/ metastatic HCC, a third of patients who received 1L therapy subsequently received 2L therapy. Next steps include investigating factors associated with non-receipt of 2L therapy, sequencing of therapies when multiple lines of therapies are received, and evaluating outcomes by type of agent received in 2L and beyond. Research Sponsor: Eli Lilly.

280 Poster Session

The dose-optimisation of lenvatinb for patients with unresectable hepatocellular carcinoma in clinical practice: A retrospective analysis of real-world evidence in China. *First Author: Lan Zhang, Liver Cancer Institute & Zhong Shan Hospital, Fudan University, Shanghai, China*

Background: Lenvatinib has become available as first-line therapy in patients with unresectable hepatocellular carcinoma (u-HCC). Although 8mg or 12mg/day is the standard starting dose according to weight, the high rate of adverse events (AEs) leading to dose reduction often limits its application. Various dosing schedules are used clinically to alleviate toxicities in practice. This study evaluated the safety and antitumor activity of two dosing strategies for lenvatinib administrations. **Methods:** Patients administered lenvatinib for u-HCC between April 2018 and July 2019 were enrolled. The dose-escalation strategy was conducted as follow, starting dose 4mg/day orally with biweekly escalation (As common AE always occurred within 2 weeks after administered), per 4 mg increment, to 8 or 12mg finally per body weight if no significant drug-related (no more than G2) adverse events occurred. Patients with a standard-dose strategy (8/12mg/day orally per body weight) were also included for comparison.Objective response rate(ORR) and progression-free survival (PFS) were assessed according to RECIST1.1 criteria. Dose-reduction rate was recorded and treatment-related adverse events (TRAE) was evaluated according to the CTCAE 5.0. **Results:** Totally 56 patients were included (37 in dose-escalation group and 19 in standard-dose group). The mean weight was 64.79±1.66 kg in dose-escalation group and 58.76±2.45 kg in standard-dose group, BCLC stage C proportion was 51.4% and 63.2%, Child-pugh B proportion was 16.2% and 5.3% respectively. Baseline demographic parameters were comparable between two groups (P>0.05). There was no significant difference in response rate (32.43% vs 42.1%, P=0.335), disease control rate (86.4% vs 84.2%, P=0.686) and PFS (P=0.631). The proportion of patients who reached the full dose (per weight) was also similar (48.6% vs 63.2%, p=0.399). Dose reduction rate was significantly higher in standard-dose group than dose-escalation group (36.8%vs 13.5% , p=0.044). Although, no difference in grade 3/4 adverse events was found between two groups (P=0.083), patients in standard-dose group(36.8%,7/19) have a higher incidence trend of G3/4 AEs than those of dose-escalation group(16.2%,6/37). **Conclusions:** The dose-escalation strategy may be an alternative approach to prolong lenvatinib treatment period, with comparable efficacy and more tolerance. More data are needed to confirm the long-term efficacy and safety of the dose-escalation strategy. Research Sponsor: None.

281 Poster Session

When will it be better? Lenvatinib combined with TACE for unresectable hepatocellular carcinoma: A retrospective analysis of real-world evidence in China. *First Author: Lan Zhang, Liver Cancer Institute & Zhong Shan Hospital, Fudan University, Shanghai, China*

Background: TACE and lenvatinib has each shown to prolong overall survival in patients with unresectable HCC, combination of which may also improve clinical outcomes and have been widely used in the real world accordingly. However, the optimal timing of adding on lenvatinb to TACE remains unclear. We are aiming to evaluate the efficacy and safety between two combination strategies. **Methods:** From Nov 2018 to Jun 2020, 79 consecutive patients had received a combination treatment of lenvatinib and TACE. Patients followed up for more than 2 months were included in this analysis. They were classified as early-combination group(add on lenvatinib before or after the first TACE) and late-combination group(add on lenvatinib after at least two procedures of TACE). Tumor response and progression-free survival (PFS,time from the first day of prescribing lenvatinib to progression or death) were assessed according to RECIST1.1 criteria. Liver function were also evaluated at baseline and every 2 months later. AEs were recorded during the combination treatment period according to CTCAE 5.0. **Results:** A total of 48 u-HCC patients was finally enrolled. Median follow-up in all patients was 9.3 (5.3-14.3) months. Patients' baseline characteristics were similar in two groups. For early-combination group(n=22)and late-combination group(n=26), the mean age was 65±9.7 and 61±11.6years(p=0.2);BCLC stage C HCC was 59% and 54%(p=0.89);and Child-Pugh A proportion was 81.8% and 77%(p=0.73) respectively. The objective response rate(ORR) was 22.9% in total 48 cases. There was no significant difference in response rate (18.2% vs 26.9%, P=0.51) or disease control rate (90.9% vs 92.3%, P=1.00). Median PFS was significantly longer in the early-combination group than that in late-combination group (14.5 vs 8.9 months; p=0.048). The safety profile was similar between two groups. Grade 3/4 adverse events were 3 (13.6%) and 2 cases(7.7%) respectively (P=0.65). **Conclusions:** This is to date the first real-world data of the combination timing of lenvatinib with TACE in u-HCC patients. Early-combination strategy may be a better option for the u-HCC patients with a longer mPFS. Research Sponsor: None.

282 Poster Session

Prospective, multicenter study of apatinib combine with TACE in treating intermediate to advanced stage HCC patients: A real-world study from China. *First Author: Hailiang Li, Henan Cancer Hospital, Zhengzhou, China*

Background: Combination of transcatheter arterial chemoembolization (TACE) with apatinib are emerging as an effective treatment for patients with intermediate to advanced stage HCC. However, the data of HCC treated by apatinib in the real-world setting are not reported. In this real-world study, we aimed to explore the efficacy and safety of HCC pts which underwent TACE combine with apatinib. **Methods:** This was a prospective, multicenter observational study in a real-world setting and this study was approved by our Ethics Committee. Pts aged ≥18 years with well diagnosed intermediate or advanced stage HCC were included. The pts received apatinib plus TACE treatment as the first-line therapy. TACE treatment was performed on demand, the dose of apatinib was selected by the investigator. The primary endpoint was progression-free survival (PFS). The secondary endpoints were overall survival rate (OS), objective response rate (ORR), disease control rate (DCR) and safety profile. All of the objective response was assessed by independent central review per mRECIST criteria. **Results:** From Jun 2019 to Feb 2020, a total of 98 well diagnosed HCC pts with age from 31 to 86 were enrolled in this study. As of August 2020, the median follow-up was 9.5 months. The mPFS of 98 pts was 7 months. The ORR, DCR and 6 months OS rate was 35.7%, 76.5% and 82.6%, respectively.The PFS was 7.5 months in intermediate stage and 6.4 months in advanced stage. The ORR was 46.3% in intermediate stage (41 cases) and 28% in advanced stage (57 cases) HCC. And the 6 months OS rate was 90.2% in intermediate stage and 77.1% in advanced stage HCC. Overall, 17 (17.3%) pts had grade≥3 treatment-related AEs. All of the safety adverse effects can be tolerated or reduced after symptomatic treatment and no unexpected adverse events were observed. **Conclusions:** In this real-world study, apatinib showed a favorable efficacy and safety profile in pts with intermediate and advanced stage cancer. Apatinib combination TACE therapy might lead to better survival benefit in first-line treatment for HCC pts. Clinical trial information: ChiCTR1900024030. Research Sponsor: None.

283 Poster Session

Treatment patterns and outcomes of hepatocellular carcinoma (HCC) patients (pts) in the CancerLinQ Research Database (CLQ). *First Author: Shaum Kabadi, AstraZeneca, Gaithersburg, MD*

Background: Treatment and management of pts with HCC is complicated by the presence of underlying chronic liver disease. Clinical trials with unresectable HCC pts are generally limited to Child-Pugh A or pts with good performance status. Therefore there is limited data for less fit HCC pts, particularly those treated in the community practice setting. **Methods:** The study design was a retrospective cohort study using the US-based CancerLinQ Discovery Database (CLQ). CLQ was launched by the American Society of Clinical Oncology in 2016 and consists of longitudinal, demographically, and geographically diverse data aggregated from oncology practice Electronic Health Record databases. Eligible pts were ≥18 years at time of HCC diagnosis, had a diagnosis of stage IV HCC within the record, and had ≥2 clinical encounters on separate dates during follow-up after the date of diagnosis. The study period and patient identification period was Jan 1997–Aug 2019; follow up continued through May 2020. Patient demographics, clinical characteristics, and general treatment characteristics were summarized using descriptive statistics. **Results:** 460 pts were eligible for analysis. Of these, 141 pts (31%) had a Child-Pugh score as reported in medical charts or imputed based on structured and curated data. 76 (54%) pts were Child-Pugh class A, 59 (42%) Child-Pugh class B, and 6 (4%) Child-Pugh class C. The proportion of pts with chronic hepatitis C infection and liver cirrhosis was higher in pts with Child-Pugh classes B and C compared to A. Time from diagnosis to first systemic therapy decreased from a median of 126 days for pts with Child-Pugh class A, to 47 and 16 days for class B and C, respectively. Sorafenib was the most common regimen regardless of line of therapy, followed by PD-1 pathway inhibitors and chemotherapy. Median duration of sorafenib therapy decreased from Child-Pugh class A to C (table). There was a similar decrease in duration of therapy for pts receiving PD-1 pathway inhibitors and chemotherapy when moving from class A to class C. **Conclusions:** This is the first published retrospective study in HCC using the CLQ. Pts with Child-Pugh class B or C, who are typically excluded from clinical trials, represented 48% of the pts with a Child-Pugh score included in this analysis. Duration of therapy was numerically lower for pts with Child-Pugh class B or C compared to Child-Pugh class A. Further research is needed to describe real-world evidence outside the context of a clinical trial for HCC pts. Funding: AstraZeneca.

Child-Pugh score class	Variable	Bevacizumab	Chemotherapy	Other TKI	Others	PD-1 pathway	Sorafenib
A	Obs	2	25	8	1	25	58
	Avg days	216	383	282	57	156	247
	Median days	216	235	157.5	57	81	147
B	Obs	1	14	5	1	21	35
	Avg days	166	229	160	15	105	244
	Median days	166	32.5	98	15	60	126
C	Obs	-	-	-	-	1	2
	Avg days	-	-	-	-	1	44
	Median days	-	-	-	-	1	43.5

Avg, average; obs, observed; TKI, tyrosine kinase inhibitor Research Sponsor: AstraZeneca.

284 Poster Session

Risk factors, treatment patterns and survival of patients with incident hepatocellular carcinoma in France: A retrospective data analysis. *First Author: Philippe Mathurin, Centre Hospitalo-Universitaire Claude Huriez, Service d'Hépatologie, Lille, France*

Background: Despite the screening of patients at risk, hepatocellular carcinoma (HCC) is often diagnosed at an advanced stage disease, with a very poor prognosis. Aim: To describe risk factors, treatment patterns and survival of patients with newly diagnosed HCC in France over the period 2015-2017 using SNDS, the national administrative healthcare database covering around 99% of the population. **Methods:** The database was searched for patients with a diagnosis of HCC (ICD-10: C220) from 1 January 2015–31 December 2017. Disease stage (Barcelona Clinic Liver Cancer B, C or D classification) was defined by the identification of treatment: transcatheter arterial chemoembolization (TACE) or radioembolization (TARE), HCC systemic therapy and/or best Supportive Care (BSC). Patients were followed up for a maximum of 2 years. **Results:** 21,071 patients were identified, mean age 69.2 years (SD: 11.1), 82.2% were male. Liver disease or diabetes was identified in 86.4% of patients. The most frequent risk factors were alcohol liver disease (42.7%), viral hepatitis and alcohol liver disease (7.2%), viral hepatitis alone (12.6%), NASH/NAFLD or diabetes (17.7%). At diagnosis, 6,571 (31.2%) received a curative HCC treatment. Within the total population, 8,616 patients (40.9%) were only managed by BSC, 6,571 (31.2%) received a treatment therapy, of which 3,184 (15.1%) had a TACE or TARE and 2 700 (12.8%) sorafenib. The 1-year survival rates by initial treatment were: curative (88.7%), TACE or TARE (70%), systemic therapy (32.2%) and only 17.8% with BSC. **Conclusions:** These results show the high burden of HCC, with more than two thirds of patients not receiving active treatment. Research Sponsor: Ipsen.

285 Poster Session

Anti-PD-1 antibody SHR-1210 combined with apatinib as adjuvant treatment in patients with hepatocellular carcinoma at high risk of recurrence after radical resection: Preliminary results from a multicenter, randomized, controlled phase II trial. *First Author: Hong Zhao, Department of Hepatobiliary Surgery, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China*

Background: There is no globally recognized standard adjuvant therapy for HCC after radical resection. Herein, we explored to evaluate the efficacy and safety of anti-PD-1 antibody SHR-1210 combined with apatinib as adjuvant treatment versus hepatic arterial infusion (HAI) in HCC patients with high risk of recurrence after radical resection. **Methods:** This was an ongoing multicencer, randomized, controlled phase 2 trial. All HCC patients were Child-Pugh Class A, and confirmed as high risk of recurrence such as portal vein tumor thrombus (PVTT) involved in second-order branch or above, microvascular invasion (MVI) and microsatellite leisions. Eligible patients were randomly assigned (1:1) to receive SHR-1210 (200mg, q2w) and apatinib (250mg, q.d.) for 12 cycles, or two times of standard HAI treatments (epirubicin 80-100mg or epirubicin 50mg+oxaliplatin 50mg). The primary endpoint was recurrence-free survival (RFS), and the secondary endpoints included safety and quality of life score (QoL). **Results:** From Jun 12, 2019 to Sep 15, 2020, 32 Chinese HCC patients (pts) (16pts in SHR-1210-apatinib group and HAI group, respectively) had been recruited. Full analysis (FAS) population contained 29 pts and intention to treat (ITT) population included 32 pts. The hadzard ratio for relapse or death with SHR-1210-apatinib as compared with HAI was 0.48 (95% CI 0.12-1.75; P = 0.2992) and 0.38 (95% CI 0.11-1.20; P = 0.0910) in FAS and ITT population, respectively, at date cutoff. Median RFS was not reached and 10.5 months in SHR-1210-apatinib group and HAI group, respectively. The average QoL score during treatment was 48.8 and 49.2 in SHR-1210-apatinib group and HAI group, respectively. The most common grade 3 or 4 adverse events occurred in SHR-1210-Apatinib were γ-glutamyltransferase (GGT) increase (18.75%), leukopenia (12.50%), neutrophil count decrease, alanine and aspartate aminotransferase increase (12.50%), while in HAI group were lymphocyte count decrease (7.69%), hemoglobin increase (7.69%) and GGT increase (7.69%). **Conclusions:** In HCC patients with high risk of recurrence after radical resection, SHR-1210 combined with apatinib was tolerable, and might offer a new promising choice superior to HAI for adjuvant therapy in HCC, further study is needed to reach the pre-defined primary endpoint. Clinical trial information: NCT03839550. Research Sponsor: None.

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The lines of loco-regional therapies received and the healthcare economic burden of patients newly diagnosed with hepatocellular carcinoma in the United States. *First Author: Brian Seal, AstraZeneca Pharmaceuticals LP, U.S. Medical Affairs: Evidence Generation, Gaithersburg, MD*

Background: Hepatocelluar carcinoma (HCC) is one of the fastest growing causes of cancer-related deaths in the US. The objectives of this study were to examine the lines of loco-regional therapies received and the healthcare economic burden of patients newly diagnosed with HCC in the US. **Methods:** Patients (≥18 years of age) diagnosed with HCC who received ≥1 loco-regional therapy (index date) after diagnosis were identified from the MarketScan Commercial and Medicare Supplemental databases (July 1, 2013-May 31, 2018). Patients were required to have ≥6 months of continuous insurance enrollment before the index date and ≥1 month after (follow-up period). The follow-up period was censored when patients received any systemic therapy. During the follow-up periods, the number of patients who received radiation therapy, ablative therapy, and embolization procedures (transarterial embolization/chemoembolization [TAE] and radioembolization [TARE]) were examined. All-cause and HCC-related healthcare costs (total and patient out-of-pocket [OOP] payments per patient per month [PPPM]) were also measured. **Results:** Among the 2,101 patients newly diagnosed with HCC who received ≥1 loco-regional therapy, median age was 64 years and 75.0% were male; the mean follow-up duration was 11.5 months. During the follow-up periods, 28.1% (n = 590) received radiation therapy, 27.3% (n = 574) ablative therapy, and 77.3% (n = 1,623) embolization therapy (TAE: 68.7% [n = 1,443]; TARE: 20.7% [n = 434]); 30.9% of patients received multiple loco-regional therapies. During the follow-up periods, total all-cause healthcare costs were a mean of $20,316 (OOP: $378) PPPM, of which 70.7% ($14,359; OOP: $227 PPPM) were HCC-related. The breakdown of healthcare costs is shown in the table. **Conclusions:** According to the findings of this large-scale real-world analysis of patients newly diagnosed with HCC in the US, a vast majority received at least one embolization procedure. The monthly healthcare economic burden of patients with HCC treated with local-regional therapies is relatively high. Research Sponsor: AstraZeneca Pharmaceuticals LP.

	All-cause Mean (st dev)	HCC-related Mean (st dev)	
Total healthcare cost PPPM	$20,316 ($26,447)	$14,359 ($23,064)	
	Inpatient	$5,675 ($19,489)	$4,160 ($16,966)
	Outpatient	$12,762 ($17,820)	$10,199 ($16,455)
	Pharmacy	$1,878 ($5,425)	-

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Safety, tolerability and efficacy of transarterial chemoembolization using anthracyclines-loaded drug eluting microspheres for treatment of patients with unresectable hepatocellular carcinoma: Pooled analyses. *First Author: Thierry De Baere, Gustave Roussy Cancer Institute/Paris-Sud University, Villejuif, France*

Background: Transarterial chemoembolization either with Lipiodol (cTACE) or with drug eluting microspheres (DEM-TACE) is indicated for the treatment of hepatocellular carcinoma (HCC) not amenable to curative treatments in patients with preserved liver function. Safety of TACE is becoming more important with its increased use as a bridge to transplant or downstaging to resection, but also for preservation of liver function in case of subsequent immuno-combination therapies. LifePearl microspheres is a novel DEM comprised of polyethylene-glycol with reported good safety profile and efficacy in smaller series. Our purpose was to assess safety and efficacy of TACE using anthracycline loaded LifePearl for the treatment of patients with unresectable HCC in a pooled analysis of studies with available more than 500 patient's level data. **Methods:** We pooled patient level data from 5 single arm studies. Safety was assessed by close monitoring of adverse events according to CTCAE (v4.03). Tumor response was assessed, according to mRECIST and RECIST1.1 and analyzed as best overall response to account for differences in time of imaging follow-up between studies. The Kaplan-Meier method was used to estimate event rates for time to event outcomes: progression free survival (PFS), time to unTACEable progression (TTUP) and overall survival (OS) censoring patients at time of surgery or transplantation. **Results:** Out of 586 patients, 85.5%, 13.5% and 1.0% were Child Pugh A, B and C, respectively. BCLC stages 0, A, B and C were 13.6%, 43.4%, 41.1% and 1.9% respectively. The mean number of HCC lesions was 2.1±1.5 and mean sum of tumor diameters was 49.3±32.9mm. In 19% of patients alpha-feto protein level was > 200ng/ml. A mean of 1.9±1.3 DEM-TACEs were performed per patient. A total of 197 events were reported including 2.6 % grade 4 and 1.5% grade 5, mostly related to post-embolization syndrome. Complete response, partial response and stable disease were 60.2%, 27.1% and 7.4% respectively providing an objective response and disease control rates of 87,3% and 94,7% respectively. 10% of patients were transplanted or resected. Median OS, PFS and TTUP is indicated in the table below. OS was 89.2%, 80.2% and 69.7% at 12, 18 and 24 months respectively. **Conclusions:** The treatment of patients with unresectable HCC with anthracycline loaded LifePearl showed good tolerance with acceptable toxicity and high tumor response rate that translated into promising PFS, TTUP and OS. Research Sponsor: Terumo Europe.

Median OS, PFS and TTUP.

Endpoint	Total population	BCLC O&A	BCLC B&C	
Median OS (months)	35.8 [30.3; n.e.]	n.e [35.8; n.e.]	29.9 [27.0; 37.0]	
	Median PFS (months)	12.0 [10.1; 13.4]	12.9 [11.3; 14.9]	9.7 [7.9;12.6]
	Median TTUP (months)	19.4 [16.7; 28.3]	n.e [24.6; n.e]	14.1[9.7;16.7]

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Treatment patterns and survival in patients with late-stage hepatocellular carcinoma in France: A retrospective database analysis. *First Author: Jean-frederic Blanc, Service d'Hépato-Gastroentérologie et d'Oncologie Digestive, Groupe Hospitalier Saint André, Bordeaux, France*

Background: The prognosis for patients with late-stage hepatocellular carcinoma (HCC) is poor, with only one systemic treatment option available for patients until 2017. **Aim**: To describe treatment patterns and survival of French patients following diagnosis of late-stage HCC (Barcelona Clinic Liver Cancer classification B, C or D), using a comprehensive nationwide claims database, SNDS. **Methods:** The SNDS database was searched from 1 January 2015 to 31 December 2017 for patients with a diagnosis of HCC (ICD-10: C220) and late-stage disease, defined by the identification of transcatheter arterial chemoembolization (TACE) or radioembolization (TARE), HCC systemic therapy and/or best supportive care (BSC). Patients were followed up for a maximum of 2 years. **Results:** 17,298 patients (mean age: 68.7 years (SD: 11.3), 82.6% male) were identified, with 72.4% diagnosed at late stage. During follow-up, 29.6% of patients were treated with TACE or TARE, and 27.1% received systematic therapy (sorafenib in 99.5% of cases). The median duration of systemic treatment was 7.9 (95% CI: 7.4-8.5) months. In 62.5% of cases, this treatment was discontinued at 12 months; this proportion fell to 40.3% when using mortality as a competitive risk. Survival since diagnosis of late stage HCC differed according to the type of first treatment received. Median overall survival was 23.7, 11.9, 7.4 and 1 month in patients initially receiving TACE, TARE, systemic therapy or no treatment, respectively. **Conclusions:** These results confirm the high clinical burden of late-stage HCC over this period and the need for second-line systemic treatments to improve patient outcomes. Research Sponsor: Ipsen.

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Impact of NAFLD on clinical outcomes in hepatocellular carcinoma treated with sorafenib: An international cohort study. *First Author: Jessica Howell, University of Melbourne, Melbourne, Australia*

Background: The incidence of non-alcoholic fatty liver disease (NAFLD)-associated hepatocellular carcinoma (HCC) is increasing. The impact of NAFLD on overall survival (OS), treatment response and toxicity in patients with HCC treated with sorafenib is unknown. We examined the impact of NAFLD on OS and toxicity in an international cohort of patients receiving sorafenib. **Methods:**Clinical and demographic data were collected from patients consecutively treated at specialist centres in Europe and North America. The impact of NAFLD on OS, sorafenib-specific survival and sorafenib-related toxicity compared to other aetiologies of liver disease using multivariable Cox-proportional hazards and logistic regression modelling was assessed. **Results:** 5201 patients were treated with sorafenib; 183 (3.6%) had NAFLD-associated HCC. NAFLD-associated HCC patients were more likely to be older women(-median age 65.8 vs 63.0 years, $p < 0.01$ and 10.4% vs 2.3%, < 0.01), with a median BMI of 29.4. After controlling for known prognostic factors, no difference in OS in patients with or without NAFLD was observed(adjusted HR 0.94 (95% CI 0.76 -1.16), p = 0.57). NAFLD-associated patients had more advanced stage HCC when they commenced sorafenib (BCLC C/D 70.9% vs 58.9%, $p < 0.01$) and were more likely to be commenced on a lower starting dose of sorafenib (51.4 vs. 36.4%, $p < 0.01$). However, there was no difference in sorafenib-specific survival between NAFLD and other aetiologies(HR 0.99, 95% CI (0.85 – 1.16, p=0.92). Adverse events were similar between NAFLD and non-NAFLD HCC groups, including rates of $\geq$ grade 2 hypertension(6.3 vs. 5.8%, p = 1.00). A lower rate of severe hand foot syndrome was observed in the NAFLD population(3.8 vs. 12.4%, p = 0.03). **Conclusions:** OS in HCC does not appear to be influenced by the presence of NAFLD. NAFLD-associated HCC derive similar clinical benefit from sorafenib compared to other aetiologies. Research Sponsor: None.

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Low energy amplitude modulated radiofrequency electromagnetic fields in combination with standard treatment or as monotherapy to show improvement in quality of life in patients with advanced hepatocellular carcinoma. *First Author: Micelange Carvalho Sousa, Hospital Sírio Libanês, São Paulo, Brazil*

Background: Hepatocellular carcinoma (HCC) is a fatal cancer without curative option for most patients. Hence the importance to improve health related quality of life (HRQoL). Amplitude-modulated radiofrequency electromagnetic fields (EMF), as a novel and non-toxic therapy, has potential for improving HRQoL in advanced HCC patients. **Methods:** An open-label, single center, prospective clinical protocol was performed in advanced HCC patients as an initial and salvage treatment modality. Systemic exposure to EMF was used in combination with a systemic conventional treatment or as a single treatment. A spoon-shaped antenna placed in the oral cavity delivered EMF over 90 minutes with monthly repetitions until death or consent withdrawal. The effect on HRQoL was the primary objective of this study. Patients answered the EORTC-C30 v3.0 questionnaires prior to every EMF exposure. Clinically meaningful change (CMC) and time to deterioration (TTD) for Global Health (QoL), Role Functioning (RF) and Physical Functioning (PF) were used in the analysis. **Results:** From March 2018 to April 2020, 55 advanced HCC patients were submitted to 373 EMF exposures. 41/55 (75%) patients had repetitive exposures (mean # 4, ranging from 2-16). 87% were male, median age was 67, 84% were BLCL-C, 16% were Child-Pugh B, 29% had extra-hepatic metastasis, 55% had failed previous treatment and 71% had documented radiological progression. 31(56%) patients received EMF in combination with systemic therapy (28 TKI and 3 anti-PDL1). 24 patients received EMF as a single treatment modality. The mean baseline score was 68.1 for QoL and 77.1 for RF and PF. 61%, 76% and 49% of patients experienced positive change in QoL, RF and PS scores immediately prior to the second exposure, respectively. +CMC was reported in 20%, 17% and 32% of patients, respectively for QoL, RF and PS. The median QoL TTD was not reached. The median RF TTD was 7.2 month and the median PF TTD was 11.9 month. The median RF TTD for patients in combination treatment was 11.4 months and in a single treatment was 13.5 month. The median PF TTD for patients in combination treatment was 12.8 months and in single treatment was 14.5 month. **Conclusions:** Advanced HCC patients showed positive changes in QoL, RF and PF HRQoL scores after single exposure to EMF. The benefit from EMF in HRQoL was durable both in combination with TKI or as a single modality in advanced HCC patients. These results support future development as a novel palliative treatment modality in advanced HCC patients. Clinical trial information: NCT 01686412. Research Sponsor: None.

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The implications of treatment delays in adjuvant therapy for cholangiocarcinoma patients. *First Author: Matthew Parsons, University of Utah, Salt Lake City, UT*

Background: To understand the factors associated with timing of adjuvant therapy in the management of intrahepatic and extrahepatic cholangiocarcinoma and the impact of delays on overall survival (OS). **Methods:** Data from the NCDB for patients with pathologically proven non-metastatic adenocarcinoma of the bile ducts from 2004 to 2014 were pooled and screened. Patients were included only if they underwent surgery and adjuvant chemotherapy (CMT) and/or radiotherapy (RT). Patients who underwent neoadjuvant therapy or received CMT or RT with palliative intent were excluded. Pearson's chi-squared test and multivariate logistic regression analyses were used to assess the distribution of demographic, clinical, and treatment factors. After propensity-score matching with inverse probability of treatment weighting, OS was compared between patients who had initiation of adjuvant therapy past various time points using Kaplan Meier analyses and doubly-robust estimation with multivariate Cox proportional hazards modeling. **Results:** In total, 7,422 patients in our analysis underwent adjuvant treatment. This represented 43% of the study cohort of 17,123 patients. Of the patients who underwent adjuvant treatment, 3,956 (53%) initiated adjuvant therapy by two months, 6,234 (84%) by 3 months and 6,987 (94%) by four months. High-grade disease, macroscopically positive margins, tumors larger than five centimeters, and unknown LVSI status, were associated with earlier initiation of adjuvant treatment at two months or earlier. Patients who received early adjuvant therapy were also more likely to be treated with a combination of CMT and RT. Factors associated with delay of adjuvant therapy beyond three months post-surgery included Charlson scores of one or greater and Hispanic race. After propensity score weighting, there was no survival difference between groups when comparing initiation of adjuvant therapy before or after two, three or four month time points **Conclusions:** We identified a number of patient characteristics related to the timing of initiating adjuvant therapy in patients with biliary cancers. There were no significant difference in OS associated with delaying adjuvant therapy beyond two, three or four month time-points. Our findings are relevant in the era of COVID-19 when minimizing patient exposure to health-care settings during a pandemic may need to be considered when deciding on the timing of adjuvant therapy. If a delay is necessary, our results suggest that there is no survival detriment to initiating adjuvant therapy beyond three or four months after surgery for biliary cancers. Research Sponsor: None.

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Anlotinib plus TQB2450 in patients with advanced refractory biliary tract cancer (BTC): An open-label, dose-escalating, and dose-expansion cohort of phase Ib trial. *First Author: Jun Zhou, Beijing Cancer Hospital and Institute, Beijing, China*

Background: Anti-angiogenic agents have been clinically investigated in combination with anti-PD-1/L1 mAbs due to their immuno-modulatory effects. Anlotinib (A), a potent oral multi-target tyrosine kinase inhibitor, has anti-angiogenic properties and anti-tumor efficacy with a favorable toxicity profile. The combination of A and TQB2450 (T), an anti-PD-L1 mAb, exhibited superior tumor growth suppression compared to either monotherapy in murine models. This ongoing phase 1b study cohort is aimed to assess the safety and efficacy of A+T in pts with advanced BTC. **Methods:** In this study cohort, patients (pts) with previously treated, advanced BTC were enrolled. A 3+3 dose escalation was used to determine the maximum tolerated dose (MTD) and a recommended phase 2 dose (RP2D) in a dose-escalating stage. Additional pts were enrolled in a dose-expansion stage to further establish the safety and determine the preliminary efficacy. Oral A of 10 and 12 mg was administered once daily for 14 days on / 7 days off with intravenous T of 1200 mg every 3 weeks. The primary endpoint was dose-limiting toxicity (DLT) during first cycle (first 3 weeks) to estimate the MTD, RP2D and overall response rate (ORR). Tumor response was assessed according to RECIST version 1.1 and iRECIST. The Secondary endpoints were progression-free survival (PFS), disease control rate (DCR) and safety. **Results:** 25 pts were enrolled (8 with intrahepatic cholangiocarcinoma [IHCC]; 8 with extrahepatic cholangiocarcinoma [EHCC]; 9 with gall bladder cancer [GBC]) until August 2020. Median number of prior lines of therapy was 1 (range 1-5). During dose-escalation, no DLT was observed and 12 mg anlotinib was determined as RP2D for expansion. Among 24 evaluable pts (with at least once tumor assessment), 3 had achieved complete response (CR) and 7 had partial response (PR), which were all treated by 12 mg anlotinib plus TQB2450, 8 had stable disease (SD) and 6 had progression disease (PD). ORR was 41.67% and DCR was 75%. 10 pts were still on treatment. The median PFS was 240 days (95% CI, 83~NR).Treatment-related adverse events (TRAEs) occurred in 83.3% of pts (G3/4 in 16.7% [4/24], and leading to treatment discontinuation in 4.2% [1/24]). The most common TRAEs were hypertension (33.3%), decreased white blood cell counts (25.0%), increased TBIL (20.8%), decreased neutrophil counts (20.8%), increased DBIL (12.5%), and increased IBIL (12.5%). **Conclusions:** A+T had a manageable safety profile and encouraging antitumor efficacy in pts with previously treated, advanced BTC. No unexpected AEs were identified beyond the established safety profile for each agent. Clinical trial information: NCT03996408. Research Sponsor: Chia Tai Tianqing Pharmaceutical Group Co., Ltd.

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Comparison of systemic therapy efficacy in advanced hepatocellular carcinoma: Systematic review and frequentist network meta-analysis of randomized controlled trials. *First Author: Robin Park, MetroWest Medical Center, Framingham, MA*

Background: Several systemic agents are approved for use in the first line and second line treatment settings for advanced hepatocellular carcinoma (aHCC). However, choosing among available options in both first and second line settings remain difficult due to the paucity of head-to-head comparative trials. Therefore, we have conducted a systematic review and network meta-analysis for the indirect comparison of the systemic agents in the first line and second line settings. **Methods:** Published clinical trials that have evaluated systemic agents in the first line and second line settings in advanced HCC from inception to April 2020 were identified by searching PubMed, EMBASE, and Cochrane Databases and abstracts presented in the main annual ASCO and ESMO conferences from 2017 to 2020. Studies published in English providing clinical outcomes data including overall survival (OS), progression free survival (PFS) and objective response rate (ORR) were included in the analysis. The primary outcomes of interest were pooled hazard ratios (HR) of OS and OR of ORR in first line studies and HR of PFS and OR of ORR for second line studies. OS for second line agents were synthesized in a qualitative analysis. **Results:** Overall, 8,335 patients (13 studies) and 4,612 patients (11 studies) were analyzed in phase II/III trials for first line and second line settings respectively. In the first line setting, atezolizumab plus bevacizumab and lenvatinib were ranked highest as the regimens associated with the greatest OS (A+B, HR 0.58, 95% CI, 0.42-0.80; P-score 0.993) and ORR (lenva, OR 3.34, 95% CI, 2.17-5.14; P-score 0.080) respectively. In the second line setting, cabozantinib showed the highest probability of greatest PFS benefit (HR 0.44, 95% CI, 0.29-0.66; P-score 0.854) as well as the highest probability of greatest ORR benefit (cabo, OR 9.40, 95% CI, 1.25-70.83, P-score, 0.266). **Conclusions:** In the first line setting, atezolizumab plus bevacizumab may be the superior regimen whereas lenvatinib may be considered as the initial option when robust tumor responses are preferred. In the second line setting, cabozantinib may be the preferred option including in cases when robust tumor responses are favored. Research Sponsor: None.

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DEDUCTIVE: A study of tivozanib in combination with durvalumab in subjects with untreated advanced hepatocellular carcinoma—Phase Ib results. *First Author: Renuka V. Iyer, Roswell Park Comprehensive Cancer Center, Buffalo, NY*

Background: A recent ph3 study combining bevacizumab (VEGF-A Mab) with atezolizumab (PD-L1 inhibitor) has shown significant improvements in OS and PFS demonstrating that a combination of VEGF and PDL1 inhibition can improve patient outcomes over sorafenib. Tivozanib (T, a potent and selective VEGFR 1, 2 & 3 TKI) and durvalumab (D, a PD-L1 antibody) have both demonstrated single agent activity in HCC and have been combined safely with other therapies. T blocks all three VEGF receptors, and when combined with a PD-L1 inhibitor may improve patient outcomes. The ph1 portion of this study combines T with D to establish the recommended phase II dose (RP2D) and provide preliminary safety and efficacy data. **Methods:** Major eligibility criteria are adults with documented advanced HCC, Child-Pugh Class A, ECOG 0 or 1, creatinine clearance $>$ 40 ml/min. Major exclusion criteria are co-infection with HBV and HCV and significant organ dysfunction. The starting dose is the combination of T 1 mg orally for 21 days followed by 7 days off treatment and D 1500 mg intravenously every 28 days. A DLT is generally defined as the occurrence of any Grade $\geq$3 immune or non-immune adverse event (AE) in Cycle 1 that is at least possibly related to the investigational regimen other than any grade of vitiligo or alopecia or Grade 3 controllable hypertension in cycle 1. The primary objective is to establish the RP2D and the safety and tolerability for this combination in patients with advanced HCC. Patients will be treated until progression of disease, unacceptable side effects, or death. Outcome measures will be AEs per CTCAE v.5 and cross-sectional imaging performed every 8 weeks. **Results:** Seven patients were enrolled in phase I. Six were male; the median age was 75 (range 40 to 82). One patient had mild elevation of LFTs and did not complete the 21-day course of T and was replaced. No patient experienced a $>$=grade 3 AE in cycle 1. The most common AEs, each seen in two of seven patients, were anorexia, cough, diarrhea, dysphonia, fatigue, hypertension, and palmar-plantar erythrodysesthesia. Two of seven have achieved a partial response. **Conclusions:** The combination of T with D in patients with untreated advanced HCC is well tolerated. The RP2D for the combination is T 1 mg orally for 21 days on treatment followed by 7 days off treatment and D 1500 mg intravenously every 28 days. In the phase II portion of the study an additional 30 patients will be treated at the RP2D. Secondary objectives are to assess the objective response rate, progression free survival, and overall survival in this population. Clinical trial information: NCT03970616. Research Sponsor: AVEO Oncology.

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Atezolizumab plus bevacizumab for unresectable or metastatic hepatocellular carcinoma: A cost-effectiveness analysis. *First Author: Wenjun Wang, Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China*

Background: In May 2020, atezolizumab plus bevacizumab was approved by US Food and Drug Administration for patients with unresectable or metastatic hepatocellular carcinoma (HCC) who have not received prior systemic therapy due to improvement in overall and progression-free survival compared with standard sorafenib treatment. However, because of the high cost of atezolizumab plus bevacizumab, there is a need to assess its value by considering both efficacy and cost. The aim of this study is to evaluate the cost-effectiveness of atezolizumab plus bevacizumab vs sorafenib for patients with unresectable or metastatic HCC from the US payer perspective. **Methods:** A partitioned-survival model was developed to compare health care costs and clinical outcomes of atezolizumab plus bevacizumab vs sorafenib in first-line treatment of unresectable or metastatic HCC over 6-year horizon. Treatment effects were extracted from the IMbrave150 trial. Health care cost and health utility data were obtained from published studies and databases. Incremental cost-effectiveness ratio (ICER) was calculated as the ratio of the incremental cost to the incremental quality-adjusted life years (QALYs). One-way deterministic and probabilistic sensitivity analyses were used to examine model uncertainty. Additional subgroup analyses were performed. **Results:** Atezolizumab plus bevacizumab resulted in increase of 0.623 life-years, 0.484 QALYs and $158,781 per patient at the base case analysis. The ICER was $322,500 per QALY (95% confidence interval, $136,275 to $801,509 per QALY), with 0.5% and 4.1% chance of being cost-effective at a willingness-to-pay threshold of $100,000 and $150,000 per QALY, respectively. The ICER never went below $150,000 per QALY in the one-way sensitivity analyses and among patients of clinically relevant subgroups in the subgroup analyses. **Conclusions:** Atezolizumab plus bevacizumab is unlikely to be cost-effective compared with sorafenib in first-line treatment of patients with unresectable or metastatic HCC from the US payer perspective. Research Sponsor: Chinese foundation for hepatitis prevention and control——TianQing liver disease research fund subject.

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Association of early recurrence within one year of liver transplant for hepatocellular carcinoma with poor survival. *First Author: Bryan Cho Wing Li, HKU, Hong Kong, China*

Background: Treatment of hepatocellular carcinoma (HCC) recurrences following liver transplant is challenging. All the clinical trials of systemic therapies for advanced HCC excluded patients with any history of organ transplant. Here we review outcome, and the safety and efficacy of the application of systemic medical therapies in this clinical setting. **Methods:** This is a retrospective cross-sectional study of consecutive adult patients with recurrence of HCC following liver transplant for the indication of treatment of HCC in Queen Mary Hospital from January 2005 to January 2018. **Results:** Forty-three consecutive patients with a recurrence of HCC following liver transplant were identified from 2005 to 2018. Median survival from diagnosis of recurrence was 17 months (CI 11.3, 22.7). Early recurrence within 12 months of transplant was associated with a significantly worse median survival of 10 months CI 8.5, 11.4) compared to 26 months (CI 18.8, 33.2) when recurrences occurred after 12 months from transplant ($p< 0.001$) after adjustment with peritumoural vascular invasion, first line therapy with sorafenib, any second line therapy and use of mTOR inhibitors as immunosuppressants, with a hazard ratio of 0.104 (log-rank test, $p<0.001$). 41 patients who received medical systemic therapies, 34 (79.1%) received sorafenib as the first line systemic therapy. 47.1% (N= 16) received subsequent lines of systemic therapies (ranging from 1 to 4 lines). Hand-foot syndrome was most common among the adverse events and it was observed in 34.7% patients treated with sorafenib. It led to dose interruptions in 8.8 % of patients who were given sorafenib. 26.7% had grade 1 diarrhoea. 14.3% had grade 1 transaminase rise. **Conclusions:** Early recurrence within one year from transplant was the most significant risk factor. Treatment efficacy and adverse events and tolerability of sorafenib were comparable with those in the setting of advanced HCC without transplant. Research Sponsor: None.

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Pembrolizumab (pembro) monotherapy for previously untreated advanced hepatocellular carcinoma (HCC): Phase II KEYNOTE-224 study. *First Author: Jean-Luc Van Laethem, Erasme Hospital, Brussels, Belgium*

Background: Results from cohort 1 of KEYNOTE-224, an open-label, single-arm, multicountry phase II trial, demonstrated that pembro monotherapy was efficacious and tolerable in patients (pts) with advanced HCC previously treated with sorafenib. Here, we report results from KEYNOTE-224 cohort 2, which enrolled pts with advanced HCC and no prior systemic therapy. **Methods:** Eligible pts in cohort 2 had radiologically, histologically, or cytologically confirmed, incurable HCC not amenable or refractory to locoregional therapy, Child Pugh A liver disease, measurable disease based on RECIST 1.1 by blinded independent central review (BICR), ECOG PS 0-1, and BCLC stage C or B. Pts received pembro 200 mg IV Q3W for ~2 years or until disease progression, unacceptable toxicity, consent withdrawal, or investigator decision. Primary endpoint was ORR (RECIST 1.1 by BICR). Secondary endpoints included DOR, DCR, TTP, PFS, OS, and safety/tolerability. Response was assessed every 9 weeks. Efficacy and safety were assessed in pts who received ≥1 dose of study treatment. DOR was assessed in responders. The estimate and 95% CI of the ORR and DCR were based on the Clopper-Pearson method. Kaplan-Meier method was used to estimate OS, PFS, and DOR. A sample size of ~50 pts was chosen to provide acceptable precision for the assessment of ORR. **Results:** Cohort 2 enrolled 51 pts. The median time from the first dose to data cutoff (July 31, 2020) was 21 (range, 17-23) mo. The median age of pts was 68 (range, 41-91) years, one pt was HBV+, 80% had alcohol use, 8% were HCV+, 18% had vascular invasion, 35% had extrahepatic disease, 33% had BCLC Stage B disease, and 67% had BCLC Stage C HCC. ORR was 16% (95% CI, 7-29) and was similar across most subgroups. Median DOR was not reached (range, 3-20+ mo); 70% were estimated to have response duration ≥12 mo. Best overall responses were 0 CR, 8 (16%) PRs, 21 (41%) SDs, and 17 (33%) PDs; response was not evaluable or not assessed for 5 (10%) pts. DCR was 57%. The median TTP was 4 (95% CI, 3-8) mo. The median PFS was 4 (95% CI, 2-6) mo, and median OS was 17 (95% CI, 8-NA) mo. PFS rate at 18 mo was 16%, and OS rate at 18 mo was 46%. Treatment-related AEs (TRAEs) occurred in 27 (53%) pts; the most common TRAEs were diarrhea, fatigue, hypothyroidism, and myalgia. Grade ≥3 TRAEs occurred in 7 (14%) pts. TRAEs led to treatment discontinuation in 6% of pts. Immune-mediated AEs and infusion reactions occurred in 11 (22%) pts. One treatment-related death occurred due to myocarditis, with associated immune-related hepatitis. **Conclusions:** In pts with advanced HCC and no prior systemic therapy, pembro monotherapy provided durable anti-tumor activity, promising overall survival, and demonstrated a safety profile consistent with that previously observed for pembro in advanced HCC. These findings support further evaluation of pembro-based regimens for the treatment of HCC in the frontline setting. Clinical trial information: NCT02702414. Research Sponsor: Funding for this research was provided by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

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Post hoc analysis in patients (pts) with unresectable hepatocellular carcinoma (uHCC) who progressed to Child-Pugh B (CPB) liver function in the phase III REFLECT study of lenvatinib (LEN). *First Author: Jasmine Huynh, University of California Davis Comprehensive Cancer Center, Sacramento, CA*

Background: The treatment landscape for pts with uHCC has recently expanded. However, there is an unmet need for effective treatment options in CPB pts. LEN is approved first-line in uHCC based on the REFLECT study (Child-Pugh A [CPA] pts were allowed, per inclusion criteria). In a prior analysis of REFLECT, pts treated with LEN benefited irrespective of baseline liver function (ALBI grade 1 or 2; Child-Pugh score 5 or 6). To determine outcomes in pts with reduced liver function, we report a post hoc analysis of key efficacy and safety results in LEN-treated pts from REFLECT who progressed to CPB and those who did not within the first 8 weeks of treatment. **Methods:** In REFLECT, pts with uHCC were randomized 1:1 to LEN (per bodyweight: 12 mg/day for ≥60 kg; 8 mg/day for < 60 kg) or sorafenib (400 mg twice daily) in 28-day cycles. This analysis assessed ORR. Landmark analyses (starting at week 8) of PFS, time-to-progression (TTP), and OS in CPB pts and in pts who remained CPA at 8 weeks post-randomization were also conducted. Tumors were assessed by mRECIST by independent imaging review. Safety was also assessed from baseline. **Results:** This subgroup analysis included LEN-treated pts (n = 60) who progressed to CPB within the first 8 weeks of treatment (CPB pts) and 413 pts who did not (CPA pts). At baseline, 26.7% and 73.1% of pts had an ALBI grade of 1 and 73.3% and 26.9% of pts had an ALBI grade of 2 in CPB and CPA pts, respectively. ORR was 28.3% (95% CI 16.9–39.7) for CPB pts and 42.9% (95% CI 38.1–47.6) for CPA pts. A landmark analysis showed a median PFS of 3.7 mos (95% CI 1.8–7.4) for CPB pts and 6.5 mos (95% CI 5.6–7.4) for CPA pts from the week 8 timepoint. Landmark analyses at week 8 also showed that the median TTP was 5.6 mos (95% CI 3.5–9.3) for CPB pts and 7.3 mos (95% CI 5.6–7.4) for CPA pts; the median OS was 6.8 mos (95% CI 2.6–10.3) for CPB pts and 13.3 mos (95% CI 11.6–16.1) for CPA pts per week 8 landmark analyses. As expected, efficacy appeared to be greater in CPA pts versus CPB pts; however, OS of 6.8 months in CPB pts after the week 8 landmark is notable. Moreover, median duration of treatment was 3.2 mos for CPB pts and 6.9 mos for CPA pts, thereby suggesting CPB pts can remain on LEN. The incidence of grade ≥3 treatment-related AEs (TRAEs) was 71.7% in CPB pts and 54.7% in CPA pts. TRAEs leading to discontinuation occurred in 18.3% of CPB pts and 7.5% of CPA pts. **Conclusions:** In this post hoc analysis of pts in REFLECT, we examine the key efficacy and safety results for LEN-treated pts who progressed to CPB by week 8. This post hoc analysis is limited by its descriptive nature; however, the results indicate that further study of LEN in CPB pts with uHCC is warranted. Clinical trial information: NCT01761266. Research Sponsor: Eisai Inc., Woodcliff Lake, NJ, USA, and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

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Zanidatamab (ZW25) in HER2-positive biliary tract cancers (BTCs): Results from a phase I study. *First Author: Funda Meric-Bernstam, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Treatment options are limited for patients with unresectable, locally advanced or metastatic BTCs progressing after first line treatment. Standard second line chemotherapy yields objective response rates (ORR) of < 10% and median overall survival of these patients is < 6 months. Human epidermal growth factor receptor 2 *(HER2)* overexpression/ amplification is observed in 5–19% of BTCs. Zanidatamab is a bispecific HER2-targeted antibody that has demonstrated durable single agent activity with good tolerability in a range of HER2-overexpressing cancers. **Methods:** In the expansion cohort of this phase I study (NCT02892123), the primary objective is to characterize safety and tolerability of zanidatamab and secondary objectives include evaluation of anti-tumor activity. This cohort includes BTC patients with centrally confirmed HER2 overexpression (immunohistochemistry [IHC] 3+ or IHC 2+/ fluorescence *in situ* hybridization [FISH]+), disease progression after standard of care therapy, and measurable disease per RECIST 1.1. Zanidatamab is administered at the previously identified recommended dose of 20 mg/kg every 2 weeks (Q2W). Tumors are assessed every 8 weeks (response confirmed at ≥ 4 weeks). **Results:** As of the data cutoff date (Jul 28, 2020), 20 patients (median age: 63 years [range, 42–78]) with BTC (11 gallbladder cancers, 5 intra- and 4 extra-hepatic cholangiocarcinomas) have been treated with zanidatamab. The median number of prior systemic therapies was 2.5 (range, 1–8), including five patients who had received prior HER2-targeted therapy (trastuzumab). Fourteen (70%) patients experienced zanidatamab-related adverse events (AEs), all of which were grade 1 or 2 in severity. The most common (occurring in ≥ 20%) zanidatamab-related AEs were diarrhea (n = 9) and infusion-related reactions (n = 6). A single treatment-related serious AE of grade 2 fatigue was reported in one patient. Among patients evaluable for response (n = 17), the confirmed ORR was 47% (n = 8; 95% confidence interval [CI]: 23, 72), the disease control rate was 65% (n = 11; 95% CI: 38, 86) and the median duration of response was 6.6 months (95% CI: 3.2, not estimable). **Conclusions:** Zanidatamab is well tolerated with promising and durable anti-tumor activity in patients with HER2 overexpressing BTC. Based on these data, zanidatamab is now being evaluated in an ongoing global Phase 2b study in patients with advanced HER2+ BTC that have progressed after treatment with a gemcitabine-containing regimen (NCT04466891). Clinical trial information: NCT02892123. Research Sponsor: Zymeworks Inc.

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Use of yttrium-90 (Y90) glass microspheres (TheraSphere) as neoadjuvant to transplantation/resection in hepatocellular carcinoma: Analyses from the LEGACY study. *First Author: Robert Lewandowski, Northwestern University Feinberg School of Medicine, Chicago, IL*

Background: The objective of the LEGACY study was to assess the Objective Response Rate (ORR) and Duration of Response (DoR) following treatment with Yttrium-90 (Y90) glass microspheres in patients with unresectable solitary hepatocellular carcinoma (HCC). The objective of the analyses presented here are to evaluate ORR, DoR, and Overall Survival (OS) by transplant/resection status and to compare these outcomes with patients who did not go on to transplantation/resection after receiving treatment with Y90. **Methods:** LEGACY is a single-arm, multicenter, retrospective study of patients with unresectable HCC who received treatment with Y90 glass microspheres (TheraSphere) at one of three sites in the United States. LEGACY included all consecutive eligible patients who received treatment between January 2014 and December 2017 and met the eligibility criteria (Child-Pugh A; ECOG score of 0 or 1; BCLC A or C; and a solitary tumor > 2 and ≤8 cm). Primary efficacy endpoints included ORR and DoR. ORR included patients who achieved either a complete response or partial response based on localized mRECIST; response was assessed via blinded, independent, central review. Secondary endpoints include OS and number and type of subsequent treatments, including transplantation and resection. **Results:** Among all 162 patients enrolled in LEGACY, ORR was 72.2% (117/162; 95% CI = 64.9%, 78.5%); the majority of patients experienced DoR ≥ 6 months (89/117, 76.1%, 95% CI = 67.6%, 82.9%). Median follow-up time for all 162 patients enrolled in LEGACY was 29.9 months by reverse Kaplan-Meier analysis; 3-year OS was 86.6%. For 45/162 (27.8%) of patients, Y90 treatment served as neoadjuvant therapy; 34 went on to transplantation (21.0%) and 11 (6.8%) went on to resection. For neoadjuvant treatment, ORR was 80.0% (36/45, 95% CI = 66.2, 89.1), DoR ≥ 6 months was 30.6% (11/45, 95% CI = 18.0, 46.9), and 3-year OS was 92.8% (95% CI = 74.2, 98.2). Of these 45 patients, 35 patients achieved complete response (CR), 1 achieved partial response (PR), and 9/45 (20.0%) were deemed not evaluable as they underwent surgery prior to the 6-month mark and did not have imaging assessments post-Day 46. These nine patients were censored, lowering the DoR; however, histopathology revealed that 7/9 (77.8%) achieved complete pathologic necrosis, 1/9 (11.1%) had extensive pathologic necrosis, and 1 (11.1%) had partial pathologic necrosis. For the 117/162 (72.2%) patients who did not go on to surgical treatment, ORR was 91.5% (107/117, 95% CI = 85.0, 95.3), DoR ≥ 6 months was 72.9% (78/117, 95% CI = 63.8, 80.4), and 3-year OS was 83.5% (95% CI = 72.2, 90.5). **Conclusions:** Treatment of solitary unresectable HCC with Y90 glass microspheres provides strong ORR, DoR, and OS both as neoadjuvant therapy to transplantation/resection and as treatment in non-surgical candidates. Research Sponsor: Boston Scientific Corporation.

301 Poster Session

Analysis of early tumor shrinkage and depth of response in patients with advanced biliary tract cancer treated with gemcitabine plus cisplatin or gemcitabine plus S-1: An exploratory analysis of JCOG1113. *First Author: Naohiro Okano, Kyorin University Faculty of Medicine, Tokyo, Japan*

Background: JCOG1113 is a randomized phase III trial to confirm the non-inferiority of gemcitabine (GEM) plus S-1 (GS) compared with GEM plus cisplatin (GC) regarding overall survival (OS) in patients with advanced biliary tract cancer (BTC). Although the non-inferiority of GS to GC was demonstrated, the difference in the nature of tumor shrinkage effects between GC and GS is not clear. Early tumor shrinkage (ETS) and depth of response (DpR) are considered as on-treatment markers that reflect the anti-tumor effect to chemotherapy and have been reported to be associated with survival in metastatic colorectal cancer. However, there are few studies assessing ETS or DpR in advanced BTC. Therefore, we evaluated the association between ETS, DpR, and clinical outcomes in JCOG1113. **Methods:** We conducted an exploratory analysis of JCOG1113, which included chemotherapy-naïve patients with recurrent or unresectable BTC. ETS was defined as tumor reduction in the sum of the longest diameters of the target lesions at week 6 when compared with that at baseline. DpR was defined as the maximum tumor shrinkage observed until 12 weeks from enrollment. Survival curves were estimated using the Kaplan–Meier method. Progression-free survival (PFS) and OS for ETS and DpR were estimated from week 6 and 12 (landmarks) after enrollment, respectively. Multivariable analyses for PFS and OS, adjusted for baseline factors, were performed using a stratified Cox regression model. **Results:** Of the 354 registered patients in JCOG1113, 277 patients in the ETS group and 230 patients in the DpR group were included in this study. Seventy-seven patients (27.8%) achieved ETS ≥ 20% (ETS high group) and 52 patients (22.6%) achieved DpR ≥ 40% (DpR high group). The proportion of ETS high group (GC, 25.4%; GS, 30.4%) and DpR high group (GC, 21.2%; GS, 24.1%) was similar between the arms. The patient characteristics of ETS high group were not different between GC and GS. The hazard ratio (HR) of the ETS high group compared with the ETS low group for PFS and OS was 0.76 (95% confidence interval [CI] 0.58–1.00) and 0.80 (95% CI 0.60–1.07), respectively. The impact of ETS was higher in GC (HR 0.64, 95% CI 0.43–0.95) than GS (HR 0.88, 95% CI 0.60–1.28) in PFS. The HR of DpR high group compared with DpR low group for PFS and OS was 0.75 (95% CI 0.55–1.03) and 0.79 (95% CI 0.57–1.09), respectively. The impact of DpR was higher in GC (HR 0.63, 95% CI 0.40–0.998) than GS (HR 0.88, 95% CI 0.57–1.37) in PFS. ETS and DpR were significantly associated with both PFS and OS in the multivariable analyses. **Conclusions:** ETS and DpR may be useful as on-treatment markers associated with PFS and OS in patients with advanced BTC, especially in those treated with GC. Clinical trial information: UMIN000010667. Research Sponsor: the National Cancer Center Research and Development Funds, and Japan Agency for Medical Research and Development.

302 Poster Session

Advances in the treatment of cholangiocarcinoma: Effect of online education on clinician knowledge and confidence. *First Author: Geoff Roy Fisher, Medscape Global Education, New York, NY*

Background: This study determined whether online continuing medical education could improve the knowledge and confidence of cliniciansonthe latest developments in the treatment of cholangiocarcinoma (CCA). **Methods:** A 30-minute online video panel discussion was launched for countries outside the USA in March 2020. Data was collected to June 2020. Educational effect assessed with repeated-pairs pre-/post-activity, where individual participants served as their own control. Three multiple-choice, knowledge questions and one self-efficacy, five-point Likert scale confidence question were analyzed. Chi-squared test assessed pre- to post-activity change (5% significance level, $P < .05$). Magnitude of change in total number of correct responses overall, and for each question, were determined with Cramer's V (<.06=Modest, 0.06-0.15=Noticeable, .16-.26=Considerable, >.26=Extensive). **Results:** 85 oncologists (oncs) and 44 gastroenterologists (gastros) completed pre- and post-activity questions. A considerable educational effect was observed for both oncs (V=.174, P<.0001) and gastros (V=.246, p<.0001) with average % of correct responses increasing from 62 to78% and 47 to 71%, respectively. Clinicians with 3/3 answers correct increased post-activity (11 to 48% for oncs, 28 to 51%, for gastros). Improvements in % of correct responses post-activity were seen for questions on the molecular target for pemigatinib, the subtype of CCA where IDH mutations are detectable, and the need for comprehensive molecular testing at diagnosis of metastatic CCA (relative improvements: 31%, 38%, and 11% for oncs; 155%, 50% and 14%, for gastros). 78% of oncologists' and 72% of gastros' responses were improved or reinforced post-activity. 21% of all participants stated they would modify treatment plans. Confidence in incorporating routine broad molecular testing in the treatment of CCA improved post-activity with a total average confidence shift of 25% for oncs and 32% for gastros. **Conclusions:** This on-demand, online video panel discussion resulted in a considerable education effect. Online medical education is valuable in improving knowledge and confidence, as well as identifying areas of continued educational need. Research Sponsor: Incyte.

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Effect of *FGFR2* alterations on survival in patients receiving systemic chemotherapy for intrahepatic cholangiocarcinoma. *First Author: Ghassan K. Abou-Alfa, Memorial Sloan Kettering Cancer Center & Weill Medical College at Cornell University, New York, NY*

Background: Most patients (pts) with cholangiocarcinoma (CCA) are diagnosed with advanced disease and are ineligible for surgery. *FGFR2* fusions/rearrangements are oncogenic drivers and are present almost exclusively in pts with intrahepatic CCA (iCCA; 10–16% of pts); however, little is known about the effects of *FGFR2* status on response to systemic chemotherapy. Memorial Sloan Kettering (MSK) obtains genomic sequencing data from almost all iCCA pts treated at the institution. This provides a unique, rich database from which genomic profiling data can be overlaid with clinical data to facilitate a meaningful understanding of pt outcomes, and to suggest potential therapeutic options. This retrospective analysis evaluated progression free survival (PFS) and overall survival (OS) in pts receiving standard systemic chemotherapy (CXT) for iCCA harboring *FGFR2* fusions/rearrangements (*FGFR2* $^{+}$), or harboring wild-type *FGFR2* (*FGFR2*^{wt}). **Methods:** Clinical and genomic data were obtained from the MSK database for all iCCA pts to determine disease history and exposure to prior lines (PL) of CXT in the advanced setting. Only pts with complete data for PL of CXT were analyzed. Median PFS and OS were calculated using the Kaplan-Meier method. OS was calculated from diagnosis until death; PFS was calculated from first dose of first line of CXT until progression, death, last visit, relevant dates of later CXT lines; pts with unconfirmed outcomes were censored at last known follow-up date. **Results:** One-hundred-thirty-two pts were included in this analysis (median age at diagnosis: 62.0 y; 54.5% female; *FGFR2*$^{+}$, n = 15; *FGFR2*^{wt}, n = 115; other *FGFR2* alterations, n = 2). Among pts receiving first-line CXT, median PFS was 7.1 months (95% CI: 5.0–8.3) for all pts (n = 124), 6.2 months (2.0–16.8) for *FGFR2*$^{+}$ pts (n = 15), and 7.2 months (5.0–8.3) for *FGFR2*^{wt} pts (n = 107). Among pts with ≥2 PL of CXT (n = 90), median PFS on second-line chemotherapy was 5.6 months (95% CI: 2.8–10.3) for *FGFR2*$^{+}$ pts, and 3.7 months (2.6–5.6) for *FGFR2*^{wt} pts. Median OS was numerically longer in *FGFR2*$^{+}$ pts compared with *FGFR2*^{wt} pts (31.3 months [95% CI: 5.8–not estimable] vs 21.8 months [16.7–26.6]). **Conclusions:** Among pts receiving standard systemic chemotherapy for iCCA, median PFS was similar in pts harboring *FGFR2*$^{+}$ vs *FGFR2*^{wt} receiving first-line chemotherapy, and relatively longer in pts harboring *FGFR2*$^{+}$ receiving second-line chemotherapy. Median OS was longer in *FGFR2*$^{+}$ vs *FGFR2*^{wt} pts. Compared with recently published data in molecularly unselected CCA pts (Lowery. *Cancer*. 2019; 125: 4426), PFS was similar in pts receiving first-line chemotherapy, and slightly longer for second-line chemotherapy. Data interpretation is limited by the retrospective nature of this analysis of investigator-reported data, the study size, and by the possibility that the analysis population may not reflect the general population of pts with CCA. Research Sponsor: Incyte Corporation.

304 Poster Session

Early tumor marker decrease to predict the efficacy of combination therapy with lenvatinib plus anti-PD-1 antibodies in unresectable hepatocellular carcinoma (uHCC). *First Author: Hui-Chuan Sun, Liver Cancer Institute and Zhongshan Hospital, Fudan University, Shanghai, China*

Background: Combination therapy with anti-angiogenic agents plus anti-PD-1 antibodies has shown high anti-tumor activity in uHCC. However, predicting the efficacy of this combination therapy remains a challenge. **Methods:** This study included consecutive patients with uHCC who received lenvatinib (8 mg/d regardless of body weight) and an anti-PD-1 antibody as first-line systemic therapy between Sep 2018 and July 2020, and had at least one imaging evaluation. Tumor response was assessed every 2 months (± 2 week) by the investigators using modified RECIST criteria. Patients were evaluated as having a radiological response (complete or partial response) or non-radiological response (stable disease or progressive disease) at the best overall response evaluation. Serum tumor markers for HCC, including alpha-fetoprotein (AFP) and protein induced by vitamin K absence or antagonist-II (PIVKA-II), were evaluated at baseline and 2-3 weeks after therapy was initiated and their association with radiological response were assessed. Patients with baseline AFP or PIVKA-II between the upper limit of normal and the maximum measuring range of the kit were evaluable for AFP decrease or PIVKA-II decrease. **Results:** A total of 76 patients were eligible for this study. Baseline AFP ≥400 ng/mL or PIVKA-II ≥400 mAU/mL was not associated with radiological response (P = 0.167 and P = 0.916, respectively). At 2-3 weeks after the initiation of therapy, 51 patients were evaluable for AFP decrease; 78.4% experienced a > 20% AFP decrease and 51.0% experienced a > 50% AFP decrease. Patients with a > 50% AFP decrease had a higher rate of radiological response than those with AFP increase or a ≤50% AFP decrease (73.1% vs 32.0%, P = 0.003). In 57 patients evaluable for PIVKA-II decrease, 50.9% and 35.1% experienced a > 20% and > 50% PIVKA-II decrease, respectively. Patients with a > 50% PIVKA-II decrease had a higher rate of radiological response than those with PIVKA-II increase or a ≤50% PIVKA-II decrease (85.0% vs 29.7%, P < 0.001). Both AFP decrease > 50% and PIVKA-II decrease > 50% predicted radiological response, with an area under receiver operating characteristic curve of 0.706 (95% CI, 0.560-0.852, P = 0.012) and 0.752 (95% CI, 0.621-0.883, P = 0.001), respectively. Furthermore, patients with a > 20% AFP or PIVKA-II increase from baseline had a lower rate of radiological response (0% vs 57.4%, P = 0.043; and 21.7% vs 69.7%, P < 0.001, respectively). **Conclusions:** A tumor marker decrease was seen in most patients as early as 2-3 weeks after the initiation of the combination therapy. Early on-treatment AFP or PIVKA-II decrease may serve as a predictor for objective response for patients with uHCC receiving combination anti-angiogenic and immune therapy. Research Sponsor: None.

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Phase II study of modulation of sorafenib (SOR)-induced autophagy using hydroxychloroquine (HCQ) in advanced hepatocellular cancer (HCC): Planned interim efficacy and safety analysis. *First Author: Sukeshi Patel Arora, Mays Cancer Center, University of Texas Health San Antonio, San Antonio, TX*

Background: SOR is the first systemic therapy approved for advanced HCC, but has shown only modest improvements in survival. Resistance to SOR in pre-clinical models has been attributed to autophagy induction. Autophagy inhibition with HCQ enhanced SOR-induced cell death and apoptosis in early pre-clinic and clinical studies. Data from the phase I study of SOR plus HCQ in advanced solid tumors at showed clinical safety and efficacy. Therefore, we conducted a prospective study to evaluate efficacy of SOR and HCQ in advanced HCC patients (pts) (NCT03037437) and report planned interim analysis for our first-line cohort. **Methods:** Prospective phase II study of SOR 400 mg po BID + HCQ 400 mg daily in pts with advanced HCC (CP A-B8 cirrhosis). Cohort 1: first-line SOR/HCQ. Cohort 2: add HCQ upon progressing on SOR. CP B pts started at 200 mg BID, with dose escalation as tolerated. Cycle = 4 weeks. Primary endpoint: mTTP. Secondary endpoints: mOS, response by RECIST; AEs (NCI-CTCAEv3.0); PD analysis for markers of autophagy and immunity. Pts evaluable for efficacy if completed C1. Planned interim efficacy and safety analysis approved by DSMB is reported here. **Results:** For cohort 1, n = 19. Median age 63.5 (51-80). 80% Male; 65% Hispanics. ECOG 0-1: 100%. CP B cirrhosis: 32%. Etiology of cirrhosis: HCV 84%, ETOH 26%, NASH 5%. BCLC B 21%, C 70%. AFP > 400: 47%, PVT: 32%, metastases: 64%, post-transplant: 21%. Reason off study: PD (n = 10), toxicity (n = 2), lost to f/u (n = 1), withdrew (n = 1). N = 16 completed C1, n = 2 remain on study. mTTP is 4.2 months (95% CI: 3.7-NA). mOS 13.8 months (95% CI: 13.8-NA). Response Rate (CR+PR): 25%. Best response: CR n = 1 (6%), PR n = 3 (19%), SD n = 7 (44%). 4+ cycles: n = 9 (56%). % alive. Median duration of response 7.6 months (3.67-20). Gr 1/2 AEs as expected from SOR. Gr 3: AST elevated (n = 1), diarrhea (n = 1) due to SOR. Gr 2 rash (n = 1) due to HCQ. No Gr 4/5. Dose reduction: 70% for SOR, 0% for HCQ. PD analysis on the 3 responders show favorable immune profile changes (increase in cytotoxic T cells and decrease T Regs). **Conclusions:** SOR/HCQ had a better response rate (25%) than historically SOR alone (2%) in pts with advanced HCC, predominantly BCLC C, with CP A and B cirrhosis. While immune checkpoint inhibitors (ICIs) are taking the forefront in advanced HCC, SOR/HCQ may have a role in patients with CP B cirrhosis, transplant or contraindications to ICIs. Further, analysis of predictive markers of response is ongoing. Clinical trial information: NCT03037437. Research Sponsor: U.S. National Institutes of Health.

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Penpulimab (Anti-PD-1) combined with anlotinib as first-line therapy for unresectable hepatocellular carcinoma (uHCC): Updated results from a phase Ib/II study. *First Author: Shun Chang Jiao, Department of Oncology, Chinese PLA General Hospital, Beijing, China*

Background: Combined therapy of an immune checkpoint inhibitor with a targeted antiangiogenic agent had been proved to be effective for the treatment of uHCC. Penpulimab was engineered to eliminate Fcγ$R binding and ADCC/ADCP completely, where ADCC/ADCP effects could induce T-cell apoptosis and clearance and then compromise anti-tumor activity. Penpulimab demonstrated a slower PD-1 antigen binding off-rate, which resulted in better cellular activity and higher receptor occupancy. Penpulimab also showed numerous contacts with N58 glycosylation on the BC loop of PD-1 which could be an advantage to facilitate interaction of PD-1 antibody and might contribute to slower binding off-rate. These structural differentiations offer more robust biological effect and enhance anti-tumor activity of penpulimab. Anlotinib is a multi-targeted tyrosine kinase inhibitor selective for VEGF receptors 1/2/3, FGF receptors 1-4, PDGF receptors α and β, and c-kit. **Methods:** In this open-label, multicenter phase Ib/II study, patients (pts) without prior systemic treatment, and classified as BCLC stage B (not amenable for locoregional therapy) or C, Child-Pugh $\leq$7, and ECOG PS $\leq$ 1 received Penpulimab (200mg IV Q3W) and Anotinib (8 mg PO 2weeks on/1 week off). Primary endpoint was ORR (RECIST v1.1); secondary endpoints were safety, DCR, DoR, TTP, PFS and OS. **Results:** 31 pts (median age 56 years [23–74], ECOG 0/1 [64%/36%], BCLC B/C [23%/77%], HBV/HCV [61%/7%]) received combined therapy. As of August 31, 2020, median follow-up time was 11.9 mons (range 3.7-17.7). Median PFS was 7.6 mons with 6-mons PFS rate was 57.6% while median TTP was 8.5 mons with 6-mons TTP rate was 62.7%. Median overall survival had not been met and 6-mons OS rate was 93.2%. The ORR was 31.0% (9/29) and DCR was 82.8% (24/29). At data cutoff, 77.8% of responders remained ongoing and still on treatment. Treatment-related adverse events (TRAEs) occurred in 90.3% of pts ($\geq$G3 in 16.1% [5/31], no G5, treatment discontinuation in 9.7% [3/31]). Most common TRAEs ($\geq$15%) were increased AST (38.7%) and ALT (35.5%), increased blood bilirubin (22.6%) , asthenia (22.6%) , decreased platelet count (19.4%) and rash (16.1%). **Conclusions:** Penpulimab plus Anlotinib showed favorable antitumor efficacy and an acceptable safety profile in pts with uHCC. The further randomized, phase 3 study of Penpulimab in combination with Anlotinib at a higher dose (10 mg PO 2 weeks on/1 week off) in this setting is ongoing (NCT04344158). Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology.

307 Poster Session

Phase II study of anlotinib plus sintlimab as second-line treatment for patients with advanced biliary tract cancers. *First Author: Hong Zong, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China*

Background: Gemcitabine combined with cisplatin (GP) has been established as the standard first-line treatment in patients with unresectable biliary tract cancers (BTC), a heterogeneous group of rare and aggressive malignancies arising from the epithelium of the biliary duct system. Nevertheless, there has been no approved standard of care for second-line treatment. In this study, we explored the efficacy and safety of the combination of anlotinib and sintlimab as a novel second-line regimen in BTC. **Methods:** In this phase II trial, patients with advanced BCT, who experienced progression after first-line chemotherapy, received anlotinib (12 mg, PO, D1-14, Q3W) combined with sintlimab (200 mg, iv, D1, Q3W) until disease progression or unacceptable toxicity. The primary endpoint was OS, and the secondary endpoints included ORR, PFS, DCR, and safety. The exploratory endpoint was the correlation of clinical outcomes with biomarkers. **Results:** From Aug 2019 to Sep 2020, 17 patients were enrolled. 9(52.9%) were men, and the median age was 59(43-69) years. Nine patients were diagnosed with ICC, 2 with ECC, and 6 with GBC. 15 patients were assessable for response. At a median follow-up of 8.76 months (95%CI: 3.60-13.94 months), the primary endpoint OS has not been reached, the median PFS was 6.50 months (95%CI: 3.60-9.40 months). ORR was 40.00%, and DCR was 86.67%. The incidence of treatment-related adverse events (TRAEs) was 70.60%, and the most common grade 1-2 AEs were hypertension (70.60%), diarrhea (17.65%), and hypothyroidism (17.65%). **Conclusions:** Anlotinib plus sintlimab demonstrates significant clinical activity and acceptable toxicity in patients with advanced BTC who failed first-line chemotherapy. Clinical trial information: ChiCTR1900022003. Research Sponsor: None.

308 Poster Session

Real-world outcomes of patients with intrahepatic cholangiocarcinoma treated with trans-arterial radioembolization: Results from the CIRSE Registry for SIR-Spheres Therapy (CIRT), a large European prospective multi-center observational study. *First Author: Thomas Helmberger, Department of Radiology, Neuroradiology and Minimal-Invasive Therapy, Klinikum Bogenhausen, Munich, Germany*

Background: Trans-arterial radioembolization (TARE) is a treatment option for patients with intrahepatic cholangiocarcinoma (ICC). The CIRSE Registry for SIR-Spheres Therapy (CIRT) is the first European prospective multi-centre observational study designed to evaluate the clinical outcomes of patients treated with TARE with SIR-Spheres Y90 resin microspheres for ICC in the multi-institutional real-life clinical setting. The study was conducted by the Cardiovascular and Interventional Radiological Society of Europe (CIRSE). **Methods:** Patients were enrolled prospectively between Jan 2015 and 31 Dec 2017. Eligible patients were adults treated with TARE with Y90 resin microspheres for ICC. Data on baseline characteristics and treatment intention/clinical context and dosimetry were collected, as well as follow-up data (every 3 months; for 24 months after treatment), including overall survival (OS), (hepatic) progression-free survival [(h) PFS], safety and Global Health Status (GHS, using the *European Organisation for the Research and Treatment of Cancer* QLQ-C30). **Results:** 120 patients were included from 18 sites in 8 European countries. Median age was 63 years (range: 29-86) and 54.2% were male. Median tumour to liver percentage was 12.8%. Median prescribed activity was 1.32 GBq for whole liver treatments (n = 49), 1.20 GBq for right lobe treatments (n = 56) and 0.82 GBq for left lobe treatments (n = 51). 97.5% of the delivered activity was within 90% of the prescribed activity. TARE treatment as a first line (L1) global strategy was applied in 39.1%, 27.4% as second line (after systemic therapy). Treatment intention was predominantly palliative (69.2%) or tumour shrinkage (20.8%). Median OS was 14.7 months (95% confidence interval (CI) 10.9 – 17.9). Median PFS was 5.7 months (95% CI 3.9 – 7.5), whereas hPFS was 6.2 months (95% CI 4.1 – 8.5). Mean GHS was 59.3 at baseline, 61.0 after 3 months, 56.0 at 6 months, 54.4 at 9 months and 63.0 after 1 year. Severe adverse events (grade 3 and 4) were found in 13 (10.8%) patients: (abdominal pain 3.3%, fatigue 1.7%, gastrointestinal ulceration 0.8%, gastritis 0.8%, radiation cholecystitis 0.8%, radiation-induced liver disease 1.7%, other 5.8%). Detailed subgroup analyses are currently being performed. Updated data describing OS, PFS and hPFS for L1 TARE vs TARE after systemic chemotherapy, as well as prognostic factors for OS, PFS and hPFS will be shown. **Conclusions:** The results from this large prospective multi-centre observational study shows that in the real-world context, TARE is applied early and successfully in the treatment pathway. TARE is shown to be an effective and safe treatment with no meaningful deterioration of quality of life. Clinical trial information: NCT02305459. Research Sponsor: Sirtex Medical Europe.

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Phase I study of the novel pro-drug MIV-818 in patients with hepatocellular carcinoma, intra-hepatic cholangiocarcinoma or liver metastases. *First Author: T.R. Jeffry Evans, University of Glasgow, Beatson West of Scotland Cancer Center, Glasgow, United Kingdom*

Background: MIV-818 is an orally administered troxacitabine (TRX)-based nucleotide prodrug. It is highly metabolized by human hepatocytes, directing high levels of the chain-terminating nucleotide tri-phosphate to the liver, while minimizing exposure to other organs. The tri-phosphate is incorporated into DNA during replication, which leads to DNA double strand breaks, DNA damage responses, and cytotoxicity. **Methods:** Patients (pts), ≥18 years, ECOG performance status < 1, adequate organ function, with treatment-refractory hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (iCCA) or liver metastases (LM) from solid tumors were enrolled. In phase Ia, MIV-818 monotherapy was administered in an intra-patient dose-escalation design with doses of 3-70mg for 3-5 days in cycles of 21 days. Phase Ib is an inter-patient dose escalation in a 3+3 cohort design and is currently ongoing. Treatment is given until disease progression or unacceptable toxicity. The primary objective is to assess safety and tolerability and, for phase Ia, also to establish the starting dose for phase Ib. Key secondary objective was to evaluate the overall response rate based on RECIST v1.1. The pharmacokinetics of MIV-818 and its metabolites were evaluated, and on-treatment liver biopsies were collected to assess the pharmacokinetics and the pharmacodynamic effects of MIV-818. **Results:** Nine patients (7M; 2F), ECOG performance status 0 (n=3) or 1 (n=6), median age = 57 years (range: 50-84) with HCC (2 pts), iCCA (1) or LM (6) from solid tumors (mainly GI tract), previously treated with median 2 (1-5) lines of therapy, were included in phase Ia. Patients were dosed up to 60 mg 5 days/week. The most common treatment related AEs were those in the hematological system: neutropenia grade (gr) 1-4, neutropenic sepsis gr 4; thrombocytopenia gr 1-2, anemia gr 1-2. Elevated bilirubin gr 1-3 and liver enzymes gr 3 were also reported. Most of the AEs were reversible. Five pts discontinued due to AE and 4 pts discontinued due to progressive disease outside the liver after 2-4 cycles. Starting dose of phase Ib was determined to be 40mg 5 days/week. Tumor biopsies showed evidence of selective DNA damage in tumor tissue, including in hypoxic regions, with minimal or no impact of MIV-818 observed in healthy liver tissue. **Conclusions:** MIV-818 had an acceptable safety and tolerability profile. Biomarker data of liver biopsies demonstrated a selective effect of MIV-818 on cancer cells. Updated safety and efficacy data from phase Ib will be presented at the meeting. (NCT03781934). Clinical trial information: 2018-000995-14. Research Sponsor: Medivir AB, Sweden.

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Evaluation of neratinib (N), pembrolizumab (P), everolimus (E), and nivolumab (V) in patients (pts) with fibrolamellar carcinoma (FLC). *First Author: Ghassan K. Abou-Alfa, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: FLC, a rare liver cancer of young adults, has no effective systemic therapies. Surgical resection is used extensively with non-curative intent. FLC is associated with a *DNAJB1-PRKACA* chimeric transcript that produces a fusion protein with retained kinase activity and increased expression of several oncogenic signaling pathways including, but not limited to, *HER2* (*ERBB2*). **Methods:** N (240 mg oral daily) was studied in FLC pts in the SUMMIT study (NCT01953926); and later under compassionate use for N-based combinations (combo): P (2 mg/kg q3w), E (7.5 mg daily), and V (240 mg q2w) in doublet or triplet regimens. Eligible pts: ≥12y; histologically confirmed FLC; adequate organ function; any number of prior therapies. Primary endpoint: objective response rate (ORR; RECIST v1.1). Secondary endpoints: duration of response; clinical benefit rate (CBR); safety (CTCAE v4.0); somatic and germline sequencing (MSK IMPACT). **Results:** As of 03-Sep-2020, 15 pretreated pts received N in SUMMIT (confirmed ORR 0%; CBR 13%). Efficacy data for 5 pts from SUMMIT and 2 more pts receiving combo under compassionate use (4 male, 3 female, median age 26 years, median 0 [range 0–4] prior systemic therapies) are in shown in the table. The most common adverse events (AE) with single-agent N (n = 5) were diarrhea (grade 1 80%; grade 2 20%) and nausea (grade 1 60%); other AEs were grade ≤1 in ≤20% of pts. **Conclusions:** N monotherapy had limited benefit as a single agent in FLC pts. Several case studies evaluating N-based combo with checkpoint inhibitors administered under compassionate use demonstrated that NP led to 1 PR, and the triplet of NPE to prolonged SD. These are case-limited observations but are critical and worth evaluating further in upcoming clinical trials given the continued lack of a standard of care therapy for pts with FLC. Clinical trial information: NCT01953926. Research Sponsor: Puma Biotechnology Inc.

Patient sequential number	Somatic IMPACT Germline IMPACT	Combo received	Response (DOR, months) N	Response (DOR, months) Combo	Current status
1	TERT non-coding mutation, *DNAJB1-PRKACA* deletion Germline negative	NV	SD (6)	PD (3)	Alive, off combo; receiving GO
2	N/A[1]	NP NPE	PD (2)	SD (9) SD (10)	Alive, off combo; receiving GO
3	TERT inversion, *DNAJB1-PRKACA* fusion	NE	SD (4)	SD (6)	Alive, off combo; unknown current treatment
	Germline negative	NPE		PD (3)	
4[2]	N/A[1]	NP	PD (2)	SD (3)	Alive, off combo; receiving G
5	*TERT* non-coding mutation, *DNAJB1-PRKACA* fusion, *HIST1H3I* mis-, *IRS1* exon 1 mis-, *PIK3R3* exon 7 mis-, *SF3B1* exon 19 mis- Germline BLM pathogenic variant	NP	SD (4)	PR (6)	Alive, on treatment
6	*DNAJB1-PRKACA* fusion Germline negative	NPE[3]	N/A	SD (4)	Alive, on treatment; allergy to E, pending sunitinib
7	N/A[1]	NP	N/A	PD (2)	Alive, on treatment; pending E

[1]Not done or results not available; [2]Pt stopped from treatment due P-related AE; [3]Not evaluable; E stopped due to AE.
DOR, duration of response; G, gemcitabine; mis-, missense; O, oxaliplatin; PD, progressive disease; PR, partial response; SD, stable disease.

311 Poster Session

A phase I/II study of safety and efficacy of the arginase inhibitor INCB001158 plus chemotherapy in patients (Pts) with advanced biliary tract cancers. *First Author: Milind M. Javle, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Arginase, secreted in the tumor microenvironment by myeloid suppressor cells, is a major regulator of arginine-mediated immune response. Arginase inhibition by INCB001158 increases arginine, which reverses the immunosuppressive effects of neutrophils and myeloid-derived suppressor cells on T cells. The current standard first-line (1L) treatment for advanced biliary tract cancers (BTC) is gemcitabine/cisplatin chemotherapy. The combination of INCB001158 immunotherapy and standard 1L treatment may provide additional clinical benefit in pts with advanced or metastatic BTC. **Methods:** This open-label phase 1/2 study evaluated the safety, tolerability, and antitumor activity of INCB001158 in pts with advanced or metastatic solid tumors. In phase I, dose escalation of INCB001158 (50, 75, and 100 mg twice daily [BID]) was used to determine the recommended phase II dose (RP2D) of INCB001158 + gemcitabine/cisplatin. Phase II used a Simon 2-stage design and evaluated objective response rate (ORR; RECIST v1.1), duration of response (DOR), disease control rate (DCR), and progression-free survival (PFS) of INCB001158 RP2D + gemcitabine (1000 mg/m^2)/cisplatin (25 mg/m^2 Days 1 and 8 of 21-day cycle). Here we report preliminary safety and activity from the cohort of pts with BTC. **Results:** The phase I dose-escalation group identified a RP2D for INCB001158 of 100 mg BID. At a data cutoff of July 1, 2020, 33 pts with BTC in phase II treated with INCB001158 100 mg BID + gemcitabine/cisplatin were evaluable. Adverse events (AEs) related to INCB001158 and/or chemotherapy occurred in 88% of pts and 73% of pts had AEs related specifically to INCB001158 (Table). Treatment was interrupted due to INCB001158-related TEAEs in 30% of pts (n=10); discontinuation related to INCB001158 occurred in 3% (n=1). Treatment did not result in immune-related or significant additive chemotherapy-associated toxicity. ORR was 24% (8/33; 95% CI, 11.1–42.3) based on confirmed response per investigator's assessment; stable disease occurred in 42% of pts. Median DOR (95% CI) was 5.8 (4.1–not reached) mo, and the DCR was 67%. Median PFS (95% CI) was 8.5 (5.7–10.1) mo. **Conclusions:** Preliminary data suggest the combination of INCB001158 100 mg BID + gemcitabine/cisplatin was tolerable and did not result in significant added toxicity. Response rates and PFS suggest that some pts with BTC may benefit from this combination. Clinical trial information: NCT03314935. Research Sponsor: Incyte Corporation.

Phase 2 most common treatment emergent AEs (>25%) in the BTC cohort (n=33).

Preferred Term, n (%)	Any Grade	Grade ≥3	Related to INCB001158	Related to Gemcitabine/Cisplatin
Fatigue	16 (49)	3 (9)	11 (33)	10 (30)
Anemia	15 (46)	7 (21)	3 (9)	13 (39)
Nausea	13 (39)	2 (6)	4 (12)	8 (24)
Neutrophil count decreased	11 (33)	10 (30)	3 (9)	11 (33)
Constipation	10 (30)	0	1 (3)	1 (3)
Platelet count decreased	10 (30)	3 (9)	2 (6)	10 (30)
Vomiting	10 (30)	4 (12)	1 (3)	6 (18)
Pyrexia	9 (27)	1 (3)	0	3 (9)

312 Poster Session

Silmitasertib (CX-4945) in combination with gemcitabine and cisplatin as first-line treatment for patients with locally advanced or metastatic cholangiocarcinoma: A phase Ib/II study. *First Author: Mitesh J. Borad, Mayo Clinic, Scottsdale, AZ*

Background: Silmitasertib (CX-4945), an oral small molecule inhibitor of casein kinase 2 (CK2), has exhibited preclinical antitumor activity and strong synergism with gemcitabine + cisplatin. We investigated the safety and efficacy of silmitasertib in combination with gemcitabine + cisplatin in patients with unresectable cholangiocarcinoma (CCA). **Methods:** S4-13-001 is a multicenter, open-label, phase Ib/II study of silmitasertib in combination with gemcitabine + cisplatin in patients with locally advanced or metastatic CCA. The phase Ib portion included dose-escalation, expansion, and exploratory cohorts of silmitasertib with doses ranging from 200 to 1000 mg bid (6 days for the escalation/expansion cohorts and 10 and 21 days' continuous dosing for the exploratory cohorts). In the phase II portion patients received silmitasertib 1000 mg bid for 10 days in combination with gemcitabine + cisplatin on days 1 & 8 over a 21-day cycle. In this interim analysis, we present findings from the combined population of patients from the phase Ib and II portions of the study. Response to treatment was assessed by RECIST v1.1 every 6 weeks. Primary efficacy outcome measure was progression-free survival (PFS). ClinicalTrials.gov (NCT02128282). **Results:** A total of 87 patients were enrolled and received silmitasertib in the phase Ib (n=50) and phase II (n=37) portions of the study. Of these, 55 patients were evaluable for efficacy with details as follows: median PFS 11.1 (95% CI 7.6–14.7) months; median overall survival (OS) 17.4 (95% CI 13.4–25.7) months; overall response rate (ORR) 32.1%; and disease control rate (DCR) 79.3%. Almost all patients (79/87; 90.8%) evaluable for safety reported ≥1 treatment-related adverse event (TEAE). The most common TEAEs (all grades) with silmitasertib were diarrhea (65.5%), nausea (50.6%), vomiting (33.3%), fatigue (31.0%), and anemia (21.8%). The most common grade ≥3 TEAEs were diarrhea (13.8%), neutropenia (11.5%), nausea (9.2%), anemia (8.0%), and thrombocytopenia (8.0%). Eleven patients (12.6%) discontinued treatment due to TEAEs. **Conclusions:** Silmitasertib in combination with gemcitabine + cisplatin yields promising preliminary evidence of efficacy in patients with locally advanced or metastatic CCA. Based on these data a randomized phase III trial is planned. Clinical trial information: NCT02128282. Research Sponsor: Senhwa Biosciences Corporation.

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Exposure-response (E-R) efficacy and safety (E-S) analyses of tremelimumab as monotherapy or in combination with durvalumab in patients (pts) with unresectable hepatocellular carcinoma (uHCC). *First Author: Xuyang Song, AstraZeneca, Gaithersburg, MD*

Background: In a phase II study in uHCC (Study 22, NCT02519348), a novel, priming combination regimen of tremelimumab (T; anti-CTLA-4) and durvalumab (D; anti-PD-L1) (T300+D) has shown favorable clinical activity vs each agent as monotherapy or vs another combination (T75+D). The analyses presented here assess the pharmacokinetics (PK) and relationships between tremelimumab exposure, as monotherapy or in combination, and safety, efficacy, and pharmacodynamics (PD) in this study. **Methods:** Overall, 216 pts were included in these analyses (T, n=65; T300+D, n=72; T75+D, n=79). Safety, antitumor activity, PK, PD, and immunogenicity were analyzed using standard pharmacometrics methods. A previously developed population PK model for T across solid tumors was validated using T monotherapy and combination therapy data from Study 22, including a post-hoc covariate analysis to assess the impact of covariates on individual PK parameters. Population PK and PD models related individual T exposures to safety parameters, PD, and efficacy (overall survival, OS; progression-free survival, PFS; and objective response rate, ORR). The E-R relationships for time-to-event variables OS and PFS were explored by Kaplan-Meier estimates and analyzed by Cox proportional-hazards models (CPHM). **Results:** For T monotherapy and T+D combinations, no significant E-S relationships were observed for grade 3/4 treatment-related adverse events (TRAEs), grade 3/4 TRAEs of special interest, and AEs leading to treatment discontinuation. Analyses of each quartile of T exposure suggest pts with higher exposure (3^{rd} and 4^{th} quartile) may have longer OS vs lower quartiles. The CPHManalysis showed that after accounting for prognostic factors (baseline albumin and neutrophil-to-lymphocyte ratio), neither AUC nor C_{min} appeared to be a significant factor for OS hazard. There was no significant relationship between response and ORR, PFS and any T PK exposure metric in T-treated pts. Saturable relationships (described by E_{max}) were observed for maximum change from baseline for proliferating T-cell counts as functions of exposure. **Conclusions:** The observed PK data are generally consistent with predictions based on a historical population PK model, suggesting the PK of T in uHCC pts is consistent with pts with other solid tumors. No significant relationships were observed between E-S and E-R; therefore, PK is not a significant predictor to evaluate for T efficacy or safety. Considering the small sample size limitation, still the saturable relationships observed in proliferating T-cells appear to support a dose of T300. Future studies of pooled data from Study 22 and the larger phase III HIMALAYA study (NCT03298451) will be conducted to further the characterization of E-R relationships and the development of the T300+D regimen. Clinical trial information: NCT02519348. Research Sponsor: AstraZeneca.

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Preliminary results of the phase II ALTER-HOO3 trial: Anlotinib plus toripalimab as a first-line treatment for patients with unresectable hepatocellular carcinoma. *First Author: Haifeng Lin, The Second Affiliated Hospital of Hainan Medical University, Haikou, China*

Background: Hepatocellular carcinoma (HCC) is particularly prevalent in China because of the high prevalence of chronic hepatitis B infection. In the last decade, sorafenib was the first molecular target drug approved for the treatment of advanced liver cancer. Until recently, the combination of angiogenic inhibitor with anti-PD-1 /L1 monoclonal antibody has represented significant efficacy over sorafenib monotherapy in the first-line regimen of unresectable HCC. Nevertheless, there are still unmet needs in clinical practice due to limited choice of drugs. Anlotinib is a novel oral multi-targeted tyrosine kinase inhibitor that targets VEGF receptors 1/2/3, FGF receptors 1-4, PDGF receptors α and β, and c-kit, and has been approved for standard treatment of non-small cell lung cancer, small cell lung cancer and soft tissue sarcoma in China. Toripalimab, a humanized IgG4 mAb against PD-1, is the first Chinese-produced PD-1 inhibitor marketed, which has been approved as a second-line treatment for metastasis melanoma. This study aims to evaluate the efficacy and safety of anlotinib plus toripalimab as the first-line treatment for unresectable HCC. **Methods:** This was a single-arm, multicenter, phase II trial. 30 patients with unresectable HCC, Child-Pugh $\leq$7 and ECOG PS $<$2 will be enrolled if they had not been treated with prior treatment. Pts received anlotinib (12 mg, p.o., qd, d1-14, q3w) and toripalimab (240 mg, iv, d1, q3w) until disease progression or unacceptable toxicity. The primary endpoint was objective response rate (ORR) assessed by investigator according to mRECIST and irRECIST. Secondary endpoints included progression-free survival (PFS), overall survival (OS), disease control rate (DCR), duration of response (DoR) and safety. **Results:** By the cutoff date of September 21, 2020, 11 pts were enrolled and of those 8 pts were evaluable. 9 pts (81.8%) experienced treatment related adverse events (TRAEs) and grade 3 TRAEs occurred in 5 pts (45.5%). No grade 4 or above TRAEs occurred. The most common TRAEs were decreased appetite (n =6, 54.5%) and fatigue (n =5, 45.5%).Among 8 evaluable pts, unconfirmed ORR was 25% (95% CI 0.032-0.651) with 1 unconfirmed CR and 1 unconfirmed PR, and DCR was 87.5% (95% CI 0.473-0.997) according to mRECIST. **Conclusions:** Anlotinib in combination with toripalimab showed tolerant toxicity and preliminary anti-tumor efficacy in first-line regimen for uHCC patients. Furthermore, it is needed to be proved in update results and large scale studies. Clinical trial information: ChiCTR1900028295. Research Sponsor: None.

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Safety profile of immune checkpoint inhibitors versus sorafenib as first-line treatment in advanced hepatocellular carcinoma: A meta-analysis of randomized controlled trials. *First Author: Alessandro Rizzo, Department of Experimental, Diagnostic, and Specialty Medicine–DIMES, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy*

Background: Systemic treatment with tyrosine kinase inhibitors such as sorafenib represents the mainstay of advanced-stage hepatocellular carcinoma (HCC). However, survival outcomes remain disappointing, mostly because of the onset of acquired resistance and a suboptimal safety profile, which frequently requires treatment modifications and early discontinuation of treatment – thus, interfering with compliance and long-term outcomes of patients. With immune checkpoint inhibitors (ICIs) quickly expanding as a novel therapeutic option in advanced HCC, the toxicity profiles of these agents should be kept in mind. We performed a meta-analysis with the aim to compare all-grade (G) adverse drug events (ADEs) of ICIs (alone or in combination with other anticancer agents) versus sorafenib monotherapy across randomized controlled trials (RCTs) of first-line treatment for advanced HCC. **Methods:** Eligible studies included RCTs comparing ICIs versus sorafenib as first-line treatment in HCC. Safety profile from each selected study was investigated for all-G most common ADEs. Outcomes of interest were as follows: pruritus, diarrhea, hand-foot skin reaction (HFSR), fatigue, aspartate aminotransferase (AST) increase, rash, hypertension and decreased appetite. Results were compared by calculating odds ratios (ORs) with 95% confidence intervals (CIs); ORs were combined with Mantel-Haenszel method. All statistical analyses were performed using R studio software. **Results:** Two RCTs (CheckMate 459, IMbrave 150) involving 1,228 patients were included in the analysis. Patients treated with ICIs showed higher risk of pruritus (OR 1.99, 95% CI = 1.22-3.24) while sorafenib treatment was associated with higher risk of diarrhea (OR 0.26, 95% CI = 0.18-0.37) and HFSR (OR 0.01, 95% CI = 0-0.04). Conversely, no statistically significant differences were observed in terms of fatigue (OR 0.84, 95% CI = 0.45-1.58), AST increase (OR 1.21, 95% CI = 0.78-1.88), rash (OR 0.71, 95% CI = 0.46-1.11), hypertension (OR 0.28, 95% CI = 0.01-9.76) and decreased appetite (OR 0.41, 95% CI = 0.14-1.21) between the two groups. **Conclusions:** Although the substantial heterogeneities affecting our analyses, ICIs appear feasible in advanced HCC, being endowed with an acceptable safety profile. Beyond activity and efficacy, careful consideration should be given to toxicity while choosing the appropriate first-line treatment in advanced HCC. Research Sponsor: None.

316 Poster Session

The use of cabozantinib in advanced hepatocellular carcinoma (HCC): Hong Kong multi-center experience. *First Author: Yawen Dong, University of Hong Kong, Wien, Austria*

Background: In the phase III CELESTIAL trial, cabozantinib showed significant improvement in overall survival with good tolerability in advanced HCC population. We aimed to evaluate the efficacy, survival and tolerability of cabozatinib in advanced hepatocellular carcinoma (HCC) patients in a real life setting. **Methods:** Between February 2018 and October 2019, consecutive advanced HCC patients who received cabozatinib alone or in combination at University of Hong Kong Health System hospitals were analysed. Cabozantinib was administered at 60 mg continuously daily. Objective response rate (ORR), time-to-progression (TTP), overall survival (OS), and tolerability were evaluated. **Results:** Overall, 22 patients were included. The median age was 57.1 years (range 48.5-58.6). All patients except one were hepatitis B carriers. More than 80% of the patients had underlying Child-Pugh A cirrhosis. Most patients had metastatic disease (95.5%). More than 70% of patients received cabozantinib beyond second-line, and most of the patients had prior exposure to tyrosine kinase inhibitor (TKI) and/or immunotherapy. The median time from the start of first-line systemic treatment to the start of cabozantinib was 11.2 months. Cabozantinib was administered to 11 patients (50%) as single agent, while the other half received cabozantinib in combination with mostly immune checkpoint inhibitors. The median follow-up was 7.6 months. The table below shows the ORR. The overall median TTP and OS were 4.2 and 8.90 months, respectively. Interestingly, among those who received single agent cabozantinib, the median OS was 5.36 months in contrast to 12.32 months in the patients received combination. Overall, 90.9% of patients experienced treatment related adverse events (TRAEs) with transient liver function occurred in nearly 50% patients. Nevertheless, Grade 3/4 TRAEs was only 12%. **Conclusions:** Our present study showed that the use of cabozatinib in advanced HCC patients had good anti-tumour activity and survival benefits with acceptable toxicity profile. Research Sponsor: Ipsen education grant.

	Overall (n=22)	Single-agent (n=11)	Combination (n=11)
Complete response	0 (0%)	0 (0%)	0 (0%)
Partial response	1 (4.5%)	1 (9.1)	0 (0%)
Stable disease	7 (31.8%)	2 (18.2%)	5 (45.5%)
Progressive disease	11 (50.0%)	5 (45.5%)	6 (54.5%)
Not evaluable	3 (13.6%)	3 (27.3%)	0 (0%)

317 Poster Session

Transition of molecular target agent therapy in advanced hepatocellular carcinoma: A multicenter, retrospective study. *First Author: Kazufumi Kobayashi, Department of Gastroenterology, Graduate School of Medicine, Chiba University, Chiba, Japan*

Background: There have been considerable advances in systemic chemotherapy for hepatocellular carcinoma (HCC) in recent times. Currently, four molecular target agents (MTA) are available for HCC treatment in Japan. Sequential therapy using multiple MTAs is being considered as the gold standard of treatment. However, the effectiveness of the treatment strategy transition for HCC remains unclear. The present study aimed to clarify the current practical use of MTAs and its effectiveness in HCC treatment. **Methods:** In this multicenter, retrospective study, we collected and analyzed the clinical data of 877 patients who underwent MTA therapy for HCC from June 2009 to March 2019 at several institutes in Japan. The patients were classified into 3 groups as per the period of initial MTA treatment beginning (period 1: 2009–2012, n = 267; period 2: 2013–2016, n = 352; period 3: 2017–2019, n = 258). These 3 periods were defined to have approximately same term. Period 3 means the era of multiple MTAs because of the approval of regorafenib in Japan in 2017. We assessed the patient characteristics, MTA use, and prognosis of the 3 groups. **Results:** The proportion of patients with advanced-stage HCC, defined according to the Barcelona Clinic Liver Cancer staging system, in each period was 70.1%, 66.5%, and 62.0% in period 1, 2, and 3, respectively. MTA use for intermediate stages increased with the passage of time (p = 0.052). The proportion of multiple MTAs use was remarkably increased in the 3 groups (1.1%, 10.2%, and 42.6%, respectively, $p < 0.0001$). Child-Pugh score, proportion of macrovascular invasion, extrahepatic metastasis, and α-fetoprotein (AFP) ≥400 ng/mL showed no significant difference among the 3 groups. The median overall survival was 11.9 months for the entire cohort and 10.4, 11.3, and 15.2 months, for period 1, 2, and 3, respectively. It is noteworthy that the prognosis of patients with HCC improved over time (p = 0.016). With respect to progression-free survival, the median value was 3.0 months for the entire cohort and 2.7, 2.8, and 4.7 months for period 1, 2, and 3, respectively ($p < 0.0001$). The treatment duration was also prolonged with time (2.7, 3.2, and 6.6 months for period 1, 2, and 3, respectively; $p < 0.0001$). Multivariate analysis using Cox proportional hazard model showed that HCV infection, Child-Pugh score, performance status, α-fetoprotein ≥400 ng/mL, presence of macrovascular invasion, and period 3 for initial MTA introduction were independent prognostic factors. **Conclusions:** Sequential therapy with multiple MTAs has gained popularity with time and is considered to improve patient prognosis. The development of MTA therapy for HCC is expected to continue. Therefore, further studies are needed to help determine the appropriate drugs, the sequence of MTA use, and the precise transition time. Research Sponsor: None.

318 Poster Session

Landmark analysis of overall survival (OS) by objective response (OR) in previously treated patients (pts) with advanced hepatocellular carcinoma (aHCC): Post-hoc analysis of the randomized, phase III KEYNOTE-240 study. *First Author: Julien Edeline, Centre Eugène Marquis, Rennes, France*

Background: Studies have shown that OR is prognostic of OS in pts with HCC. KEYNOTE (KN)-224 (NCT02702414) evaluated pembrolizumab (pembro; anti-PD-1) in sorafenib (sora)-treated pts with aHCC and demonstrated an OR rate of 17% that was durable in responders receiving pembro, ultimately leading to its FDA approval. In KN-224, a landmark analysis showed that OR in pembro-treated pts was prognostic of longer OS. The KN-240 (NCT02702401) study evaluated pembro + best supportive care (BSC) vs placebo (pbo) + BSC in sora-treated pts with aHCC. Although clinical benefit was observed in KN-240 with pembro vs pbo, prespecified statistical significance criteria for OS and PFS were not met. This post hoc analysis of KN-240 was performed to determine whether OR at landmark is prognostic of longer survival after landmark time. **Methods:** Eligible pts were aged ≥18 y, had confirmed aHCC, and experienced progression during or after sora treatment or intolerance to sora. Landmark analyses of OS according to OR at 6, 12, and 18 wk after randomization were performed on the pembro arm to examine the association between survival after the landmark with response achieved prior to the landmark. OR was assessed by blinded independent central review per RECIST v1.1. Responders at each landmark were defined as pts with any response assessment of CR or PR before the landmark date; all other pts were defined as nonresponders. HRs and 95% CIs for survival after the landmark were calculated from the Cox proportional model with Efron's method of tie handling with responder status as a single covariate. Analyses were performed in the ITT population. **Results:** As of Jan 2, 2019, the median time from randomization to data cutoff was 21.2 months (range 13.4-30.4) for pembro. There were 51 pts (18.3%) with a BOR of CR or PR in the pembro arm and 6 pts (4.4%) with a BOR of PR (no CR) in the pbo arm (excluded from landmark analyses). OS after landmark time was longer for responders compared with nonresponders at the wk 6, 12, and 18 time points (Table). The HR for OS after landmark time for responders versus nonresponders were 0.37 (95% CI 0.18-0.75), 0.39 (95% CI 0.23-0.66), and 0.37 (95% CI 0.21-0.63) at wk 6, 12, and 18, respectively. **Conclusions:** This post hoc analysis demonstrates that pts with sora-treated aHCC who achieve OR by landmark time with pembro have longer OS after the landmark time, confirming the prognostic association between OR with pembro and OS observed in KN-224. Clinical trial information: NCT02702401. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Response status to pembro	n	Median OS, months (95% CI)	Responder vs nonresponder HR (95% CI)
Responder at wk 6	21	Not reached (NR) (18.2-NR)	0.37 (0.18-0.75)
Nonresponder at wk 6	248	12.1 (9.9-14.1)	
Responder at wk 12	37	20.4 (16.3-NR)	0.39 (0.23-0.66)
Nonresponder at wk 12	218	10.8 (8.5-12.9)	
Responder at wk 18	41	NR (15.4-NR)	0.37 (0.21-0.63)
Nonresponder at wk 18	191	10.8 (9.0-13.1)	

319 Poster Session

Results from the phase I dose-escalation study of the radiation enhancer NBTXR3 for the treatment of HCC and liver metastases. *First Author: Thierry De Baere, Institut Gustave Roussy, Villejuif, France*

Background: NBTXR3, a first-in-class radioenhancer composed of functionalized hafnium oxide nanoparticles, is administered by one time intratumoral injection (ITI) and activated by radiotherapy (RT), such as stereotactic body RT (SBRT). NBTXR3 increases RT energy deposit inside tumor cells and subsequently increases tumor cell death compared to RT alone, while sparing healthy tissues. SBRT is well-tolerated in hepatocellular carcinoma (HCC) or liver metastases (mets) and a valuable alternative for patients not eligible for surgery or radiofrequency ablation. However, energy dose deposit to tumor cells is limited due to potential toxicity to surrounding healthy tissues. Patients with unresectable liver cancers including patients with liver or renal dysfunction might benefit from NBTXR3. A Phase 1 clinical trial was conducted to evaluate the safety and Recommended Phase 2 Dose (RP2D) of NBTXR3 activated by SBRT [NCT02721056] in these patients, here we report the results. **Methods:** A 3+3 dose escalation scheme tested 5 NBTXR3 levels: 10, 15, 22, 33, and 42% of baseline tumor volume. NBTXR3 ITI was followed by SBRT (45 Gy / 3 fractions / 5-7 days or 50 Gy / 5 fractions / up to 15 days) in patients with HCC or liver mets. Primary endpoints included RP2D determination and early DLT incidence. Secondary endpoints include safety profile, liver disease scores evolution, and early efficacy by response rate (mRECIST for HCC/RECIST 1.1 for liver mets). **Results:** 23 patients were treated: 6 patients at 10% (2 SBRT doses tested due to organ constraints), 4 patients each at 15% and 22% (due to fiducial displacement and ITI shift), 3 patients at 33% and 6 patients at 42%. No early DLT was observed at any dose level. 1 SAE (grade 3 late onset bile duct stenosis) related to NBTXR3 and RT occurred at 22%. There were 11 AEs related to NBTXR3 and/or ITI, of which grade 3 AEs were: 2 abdominal pain (ITI related; 15%) and 1 late onset bile duct stenosis (22%), lesion close to the bile duct. No NBTXR3 or ITI related grade 4-5 AEs were observed. RT related AEs were as expected with SBRT. No clinically meaningful changes in Child-Pugh score or APRI were observed post-treatment. CT-scan showed NBTXR3 present within the tumor without leakage to surrounding healthy tissues. Best observed responses (MRI) in injected target lesions from HCC patients (n = 15) were 5 CRs (33.3%), 5 PRs(33.3%), 1 SD (6.7%), 2 NE (13.3%), 2 patients did not have post baseline MRI and for liver mets (n = 8) were 5 PRs (62.5%), 2 SD (25.0%) and 1 NE (12.5%). **Conclusions:** No early DLTs were observed and NBTXR3 demonstrated a good safety and tolerability profile. The RP2D was determined to be 42% of tumor volume. Initial efficacy is promising and highlights the potential for NBTXR3 to address an unmet medical need in patients with unresectable primary or metastatic liver cancers. Clinical trial information: NCT02721056. Research Sponsor: Nanobiotix.

320 Poster Session

Targeting *HER2* (*ERBB2*) mutation-positive advanced biliary tract cancers with neratinib: Results from the phase II SUMMIT 'basket' trial. *First Author: James J. Harding, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Genomic profiling studies have reported somatic *HER2* mutations in ~2–5% of biliary tract cancers (BTC). Clinical data from the SUMMIT study demonstrate that neratinib, a pan-HER irreversible tyrosine kinase inhibitor, has encouraging clinical activity in multiple types of *HER2*-mutant solid tumor malignancies. **Methods:** SUMMIT is a multi-histology, open-label, phase II 'basket' study of neratinib in patients with somatic *HER2* mutations (ClinicalTrials.gov NCT01953926). Patients with activating somatic HER2 mutations with different histologies, including BTC, received neratinib monotherapy (240 mg oral daily). Loperamide prophylaxis was mandatory during cycle 1. Efficacy endpoints: objective response rate (ORR, RECIST v1.1); clinical benefit rate (CBR); duration of response; progression-free survival (PFS). Adverse events (AEs) were assessed by CTCAE v4.0. Genomic profiling from fresh/archival tumor tissues and/or plasma cfDNA was performed retrospectively by next-generation sequencing (MSK-IMPACT). **Results:** As of 3-Sep-2020, 25 patients with *HER2*-mutant BTC were enrolled: gallbladder (40%); intrahepatic (24%); extrahepatic (20%); ampulla of Vater (16%). 68% of patients received ≥2 systemic regimens (96% received prior gemcitabine-based regimens). The S310F/Y variant accounted for nearly half of *HER2* mutations (n=11). Other *HER2* mutations: V777L (n=5); L755S (n=2); V842I (n=2); R678Q (n=2). Confirmed ORR in 25 evaluable patients was 12% (95% CI 3–31%) and CBR was 20% (95% CI 7–41%), including 3 confirmed PRs and 2 patients with SD for ≥16 weeks. Tumor shrinkage was observed in multiple *HER2*-activating mutations and enriched in gallbladder and extrahepatic subtypes of BTC. Median PFS was 2.8 (95% CI 1.1–3.7) months; median overall survival (OS) was 5.4 (95% CI 3.7–11.7) months. Nine (36%) patients (3 of whom with ECOG PS 2) came off study within 28 (range 6–47) days of treatment due to clinical deterioration (unrelated to study drug) followed by death. The most common treatment-related AEs (any grade) were diarrhea (56%) and vomiting (48%). Diarrhea was the most common Grade 3 event (24%); 4 patients (16%) required a neratinib dose reduction; no patients discontinued treatment due to diarrhea. **Conclusions:** Neratinib is safe and tolerable in patients with advanced BTC patients and somatic *HER2* mutations. The antitumor activity of neratinib appears comparable to current standards of care, with similar PFS and OS in heavily pretreated patients. Analysis of co-occurring oncogenic mutations and response is ongoing, and consideration is being given to neratinib-based combination regimens to further improve outcomes in this setting. Clinical trial information: NCT01953926. Research Sponsor: Puma Biotechnology Inc.

321 Poster Session

Lenvatinib plus pembrolizumab for patients with previously treated biliary tract cancers in the multicohort phase II LEAP-005 study. *First Author: Luis Villanueva, Fundación Arturo López Pérez, Providencia, Santiago, Chile*

Background: Second-line treatment options for patients with biliary tract cancers (BTC) are limited. Lenvatinib, an anti-angiogenic multikinase inhibitor, in combination with the programmed death-1 immune checkpoint inhibitor pembrolizumab, has demonstrated promising antitumor activity with a manageable safety profile in patients with select advanced solid tumors. LEAP-005 (NCT03797326) is evaluating the efficacy and safety of lenvatinib plus pembrolizumab in patients with previously treated advanced solid tumors; here we present results from the BTC cohort of LEAP-005. **Methods:** In this nonrandomized, open-label, phase II study, eligible patients were aged ≥18 years with histologically or cytologically documented advanced (metastatic and/or unresectable) BTC with disease progression after 1 prior line of therapy, measurable disease per RECIST v1.1, ECOG PS of 0–1, and tissue sample evaluable for PD-L1 expression. Patients received lenvatinib 20 mg once daily plus pembrolizumab 200 mg Q3W for up to 35 cycles (approximately 2 years) or until confirmed disease progression, unacceptable toxicity, or withdrawal of consent. Treatment with lenvatinib could continue beyond 2 years in patients experiencing clinical benefit. Primary endpoints were ORR (per RECIST v1.1 by blinded independent central review) and safety. Secondary endpoints were the disease control rate (DCR; comprising CR, PR, and SD), duration of response (DOR), PFS, and OS. Tumor imaging was performed Q9W from treatment initiation for 54 weeks, then Q12W to week 102, and Q24W thereafter. **Results:** 31 patients were enrolled in the BTC cohort (ECOG PS 1, 55%; 84% ex-US). As of April 10, 2020, median time from first dose to data cutoff (DCO) was 9.5 months (range, 3.1–11.9), with 16 patients on treatment at DCO. There were 3 (10%) PRs and 18 (58%) SDs. ORR was 10% (95% CI, 2–26), and DCR was 68% (95% CI, 49–83). Median DOR was 5.3 months (range, 2.1+ to 6.2). Median PFS was 6.1 months (95% CI, 2.1–6.4). Median OS was 8.6 months (95% CI, 5.6 to NR). Treatment-related AEs occurred in 30 patients (97%), including 15 (48%) who had grade 3–4 AEs; there were no treatment-related deaths. 2 (6%) discontinued treatment due to treatment-related AEs (myocarditis, pyrexia; n = 1 each). The most frequent treatment-related AEs were hypertension (42%), dysphonia (39%), diarrhea (32%), fatigue (32%), and nausea (32%). 14 patients (45%) had immune-mediated AEs and 1 patient (3%) had an infusion-related reaction. **Conclusions:** Lenvatinib plus pembrolizumab demonstrated encouraging efficacy and manageable toxicity in patients with advanced BTC who had received 1 line of prior therapy. Based on these data, enrollment in the BTC cohort has been expanded to 100 patients. Clinical trial information: NCT03797326. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

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Second-line chemotherapy (2L) in elderly patients with advanced biliary tract cancer (ABC): A multicenter real-world study. *First Author: Alessandro Rizzo, Department of Experimental, Diagnostic, and Specialty Medicine–DIMES, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy*

Background: The ABC-06 trial recently established the role of 2L in ABC progressing after platinum/gemcitabine combination. However, older patients are often under-represented in clinical trials and no data are currently available regarding 2L in elderly ABC. The aim of this real-world study was to explore the treatment pattern, safety and efficacy of 2L in ABC patients aged ≥ 70 years old and to compare their outcomes with younger subjects. **Methods:** Institutional registries across three academic medical centers were retrospectively reviewed and data of interest retrieved to identify ABC who had received 2L from October 2002 to July 2020. Patients older than 70 years were considered as elderly individuals. The Kaplan-Meier methods was used to estimate survival and the log-rank test to make comparison. The impact of variables on survival was assessed through univariate and multivariate analysis. **Results:** A total of 190 ABC patients treated with 2L were identified and included in the analysis. Among them, 27.3% (n = 52) were aged ≥ 70 years (range 70-87y), of whom 25 patients had iCCA (48%), 13 GBC (25%) and 15 eCCA (27%). 56% (n = 29) were female and 38 (73%) patients had an ECOG-PS 0-1. The most frequently administered 2L regimens were capecitabine monotherapy (n = 14, 27%), single-agent gemcitabine (n = 9, 17%) and gemcitabine/capecitabine combination (n = 9, 17%). No differences in terms of prior surgery (p = 0.64) and 2L treatment intensity (p = 0.34) were observed compared to patients aged < 70 years. The disease control rate of 2L was 28.8% and 29.7% in elderly and youngers, respectively. No statistically significant differences in both mOS (5.7 months in elderly vs 6.1 months in youngers, HR 0.97; p = 0.86) and mPFS (4.7 vs 4.8 months, HR 0.88; p = 0.44) were recorded. Regarding the safety profile of 2L, grade 3 or 4 treatment-related toxicities occurred more frequently in the older group (48.5% versus 8.2%; OR 6.31; p < 0.001). When looking at prognostic factors, absolute lymphocyte count < 1000/mmc (p < 0.001) and albumin level < 3 g/dL (p < 0.001) were independently associated with worse prognosis. **Conclusions:** The results of this real-world study, limited by its retrospective nature and small sample size, suggest that for patients aged ≥ 70 years, 2L could be equally effective as for youngers, with survival outcomes aligned to those from ABC-06 trial. Notably, based on the higher incidence of grade 3-4 adverse events, the delivery of 2L should be carefully evaluated and monitored in this patient subset. Research Sponsor: None.

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Results of a phase Ib study of regorafenib (REG) 80 mg/day plus pembrolizumab (PEMBRO) for first-line treatment of advanced hepatocellular carcinoma (HCC). *First Author: Richard D. Kim, H. Lee Moffitt Cancer Center, Tampa, FL*

Background: In a phase Ib study, REG 120 mg/day plus PEMBRO for first-line treatment of advanced HCC showed no unexpected safety signals and encouraging anti-tumor activity. At the maximum tolerated dose (MTD) of REG (120 mg/day), approximately three-quarters of patients (pts) had a REG dose reduction or interruption due to a treatment-emergent adverse event (TEAE). Here, we present preliminary data for the REG 80 mg/day cohort. **Methods:** This is an ongoing, dose-finding study in pts who had no prior systemic therapy. In the first cohort, pts received REG 120 mg/day orally for 3 weeks on/1 week off plus PEMBRO 200 mg intravenously q 3 weeks. In later cohorts, the REG dose could be escalated (160 mg/day) or reduced (80 mg/day); the PEMBRO dose is fixed. The primary objective is safety and tolerability. Secondary objectives are to define the MTD and recommended phase II dose and assess anti-tumor activity. **Results:** By July 24, 2020, 16 pts were treated with REG 80 mg/day. Median age was 67 years (range 56–79), 25%/75% were Barcelona Clinic Liver Cancer stage B/C, 100% Child–Pugh A, and 69%/31% had Eastern Cooperative Oncology Group performance status 0/1. Grade (Gr) 3 TEAEs occurred in 8/16 pts (50%) and there were no Gr 4 TEAEs (Table); one pt experienced Gr 5 pneumonitis (not drug related). There were no reports of Gr 3 hand–foot skin reaction or Gr 3 maculopapular rash, and one report (6%) of Gr 3 rash. TEAEs led to a REG dose reduction or interruption in 50% of pts and to a PEMBRO dose interruption in 25% of pts. Median treatment duration (range) including pts ongoing was 4.1 months (0.4–7.1) for REG and 3.8 months (0.03–7.2) for PEMBRO. Of 13 evaluable pts, 2 (15%) had a partial response and 9 (69%) had stable disease (Response Evaluation Criteria in Solid Tumors v1.1); disease control rate was 85%. **Conclusions:** These preliminary results for the combination of REG 80 mg/day plus PEMBRO for first-line treatment of advanced HCC were consistent with the REG 120 mg/day cohort. The combination showed no unexpected safety signals and encouraging anti-tumor activity. Assessment of REG 80 mg/day plus PEMBRO is ongoing. Clinical trial information: NCT03347292. Research Sponsor: Bayer.

	REG 80 mg/day plus PEMBRO (N=16)		
TEAE, n (%)	**Regardless of relation to study drug**	**REG related**	**PEMBRO related**
Any grade	13 (81)	12 (75)	8 (50)
Grade 3/4/5	8 (50)/0/1 (6)	6 (38)/0/0	3 (19)/0/0
Serious	7 (44)	3 (19)	0
Leading to REG/PEMBRO dose modification*	8 (50)/4 (25)	4 (25)/3 (19)	1 (6)/1 (6)
Leading to REG/PEMBRO discontinuation	2 (13)/2 (13)	0/1 (6)	0/0

*Modification: Reductions or interruptions of REG; interruptions of PEMBRO.

Medical Dictionary for Regulatory Activities v23.0; Common Terminology Criteria for Adverse Events v4.03 grade.

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Modeling sequential systemic therapy for unresectable hepatocellular carcinoma in the era of immunotherapy: What comes next? *First Author: Ciro Celsa, University of Palermo, Palermo, Italy*

Background: Atezolizumab plus Bevacizumab represents the new best performing first-line approach for unresectable hepatocellular carcinoma (u-HCC). However, the best sequential strategy after every first-line failure (for progression or intolerance) remains elusive, and options for retreating patients failing Atezolizumab plus Bevacizumab with multi-kinase inhibitors (MKI) or immune checkpoint inhibitor (ICI) are yet undefined. **Methods:** We developed a Markov model to analyze simulated-Overall Survival (s-OS) of second-line ICIs or MKIs after first-line Atezolizumab plus Bevacizumab over a lifetime horizon. For first-line therapy, PFS of Atezolizumab plus Bevacizumab was extracted from Imbrave 150 trial and it was used as endpoint since it is not influenced by post-progression survival. For second-line retreatment, pooled OS of MKIs (Regorafenib and Cabozantinib), or ICIs (Nivolumab and Pembrolizumab) were adopted. Survival estimates for sequential settings considered the proportion of patients who did not receive second-line therapy due to death during first-line therapy. Individual patient survival data were extracted from PFS and OS Kaplan-Meier curves of RESORCE trial for Regorafenib, CELESTIAL trial for Cabozantinib, CheckMate-040 for Nivolumab and Keynote-240 for Pembrolizumab. Each reconstructed survival curve was inspected for accuracy and was compared with originally published curves. **Results:** First-line Atezolizumab plus Bevacizumab followed by second-line ICIs turned on from the model as the best sequential strategy (median s-OS 24 months; 95% Confidence Interval (CI) 23-26 months) and extends survival when compared Atezolizumab plus Bevacizumab followed by MKIs (median s-OS 20 months; 95% CI 19-21 months). **Conclusions:** To our knowledge and given the absence of adequately designed sequential RCTs, this is the first model to date which suggests, with a proper methodological approach, an accurate estimate of outcome of patients with u-HCC treated by sequential systemic therapies. In patients with u-HCC failing first-line treatment, modelling estimates of s-OS for each retreatment strategies may assist in choosing the most promising sequences in order to plan appropriate RCTs. Research Sponsor: None.

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Alliance/CALGB 80802: Impact of hepatitis C (HCV) on doxorubicin (DO) + sorafenib (S) versus S in patients (pts) with advanced hepatocellular carcinoma (aHCC). *First Author: Imane H. El Dika, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: Alliance/CALGB 80802 randomized phase III trial evaluated DO+S vs. S in pts with aHCC, and showed no improvement in median OS. Multi-drug resistant pathway mitigation by the Ras/Raf/MEK/ERK pathway and bFGF-mediated activation of Raf-1 promotes the formation of antiapoptotic Raf-1 and ASK1 complex, induced by anthracyclines. S efficiently blocks NS5A-recruited c-Raf mediated HCV replication and viral gene expression. Once inhibited by S, VEGF expression of HepG2 may limit HCV cellular entry. Release of Raf-1-Ask-1 dimer and inhibition of Raf-1 via S putatively differ in the presence or absence of DO. We hypothesize treatment with S reduces HCV titer levels (TL) and influence pts' outcome. **Methods:** In 80802 HCV pts, TL were evaluated in both arms at baseline and post-baseline at Day 1 of Cycles 2, 3, and every 2 cycles and at progression or discontinuation of therapy. HCV undetectable (HCV-UN) levels were defined as < 50 copies/mL. TL were evaluated in relation to OS and PFS. HCV RNA levels were measured by TaqMan PCR and by genotype. **Results:** Of 356 pts, 83 were HCV+ with more Black/African American (25/50 = 50%) vs. White (54/239 = 23%) or other race groups (4/67 = 6%) (p < 0.0001). HCV titer data were available on 54 pts (S: 28, DO+S: 26). At baseline, 12 pts (S: 7, DO+S: 5) were HCV-UN, and post-baseline HCV TL did not significantly differ between treatment arms; one patient in each arm went from detectable (HCV-D) to HCV-UN. Post-baseline, 40 pts were HCV-D vs. 14 who were HCV-UN (S+DO: 8, S: 6 pts). Except for the two pts who became HCV-UN, baseline HCV-D vs. HCV-UN titers was similar to that status post-baseline. PFS and OS between HCV-D and HCV-UN both at baseline and post-baseline are delineated in the table. **Conclusions:** We observed that S did not influence HCV TL. Pts treated with DO+S vs. S had worse PFS if they had HCV-UN, and further that higher levels of HCV titers at baseline were associated with significantly improved PFS. Given the small sample size, these findings warrant further prospective evaluation. Support: U10CA180821, U10CA180882, U24CA196171; Bayer, Bristol-Myers-Squibb, and Sanofi. https://acknowledgments.alliancefound.org. Clinical trial information: NCT01015833. Research Sponsor: U.S. National Institutes of Health., Pharmaceutical/Biotech Company., U10CA180863 (CCTG), U10CA180820 (ECOG-ACRIN), U10CA189859, U10CA180888 (SWOG).

	PFS			OS		
All pts	**Median (months)**	**HR* (95% CI)**	**p-value**	**Median (months)**	**HR* (95% CI)**	**p-value**
Baseline HCV-UN (vs. HCV-D)	3.9 (vs. 5.8)	3.51 (1.58 - 7.78)	0.002	7.95 (vs. 8.31)	1.19 (0.59 - 2.43)	0.63
Post-baseline HCV-UN (vs. HCV-D)	2.8 (vs. 5.5)	3.00 (1.48 - 6.12)	0.002	7.95 (vs. 7.6)	1.14 (0.58 - 2.23)	0.68
DO+S pts						
Baseline HCV-UN (vs. HCV-D)	3.94 (vs. 7.13)	3.26 (1.17 - 9.1)	0.024	7.95 (vs. 9.33)	1.36 (0.52 - 3.51)	0.53
Post-baseline HCV-UN (vs. HCV-D)	2.8 (vs. 7.13)	4.12 (1.47 - 11.5)	0.007	9.1 (vs. 8.95)	1.22 (0.49 - 3.03)	0.67
S pts						
Baseline HCV-UN (vs. HCV-D)	1.5 (vs. 5.2)	3.91 (1.13 - 13.6)	0.032	8.29 (vs. 7.33)	1.02 (0.34 - 3.02)	0.97
Post-baseline HCV-UN (vs. HCV-D)	2.7 (vs. 4.9)	2.22 (0.78 - 6.28)	0.13	7.75 (7.03)	1.06 (0.39 - 2.86)	0.91

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Safety and efficacy of combination of GT90001, an anti-activin receptor-like kinase-1 (ALK-1) antibody, and nivolumab in patients with metastatic hepatocellular carcinoma (HCC). *First Author: Chiun Hsu, Department of Medical Oncology, National Taiwan University Cancer Center, Taipei, Taiwan*

Background: GT90001, a fully human anti-ALK-1 mAb (IgG2) that may inhibit ALK-1/ TGF-β signaling and tumor angiogenesis, has shown good single-agent safety profile in humans. This study aimed to assess the safety and efficacy of GT90001 in combination with nivolumab in patients with advanced HCC who had progressive disease after or were intolerant to first-line sorafenib or lenvatinib therapy (NCT03893695). **Methods:** We did a phase I/II, open-label, single arm, dose de-escalation and expansion trial of GT90001 in combination with nivolumab in patients with histologically or cytologically confirmed HCC with Child-Pugh class A, ECOG performance status of 0 or 1 at three sites in Taiwan. Patients previously treated with immune checkpoint inhibitors were excluded. Stage 1 (dose de-escalation cohort) tested 3 doses of GT90001 (7 (starting dose), 4.5, and 3 mg/kg every 2 weeks) plus nivolumab 3 mg/kg every 2 weeks in 6 subjects at each dose level. Dose-limiting toxicity (DLT) was defined as any treatment-emergent grade 3-4 adverse events (AEs) (CTCAE V5.0) in the first 28 days of treatment. Stage 2 (expansion cohort) tested the combination regimen in 14 patients until loss of clinical benefit or unacceptable toxicity. The primary efficacy endpoint was investigator-assessed objective response as per RECIST v1.1. **Results:** Between July 9th, 2019 and June 26th, 2020, twenty eligible patients were treated. No DLT was observed in stage 1, and GT90001 7.0 mg/kg + nivolumab 3.0 mg/kg every 2 weeks were given in stage 2. The pharmacokinetics of GT90001 and nivolumab were similar to those observed in monotherapy. As of June 26, 2020, 20 patients were evaluable for safety. The common AEs (occurring to more than 20%) included platelet count decreased, rash, fatigue, dizziness, peripheral edema, and constipation. Three patients had treatment-related serious AEs (renal dysfunction, autoimmune hepatitis, hyperamylasemia). Nine patients had GT90001 dose interruption due to AEs and the most common reasons were platelet count decrease (3 patients). No patient discontinued the treatment due to AEs. The median duration of follow-up was 3.7 months (range 0.6-11.1). An objective response assessed was observed in 7 patients (43.75%) out of 16 evaluable patients, all were partial response and 4 of them had confirmed responses. The disease control rate (complete response + partial response + stable disease) was 56.2%. Updated efficacy data will be presented at the congress. **Conclusions:** The combination of GT90001 with nivolumab showed a manageable safety profile, and no new safety signals were identified. The promising preliminary antitumor activities show the potential of GT90001 combined with nivolumab as second-line treatment for advanced HCC. Clinical trial information: NCT03893695. Research Sponsor: Kintor Pharmaceutical Limited.

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Trends of clinical outcomes with sorafenib in randomized controlled trials for patients with treatment-naïve advanced hepatocellular carcinoma. *First Author: Timothy J Brown, Abramson Cancer Center, Hospital of the University of Pennsylvania, Philadelphia, PA*

Background: Sorafenib was first approved by the US FDA to treat patients with advanced hepatocellular carcinoma (HCC) after two landmark trials (SHARP and Asia-Pacific) showed improved overall survival (OS). Since those two landmark trials, median OS has increased in the sorafenib arms in several recent phase III trials in HCC. We analyzed trends in OS, progression-free survival (PFS), and objective response rates (ORR) in published randomized clinical trials of sorafenib in HCC to better understand factors underlying the improvements. **Methods:** We searched PubMed for all published trials of sorafenib in advanced HCC. Trials were included if the patients were naïve to systemic therapy and had a comparison arm that was active systemic therapy or placebo. We extracted demographic and trial-level outcome data to correlate outcomes such as OS, PFS, ORR, and duration of therapy. T-tests were used to compare outcomes and linear regression was used to identify temporal trends with significance set at p£0.05. **Results:** The PubMed search returned 100 studies. A total of 15 studies met inclusion criteria with a total of 3755 patients treated with sorafenib (9 phase III and 6 phase II). Included trials enrolled patients from 2005-2019. The median OS in all trials was 10.0 mos (range: 6.5-14.8 mos). OS has significantly improved since the first trial began accruing (p = 0.04). A total of 12 studies provided data on PFS using RECIST 1.1, with a median PFS of 4.0 months (range: 2.7-6.6 mos). PFS has not changed over time (p = 0.99). However, ORR assessed by RECIST 1.1 have trended toward improvement over time (p = 0.08). Median duration of therapy with sorafenib has decreased by 53% since the enrollment of the first clinical trial in 2005, from 23.1 weeks to 12.2 weeks (p = 0.02). Despite this, no significant correlations were observed with the interaction of duration of therapy and OS (p = 0.92). Further, there was no significant change in the age of patients included, proportion of patients with Childs-Pugh A, Barcelona Clinic Liver Cancer (BCLC) B, BCLC C, ECOG performance status 0, HBV or HCV, proportion of patients with extrahepatic spread or vascular invasion at time of enrollment, or proportion of patients who have undergone prior locoregional therapies to explain the OS findings. **Conclusions:** The OS of patients with advanced HCC on the sorafenib arm in published trials has been increasing, however the reasons for this increase are not apparent from data available in the published literature. At the same time, the median duration of treatment with sorafenib has been decreasing over time and PFS is unchanged, suggesting improvements in sorafenib delivery may not be the primary factor. It is possible these trends represent heretofore unquantified changes in patient selection for systemic therapy, improvements in supportive care, or post-progression treatment for patients on HCC clinical trials. Research Sponsor: None.

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Outcome of early and intermediate-stage hepatocellular carcinoma (HCC): A single institution experience at MGUH. *First Author: Chao Yin, Lombardi Cancer Center MedStar Georgetown University Hospital, Washington, DC*

Background: Liver transplant (LT) remains the best curative standard for HCC within Milan criteria (Milan). Nonsurgical locoregional treatments, including TACE and ablation, offer a bridge to surgical management and attempt to downstage or maintain patients (pts) within Milan pending liver transplant and donor organ availability. We investigated clinical factors that predict successful downstaging of HCC and liver transplant. **Methods:** In this single-institutional retrospective analysis, pts with early-intermediate stage HCC within Milan (control) vs beyond Milan were evaluated for clinical outcome. Clinical factors including treatment and response, demographics, TACE distribution (number of treatments, timing, and response), and status of liver transplantation (timing and if received) were correlated to overall survival (OS). OS was calculated using the Kaplan-Meier method. **Results:** HCC pts (n = 343) considered for LT or downstage to LT were included in the study: 75% male, 13% African American, 55% Caucasian, and 14% Asian. 12% of pts had HBV, 53% had HCV, 2% had both HBV and HCV. 221 pts were diagnosed within Milan vs 122 beyond Milan, in which 36% (n = 44) were still within UCSF criteria (UCSF). 43% of those diagnosed within Milan ultimately received LT vs 16% of those diagnosed beyond Milan. 49% of pts (n = 60) initially beyond Milan were downstaged to within Milan, via TACE, wherein 27% received LT; this group accounted for 13% all LT. However, in the subset of pts beyond Milan but within UCSF, 68% were downstaged to within Milan, wherein 40% received LT. In pts initially within Milan, 21% (n = 47) progressed beyond Milan, but 40% of this subset was downstaged back to within Milan. Pts both within and beyond Milan had a median of 2 TACE procedures. Differences in the rates of LT relative to the number of TACE were significant (p = 0.022) for pts initially within Milan; for < / = 2 TACE, 54% had LT; for > 2 TACE, 26% had LT. Similar comparison was nonsignificant for pts initially beyond Milan (p = 0.95); rates of LT for < / = 2 TACE and > 2 TACE were 17% and 16% respectively. Median OS for non-LT recipients was 5 years vs not reached for LT recipients (> 70% alive at 8 years, p < 0.001). Pts initially beyond Milan but within UCSF criteria had similar OS vs those initially within Milan (both 75% at 4 years), but OS was worse (50% at 4 years) for those beyond UCSF (p = 0.024). **Conclusions:** Liver transplantation significantly increased OS in early-intermediate stage HCC. Increased number of TACE procedures was associated with decreased likelihood of ultimate LT in pts initially diagnosed within Milan, particularly when they had > 2 TACE. Pts initially beyond Milan but within UCSF criteria had similar OS vs those initially within Milan; this former subset had a good chance of being downstaged to Milan and ultimately receive LT. Additional clinical factors that predict successful downstaging of HCC and LT are being investigated. Research Sponsor: None.

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Activity of tepotinib in hepatocellular carcinoma (HCC) with high-level *MET* amplification (*MET*amp): Preclinical and clinical evidence. *First Author: Sandrine Faivre, Saint-Louis Hospital & Paris 7 University, Paris, France*

Background: Tepotinib, a potent and highly selective MET inhibitor, showed promising activity in advanced HCC with MET overexpression in two Phase Ib/II trials, which both met their primary endpoints. One trial enrolled Asian patients (pts) without prior systemic therapy (first line [1L]; NCT01988493) and one enrolled US/European pts with prior sorafenib (second line [2L]; NCT02115373). By investigator assessment, objective response rates and disease control rates with tepotinib in Phase II were 15.8% and 60.5% in 1L (n = 38), and 8.2% and 57.1% in 2L (n = 49). Outcomes appeared better in pts with *MET*amp. Thus, we further investigated the preclinical and clinical activity of tepotinib in HCC, focusing on high-level *MET*amp, which could be an oncogenic driver in this tumor type. **Methods:** Preclinical activity was assessed in 37 HCC pt-derived xenografts (PDXs) in nude mice treated with tepotinib (100 mg/kg, Days 1–5, every 7 days for five cycles; 6–12 replicates per PDX). Clinical activity was assessed by analyzing pts with *MET*amp or high-level *MET*amp (defined as mean *MET* gene copy number [GCN] ≥5 and ≥10, respectively; by fluorescence *in situ* hybridization), who received tepotinib 500 mg in Phase Ib or II of the 1L and 2L trials (n = 121). In the Phase Ib part of the 1L trial, pts could have received prior treatment. **Results:** Molecular profiling revealed high-level *MET*amp in two of 37 HCC PDXs: LIM612 (*MET* GCN 47.1) and LIPF210 (*MET* GCN 44). Tepotinib induced significant tumor regression in both of these high-level *MET*amp HCC PDX models (mean tumor volume reduction: 97% and 96%, respectively). Across the two trials, 15 pts treated with tepotinib 500 mg had *MET*amp, of whom five had an objective response (one complete response [CR] and four partial responses [PRs]) and six had stable disease (SD) as best overall response. Four pts had high-level *MET*amp (mean *MET* GCN 14.3, 18.1, 30.2, and 36.2), with best overall response of CR in one pt, PR in two pts and SD in one pt (Table). One pt with high-level *MET*amp (mean *MET* GCN 14.3) treated with 1L tepotinib was still receiving treatment as of Sept 2020 (total tepotinib treatment duration: > 45 months). **Conclusions:** High-level *MET*amp may be an oncogenic driver in HCC that sensitizes tumors to MET inhibition with tepotinib. Compared with MET overexpression, high-level *MET*amp could be a better predictive biomarker for MET inhibitors in this setting. Clinical trial information: NCT01988493, NCT02115373. Research Sponsor: Merck KGaA, Darmstadt, Germany.

Pt no.	Line of tepotinib	Study	Phase	Mean *MET* GCN	*MET*: *CEP7* ratio	MET IHC	Best overall response*	Progression-free survival, months*	Treatment duration, months
1	1L	NCT01988493	II	14.3	8.1	3+	PR	10.9	14.0†
2	2L‡	NCT01988493	Ib	30.2	12.1	3+	PR	20.3	20.0
3	2L‡	NCT02115373	II	18.1	7.5	3+	CR	13.8	14.3
4	2L‡	NCT02115373	II	36.2	15.1	3+	SD	2.8	2.8

*By investigator assessment per each study data cut-off; †Treatment ongoing as of Sept 2020 (currently > 45 months of treatment); ‡Prior treatment was sorafenib. IHC, immunohistochemistry.

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Ipilimumab and nivolumab/pembrolizumab in advanced hepatocellular carcinoma refractory to prior immune checkpoint inhibitors. *First Author: Jeffrey Sum Lung Wong, University of Hong Kong, Hong Kong, China*

Background: Programmed cell death protein 1 (PD-1) pathway blockade with immune checkpoint inhibitors (ICI) is a standard therapy in advanced hepatocellular carcinoma (HCC) nowadays. No strategies to overcome ICI resistance have been described. We aimed to evaluate the use of ipilimumab and anti-PD-1 ICIs (nivolumab or pembrolizumab) combinations in advanced HCC patients with progression on prior ICIs. **Methods:** Advanced HCC patients with documented tumour progression on prior ICIs and subsequently received ipilimumab with nivolumab/pembrolizumab were analysed. Objective response rate (ORR), median duration of response (DOR), time-to-progression (TTP), overall survival (OS), and treatment-related adverse events (TRAEs) were assessed. **Results:** Twenty-five patients were included. The median age was 62 (range 51-83). 68% were of Child-Pugh (CP) grade A and 48% had primary resistance to prior ICI. At median follow-up of 37.7 months, the ORR was 16% with a median DOR of 11.5 months (range 2.76-30.3). Three patients achieved complete response. The median TTP was 2.96 months (95% C.I. 1.61-4.31). Median OS was 10.9 months (95% C.I. 3.99-17.8) and the 1-year, 2-year and 3-year survival rates were 42.4%, 32.3% and 21.6% respectively. The ORR was 16.7% in primary resistance group and 15.4% in acquired resistance group (p=1.00). All responders were of CP A and Albumin-Bilirubin (ALBI) grade 1 or 2. CP and ALBI grades were significantly associated with OS (p=0.006 and p<0.001 respectively). Overall, 52% of patients experienced TRAEs and 12% experienced grade 3 or above TRAEs. **Conclusions:** Ipilimumab and nivolumab/pembrolizumab can achieve durable antitumour activity and encouraging survival outcomes with acceptable toxicity in patients with advanced HCC who had prior treatment with ICIs. Research Sponsor: Research Grant Council, Hong Kong.

331 Poster Session

Telotristat ethyl to enhance cytotoxic chemotherapy response in preclinical cholangiocarcinoma models. *First Author: Niranjan Awasthi, Indiana University School of Medicine, South Bend, IN*

Background: Cholangiocarcinoma (CCA) is the second-most common primary liver cancer after hepatocellular carcinoma. It has a poor prognosis with a 5-year survival rate of 5-15%. The current standard first-line therapy for advanced unresectable CCA is a combination of gemcitabine and cisplatin (GemCis) chemotherapy that leads to a median survival of 6-12 months. Nanoparticle albumin-bound paclitaxel (*nab*-paclitaxel, NPT) is an approved therapy for breast, NSCLC and pancreatic cancer. Elevated levels of serotonin have been reported in CCA that has protumorigenic activity. We tested the hypothesis that telotristat ethyl (TE), an inhibitor of serotonin biosynthesis, has antitumor activity in CCA and it augments GemCis and nab-paclitaxel response in preclinical CCA models. **Methods:** Tumor growth experiments were performed in mice subcutaneous CCA intrahepatic CCLP-1 xenografts, extrahepatic TFK-1 xenografts and patient-derived xenografts. Animal survival studies were performed using human CCA intrahepatic CCLP-1 cells in the peritoneal dissemination model in NOD/SCID mice. **Results:** In intrahepatic CCLP-1 subcutaneous xenografts, compared with controls, reduction in tumor growth was observed by TE (53%), GemCis (53%) or NPT (69%). The combination of TE with GemCis or NPT exhibited an additive tumor growth inhibition response, GemCis+TE (85%) and NPT+TE (90%). In extrahepatic TFK-1 subcutaneous xenografts, TE led to a significant reduction in tumor growth (51%), while GemCis and NPT reduced tumor growth by 37% and 56%, respectively. Again, an additive tumor growth inhibition effect was observed by the addition of TE to chemotherapy, GemCis+TE (67%) and NPT+TE (74%). In CCA patient-derived subcutaneous xenografts, GemCis caused the greatest tumor growth reduction (80%) followed by NPT (57%) and TE (40%). Combinations increased tumor inhibition further: GemCis+TE (95%) and NPT+TE (91%). Mouse survival in peritoneal dissemination xenografts was only marginally enhanced by TE (11%) or GemCis (9%) while NPT led to a substantial extension (60%). Interestingly, the combination of TE with GemCis or NPT demonstrated a further extension in mice survival: GemCis+TE (26%) and NPT+TE (68%). **Conclusions:** TE had antitumor activity and it enhanced chemotherapy effects in several CCA preclinical models indicating that this therapeutic combination has the potential to ameliorate clinical therapy for CCAs of different origin. Research Sponsor: TerSera Therapeutics, Indiana University School of Medicine funds.

332 Poster Session

Low energy amplitude modulated radiofrequency electromagnetic fields to show antitumor effect in combination with standard treatment or as monotherapy in patients with advanced hepatocellular carcinoma. *First Author: Yone De Camargo Setogute, Hospital Sirio Libanes São Paulo, São Paulo, Brazil*

Background: Exposure to amplitude-modulated radiofrequency electromagnetic fields (EMF) in immortalized hepatocellular carcinoma (HCC) cell cultures and xenograft models demonstrated anti-tumor effect. Patients with advanced HCC exposed to systemic EMF showed objective response with potential survival benefit. **Methods:** An open-label, single center, prospective clinical protocol was performed in advanced HCC patients as an initial, second or third treatment modality. Systemic exposure to EMF modulated at patient-specific frequencies was applied as an add-on strategy (combination) to systemic conventional treatment or as a single therapeutic modality. A spoon-shaped antenna placed in the oral cavity delivered EMF over 90 minutes with monthly repetitions until death or consent of withdrawal. The primary objective was overall survival (OS) in comparison with historical control group of 45 advanced patients HCC from the same institution. Retrospective radiological review was conducted by two independent radiologists for objective response (OR) using RECIST1.1 criterion. **Results:** From March 2018 to April 2020, 55 advanced HCC patients were submitted to 373 EMF exposures. 87% were male, median age of 67, 84% were BLCL-C, 16% were Child-Pugh B, 29% had extra-hepatic metastasis, 55% had failed previous treatment and 71% had documented radiological progression. 31(56%) patients received EMF in combination with systemic therapy (25 sorafenib, 3 lenvatinib, 3 nivolumab). 24 patients received EMF as single treatment modality. The median OS for the entire patient cohort was 11.5 months. The median OS for combination treatment was 12.0 month and the median OS for single modality was 11.3 months. The median OS for the historical control was 5.3 month. The median OS from the entire cohort and the historical control were significant different (p = 0.0026) but the median OS from combination and single modality were not (p = 0.3434). Radiological images were available from 38(69%) patients. There were 6/38 (16%) documented objective responses (1 CR and 5 PR) and 30/38 (79%) patients experienced disease control. 4/21 (19%) OR were in patients using TKIs + EMF and 2/17 (12%) OR were in patients using EMF alone. **Conclusions:** EMF showed objective anti-tumor effect in combination with TKI or as single modality in advanced HCC patients. EMF showed improvement in overall survival in comparison with the historical control group supporting future development as a novel systemic treatment modality in advanced HCC patients. Clinical trial information: NCT 01686412. Research Sponsor: None.

333 Poster Session

Dissecting novel mechanisms of hepatitis B virus-related hepatocellular carcinoma using meta-analysis of public data. *First Author: Jihad Aljabban, The Ohio State University College of Medicine, Columbus, OH*

Background: Hepatitis B is a cause of hepatocellular carcinoma (HCC) globally, irrespective of viral loads. Interestingly, this process is not necessarily mediated through cirrhosis and may in fact involve oncogenic processes. Prior studies have suggested specific oncogenic gene expression pathways affected by viral regulatory proteins. Thus, identifying these genes and associated pathways could highlight predictive factors for HCC transformation, and has implications in early diagnosis and treatment. **Methods:** We employed our Search, Tag, Analyze, Resource (STARGEO) platform to conduct a meta-analysis of public data from NCBI's Gene Expression Omnibus. We performed meta-analysis consisting of 155 tumor samples compared against 185 adjacent non-tumor samples. We present the results from the meta-analysis in Ingenuity Pathway Analysis. **Results:**Our analysis revealed LXR/RXR activation, LPS-IL-1 mediation inhibition of RXR, and FXR/RXR activation as top canonical pathways amongst others. Top upstream regulators identified included the Ras family gene RABL6. The role of RABL6 in oncogenesis is beginning to unfold but its specific role in HBV-related HCC remains undefined. Our causal analysis suggests RABL6 mediates pathogenesis of HBV-related HCC through promotion of genes related to cell division, epigenetic regulation, and Akt signaling. Additionally, HOXA10 was a top upstream regulator and was strongly upregulated in our analysis. While described in other cancer, HOXA10 has not been well documented in HBV-related HCC and our causal analysis suggests it mediates pathogenesis through downregulation of tumor suppressors and its protective effect from oxidative stress. **Conclusions:** This meta-analysis describes possible role of viral regulatory proteins such as RABL6 and HOXA10 in the pathogenesis of HBV -related HCC. Further prospective studies are needed to confirm our findings. Research Sponsor: None.

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Approaching the tumor microenvironment in patients with advanced hepatocellular carcinoma using needle biopsy samples. *First Author: Hiroaki Kanzaki, Department of Gastroenterology, Graduate School of Medicine, Chiba University, Chiba, Japan*

Background: Currently, combined immunotherapy of atezolizumab (anti-PD-L1 antibody) plus bevacizumab (a humanized anti-VEGF monoclonal antibody) is the standard first-line treatment in patients with advanced hepatocellular carcinoma (HCC). At the threshold of this new era, there is limited information about tumor microenvironment (TME) in advanced HCC. Several studies on TME in HCC have analyzed samples obtained via hepatic resection. In general, hepatic resection is indicated for patients with limited size and number of intrahepatic nodules, i.e., early stage HCC. In contrast, most patients who have an indication for systemic therapy have developed macroscopic vascular invasion (MVI) or/and extrahepatic metastasis, namely in advanced stage HCC. Progression from an early stage HCC to an advanced stage HCC involves a lengthy clinical course, therefore, the TME at the time of initial diagnosis may differ from that at the time of systemic therapy indication. The present study was aimed to analyze the TME by using needle biopsy samples obtained prior to initiation of systemic therapy in patients with advanced HCC. **Methods:** Between March 2019 and May 2020, 80 patients underwent liver tumor biopsy at the time of indication for systemic chemotherapy. HCC was confirmed via pathological examination in 70 patients and their samples were analyzed. Microsatellite instability (MSI) was evaluated using polymerase chain reaction. Programed death-ligand 1 (PD-L1) expression and the levels of tumor-infiltrating lymphocytes (TIL) were evaluated using immunohistochemical staining. PD-L1 expression was defined as per the tumor proportion score (TPS; the number of PD-L1-positive cells/total number of tumor cells) and was classified as low (TPS $<$ 1%) or high (TPS $>$1%). Levels of TIL were defined as the mean number of CD8-positive lymphocytes in the tumor per 1 mm^2 and classified as low or high using the median value. **Results:** Out of the 70 tumors, one was MSI-high and 69 were MSI-negative. The PD-L1 expression was $<$ 1% in 50 samples, 1%–10% in 12, 11%–20% in 7, and 21%–30% in 1. The median level of TIL was 266/mm^2. PD-L1^{high}TIL^{high}was present in 20.0%, PD-L1^{low}TIL^{low}in 38.5%, PD-L1^{high}TIL^{low}in 8.6%, and PD-L1^{low}TIL^{high}in 32.9%. In the MSI-high tumor, PD-L1 expression was $<$ 1% and the level of TIL was 142/mm^2. High PD-L1 expression and high levels of TIL were associated with hepatitis C virus infection, high alpha-fetoprotein levels, and presence of MVI respectively. We are currently performing RNA-sequencing in order to obtain more details about TME in patients with advanced HCC. **Conclusions:** MSI-high advanced HCC was detected in 1.4% patients and was not necessarily associated with a "hot" immune microenvironment. PD-L1 expression and levels of TIL were associated with some clinical parameters. In the present study, we also reported the changes in the TME over time. Research Sponsor: Gilead Sciences, Abbie, Sumitomo Group, Bristol-Myers Squibb, Chugai Pharma, Astellas Pharma, Takeda, Shionogi, Otsuka.

335 Poster Session

Feasibility and efficacy of neoadjuvant cabozantinib and nivolumab in patients with borderline resectable or locally advanced hepatocellular carcinoma (HCC). *First Author: Mark Yarchoan, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD*

Background: Only 10-15% of newly diagnosed HCC patients are candidates for a potentially curative resection, and most patients who receive resection eventually recur. Historical systemic therapies including sorafenib, as well as locoregional therapies, have not demonstrated benefit in the perioperative setting. Novel combinations of targeted therapies and immunotherapies demonstrate higher response rates than sorafenib in HCC. Here, we report the feasibility and efficacy of neoadjuvant combination therapy with cabozantinib plus nivolumab, followed by surgical resection, in patients with borderline resectable or locally advanced HCC. **Methods:** We conducted an open-label, single-arm, phase I study in patients with HCC with borderline resectable or locally advanced HCC (including multinodular disease, portal vein involvement, or other high-risk features). Patients received 8 weeks of therapy with cabozantinib 40 mg oral daily plus nivolumab 240 mg IV every two weeks, followed by restaging and possible surgical resection. The primary endpoint was feasibility, defined by the percentage of patients experiencing a treatment-related adverse event that precluded continuing on to surgery within 60 days of the planned date for surgical evaluation. **Results:** We enrolled 15 patients of whom 14 patients completed neoadjuvant therapy and underwent surgical evaluation. Adverse events were consistent with prior experience with these agents, and the trial met its primary endpoint, with no patients experiencing a treatment-related adverse event that precluded timely surgical assessment. Of patients completing neoadjuvant therapy, 1 patient declined surgery, 1 tumor could not be resected, and 12 patients underwent successful R0 surgical resection. 5/12 (41.7%) resected patients had a major or complete pathologic response. At a median follow up of one year, 4/5 pathologic responders are without recurrence. We performed an in-depth profiling of the surgical resection biospecimens and identified an enrichment of IFNγ+ effector memory CD4+ and granzyme B+ effector CD8+ T cells as well as tertiary lymphoid aggregates in the pathologic responders. We further analyzed the spatial relationships of cell types in responders and non-responders, which identified distinct spatial arrangement of B cells in responders, and proximity of arginase-1 expressing myeloid cells to T cells in nonresponders. **Conclusions:** This study is, to our knowledge, the first use of a targeted therapy in combination with an immune checkpoint inhibitor in the neoadjuvant setting in HCC, and the first use of modern systemic therapies to expand surgical resection criteria. Neoadjuvant cabozantinib and nivolumab is feasible, and may result in pathologic responses and long-term disease-free survival in a group of patients who may be outside traditional resection criteria. Clinical trial information: NCT03299946. Research Sponsor: Bristol Myers Squibb, Exelixis.U.S. National Institutes of Health.

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Role of ctDNA to predict risk of recurrence following potentially curative resection of biliary tract and pancreatic malignancies. *First Author: Angela Lamarca, The Christie NHS Foundation Trust, Manchester, United Kingdom*

Background: The potential role of ctDNA to identify residual disease after potentially curative resection has been suggested in some malignancies; its role in resected pancreatico(P)-biliary(B) malignancies is unknown. **Methods:** Patients diagnosed with PB malignancies underwent molecular profiling (ctDNA) using FoundationMedicine Liquid (72 cancer-related genes) following potentially curative resection. Baseline patient characteristics and molecular profiling outcomes, including mutant allele frequency (MAF) for pathological alterations were extracted. Primary objective: prevalence of ctDNA identification and its correlation with recurrence (relapse-free survival (RFS) and relapse rate). **Results:** Total of 11 individuals had ctDNA analysed following potentially curative resection for PB malignancies: 8 B (4 extra-hepatic cholangiocarcinoma (eCCA), 2 ampulla, 1 intrahepatic cholangiocarcinoma (iCCA), 1 gallbladder cancer (GBC)) and 3 P. Baseline characteristics: 6 female (54.55%), median age 71.59 years (range 39.98-81.19). Most were pT2 (45.45%), pN0 (54.55%) and R0 (63.64%). Following surgery, 6 patients were started on adjuvant chemotherapy; at the end of follow-up (data cut-off 25/6/2020; median follow-up 11.15 months (range 5.45-13.52); 5 relapsed (45.45%) and 2 died (18.18%). Estimated median RFS was 11.43 months (95% CI 2.28-not reached); median overall survival was not reached. No sample failed ctDNA analysis; presence of ctDNA was identified in 3/11 (27.27%) of the samples; 2 and 1 samples had 2 and 1 pathological alterations identified, respectively: ALK fusion (1 sample; GBC), TP53 mutation (2 samples; eCCA and GBC), CHEK2 mutation (1 sample; pancreas), IDH2 mutation (1 sample; eCCA). Mean maximum MAF was 1.47 (2 in biliary; 0.43 in pancreas). Variants of unknown significance were identified in 72.73% of the samples (87.5% in B; 33.33% in P; p-value 0.152). None of the baseline characteristics explored correlated with presence of ctDNA. There was a trend towards increased relapse risk in the patients with ctDNA present following potentially curative surgery; Cox regression for RFS [HR 2.64 (95% CI 0.36-19.31); median RFS 11.44 months (95% CI 2.28-not reached) vs 10.87 (95% CI 2.21-not reached)]; relapse rate 37.5% (ctDNA absent) vs 66.67% (ctDNA present); statistical significance was not reached (p-value 0.340 and p-value 0.545, respectively). **Conclusions:** This pilot study demonstrates the feasibility of testing for ctDNA following potentially curative resection in PB malignancies. Presence of ctDNA may be associated with increased relapse risk; further studies are required to increase sample size and assess clinical implications. Research Sponsor: None.

337 Poster Session

In search of novel synthetic lethality anti-cancer drug targets in intrahepatic cholangiocarcinoma: *MTAP* genomic loss. *First Author: Jeffrey S. Ross, Foundation Medicine, Cambridge, MA*

Background: The association of *BRCA* tumor suppressor gene (TSG) inactivation and PARP inhibitor efficacy through a mechanism of synthetic lethality (SL) is now well-established. Recently, the PRMT5 arginine methyltransferase dependence in cells with *MTAP* (S-methyl-5'-thioadenosine phosphorylase) genomic alterations (GA) has been proposed as a new SL based anti-tumor strategy and under consideration for development for intrahepatic cholangiocarcinoma (IC). **Methods:** 2,170 cases of clinically advanced IC were submitted for comprehensive genomic profiling (CGP) to detect genomic alterations (GA), tumor mutational burden (TMB) and microsatellite instability (MSI) using a hybrid capture based assay (F1CDx). PD-L1 expression in tumor cells (Dako 22C3) was measured by IHC and scored using the tumor proportion score (TPS) method. **Results:** 328 (15%) ICs featured *MTAP* inactivation (MTAP-IC). 48% of MTAP-IC cases were female and 52% were male with a median age of 66 years (range 26-93 years). MTAP-IC featured 6.3 GA per sample. The median TMB was 2.5 mut/Mb with only 2% of cases with TMB ≥10 mut/Mb. No (0%) MTAP-IC cases were MSI-high. Of 112 MTAP-IC IHC stained for PD-L1, 4% were PD-L1 high (> 50%), 14% were PD-L1 low (1-49%) and 82% were PD-L1 negative. 99% of *MTAP* inactivation was by copy number (CN) loss and 1% was due to non-CN mutation. In MTAP-IC, 99% featured *CDKN2A* loss and 95% featured *CDKN2B* loss (9p21 co-deletion). *TP53* was mutated in 31% and *KRAS* in 24% (3% G12C). Other currently non-targetable GA included *ARID1A* (19%), *BAP1* (16%) and *SMAD4* (13%). Among potentially targetable GA, the MTAP-IC featured 12% *FGFR2* GA (8% rearrangements), 10% *BRAF* (8% V600E), 7% *IDH1*, 7% *PIK3CA*, 4% *BRCA2*, 4% *ERBB2* (2% amplification) and 3% *MET*. **Conclusions:** Comprehensive genomic profiling elucidated that *MTAP* GA are frequent in IC and features relatively high GA/tumor, including 9p21 co-deletion, but relatively low TMB and PD-L1 expression. Isolated *MTAP* deletion without *CDKN2A/B* co-deletion was extremely rare. In addition to the potential targeting of PRMT5 in MTAP-IC tumors, co-altered genes known to be targets in IC such as *FGFR2*, *IDH1* and *BRAF* are still prevalent in MTAP-IC, indicating potential for combining targeted therapies in some MTAP-IC patients. Research Sponsor: Foundation Medicine Inc.

338 Poster Session

Results of biomarker analysis from phase II trial of nivolumab in refractory biliary tract cancer. *First Author: Elaine Tan, University of South Florida, Tampa, FL*

Background: Our previous phase II study demonstrated that nivolumab provides modest but durable clinical efficacy in patients (pts) with refractory biliary tract cancer (BTC), suggesting the significant clinical benefit of nivolumab in selected pts and identification of potential predictive biomarkers. Here, we report outcomes from the biomarker analysis. **Methods:** Pretreatment tumor samples were obtained and assessed for immunohistochemistry (IHC) with PD-1 and PDL-1 antibodies, mRNA sequencing (RNAseq), and whole exome sequencing (WES). Clinical efficacy was correlated with the molecular analysis. Prior cisplatin exposure was reviewed to evaluate the impact of cisplatin on the tumor mutational burden (TMB) and clinical outcome. **Results:** Among 46 pts who had tumor response evaluation, 31 pts received cisplatin prior to nivolumab, and 15 were cisplatin-naive. Pre-treatment tumor samples were assessed for IHC (n = 42), RNAseq (n = 11), and WES (n = 11) based on tissue availability. There was no statistically significant correlation between prior cisplatin exposure and clinical outcome. Among 42 available tumor samples, 18 (43%) expressed PD-L1 positivity (> 1%), which was associated with a statistically significant prolonged progression free survival (PFS). Median PFS was 10.4 months for PD-L1 positive vs 2.4 months for PD-L1 negative (HR 0.23, 95% CI 0.10-0.51; P < 0.001), while there was no statistically significant correlation between PD-1 expressing tumor infiltrating lymphocytes and clinical outcome. There was also no statistically significant difference in TMB of cisplatin-exposed (n = 8) vs. cisplatin-naive tumor samples (n = 3) (9162, SD = 150 vs. 8898, SD = 806, p = 0.62). In comparing the group with prolonged disease control of at least 16 weeks (n = 4) to those with rapid disease progression (n = 7) who had mRNA sequencing performed, levels of AC005609.1, FAT3, TMEM151A, ADARB2, FAM153A were all significantly upregulated (p < 0.01), while levels of CLCA1, MUC2, IGHV3-43, SWORA6, and CRISP3 were all significantly downregulated (p < 0.01). **Conclusions:** Prior cisplatin exposure did not lead to statistically significant differences in clinical outcome or TMB in advanced BTC pts treated with nivolumab. However, PD-L1 expression > 1% correlated with improved PFS, and variations in level of certain mRNA sequences were noted when comparing pts who had rapid disease progression vs. prolonged disease control with nivolumab. This suggests that BTC pts with positive PD-L1 expression and a particular mRNA profile may have a favorable response to nivolumab. Further studies are needed to confirm these findings. Clinical trial information: NCT02829918. Research Sponsor: Bristol Myers Squibb.Chemical Biology & Molecular Medicine (CBMM) Program at Moffitt Cancer Center.

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Characterization of hyperprogressive disease in patients with advanced biliary tract cancer treated with anti-PD-1 inhibitor: A multicenter retrospective study. *First Author: Choong-kun Lee, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea*

Background: Immunotherapy, including anti-PD-1 inhibitor, represents a promising breakthrough treatment in poor prognostic cancers such as biliary tract cancer (BTC). However, subset of pts suffer from unexpected acceleration of tumor growth following the initiation of immunotherapy, termed hyperprogressive disease (HPD). We assessed HPD in BTC pts treated with anti-PD-1 inhibitor in association with clinicopathologic features. **Methods:** This retrospective study included pts with BTC who were treated with pembrolizumab 200mg IV as palliative second or third line treatment in 4 tertiary hospitals in South Korea. Previous proposed tumor dynamic parameters including time to treatment failure (TTF), tumor growth kinetics (TGK) and tumor growth rate (TGR) were calculated per RECIST v1.1. Neural network modeling technique was adopted to find clinicopathologic features that can predict HPD. **Results:** Total of 223 pts with BTC were treated with palliative second or third line pembrolizumab between December 2015 to August 2020. ORR was 11.2% (n=1 for CR, n=24 for PR, n=70 for SD, n=118 for PD, and 10 pts not evaluable). Among patients with best response as PD (n=118), 41 patients (18.4% from total pts) met the criteria for HPD definition (>2-fold increase in both TGK and TGR in the experimental period compared to the reference period). HPD pts had worse prognosis compared to non-HPD pts in terms of TTF (median 1.4 vs 2.7 months, *P* =<0.0001) and OS (median 3.57 vs 5.27 months, *P* =0.03). Clinicopathologic features including age, ECOG performance status, primary tumor site, pathology, metastatic organ, previous treatment history (surgery or radiotherapy), pretreatment PD-L1 score, tumor markers, and baseline laboratory results (LDH, albumin, or neutrophil-to-lymphocyte ratio) did not predict HPD (compared to non-HPD pts or PD without HPD pts). By neural network modeling and plotting with hidden vectors, we could define HPD-high-risk cluster (n=37) and HPD-lower-risk cluster (n=80). Higher CA 19-9-to-lymphocyte ratio (*P* =0.0004) or higher platelet-to-PD-L1 CPS (combined positivity score) ratio (*P* =0.002) predicted HPD-high-risk-cluster. HPD pts (n=41) tend to have progression due to liver (73.2% vs 45.6%, *P* =0.0026) or peritoneum (53.7% vs 21.4%, *P*=<0.0001) metastases, compared to non-HPD pts (n=182). **Conclusions:** This study for the first time describe the clinicopathologic features of HPD among pembrolizumab treated BTC pts. Baseline pathology and laboratory tests may help optimal patient selection for immunotherapy to avoid HPD in BTC pts. Further validation of BTC-specific HPD predictive features and definition (TGK or TGR ratio cut-off) will be presented after comparison with clinicopathologic features among second line 5FU-based chemotherapy treated BTC pts. Research Sponsor: None.

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Whole-genome sequencing of cholangiocarcinoma to reveal distinct profiles of patients with underlying cirrhosis or inflammatory disorders. *First Author: Nicholas Timothy Holzapfel, University of Toronto, Toronto, ON, Canada*

Background: Cholangiocarcinoma (CCA) is a lethal malignancy with limited treatment options. Molecular profiling of these tumours has revealed a number of actionable mutations and four clusters have been defined through integrative genomic analysis. We sought to explore whole genome sequencing (WGS) data in 20 patients enriched for CCA arising in the setting of cirrhosis or inflammatory disorders. **Methods:** A previously established Biliary Tract Cancer (BTC) database at the Princess Margaret Cancer Centre (PMCC)/University Health Network (UHN) was used to identify patients of clinical interest including long-term survivors, those with germ-line mutations, and those with chronic inflammatory disorders. WGS and bioinformatic analyses were performed at the Ontario Institute for Cancer Research. **Results:** The 20 resected samples included 12 patients (pts) with intrahepatic CCA, 7 perihilar CCA, and 1 distal CCA. 8 pts were alive > 8 years post resection and one patient harboured a germline MLH1 pathogenic variant (MLH1 G67R). 3 pts had documented cirrhosis (hepatitis B n = 2, haemochromatosis n = 1); other inflammatory disorders (n = 4) included ulcerative colitis (UC) without documented PSC (n = 1), PSC alone (n = 1), UC with PSC (n = 1), and ankylosing spondylitis (n = 1). The remaining cases were randomly selected. The predominant COSMIC single base substitution (SBS) mutational signatures were 1, 8 and 5, and the median TMB was 1.75 mutations per MB (0.73-33.23). The pt with an MLH1 mutation exhibited a TMB of 33.23 with predominance of SBS26. Actionable variants were enriched in the 8 pts who are alive and disease free including 2 predicted FGFR fusions and mutations in IDH1 (n = 1), BRAF V600E (n = 1), and BAP1 (n = 1). TP53 mutations (n = 7) were present exclusively in patients with cirrhosis or inflammatory disorders and the median survival in the group was 12 months (3 -21 months). Although SBS signatures were similar in this group, in the two cases of UC, SBS17 (unknown etiology) was evident. SBS17 was also dominant in one case where the TMB was 13 mutations per MB and the patient died within 3 months of diagnosis. A somatic case of homologous recombination deficiency, with no causative genetic alteration identified, was evident in a further patient receiving maintenance rituximab for a coexisting stage 4 mantle cell lymphoma. **Conclusions:** WGS may provide additional biological information in CCA particularly in patients with underlying inflammatory disorders, where TP53 mutations are prevalent and mutational signatures are distinct. Research Sponsor: Princess Margaret Hospital Cancer Foundation.

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Association between post-treatment (tx) alpha-fetoprotein (AFP) reduction and outcomes in real-world (rw) U.S. patients (pts) with advanced HCC (aHCC). *First Author: Xiaoliang Wang, Flatiron Health, New York, NY*

Background: A decrease in post-tx AFP may be associated with improved outcomes in clinical trials. However, the impact of AFP reduction after initiation of a first-line (1L) tyrosine kinase inhibitor (TKI) therapy on outcomes is unclear among pts with aHCC treated in routine clinical practice. **Methods:** This analysis utilized data from the nationwide Flatiron Health electronic health record (EHR)-derived de-identified database and included pts with aHCC with ≥2 visits between 1/1/2011-7/31/2019 who received 1L TKI. Pts with a baseline serum AFP value (closest to 1L initiation within -30 to +7 days) and a post-tx AFP value (closest to 8 weeks after 1L initiation within ±2 weeks) were included. Post-tx AFP reduction was defined as a ≥20% decrease from baseline AFP, and no reduction as a <20% decrease or any increase. Rw overall survival (rwOS) was defined as time from post-tx AFP measurement to death (censored at last EHR activity). Rw progression-free survival (rwPFS) was based on clinician documentation and defined as the first progression event or death after post-tx AFP measurement (censored at last clinic note date). Adjusted hazard ratios (aHR) for reduction vs no reduction (reference) were estimated using multivariable Cox proportional hazards models adjusted for potential confounders and baseline AFP. Effect modification was assessed by conducting tests for interactions with analyses stratified by HCC risk factors. **Results:** 441 pts were included in the study. 8% had documented history (hx) of hepatitis B (HBV), 52% hepatitis C (HCV), 47% obesity/diabetes (DM), 42% heavy alcohol use, and 11% no documented risk factor. Median baseline AFP was 210 ng/mL (IQR 237 - 2981) and 150 ng/mL (IQR 17 - 1311) among pts with reduction (N = 150) and no reduction (N = 291). There was a 35% decrease in hazard of death for pts with reduction vs no reduction (median rwOS 10.3 vs 6.7 months; Table). Similarly, a 35% decrease in hazard of rw progression or death was observed for pts with reduction vs no reduction (aHR=0.65; 95% CI: 0.52-0.81; median rwPFS 4.4 vs 2.4 months). Reduction (vs no) was associated with better rwOS among pts with hx of HCV, obesity/DM or alcohol use vs without the respective risk factor, however, no statistically significant interactions were observed (Table). **Conclusions:** Results show post-tx AFP reduction may be prognostic for rwPFS and rwOS in pts with aHCC treated with 1L TKI. Further research may clarify if prognostic value differs by HCC risk factor profile. Research Sponsor: Study sponsored by Flatiron Health, Inc.

Associations between post-tx AFP reduction (vs no) and rwOS stratified by HCC risk factor.

		aHR (95% CI)	p-interaction
Overall		0.65 (0.51, 0.83)	
HBV	**Y**	1.13 (0.31, 4.16)	0.15
	N	0.61 (0.48, 0.79)	
HCV	**Y**	0.48 (0.34, 0.68)	0.06
	N	0.85 (0.59, 1.22)	
Obesity/ DM	**Y**	0.53 (0.36, 0.79)	0.07
	N	0.84 (0.59, 1.19)	
Alcohol use	**Y**	0.55 (0.37, 0.81)	0.72
	N	0.70 (0.50, 0.98)	

Y: Yes; N: No/Not Documented.

342 Poster Session

Comparative landscape of actionable somatic alterations in advanced cholangiocarcinoma from circulating tumor and tissue-based DNA profiling. *First Author: Pashtoon Murtaza Kasi, University of Iowa, Iowa City, IA*

Background: Cholangiocarcinoma (CCA) is a target-rich disease. Despite this, treatment guidelines lack recommendations for broad molecular profiling in CCA to identify potentially actionable targets. Furthermore, comparative data assessing similarities and differences in actionable ctDNA and tissue based genomic biomarkers remain limited. As such, we sought to broadly characterize the genomic alterations that are linked to targeted therapies that may facilitate a more personalized approach to therapy. **Methods:** We retrospectively analyzed NGS data obtained from 137 advanced cholangiocarcinoma patients via Tempus xT tissue biopsy assay (DNA sequencing of 648 genes in tumor and matched normal samples at 500x depth) and/or Tempus xF liquid biopsy assay (ctDNA sequencing of 105 genes in peripheral blood samples at 5,000x depth) for germline and/or somatic mutations including single nucleotide variants, specific insertion/deletions, amplifications and gene fusions. **Results:** 110 patients were tested once and 27 patients had two or more tests available. Of the 174 genomic results, 113 were tissue-based NGS results, and 61 were liquid-based NGS results. The total number of unique alterations was found to be 296. Focusing on aberrations for which there are approved therapies in the same or other tumor types or inclusion in guidelines and/or active clinical trials, we found FGFR2 fusions (6.8%), IDH1/2 (8.4%), BRAF-V600E (2.5%), HER2 (3%), MET (0.7%), BRCA1/2/ATM (2%), PIK3CA (4.7%), and ERRFI1 (0.7%). This comprises ~30% (Table). Of note, within this bucket of actionable findings, if we focus on ctDNA liquid biopsy cohort, the proportion goes up to 33.1% vs. 23.2% for tissue based genomic testing. For example, comparison of liquid to tissue, FGFR2 fusion was noted in 11.3% vs. 3.4%, BRAF-V600E in 3% vs. 1% and HER2 0% vs. 3.8%, respectively. Also, no MSI-High patients but two (1.5%) had KRAS-G12C mutation. Notable differences in the prevalence of actionable somatic mutations in solid vs. liquid results were observed (Table). **Conclusions:** These data provide an updated benchmark for guiding the development of targeted therapies in molecularly profiled CCA and support the use of both solid and liquid biopsy molecular profiling to guide therapy selection in patients with advanced cholangiocarcinoma. Additionally, liquid biopsy molecular profiling can fill the void where tissue may not be readily available. Research Sponsor: None.

Clinically relevant and actionable tissue versus liquid biopsy molecular profiling results for patients with advanced/metastatic cholangiocarcinoma.

	All	Tissue	Liquid
***FGFR2* fusions**	6.8%	3.4%	11.3%
IDH1/2	8.4%	8.1%	7.5%
BRAF-V600E	2.5%	1.0%	3.0%
HER2	3.0%	3.8%	-
MET	0.7%	1.3%	-
BRCA1/2/ATM	2.0%	2.6%	-
PIK3CA	4.7%	3.0%	8.8%
ERRFI1	0.7%	0.0%	2.5%
Total actionable	**28.8%**	**23.2%**	**33.1%**

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Radiomic signatures to predict survival in patients with advanced hepatocellular carcinoma (HCC) treated with sorafenib +/- doxorubicin: Correlative science from CALGB 80802 (Alliance). *First Author: Laurent Dercle, Department of Radiology, Columbia University Medical Center, New York-Presbyterian Hospital, New York, NY*

Background: Alliance/CALGB 80802, a randomized phase III trial, evaluated sorafenib plus doxorubicin vs. doxorubicin in pts with HCC and showed no improvement in median overall survival (OS) (HR[95CI] 1.05 [0.83-1.31]) or PFS (HR[95CI] 0.93[0.75-1.16]). In HCC surrogacy of tumor response with OS remains controversial, in part due to varying criteria used for response evaluation (e.g., RECIST1.1 and mRECIST). We evaluated the performance of several models to predict OS using pretreatment clinical and radiomic variables. **Methods:** In CALBG 80802, we segmented all measurable tumor lesions on sequential CT scans. A lesion's imaging phenotype was deciphered with 23 uncorrelated quantitative imaging features measured at baseline and week (wk) 10 (first follow-up). An OS landmark survival analysis was conducted at wk 10. Patients were randomly assigned (3:1) to training (n = 92) and validation (n = 37) sets. In a training set, 6 random forest predictive models (6 signatures) used features that best predicted OS using 3 sets of variables: radiomics only (n = 23), clinical only (n = 9), radiomics and clinical (n = 32). Two time points (baseline only or baseline + wk 10) were assessed. Each signature's output was an individualized prediction and a continuous value ranging from 0 to 1 (from most to least favorable predicted OS). The primary endpoint was to compare these models' performance to predict OS using error rate (Harrell's concordance-index) in the validation set. **Results:** Of the 6 training signatures evaluated, the one achieving the highest performance in the validation set was an 8-feature signature combining radiomics and clinical variables measured at two time points (baseline + wk 10) with an error rate of 35.6%. The variables [rank of importance] (table) selected by the signature included baseline clinical features (albumin[1], AFP[2], Child-Pugh[4]), baseline radiomics features (component 17[3], component 1[5], component 9[7], tumor volume [8]) and wk 10 radiomics features (delta tumor volume[6]). Variable delta tumor volume [6] used a more enhanced estimation of tumor burden at baseline and a delta tumor volumetric measurement; compared to RECIST1.1 measurement of percentage change in unidimensional measurement of a subset of target lesions. The four quartiles of the signature were significantly associated with OS (Log-Rank, P < 0.0001). **Conclusions:** The selected combined radiomic and clinical composite signature provided the best prediction for OS in the 80802 study patients' population. It is a suggested way forward to go beyond single anatomic measurement techniques such as RECIST or mRECIST. Research Sponsor: U.S. National Institutes of Health.

	Variables		Time points		Error rate (%)	
Signature performance	**Clinical**	**Radiomics**	**Baseline**	**Wk 10**	**Training**	**Validation**
Best	+	+	+	+	41.7	35.6
#2	+	-	+	-	45.6	41.3
#3	-	+	+	+	52.3	45.4
#4	+	+	+	-	47.3	48.3
#5	+	+	+	-	49.6	48.9
Worst	-	+	+	-	46.7	52.4

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Clinical correlation of cadherin-17 (CA17 aka CDH17) marker with advanced tumor stages and poor prognosis of cholangiocarcinoma in a retrospective cohort of 180 patients. *First Author: Bohao Zheng, Zhongshan Hospital, Shanghai, China*

Background: Aberrant expression of cadherin-17 (CA17, aka CDH17) cancer marker is often observed in major gastrointestinal (GI) cancers. In this retrospective study, we examined the CA17 tissue expression and analyzed its clinical significance in cholangiocarcinoma (CCA). **Methods:** A total of 180 patients with detailed demographic and clinical data were enrolled in this study and randomly divided into a training cohort (N = 120) and a validation cohort (N = 60). Biopsy samples (tumor and adjacent normal tissue) collected for tissue microarray were examined by immunohistochemistry using a mouse anti-CA17 monoclonal antibody (Clone 7C5). Image pro plus was applied to score the staining intensity and expression level of CA17 marker. Kaplan-Meier analysis, Cox's proportional hazards regression, and nomogram were applied to evaluate the prognostic significance of CA17. **Results:** CA17 cancer biomarker overexpression was significantly observed in CCA compared to their non-tumor counterparts (P < 0.001), and positively correlated with aggressive tumor phenotypes, like larger tumor size (P = 0.004), lymph node metastasis (P < 0.001), and advanced TNM stage (P < 0.001). Meanwhile, patients with high expression of CA17 correlated with worse postoperative overall survival (OS)(P = 0.002) and recurrence-free survival (P = 0.03). Besides, multivariate analysis identified that CA17 expression was an independent prognostic factor for cholangiocarcinoma patients (Training cohort: HR:1.716, 95% CI:1.116-2.638; P = 0.014; Validation cohort: HR: 1.811, 95%CI:1.028-3.892; P = 0.035), which indicated that the CA17 is much more efficient than serum CA19-9 (Training cohort: HR: 1.000, 95%CI: 1.000-1.001; P = 0.006; Validation cohort: HR: 1.000,95%CI:1.000-1.001; P = 0.013) in predicting the OS of CCA patients. Notably, the nomogram integrating CA17 expression had a better prognostic performance as compared with current TNM staging systems. **Conclusions:** CA17 cancer biomarker was aberrantly expressed in CCA tumor tissues, and its high expression level positively correlated with aggressive tumor phenotypes. Furthermore, CA17 was an independent adverse prognostic factor for CCA patients' survival, which may serve as a potential drug target for CCA patients. Research Sponsor: National Natural Science Foundation of China [81872352]. Shanghai top priority Clinical Medical Center and Key Discipline Construction Plan (2017ZZ02007) and the JianFeng project of Xuhui provincial commission of health and family planning (SHXH201703).

345 Poster Session

PALBI and ALBI score as a prognosis factor for liver metastasis undergoing transarterial radioembolization. *First Author: Jorge Sanchez-Garcia, Intermountain Medical Center, Murray, UT*

Background: Liver metastasis is evident in many oncological patients at the time of initial presentation. Recently, platelet-albumin-bilirubin (PALBI) score was reported to be superior to Child-Pugh classification and albumin-bilirubin (ALBI) score in terms of mortality prediction, while Model for End-Stage Liver Disease (MELD) score is the most frequent used. Trans-arterial radioembolization (TARE) is a minimally invasive therapy used to treat liver tumors. The aim of this study is to assess prognostic performance of pre-TARE liver function scores. **Methods:** We retrospectively assessed all patients with liver metastasis that underwent TARE between February 2008 and January 2020 at a single institution. Demographic characteristics; and laboratory values were collected to calculate MELD, ALBI, PALBI, within six months before TARE administration. Results are presented as proportions and median (IQR). Multivariate Cox regression analysis was performed to identify risk factors for overall survival. **Results:** A total of 90 patients were included, 46.7% were females with a median age was 61 (50-69). Colorectal (CR) metastasis was found in 45.6% of cases, neuroendocrine tumors (NET) in 27.8% and the remainder a heterogenous group of metastatic disease. In 90% of cases, TARE was used as destination therapy. The median tumor size was 5.1 (3.3-7.1) cm with 81% having multifocal lesions. The median scores were: MELD 8 (7-10), ALBI -2.77 (-3.01 to -2.56), PALBI -2.58 (-2.77 to -2.32). Other metastatic disease (OR=2.3: 95%CI 1.3-4.3; p=0.02), MELD (OR=1.1: 95%CI 1.002-1.2; p=0.04), ALBI (OR=2: 95%CI 1.2-3.3; p=0.005) and PALBI (OR=2.4: 95%CI 1.2-4.7; p=0.01) were significant in univariate Cox regression. In the multivariate Cox regression, MELD score was not statistically significant when adjusted with diagnosis and PALBI or ALBI score. As expected due to similar variables to calculate score, ALBI and PALBI score were not statistically significance when these are used in the same model (Table). **Conclusions:** To our knowledge, this is the first report of PALBI as prognostic factor in patients undergoing TARE for metastatic liver disease. Interestingly, the multivariate cox regression showed us that MELD score is not a significant score for these patients. Further non-inferiority assessment of PALBI and ALBI over MELD score should be developed. Research Sponsor: None.

Multivariate Cox Regression Models

Variable	Model 1	Model 2	Model 3	
Diagnosis (Ref NET)	1.1 (0.6-2.2); p=0.7	1.3 (0.7-2.5); p=0.3	1.1 (0.6-2.2); p=0.7	
CR	3 (1.5-5.9); p=0.001*	2.8 (1.4-5.6); p=0.004*	2.7 (1.3-5.3); p=0.005*	
Other				
	MELD score	1.1 (1-1.2); p=0.09	1.1 (1-1.2); p=0.09	NA
	ALBI score	2.6 (1.5-4.5); p=0.0009*	NA	2 (0.9-4.4); p=0.08
	PALBI score	NA	2.6 (1.3-5.2); p=0.007*	1.6 (0.6-4.1); p=0.3
	C index	0.65	0.65	0.62
	Log rank test	<0.001	0.001	0.001

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Factors influencing adjuvant treatment decision making among Chinese patients with hepatocellular carcinoma (HCC): Results of a patient survey. *First Author: Hui-Chuan Sun, Department of Liver Surgery, Zhongshan Hospital and Liver Cancer Institute, Fudan University, Shanghai, China*

Background: This study aimed to understand patient decision-making factors for post-operative adjuvant treatment after resection of hepatocellular carcinoma (HCC) in China. **Methods:** Patients who had received surgical resection of HCC in the last 2 years at 27 hospitals in China were surveyed using a questionnaire (https://pro.wenjuan.com/t/jUZFU). Feedback was collected by telephone or online. The survey covered three domains: adjuvant treatment decision making, selection of treatment regimen and the influence of recurrence risk on willingness to receive adjuvant treatment. For each domain, participants were asked to identify decision makers and to score decision-making factors from 1 (no influence) to 7 (high influence). All factors with an average score of 6 or 7 points were considered impactful, and those with scores ≤5 were not considered impactful. Descriptive statistics were used to summarize the findings. This study was approved by the ethics committee of Zhongshan hospital and patients provided informed consent. **Results:** In total, 2,220 valid responses were collected (2,183 patients from Zhongshan Hospital, 37 from 26 other hospitals); 75% of respondents were male, 60% were aged 50-70 years, and 50% had a monthly family income ≤5,000 Chinese Yuan (~$740 USD). Among respondents, 62% had received adjuvant treatment: 56% received systemic therapy (chemotherapy, tyrosine kinase inhibitors, immune therapy and traditional Chinese medicine), 27% transarterial chemoembolization (TACE) plus systemic therapy and 17% TACE alone. The majority of respondents (75%) identified physicians as the decision makers for use of adjuvant therapy and selection of treatment regimen. Of the 38% of respondents who did not receive adjuvant treatment, 90% gave 'physician recommendation' as the reason. When patients were the decision makers, factors influencing decisions to use adjuvant treatment and selection of treatment regimen, ranked from most to least influential, were efficacy (for prevention of tumor recurrence), reimbursement status, treatment side effects and cost. Patient willingness to receive adjuvant treatment was influenced by predicted risk of recurrence; among respondents with an estimated 2-year recurrence risk > 10% and > 30%, 40% and 56%, respectively, believed they should receive adjuvant therapy. **Conclusions:** A majority of patients surveyed received adjuvant therapy, the most common of which were systemic therapy and TACE. Patients who underwent resection had a strong desire to reduce postoperative recurrence by using adjuvant therapy. Physician opinion was identified as the most important factor in treatment decision making, followed by economic factors. When patients were the decision maker, the most influential factors were treatment effectiveness followed by reimbursement status. Research Sponsor: None.

347 Poster Session

Targeted therapies in cholangiocarcinoma: Assessment of US oncologist practice patterns. *First Author: Kinjal Parikh, Medscape Oncology, New York, NY*

Background: Chemotherapy is a mainstay treatment modality for patients with advanced cholangiocarcinoma (CCA). Recent developments and new approvals have led to changing paradigms, incorporating the use of targeted therapies for patients with progressive disease. Given the need for a greater understanding of the molecular alterations, varying targets, and available and emerging therapies, education is needed to assess knowledge regarding these recent advances in unresectable CCA. The goal of this activity was to increase the knowledge of self-assess the learning needs of oncologists in treating patients with unresectable CCA. **Methods:** The education included 25 multiple choice questions in a continuing medical education (CME)-certified clinical practice assessment to assess practice gaps. The questions were designed to measure knowledge, competence, confidence, and attitudes of oncologists regarding clinical evidence, role of molecular testing, and place in the treatment paradigm for targeted therapies in unresectable CCA. The self-assessment was made available online to physicians as a learning tool to gain foundational knowledge, as well as receive feedback about their performance as compared to other test-takers, to improve self-awareness of their own personal educational gaps. The activity launched 6/24/20, and data are reported through 8/31/20. **Results:** A total of 1,009 learners, including 758 physicians, participated in the activity. Of the 104 oncologists that participated, a majority practiced in the community setting, saw patients with a range of cancers, and were not confident about using targeted therapies or recognizing targets for biomarker testing. Oncologists demonstrated the following gaps related to: NGS sequencing and biomarkers: 21% do not use; 32% use upon progressive disease; 35% did not realize that not all panels detect *FGFR2* fusions; 20% do not test for biomarkers; 29% and 56% test for *IDH or FGFR*, respectively; 60% recognize the incidence of *IDH1* mutations; Clinical trial (FIGHT202 and ClarIDHy): 45% were able to identify biomarker eligibility for pemigatinib; 9% were able to identify pemigatinib OS outcomes; 30% were able to recognize most common grade 3 AE of pemigatinib; 51% recognized the PFS endpoint with ivosidenib; 34% were able to identify eligibility for ivosidenib; 55% recognized most common AEs of ivosidenib. **Conclusions:** This CME-certified clinical practice assessment identified gaps in knowledge, competence, and confidence regarding testing and use of targeted therapies and emerging data in patients with unresectable CCA. As new data emerges and the number of targets and targeted therapies expand, continued education remains important to continue to optimize patient care. Research Sponsor: Incyte Corporation.

348 Poster Session

Gender representation in authorship in later-phase systemic clinical trials in biliary tract cancer (BTC). *First Author: Mairead Geraldine McNamara, University of Manchester, Manchester, United Kingdom*

Background: The proportion of females in medicine is increasing (approx. 50% in medical school/workforce), but disparities in female authorship in oncology research publications exist; female corresponding authorship reportedly ranges from 7.2-39.1% in oncology clinical trials (Ludmir et al 2019). This study aimed to describe and assess factors associated with female first and senior authorship in later phase systemic clinical trials in BTC and to identify any changes over time. **Methods:** Embase/Medline were used to identify final primary trial publications in BTC (2000-2020) (excluding phase I (PI) (expected to move to later phase), mixed tumour site trials, reviews, editorials and trial-in-progress publications). Gender was determined by inspection of names, google search and author communication. Chi-square tests and log regression were used to assess factors associated with female first and senior authorship, including changes over time (STATA16). **Results:** Of 501 publications, 163 met inclusion criteria; 80% single-arm PII and 15% and 5% randomised PII and PIII respectively; 73% enrolled ≤50 patients. Tumour primary sites were all BTC: 86%, cholangiocarcinoma: 8%, gallbladder cancer: 6%; 80% involved chemotherapy, 13% targeted therapy and 5% localised/systemic combinations; 65% were in first-line (1L) advanced setting, 17% post 1L, 13% advanced non-specified and 5% neo-adjuvant/adjuvant. Forty-eight percent received industry funding and 65% met primary end-point. Sixty-four percent were published post ABC-02 (Valle et al 2010). Publication impact factor (IF) was ≤5 in 50% and >20 in 12%. Median number of authors in all publications was 11. Geographic location of all first and senior authors were Asia (42%/42%), Europe (29%/29%), USA (24%/22%) and other (4%/6%), respectively. Median individual trial female author representation was 25%; there were no female authors in 12% of trials. Overall, female first and senior author representation was 21% and 11%, respectively. Median position of first female author was second. In publications with IF ≤20 and >20, there were 22% and 16% female first and 13% and 0% female senior authors, respectively. The phase of trial, journal IF, industry funding, or whether met primary end-point did not impact female first or senior author representation (all P>.05). There were more female senior authors associated with "other" geographic locations (40% in 10 trials) (P=.016) vs Asia (7%), Europe (8%) and USA (14%). There were no significant changes in female first or senior author representation over time ('00-05: 21%/18%, '06-10: 27%/5%, '11-15: 15%/15%, '16-20: 22%/9%, P=.738, and P=.508 respectively). **Conclusions:** Female first and senior author representation in later phase systemic clinical trial publications in BTC is low and has not changed significantly over time. The underlying reasons for this imbalance need to be better understood and addressed. Research Sponsor: None.

TPS349 Trials in Progress Poster Session

A phase III, double-blind, randomized study of nivolumab (NIVO) and ipilimumab (IPI), nivo monotherapy or placebo plus transarterial chemoembolization (TACE) in patients with intermediate-stage hepatocellular carcinoma (HCC). *First Author: Bruno Sangro, Clinica Universidad de Navarra and CIBEREHD, Pamplona, Spain*

Background: TACE is the most widely used locoregional therapy recommended for patients with intermediate-stage HCC (Barcelona Clinic Liver Cancer stage B). Despite the significant tumor responses that can be achieved with TACE, tumors commonly recur, progress, or are refractory. Clinical trials have explored the combination of TACE with tyrosine kinase inhibitors; however, these have not reported improved outcomes. HCC possesses a unique immunosuppressive microenvironment, which makes it an attractive target for immunotherapies, particularly immune checkpoint inhibitors. Furthermore, there is evidence that locoregional interventions induce changes in the immune environment that could promote synergy with checkpoint inhibitors. Preliminary data for the combination of TACE with nivolumab indicate an acceptable safety profile and promising efficacy (Harding et al. ASCO-GI 2020). NIVO monotherapy and NIVO+IPI combination therapy are both approved in the United States for patients with HCC previously treated with sorafenib. Together, these findings support investigation of TACE plus NIVO, IPI, or NIVO+IPI to address the therapeutic needs of patients with intermediate HCC. **Methods:** CheckMate 74W is a global, double-blind, placebo-controlled, 3-arm, randomized phase III trial. Patients with tumors that exceed the Beyond Milan and Up-to-7 criteria (7 being the sum of size [in centimeters] and number of tumors), eligible for TACE, with Eastern Cooperative Oncology Group performance status of 0 to 1 are eligible for enrollment. Patients must not have received prior locoregional therapies. Approximately 765 patients will be randomized in a 1:1:1 ratio to NIVO+IPI+TACE (arm A), NIVO+IPI placebo+TACE (arm B), or NIVO placebo+IPI placebo+TACE (arm C). Primary endpoints are the time to TACE progression (TTTP), assessed by blinded independent central review, and overall survival in arm A versus arm C. Secondary endpoints are TTTP and overall survival in arm B versus arm C, event-free survival, and progression-free survival. Clinical trial registry: NCT04340193. Clinical trial information: NCT04340193. Research Sponsor: Bristol Myers Squibb.

TPS350 Trials in Progress Poster Session

A phase I study of LY3410738, a first-in-class covalent inhibitor of mutant IDH1 in cholangiocarcinoma and other advanced solid tumors. *First Author: James Michael Pauff, Sarah Cannon Research Institute, Franklin, TN*

Background: Mutations in isocitrate dehydrogenase 1 (mIDH1) are found in approximately 20-30% of patients with intrahepatic cholangiocarcinoma (CCA), and less commonly in glioma, chondrosarcoma, and other gastrointestinal malignancies. Despite documented clinical activity of mIDH1 inhibition in solid tumors, there are no approved targeted therapies for this patient population. LY3410738 is a potent, selective, and covalent inhibitor of mIDH1 R132. LY3410738 is differentiated from prior mIDH1 inhibitors by 1) its unique covalent binding mode, 2) its increased potency, and 3) its unique binding site outside of the dimer interface, which enables activity in the setting of known common second-site IDH1 mutations. **Methods:** This is an open-label, multicenter, global phase 1 study with oral LY3410738 currently enrolling patients with advanced CCA and other solid tumor types (NCT04521686). A dose escalation cohort will be followed with 4 exploratory expansion cohorts. The primary objective for dose escalation is determination of the maximum tolerated dose (MTD)/recommended phase 2 dose (RP2D). The primary objective for dose expansion is to assess the preliminary anti-tumor activity by ORR of LY3410738 when administered alone or in combination with cisplatin plus gemcitabine. Secondary objectives include evaluating safety and tolerability, pharmacokinetics, pharmacodynamics, progression free survival, and overall survival. Key inclusion criteria include any solid tumor with the presence of mIDH1 R132, ECOG performance status $\leq$1, and adequate organ function. Any prior treatment including an IDH1 inhibitor is allowed in the dose escalation cohort. Exclusion criteria include presence of active central nervous system metastases, leptomeningeal disease, and active or uncontrolled infection. CCA patients must not have had locoregional therapy within 4 weeks prior to the initial study dose, history of hepatic encephalopathy or refractory ascites, ongoing cholangitis, or mixed hepatocellular-CCA histology. Dose escalation will follow a 3+3 design and will allow patient back-fill to dose levels previously cleared for safety. Each cycle will be 28 days (4 weeks). Once the RP2D is determined, LY3410738 will be evaluated as monotherapy in expansion cohorts 1-3, and in combination with cisplatin plus gemcitabine in expansion cohort 4. Cohort 1 will enroll CCA patients with measurable disease who have received prior chemotherapy. Cohort 2 will enroll patients with advanced solid tumors except CCA who have measurable disease and received standard therapies. Cohort 3 will enroll patients with advanced solid tumors who have non-measurable disease and received standard therapies. Cohort 4 will enroll CCA patients with measurable disease who are treatment naïve for advanced disease. Clinical trial information: NCT04521686. Research Sponsor: Loxo Oncology at Lilly.

TPS351 Trials in Progress Poster Session

Phase III study of NUC-1031 + cisplatin vs gemcitabine + cisplatin for first-line treatment of patients with advanced biliary tract cancer (NuTide:121). *First Author: Jennifer J. Knox, Princess Margaret Cancer Center, University Health Network, Toronto, ON, Canada*

Background: Biliary tract cancer (BTC) carries a poor prognosis and no first-line treatments are approved. The accepted global standard of care is gemcitabine + cisplatin (GemCis). NUC-1031 is a phosphoramidate transformation of gemcitabine designed to overcome key cancer resistance mechanisms that are associated with gemcitabine. Promising efficacy has been observed with single-agent NUC-1031 in a phase I study in advanced solid tumors and in the phase Ib ABC-08 study of NUC-1031 + cisplatin for first-line treatment of advanced BTC. Of 14 patients enrolled in 2 cohorts (NUC-1031 625 mg/m^2 or 725 mg/m^2 + cisplatin 25 mg/m^2 on Days 1 and 8 of 21-day cycle), 1 had a CR and 6 had PRs, resulting in an unconfirmed ORR of 50%. This represents an approximate doubling of ORR over SoC. The combination was well-tolerated with no unexpected AEs or DLTs. The RP2D of NUC-1031 with cisplatin was 725 mg/m^2. The tolerability profile, together with encouraging efficacy, suggested NUC-1031 + cisplatin may represent a more effective therapy than GemCis for BTC and led to initiation of a global registrational study. **Methods:** NuTide:121 is a Phase III, open-label, randomized study of NUC-1031 + cisplatin vs GemCis for first-line treatment of advanced BTC. Patients $\geq$18 years with histologically- or cytologically-confirmed BTC (including cholangiocarcinoma, gallbladder, or ampullary cancer), who have had no prior systemic chemotherapy for locally advanced/metastatic disease, are eligible. A total of 828 patients are being randomized (1:1) to either 725 mg/m^2 NUC-1031 or 1000 mg/m^2 gemcitabine, both with 25 mg/m^2 cisplatin, administered on days 1 and 8 of 21-day cycles. Primary objectives are OS and ORR. Secondary objectives include PFS, safety, PK and patient-reported quality of life. In addition to the final analysis, three interim analyses, including two designed to support accelerated approval, are planned. The study has passed an initial safety analysis, with no protocol changes required. NuTide:121 is being conducted at approximately 130 sites across North America, Europe and Asia Pacific countries. Clinical trial information: NCT04163900. Research Sponsor: NuCana.

TPS352 Trials in Progress Poster Session

A phase IIb, open-label, single-arm study of zanidatamab (ZW25) monotherapy in subjects with advanced or metastatic HER2-amplified biliary tract cancers. *First Author: Shubham Pant, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Advanced biliary tract cancers (BTCs), including gallbladder cancer (GBC) and cholangiocarcinoma (CC), have a poor prognosis. Zanidatamab (ZW25) is a novel bispecific antibody that targets HER2 domains ECD2 and ECD4, resulting in increased antibody binding density and improved receptor internalization and downregulation relative to trastuzumab. In an ongoing phase I trial (ZWI-ZW25-101; NCT02892123), single-agent zanidatamab was well tolerated and showed promising anti-tumor activity across HER2-expressing solid tumors, including BTCs. These results formed the basis for a phase IIb study of zanidatamab in patients with BTC. **Methods:** Study ZWI-ZW25-203 (NCT04466891) is a global, multicenter, open-label, single-arm, phase IIb trial designed to evaluate the anti-tumor activity of zanidatamab monotherapy in patients with HER2-amplified, inoperable and advanced or metastatic BTCs, including GBC and CC. Patients must have received at least 1 prior gemcitabine-containing systemic chemotherapy regimen for advanced disease and have experienced disease progression after (or developed intolerance to) their most recent prior therapy. New or archival tumor tissue is required from all patients for HER2 amplification and protein expression testing at a central lab using in situ hybridization (ISH) and immunohistochemistry (IHC) assays. Approximately 100 patients with HER2 amplification by ISH will be enrolled. Zanidatamab 20 mg/kg will be administered intravenously every 2 weeks until one of the treatment discontinuation criteria is met. The primary endpoint of the study is the confirmed objective response rate (ORR) by independent central review per the Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1). Secondary endpoints include duration of response (DOR), proportion of patients with DOR $\geq$ 16 weeks, disease control rate, progression-free survival, overall survival, safety, quality of life, and disease-related pain. The safety and tolerability of zanidatamab will be assessed by recording the frequency and severity of adverse events, serious adverse events, and laboratory abnormalities, as well as the frequency of zanidatamab dose modifications. The study is currently open for enrollment. Clinical trial information: NCT04466891. Research Sponsor: Zymeworks, Inc. and BeiGene Ltd.

TPS353 Trials in Progress Poster Session

Perioperative chemotherapy with gemcitabine plus cisplatin followed by radical liver resection versus immediate radical liver resection alone in gallbladder carcinoma or in front of radical resection in BTC: The phase III GAIN trial. *First Author: Thorsten Oliver Goetze, University Cancer Center Frankfurt, Institut für Klinisch-Onkologische Forschung am Krankenhaus Nordwest, Frankfurt, Germany*

Background: Radical surgical resection represents the only potentially curative treatment option for Biliary Tract Cancer (BTC) and Gallbladder Carcinoma (GBC). Nevertheless, 5-year OS is only 20–40% after curatively intended resection. GBC is the fifth most common neoplasm of the digestive tract and even the most frequent cancer of the biliary system. The majority of gallbladder carcinoma cases are discovered incidentally by the pathologist after cholecystectomy for a benign indication, so called incidental gallbladder carcinomas. For improving curative rates in BTC and GBC, early systemic therapy combined with radical resection seems to be a promising approach. The earliest moment to apply chemotherapy would be in front of radical surgery. Encouraging results of neoadjuvant/perioperative concepts in other malignancies provide an additional rationale to use this treatment in the early phase management of GBC and intrahepatic as well extrahepatic cholangiocarcinoma, especially because data regarding pure adjuvant chemotherapy in BTC`s are currently conflicting. **Methods:** GAIN is a multicenter, randomized, controlled, open-label phase III trial, including pts with GBCs in front of radical liver resection and pts with resectable/borderline resectable intra- and extrahepatic cholangiocarcinomas (ICC/ECC). Pts. are randomized to either neoadjuvant systemic chemotherapy (Gemcitabine + Cisplatin 3 cycles pre- and post-surgery) followed by radical surgery or to direct surgery without neoadjuvant treatment. Primary endpoint is OS; secondary endpoints are PFS, R0-resection rate, toxicity, perioperative morbidity, mortality and QoL. A total of N = 333 patients with GBC or BTC will be included. Recruitment has just started; first patient in was on December 6th, 2019. Clinical trial information: NCT03673072. Research Sponsor: DFG (Deutsche Forschungsgesellschaft).

TPS354 Trials in Progress Poster Session

Phase II trial of the PARP inhibitor, niraparib, in BRCA1-Associated Protein 1 (BAP1) and other DNA damage response (DDR) pathway deficient neoplasms including cholangiocarcinoma. *First Author: Thomas J. George, University of Florida Health Cancer Center, Gainesville, FL*

Background: BRCA1-Associated Protein 1 (BAP1) is a critical regulator of the cell cycle, cellular differentiation, cell death, and DNA damage response. It also acts as a tumor suppressor. Preclinical models demonstrate significant synthetic lethality in BAP1 mutant cell lines and patient xenografts when treated with PARP inhibitors, independent of underlying BRCA status, suggesting this mutation confers a BRCA-like phenotype. BAP1 is mutated, leading to a loss of functional protein, in up to 30% of cholangiocarcinomas as well as several other solid tumors. **Methods:** This phase 2, open-label, single arm multicenter study aims to exploit the concept of synthetic lethality with the use of the PARP inhibitor niraparib in pts with metastatic relapsed or refractory solid tumors. Eligible pts with measurable metastatic and incurable solid tumors are assigned to one of two cohorts: Cohort A (histology-specific): tumors harboring suspected BAP1 mutations including cholangiocarcinoma, uveal melanoma, mesothelioma or clear cell renal cell carcinoma with tissue available for BAP1 mutational assessment via NGS or Cohort B (histology-agnostic): tumors with known DNA damage response (DDR) mutations (Table) confirmed by CLIA-approved NGS. Other key eligibility criteria include age ≥18 years, adequate cardiac, renal, hepatic function and Eastern Cooperative Oncology Group performance status of 0 to 1. Pts with known BRCA1 or BRCA2 mutations or prior PARPi exposure are excluded. Pts receive niraparib 200-300mg daily (depending on weight and/or platelet count) continuously. Primary endpoint is objective response rate with secondary endpoints of PFS, OS, toxicity and exploratory biomarker determinations. Radiographic response by RECIST criteria is measured every 8 weeks while on treatment. Cohort A has fully enrolled. Cohort B enrollment continues to a maximum of 47 total evaluable subjects with expansion cohorts allowable for histologic or molecular subtypes meeting pre-specified responses. NCT03207347 Clinical trial information: NCT03207347. Research Sponsor: GSK/Tesaro., University of Florida Health Cancer Center.

DNA Damage Response Genes with Mutations Eligible for Cohort B

ARID1A	**ATM**	**ATR**	**BACH1 (BRIP1)**	**BAP1**	**BARD1**
BLM	CHEK1	CHEK2	CDK2	CDK4	ERCC
FAM175A	FEN1	IDH1	IDH2	MRE11A	NBN (NBS1)
PALB2	POLD1	PRKDC (DNA-PK)	PTEN	RAD50	RAD51
RAD52	RAD54	RPA1	SLX4	WRN	XRCC

TPS355 Trials in Progress Poster Session

Trial-in-progress: A pilot study of combined immune checkpoint inhibition in combination with ablative therapies in subjects with hepatocellular carcinoma (HCC). *First Author: Hailey Kathryn Carroll, Mater Misercordiae University Hospital, Dublin, Ireland*

Background: Locoregional therapies for hepatocellular carcinoma, such as transcatheter arterial chemoembolization (TACE) or ablation, can induce a peripheral anti-tumor immune response. This may be amplified by immune checkpoint inhibitors (ICI). Early and higher anti-CTLA4 dosing could potentially lead to better priming and a stronger immune response. Recent data has suggested that early (day 1 only), increased doses of anti-CTLA4 therapy, was associated with encouraging clinical activity and a tolerable safety profile. This study will evaluate dual immune checkpoint, CTLA4 (tremelimumab, day 1-only dosing) and PD-L1 (durvalumab) blockade in combination with TACE in patients with advanced HCC. Intensive peripheral immune-monitoring and longitudinal on-treatment tumor biopsies will focus on the role of the innate immune system, particularly Natural Killer cells, in anti-tumor responses. **Methods:** Patients with HCC (Childs Pugh A/B7; Barcelona Clinic Liver Cancer Stage B/C; ECOG 0/1; sorafenib-naïve or experienced) are being enrolled in a pilot study (Study Number UCDCRC/19/01) of tremelimumab at 2 dose levels (DL1 and DL2) in combination with durvalumab and TACE until disease progression (per irRECIST). DL1: tremelimumab (75mg q28 days for 4 doses) and durvalumab (1500mg q28 days). DL2: tremelimumab (300mg in a single dose on day 1) and durvalumab (1500mg q28 days). Subtotal TACE will be performed during study week 6 with the dose-limiting toxicity (DLT) evaluation period encompassing the first 8 weeks of the study. Primary endpoint is 6-month progression-free survival with secondary efficacy endpoints being safety, tolerability and overall survival. Exploratory objectives will evaluate changes in immune parameters in the tumor and peripheral blood of patients undergoing anti-CTLA4 therapy pre- and post-RFA or TACE. A major focus will be on the role of the innate immune system, particularly Natural Killer cells, in anti-tumor responses. Patients will be enrolled and treated at St Vincent's University Hospital in Dublin, Ireland. This study is currently open and actively recruiting. Clinical trial information: EudraCT Number 2019-002767-98. Research Sponsor: AstraZeneca.

TPS356 Trials in Progress Poster Session

A phase II study of infigratinib in previously treated advanced/metastatic cholangiocarcinoma with *FGFR* gene fusions/alterations. *First Author: Milind M. Javle, MD Anderson Cancer Center, Houston, TX*

Background: The FGFR family plays an important role in cholangiocarcinoma, with *FGFR2* gene fusions detected in about 15% of patients with cholangiocarcinoma. Infigratinib is an FGFR1–3-selective oral tyrosine kinase inhibitor under evaluation in multiple indications including front-line and pretreated cholangiocarcinoma. CBGJ398X2204 is an ongoing phase II study evaluating the efficacy of single-agent infigratinib in patients with advanced or metastatic cholangiocarcinoma with *FGFR* genetic alterations who have received prior gemcitabine. **Methods:** Study CBGJ398X2204 consists of 3 cohorts and patients in all cohorts receive oral infigratinib once daily for 21 days of a 28-day treatment cycle. Treatment will continue until progressive disease, intolerance, withdrawal of consent, or death. Cohort 1 includes patients with *FGFR2* gene fusions or translocations. Cohort 2 includes patients with *FGFR* genetic alterations other than *FGFR2* gene fusions (patients in both Cohorts 1 and 2 must not have received any prior FGFR inhibitors). Cohort 3 includes patients with *FGFR2* gene fusions who have received prior treatment with a selective FGFR inhibitor other than infigratinib. The primary endpoint is objective response rate (ORR, RECIST v1.1 per central review). Secondary endpoints include overall survival and overall response rate (per investigator). Safety, pharmacokinetics, and exploratory genetic alterations/biomarkers will also be measured. The study was initiated in 2014 and has a planned enrollment of up to 160 patients across all 3 cohorts (120 in Cohort 1, 20 in Cohort 2, and 20 in Cohort 3). Cohort 1 has completed enrollment and findings from this Cohort are the focus of a separate abstract submitted to the meeting. Results are not currently available from Cohorts 2 and 3 (trial in progress). Clinical trial information: NCT02150967. Research Sponsor: QED Therapeutics Inc.

TPS357 Trials in Progress Poster Session

A phase I/II trial to evaluate cabozantinib in patients with advanced hepatocellular carcinoma with Child-Pugh class B cirrhosis after first-line therapy. *First Author: Thomas Enzler, University of Michigan Medicine, Ann Arbor, MI*

Background: Hepatocellular carcinoma (HCC) is the 4th leading cause of cancer related death worldwide. HCC typically develops in patients with cirrhosis and has a 5-year survival estimate of 20%. Only patients with early stage disease may be eligible for a curative approach using local treatment and/or transplant. The majority of patient present with advanced HCC and will require systemic treatment for disease control. Several systemic therapies are FDA-approved for the treatment of HCC; however, they are only approved for patients with Child-Pugh class A cirrhosis. There are limited data and no approved second-line therapy for HCC with more advanced cirrhosis, including Child-Pugh class B, which represents a significant proportion of patients. The aim of this trial is to determine the safety and efficacy of cabozantinib, a multikinase inhibitor, in patients with HCC with Child-Pugh class B cirrhosis. **Methods:** This investigator-initiated, phase I/II study is enrolling 32 patients with advanced HCC, Child-Pugh B7 or B8, who have previously received first-line systemic treatment. Patients receive cabozantinib at one of 3 dose levels (20 mg, 40 mg, and 60 mg) with a starting dose level of 40 mg to evaluate the safety profile and obtain the recommended phase 2 dose (RP2D). The primary endpoint is assessment of dose-limiting toxicity with a null hypothesis greater than 35%. Secondary endpoints include ORR per RECIST v1.1, PFS, OS, and PK profile. Exploratory endpoints include whole exome/RNAseq analysis (including MET, VEGF, AXL, and immune signature), spatial profiling of immune markers by multiplex immunofluorescence, and specimen banking (tissue, blood and imaging). The trial design is based on the Time-To-Event modification of the Continual Reassessment Method (TiTE-CRM), which allows for continued monitoring of toxicity as a function of a dose-over-time, and is flexible with regard to the number of patients treated at a certain dose. The trial is open at University of Michigan as lead and coordinating site, and due to open at 3 additional high-volume centers. Clinical trial information: 04497038. Research Sponsor: Exelixis, Inc.

TPS358 Trials in Progress Poster Session

A phase II study of atezolizumab (ATEZO) and bevacizumab (Bev) in combination with Y90 TARE in patients (Pts) with hepatocellular carcinoma (HCC). *First Author: Aiwu Ruth He, Georgetown University Lombardi Comprehensive Cancer Center, Washington, DC*

Background: The anti–PD-L1 antibody ATEZO prevents PD-L1 from interacting with PD-1 and B7.1, thus reinvigorating antitumor T cell activity. Anti-VEGF BEV can increase dendritic cell maturation, enhance T cell infiltration, and reduce myeloid-derived suppressor cells and regulatory T-cells in tumors. This combination has been FDA approved for first-line treatment of advanced HCC based on the IMbrave 150 study. On the other hand, locoregional radiotherapy (e.g., Y90 TARE) enhances the diversity of the intratumoral T cell receptor repertoire. It is the standard of care for pts with intermediate-stage HCC (iHCC). Based on preclinical and clinical data, we hypothesize that the combination of Y90 TARE, BEV, and ATEZO induces synergistic tumor-killing. **Methods:** This is an open-label, multicenter, randomized phase II study of Y90 TARE and BEV plus ATEZO compared with Y90 TARE alone in pts with unresectable IHCC. The primary study objective is to assess and compare the progression-free survival (PFS) (per mRECIST 1.1) of pts in each arm. The main secondary objective is to determine the safety and tolerability (CTCAE v5) of TARE combined with ATEZO and BEV in pts with HCC. Exploratory objectives are to assess the role of the immunoscore and PD-L1 expression levels in the prediction of improved clinical outcome in pts receiving Y-90 TARE and BEV plus ATEZO; the composition of tumor-infiltrating immune cell subtypes in predicting response to a chosen therapy; how Y90 therapy affects the proportion of antigen-presenting cells in the tumor; and symptoms experienced by pts receiving TARE and BEV plus ATEZO treatment, using patient-reported outcomes. Eligible pts have either HCC that is not amenable to surgical resection, confirmed by pathology review, or at least BCLC stage B HCC outside of downstaging criteria. Other standard eligibility criteria apply. Pts must have a pretreatment liver biopsy taken and then be randomized 1:1 to TARE (Arm A) or TARE followed by ATEZO and BEV (Arm B). Pts will have TARE mapping during week (wk) 1 and TARE treatment during wk 2. In Arm B, pts will start BEV plus ATEZO 4 wks ($\pm$1 wk) after TARE treatment. Pts will have abdominal MRI or CT scans every 12 weeks, CT scans of the chest every 24 wks, and a second tumor biopsy at 4 wks. Disease progression will be captured by both RECIST 1.1 and mRECIST. We plan to assess the safety of TARE with BEV and ATEZO in the first 10 pts randomized to Arm B for two cycles. If there are no grade $\geq$ 3 unexpected toxicities possibly, probably or definitely related to combined TARE plus BEV plus ATEZO, the study will continue to accrue 128 pts in total. Pts will continue study treatment (Arm B) for a total of 24 months from initiation of TARE or until intolerable toxicity or disease progression occur, whichever is earlier. Enrollment began in September 2020. Clinical trial information: NCT04541173. Research Sponsor: Roche/Genentech, Institutional funding.

TPS359 Trials in Progress Poster Session

Trial in progress: A feasibility study of multi-platform profiling using biospecimens from patients with resected biliary tract cancer. *First Author: Adam Diehl, University of Washington School of Medicine, HEMONC-Hematology/Medical Oncology, Seattle, WA*

Background: Biliary tract cancers (BTC) are rare malignancies with a high recurrence rate after resection of localized disease. FDA-approved systemic therapies for advanced disease are limited to combination chemotherapy and FGFR inhibitors for FGFR2-altered BTC. The tools of personalized medicine may guide management and expand treatment options for this disease. In multiple tumor types, circulating tumor DNA (ctDNA) has shown significant predictive power for recurrence after resection, but its utility has not yet been established in BTC. Organoid drug sensitivity screening may also inform and expand treatment options, particularly for patients without targetable mutations on next generation sequencing (NGS). Prospective concordance between organoid drug sensitivity and *in vivo* clinical responses to a given drug is needed to establish the value of this testing in BTC. We designed a clinical trial to determine the feasibility and physician-assessed utility of multi-platform profiling of resected BTC. **Methods:** This is an observational, non-randomized feasibility study to assess the ability to obtain NGS, ctDNA monitoring, and organoid drug sensitivity screening on patients with resected localized BTC. Secondary endpoints include physician-adjudicated utility of the profiling results for patient management, prospective concordance of organoid drug sensitivity with *in vivo* drug activity, and value of ctDNA in prediction of recurrence or response to therapy. Key eligibility criteria include a biopsy or clinical presentation consistent with BTC (excluding mixed HCC-cholangiocarcinoma), surgical candidacy for resection of measurable disease, and no prior targeted or investigational therapies. ctDNA is collected pre- and post-operatively, during adjuvant chemotherapy, during surveillance for up to 5 years and during systemic therapy for recurrent disease. Physician surveys are conducted before and after receipt of profiling results and then at time points where a change in management would be considered. Enrollment began in July 2020 with 5 of a planned 20 patients enrolled at the time of submission. Clinical trial information: NCT04561453. Research Sponsor: Jacob Green Charitable Foundation.

360 Oral Abstract Session

A phase II/III randomized double-blind study of octreotide acetate LAR with axitinib versus octreotide acetate LAR with placebo in patients with advanced G1-G2 NETs of non-pancreatic origin (AXINET trial-GETNE-1107). *First Author: Rocio Garcia-Carbonero, Hospital Universitario 12 de Octubre, Imas12, CNIO, UCM, Madrid, Spain*

Background: Angiogenesis plays an important role in NET development and progression. Axitinib is a potent and selective VEGFR-1,2,3 inhibitor, with proven activity against several vascular-dependent solid tumors. The aim of this randomized, double-blind phase II/III study was to assess the efficacy of axitinib in patients with advanced G1-2 extra-pancreatic NETs. **Methods:** Eligible pts were randomized (1:1) to receive octreotide LAR (30 mg IM q4w) with axitinib (5 mg BID) or placebo BID until disease progression or unacceptable toxicity. Pteswere stratified by time from diagnosis to study entry (> or < 12m), primary tumor site (GI tract vs non-GI) and Ki-67 index (< 5% vs > 5%). Prior therapy with SSA, IFN and up to 2 lines of systemic treatment was allowed, but not prior VEGF- or VEGFR-targeted drugs. Clinical and/or radiological disease progression within 12 months prior to study entry was required. The primary endpoint was progression-free survival (PFS). Secondary endpoints included overall survival (OS), time to progression, overall response rate (ORR), duration of response, biochemical response and safety. **Results:** 256 pts were randomized (106 in the Phase II part, and 150 additional pts in the Phase III part), 126 to axitinib and 130 to placebo. The main characteristics of the study population were: median age 61 years (range: 21-85), 52% male, PS 0-1 (64-35%), G1-2 (29%-71%), primary tumor site GI (40%)-Lung (17%)-Other (32%). Prior therapies included: SSA (46%), everolimus (13%), chemotherapy (13%), TACE (5%) and PRRT (2%). ORR was significantly higher in axitinib- vs placebo-treated patients (17.5% vs 3.8%, p = 0.0004). PFS per investigator assessment also favored axitinib vs placebo-treated patients, although the difference did not reach statistical significance (median PFS 17.2 vs 12.3 months, respectively, HR 0.816, p = 0.169). Grade 3-4 treatment-related AEs occurred more frequently in the axitinib vs placebo arm (52% vs 13.8%), and included hypertension (21% vs 6 %), cardiac disorders (3.2% vs 0.7%), diarrhoea (13% vs 1.5 %), asthenia (9% vs 3%) and nausea&vomiting (2% vs 0.7%). There were 3 treatment-related deaths, 1 in the axitinib arm (cardiac failure) and 2 in the placebo arm (myocardial infarction and hepatorenal syndrome). **Conclusions:** Although the study failed to demonstrate a significant PFS benefit per investigator assessment, axitinib in combination with octreotide LAR demonstrated activity and had a tolerable safety profile in patients with advanced G1-2 extra-pancreatic NETs. Data base cleaning and central blinded radiological PFS assessment are currently ongoing. Clinical trial information: NCT01744249. Research Sponsor: Pfizer.

361 Poster Session

Discordance between central versus local response assessments in neuroendocrine tumor (NET) patients (pts) enrolled in A021202. *First Author: Susan Michelle Geyer, Mayo Clinic, Rochester, MN*

Background: Assessment of tumor response in extrapancreatic NETs with metastases can be very challenging. Previous studies suggest a high degree of discordance between local and central imaging reviews, which has implications for clinical practice and trial design. **Methods:** Serial images archived from a randomized phase II trial (A021202) of pazopanib vs placebo in progressive non-pancreatic NETs were evaluated by central review, with real-time review conducted at the time of locally interpreted progressive disease (PD). The primary endpoint of the trial was progression-free survival (PFS) by central review. Discordances between central (Alliance Imaging Core Laboratory) and local (investigator-reported) reviews were assessed. Scan-level and pt-level results across both treatment arms were evaluated. Kappa tests were used to test concordance based on source of review. **Results:** 151 pts had a total of 724 scans with response adjudication by both local and central RECIST review. Discordance was observed in both directions. Overall, 20% of scans (143/724) had discordant classifications. The most common discordances were: stable disease (SD) on local vs. PD on central review (82/143=57%), and PD on local vs. SD on central review (32/143=22%). On a pt level, 78 of 151 pts (52%) had discordant reviews; 8 had >1 type of discordance. Overall, 30% of pts (N=45) had a determination of PD on central review, but SD or better on local review, potentially resulting in excessive exposure to therapy. In contrast, 20% (N=30) were classified as PD on local read but SD or better on real-time central review (which did not necessarily translate into an abbreviated course of treatment). Cohen's kappa statistics revealed only moderate concordance between local and central reviewers both at the scan (K=0.48, 95% CI: 0.42 – 0.55) and pt (K=0.41, 95% CI: 0.32 – 0.5) levels, with no significant influence by treatment arm, primary tumor site, tumor functionality, histology, differentiation or primary disease spread. **Conclusions:** Discordance was observed in both directions, where 30% of pts were potentially kept on study drug too long (based on central read), and 20% would have been taken off study treatment early for local PD were it not for real-time central review. Although this bidirectional discordance did not affect the overall findings of the PFS outcome between arms in the trial, these analyses highlight the high prevalence of discordance, the potential to negatively influence treatment duration in both directions, and the need for more straightforward methods of assessing treatment response in carcinoid. Support: U10CA180821, U10CA180882, U24CA196171; NETRF Investigator Award; https://acknowledgments.alliancefound.org Clinical trial information: NCT01841736. Research Sponsor: U.S. National Institutes of Health.

362 Poster Session

Radiographic response of desmoplastic mesenteric lesions to peptide receptor radionuclide therapy (PRRT). *First Author: Eleonora Pelle, Moffitt Cancer Center, Tampa, FL*

Background: ^{177}Lu-dotatate PRRT is indicated in well-differentiated, SSTR+ small bowel NETs. These tumors often metastasize to mesenteric lymph nodes and produce a desmoplastic reaction, consisting of tumor cells mixed with fibrotic tissue. We hypothesized that in patients treated with ^{177}Lu-dotatate, mesenteric tumors would remain stable even as liver tumor size changes were observed. **Methods:** We retrospectively reviewed the records of all patients treated with ^{177}Lu-dotatate between 4/2018 and 12/2019. Among patients with desmoplastic mesenteric tumors and liver metastases, we evaluated changes in tumor size of mesenteric and liver lesions based on pre and post-treatment radiology reports. Due to the infrequency of objective radiographic response (ORR), any reported changes in tumor size were considered significant. Scans were subsequently reviewed by a radiologist to confirm findings. **Results:** 21 patients met the inclusion criteria: 9 had evidence of shrinkage of liver lesion(s), 1 report described mild progression of liver lesions, 7 described stable hepatic disease and 4 described mixed hepatic progression/response. 2 of the patients with hepatic tumor shrinkage met criteria for PR by RECIST 1.1. Desmoplastic mesenteric lesions remained unchanged in size, regardless of the changes detected on liver lesions. **Conclusions:** ^{177}Lu-dotatate does not impact desmoplastic mesenteric tumors typically associated with midgut NETs. Patients whose disease is confined to desmoplastic mesenteric lesions are unlikely to respond radiographically to PRRT. Moreover, the inclusion of desmoplastic mesenteric lesions as target lesions in RECIST measurements increases rates of disease stability versus response or progression. Research Sponsor: None.

363 Poster Session

A clinical score (CS) for patients with well-differentiated neuroendocrine tumors (WD NETs) under consideration for peptide receptor radionuclide therapy (PRRT) with Lu 177-dotatate. *First Author: Satya Das, Vanderbilt University Medical Center, Nashville, TN*

Background: Despite the benefit of PRRT for patients with WD NETs, questions remain regarding sequencing and optimal patient selection for the treatment. We developed a CS at Vanderbilt Ingram Cancer Center (VICC) that we hoped would predict outcomes for patients with WD NETs receiving PRRT. **Methods:** Patients with progressive WD NETs (N = 146) under consideration for PRRT with Lu 177-dotatate between 3/1/2016-3/17/2020 at VICC (N = 122) and Rush Medical Center (RMC) (N = 24) were scored. The CS included 5 categories: available non-PRRT treatments for tumor type, prior systemic treatments, patient symptoms, tumor burden in critical organs and peritoneal carcinomatosis presence. All categories were scored from 0-2 except the peritoneal carcinomatosis category which was scored from 0-1; scoring criteria were determined by the VICC NET tumor board. All patients at VICC were prospectively scored, while patients from RMC were scored retrospectively with the investigator blinded to patient outcomes. The primary outcome, progression-free survival (PFS) was estimated by the Kaplan-Meier method; a Cox proportional-hazards model adjusting primary tumor site, tumor grade and number of PRRT doses administered (none, 1-2 doses or 3-4 doses) was used to analyze effect of CS. **Results:** Median patient age was 62.7 while median CS was 5 (range 1-8); the most common primary tumor sites were small intestinal (N = 81) and pancreatic (N = 37). A total of 101 patients and 31 patients received 3-4 doses and no doses of PRRT, respectively. On multivariable analysis, in patients treated with 3-4 doses of PRRT, for each 2-point increase in CS, the estimated hazard ratio (HR) for PFS was 3.26 (95% confidence interval (CI) 2.05-5.19). On multivariable analysis, in patients who received no doses of PRRT, for each 2-point increase in CS, the estimated HR for PFS was 1.37 (95% CI .78-2.41). **Conclusions:** Among patients treated with 3-4 doses PRRT, those with lower CS had better PFS with the treatment compared to patients with higher CS. This PFS difference, based upon CS, was not observed in patients who did not receive PRRT, suggesting the predictive utility of the CS for patients with WD NETs receiving PRRT with Lu 177-dotatate. Though the CS needs to be validated, it is the first of its kind reported. Research Sponsor: U.S. National Institutes of Health.

364 Poster Session

Real-world efficacy and safety of peptide receptor radionuclide therapy (PRRT) in gastroenteropancreatic neuroendocrine tumors (GEP-NETs). *First Author: Estephany Abou Jokh Casas, Nuclear Medicine Deparment-Hospital Clinico Universitario de Santiago de Compostela, Santiago De Compostela, Spain*

Background: PRRT with ^{177}Lu-Dotatate (Lutathera) is a radiolabeled somatostatin analog indicated treatment of somatostatin receptor (STTR) positive GEP-NETs. The study aims to establish the efficacy and safety of PRRT in GEP-NETs in a real-world setting. **Methods:** We conducted an observational, retrospective, multicentric study of 40 patients with GEP-NET treated with PRRT belonging to GGNET (Galician Research Group on Neuroendocrine Tumors) network at Nuclear Medicine Department of Santiago de Compostela University Hospital (Spain). Patients characteristics, overall survival (OS), progression-free survival (PFS), overall response rate (ORR) and toxicity data were retrospectively collected and analyzed. **Results:** Data from 40 patients (pts) treated between 2016 and 2020 were recorded in this study. Median age was 63.5 years (range 41-85) and 55% were male. The baseline ECOG PS 0/1/2 was 15 (37.5%)/16 (40%)/9 (22.5%). Tumor location was intestinal 26 pts (65%), pancreas in 11 pts (27.5%) and unknown origin in 3 pts (7.5%). 25 pts (62.5%) were none functioning. Tumor grade G1/G2/G3 were 17 pts (42.5%)/ 20 pts (50%)/ 3 pts (7.5%), and Ki 67 $<$ 2/3-20/ $>$ 20%/unknown was 11 pts (27.5%)/ 21 pts (52.5%)/ 3 pts (7.5%)/ 5 pts (12.5%), respectively. The most frequent site of metastasis was liver in 32 pts (80%), lymph nodes in 19 pts (47.5%), peritoneum 11 pts (27.5%) and bone 10 pts (25%). Surgery: 22 pts (55%) primary tumor surgery and 8 pts (20%) metastasectomy. Previous systemic treatments included somatostatin analogs (SSA) in 40 pts (100%), everolimus in 26 pts (65%) and sunitnib in 11 pts (27.5%), others 7 pts (17.5%). 34 pts (85%) completed 4 cycles of treatment (6 pts (15%) non-complete due to premature death). 35 pts were evaluable for early response (after 2 cycles of treatment). Early ORR and DCR were 2.8% and 74.2%, respectively. 26 pts were evaluable after finishing treatment (6 pts premature death and 8 pending evaluation). ORR and DCR were 19.2% and 92.3%. With a median follow up of 21 months, 14 pts (35%) had died. Median OS was not reached (NR) and median PFS was 27.2 m (95% CI 16.0-38.4m). Tumor grade G1-2 ($p < 0.001$), Ki 67 $<$20% ($p = 0.002$), primary tumor surgery ($p = 0.039$) and metastasectomy ($p = 0.030$) were associated with prolonged PFS. Mild adverse events were most frequent after the 1o doses in 27.5% patients, and medium-term toxicity was present in 25.6%, mainly hematological, G1-G2 25.6%, and G3 5%. **Conclusions:** ^{177}Lu-Dotatate is a safe and effective treatment for those patients diagnosed with metastatic GEP-NET and positive somatostatin receptors, with an excellent clinical and radiological response. Furthermore, we have identified some predictive factors to OS that should be taken into consideration. Research Sponsor: None.

365 Poster Session

Cost of treatment change among patients with neuroendocrine tumors (NET) treated originally with somatostatin analogs. *First Author: Bernard Tawfik, University of New Mexico Comprehensive Cancer Center, Albuquerque, NM*

Background: Understanding the economic implications of changes in treatment among patients with NET will be important as treatment sequencing continues to evolve. This study describes treatment characteristics and healthcare costs prior to and following treatment change from somatostatin analog (SSA) monotherapy to another therapy among a privately-insured NET patient population in the U.S. **Methods:** Patients with newly diagnosed NET and treated with SSA monotherapy were extracted from IBM MarketScan claims databases in 1/1/2014-3/31/2019. NET treatment change was captured ≥30 days after SSA start date (earliest new treatment = index date). Healthcare costs (reimbursed amount in 2019 dollars) were reported for 1, 3, and 6 months pre- and post-index intervals. **Results:** A total of 1,122 NET patients with SSA monotherapy were identified; 305 had further treatment changes (mean age: 58 years; female: 52%; metastatic disease at NET diagnosis: 49%). The majority of patients started on octreotide (81%) vs lanreotide (19%). Common treatment changes included alternate SSA (38%), targeted therapy (everolimus or sunitinib) (30%) or chemotherapy (23%). Fewer than 10% of patients were treated with PRRT ^{177}Lu-dotatate or telotristat and 1% with a combination. Total healthcare cost increased from $12,376 to $25,647 (mean difference = $13,272 ±$24,189, $p<0.001$) for 1 month before/after treatment change, from $36,395 to $59,324 ($22,929 ±$41,764, $p<0.001$) for 3 months before/after, and from $66,786 to $109,224 ($42,438 ±$98,875, $p<0.001$) for 6 months before/after. Patients changing to targeted therapy had the largest 1 month interval cost increase ($19,677 ±$19,023, $p<0.001$) compared with patients changing to alternate SSA ($10,240 ±$14,112, $p<0.001$) and to chemotherapy ($4,057 ±$20,566, $p=0.155$). The differences were driven by increases in outpatient services and pharmacy prescriptions. **Conclusions:** The setting of rising costs after treatment change from SSA indicates treatment costs as the key driver, rather than NET disease severity. Future studies should investigate the clinical effectiveness of switching from SSA relative to the economic burden imposed by treatment change. Research Sponsor: Ipsen Biopharmaceuticals.

366 Poster Session

Temozolomide and capecitabine (CAPTEM) is effective in metastatic well-differentiated gastrointestinal neuroendocrine tumors. *First Author: İzzet Dogan, Istanbul University, Institute of Oncology, Medical Oncology, Istanbul, Turkey*

Background: The study aimed to evaluate patients' outcomes and prognosis with metastatic gastrointestinal neuroendocrine tumors (mgNET) who treated temozolomide and capecitabine (CAPTEM). **Methods:** The data of forty-three patients were retrospectively evaluated. Clinicopathological features and treatment approaches were recorded. Kaplan-Meier analysis was used for overall survival (OS) and progression-free survival (PFS). Prognostic factors were assessed with Cox-regression analysis. **Results:** Median age was 59 (27-85) years. The number of male and female patients was 23 (%53.5) and 20 (% 46.5), respectively. Pancreas (%51.2) was the most common site of the tumor. The number of patients with well- and poorly-differentiated mgNET was 38 (% 88.4) and 5 (%11.6), respectively. The most common metastatic sites were liver (%62.8), lymph node (%58.1), and bone (%18.6). Eleven (%25.6) of the patients previously had undergone surgery, and some patients received radiotherapy (%9.5), chemotherapy (%19), and nuclear therapy (%9.3). Also, patients received octreotide (%86) or lanreotide (%14) with CAPTEM. In patients with well-differentiated mgNET, median PFS was 17.4 months, and disease control ratio %79.4 (%3-complete response, %38.2-partial response, and %38.2-stable response). No response observed in patients with poorly differianted mgNET, and the median PFS was calculated as 4.5 months. Grade 1-2 toxicity was observed in 34 (%79.1) of the patients, and grade 3-4 toxicity in 8 (%18.6). Four (%9.5) patients discontinued therapy for the toxicity. The most common toxicities were anemia (%37.2), thrombocytopenia (%25.6), and fatigue (%16.3). At a median follow-up of 33.8 (2.9-172.73) months, the ratio of five-years OS was %61. In multivariate analysis; gender (p=0.008), age (p=0.007), and Ki-67 levels (p=0.011) were a statistically significant for OS. However, the site of the tumor (p=0.186), number of metastatic sites (p=0.255), and type of somatostatin receptor ligand (p=0.903) were not. **Conclusions:** In the study, we showed that CAPTEM + somatostatin receptor ligands (octreotide or lanreotide) were effective and well-tolerated in patients with well-differentiated mgNET. But, it was not effective in patients with poorly-differentiated mgNET. Male gender, aged over 60 years, and tumor with a high level of Ki-67 were negative prognostic factors. Research Sponsor: None.

367 Poster Session

Tumor burden in serotonin secreting pancreatic neuroendocrine tumors after initiating telotristat ethyl. *First Author: Susan Giacalone, TerSera Therapeutics USA, Deerfield, IL*

Background: Pancreatic neuroendocrine tumors (pNETs) characterized by high serotonin levels and carcinoid syndrome (CS) are rare. We evaluated tumor burden in a subgroup of patients with pNETS from the real-world TELEACE study before and after initiating telotristat ethyl (TE) in US clinical practice. **Methods:** Detailed methods of the TELEACE study have been reported previously. This was a retrospective, single arm, pre-post physician panel-based chart review of patients who received TE for at least 6 months. Descriptive statistics analyzed demographic, clinical, laboratory and radiological data extracted from medical charts of TELEACE patients with pNETS. **Results:** Fifty-two patients with pNETS initiating TE were eligible for this analysis. The average age at the time of TE initiation was 60+10.4 years; 64% were males. The majority of patients had well-differentiated (60%) tumors and low-grade (54%) tumor status. Patients received TE for an average of 11.5+7.84 months, and 21% were still receiving TE at the time of data extraction. Diarrhea and flushing were the most common CS symptoms recorded at the time of TE initiation. Urinary 5-HIAA levels were reported for 9 patients before and for 2 patients after TE initiation. Mean (median) 5-HIAA levels before and after TE initiation were 693 (211) and 22 (22) μmol/24h, respectively. Significant mean reduction in tumor size of 0.67 cm after TE initiation (P = 0.017) was observed. **Conclusions:** This subgroup analysis of the TELEACE study population showed that the addition of TE to somatostatin analog treatment may positively impact tumor burden for patients with functional pNETs. Research Sponsor: Lexicon Pharmaceuticals (now TerSera Therapeutics USA).

368 Poster Session

Treatment response and clinical outcomes of well-differentiated high-grade neuroendocrine tumors to 177Lu-DOTATATE. *First Author: Kelley Coffman, Memorial Sloan Kettering Cancer Center, New York, NY*

Background: ^{177}Lu-DOTATATE is an approved therapy for somatostatin receptor (sstr) positive gastroenteropancreatic neuroendocrine tumors (NETs). There are little data available on response and outcomes for well differentiated (WD) high grade (HG) NETs treated with ^{177}Lu-DOTATATE. **Methods:** Pts with WD HGNETs treated with ^{177}Lu-DOTATATE at MSK from 2018-2020 were identified. Demographics, response to treatment, and progression-free survival (PFS) were determined. In pts with archival tumor tissue, next-generation sequencing (NGS) was performed through an institutional platform (MSK-IMPACT). **Results:** 19 pts were identified (mean age 54, 63% female). Site of tumor origin included: pancreas (14/19, 74%), small bowel (2/19, 10.5%), rectal (2/19, 10.5%), lung (1/19, 5%). Average tumor Ki-67 was 34.8 (range 22-56). All tumors were sstr avid on pre-treatment Ga68-DOTATATE PET/CT; none of the patients had sstr negative lesions detected. Median number of prior treatments (systemic and/or liver-directed) was 4 (range 2-7). All pts had progressive disease prior to initiation of ^{177}Lu-DOTATATE. 13 pts (68%) completed all four treatment cycles; treatment was incomplete in 6 pts due to treatment-related toxicities (n = 3) and clinical progression (n = 3). Best response by radiographic report was available in 16 patients (84%): 10/16 (63%) with partial response, 1/16 (6%) with stable disease, 5/16 (31%) with disease progression. One pt with stable disease as best response received two additional cycles of ^{177}Lu-DOTATATE at progression. Median PFS (from date of first treatment with ^{177}Lu-DOTATATE until progression/death) was 11.1 months (95% CI 10.6 to NA). Five pts (26%) experienced dose modifying toxicity with ^{177}Lu-DOTATATE. The most common treatment-related toxicities were thrombocytopenia (9 pts, 47%; G3/4 in 1 pt, 5%), anemia (7 pts, 37%; G3/4 in 2 pts, 10.5%), leukopenia (6 pts, 32%; G3/4 in 0 pts), and AST/ALT elevation (4 pts, 21%; G3/4 in 0 pts). NGS results were available in the tumor tissue of 13 pts (68%). The most commonly observed alterations were in MEN1 (6/13, 46%) and DAXX (4/13, 31%). No RB1 alterations were identified. **Conclusions:** We observed a meaningful disease control rate of 69% during treatment of WD HGNETs with ^{177}Lu-DOTATATE. In this heavily pre-treated population, more than half of pts received all four treatment cycles with treatment-related toxicities largely bone-marrow related, as expected, based on historical data. As would be expected in sstr avid tumors, the vast majority had alterations in chromatin remodeling genes (MEN1, DAXX) consistent with WD NETs, with no RB1 alterations identified. Research Sponsor: Cycle for Survival.

369 Poster Session

Phase Ib/II study of pembrolizumab with lanreotide depot for advanced, progressive gastroenteropancreatic neuroendocrine tumors (PLANET). *First Author: Michael Morse, Duke University Medical Center, Durham, NC*

Background: Pembrolizumab has antitumor activity in a subset of GEP-NETs patients. We hypothesized that the lanreotide, by its antitumor effects and reduction of serotonin, a modulator of immunity, would synergize with pembrolizumab in low/intermediate grade GEPNETs. **Methods:** GEP-NETs patients who had progressed on a prior somatostatin analogue received lanreotide 90mg sq and pembrolizumab 200mg IV every 3 weeks until progressive disease or intolerable toxicity. The primary endpoint was ORR at any time on study and secondary endpoints were PFS and OS. **Results:** 22 patients were treated (F/M 10/12; Caucasian/AA/other 10/7/5; GI/pancreatic 14/8; median Ki67 5%, median time since diagnosis 5.3 yrs (IQR 2.3-7.9 yrs)). Prior octreotide LAR/lanreotide/both was administered to 20/1/1. Patients had a median of 2 prior systemic therapies (range 1-9) and six had prior locoregional therapy and 3 external beam radiotherapy. Of the 12 tumors analyzed thus far, 4 had detectable PD-L1 expression and 11 had detectable TILs. A median of 6 pembrolizumab doses (range 2-15) and 7 lanreotide doses (range 2-15) were administered. Six patients experienced treatment related SAEs (abdominal pain, pneumonitis, colitis, and hyperglycemia, all related to the pembrolizumab). Selected treatment related adverse events included: Hypothyroidism 23%, colitis 9%, hyperglycemia 14%, and pneumonitis 5%. Best response by RECIST 1.1 was SD/PD/Not available: 39/52/9% and by irRECIST was 43/48/9%. Median PFS was 5.4 months (95% CI 1.7-8.3 mo). The median overall survival at a median follow-up of 15 months was not reached. Peripheral blood immunologic correlates will be reported subsequently. **Conclusions:** In a population of GEP-NET patients, progressing on a median of 2 prior therapies, including prior somatostatin analogue therapy, a minority of whom had PD-L1 expressing tumors, the combination of lanreotide and pembrolizumab produced stable disease in approximately 40% of patients. No new safety signals were identified. Clinical trial information: NCT03043664. Research Sponsor: Ipsen, Merck.

370 Poster Session

Efficacy of ipilimumab and nivolumab in patients with high-grade neuroendocrine neoplasms. *First Author: Taymeyah E. Al-Toubah, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL*

Background: Dual checkpoint inhibitor therapy with anti-PD-1 and ant-CTLA-4 therapy has shown promising results in patients with high-grade NENs, demonstrating varying response rates of 9 – 44%. More data are needed to evaluate the true response in a real-world cohort of patients. **Methods:** Retrospective study of all patients with high-grade neuroendocrine neoplasms treated at the Moffitt Cancer Center and Mayo Clinic between 9/2017 and 7/2020 who received combination therapy with ipilimumab and nivolumab. Primary endpoint was objective response rate. **Results:** 34 patients met eligibility criteria for evaluation. Patients had received an average of 2 lines of therapy prior to treatment with ipilimumab/nivolumab, including at least one cytotoxic chemotherapy regimen. 27 (79.4%) of patients had poorly differentiated NECs and 7 (20.6%) had well-differentiated high grade NETs. The most common primary site (10, 29.4%) was pancreas; other primary sites of disease included unknown primary (n = 9), colon (n = 5), uterus (n = 3), anorectum (n = 2), esophagus (n = 2), cervix (n = 1), stomach (n = 1), and small intestine (n = 1). 5 patients (14.7%) exhibited a best response of PR per RECIST 1.1 criteria, 9 (26.5%) SD, and 17 (50%) PD: 3 patients did not have a follow-up scan and discontinued treatment shortly after initiation due to clinical progression. ORR was 14.7% and DCR was 41.2%. Median PFS was 1 month (95% CI, 0.45 – 1.55); median OS from time of treatment initiation was 5.0 months (95% CI, 3.42 – 6.59) and median OS from diagnosis was 14.0 months (95% CI, 1.49 – 26.51). Median duration on treatment was 1 month (range 0 – 10 months). 26 patients discontinued treatment for progression, 4 patients for toxicity, and 4 remain on treatment at the time of data cut off. 12 patients (35%) experienced grade 3 and 4 treatment-emergent toxicities: liver transaminitis, elevated blood bilirubin, arthralgia, myalgia, peripheral sensory neuropathy, lower extremity edema, confusion, diarrhea, encephalopathy, acute kidney injury, rhabdomyolysis, myocarditis, and colitis. **Conclusions:** The ipilimumab and nivolumab regimen has modest activity in aggressive and heavily pretreated high-grade NENs who have progressed on prior cytotoxic chemotherapy. Use of this regimen may be considered in patients with particularly aggressive, refractory high-grade NENs. Research Sponsor: None.

371 Poster Session

The role of systemic inflammatory factors in gastroenteropancreatic neuroendocrine tumors (GEP-NETs) treated with peptide receptor radionuclide therapy (PRRT). *First Author: Estephany Abou Jokh Casas, Nuclear Medicine Deparment-Hospital Clinico Universitario de Santiago de Compostela, Santiago De Compostela, Spain*

Background: Inflammation plays a key role in the pathophysiology of many diseases, including cancer. Systemic inflammatory factors have been validated as indicators of ongoing systemic inflammation that could be predictive markers of poor prognosis for oncological outcomes. However, it is unknown the prognostic impact of systemic inflammation markers in patients with GEP-NETs treated with PRRT. **Methods:** We conducted an observational, retrospective, multicentric study of 40 patients with GEP-NET treated with PRRT belonging to GGNET (Galician Research Group on Neuroendocrine Tumors) network at Nuclear Medicine Department of Santiago de Compostela University Hospital (Spain). The systemic inflammatory markers were calculated as follows: NLR = neutrophil count/lymphocyte count, PLR = platelet count/lymphocyte count, MLR= monocyte count/lymphocyte count, ALB= albumin levels and dNLR = neutrophil count/ (leucocytes count – neutrophils count). For the calculation of the different ratios, baseline analysis and after the second dose were used. The cut-off values were determined as the median of each values, correlating them with progression-free survival (PFS). **Results:** Data from 40 patients (pts) treated between 2016 and 2020 were recorded. Median age was 63.5 years (range 41-85) and 55% were male. Baseline ECOG PS 0/1/2 was 15 (37.5%)/16 (40%)/9 (22.5%). Tumor location was intestinal 26 pts (65%), pancreas 11 pts (27.5%) and unknown origin 3 pts (7.5%). 15 pts (37.5%) were functioning. Tumor grade G1/G2/G3 were 17 pts (42.5%)/ 20 pts (50%)/ 3 pts (7.5%), and Ki 67 <2/3-20/>20%/unknown were 11 pts (27.5%)/ 21 pts (52.5%)/ 3 pts (7.5%)/ 5 pts (12.5%), respectively. The most frequent site of metastasis was liver 32 pts (80%), lymph nodes 19 pts (47.5%), peritoneum 11 pts (27.5%) and bone 10 pts (25%). Surgery: 22 pts (55%) primary tumor surgery and 8 pts (20%) metastasectomy. Previous systemic treatments included somatostatin analogs (SSA) 40 pts (100%), everolimus 26 pts (65%) and sunitnib 11 pts (27.5%), others 7 pts (17.5%). The baseline cutoff-values for NLR was 2.61, for PLR 110.14, for MLR 0.31, for ALB 4.2. and for dNLR 1.71. The cutoff-values after the 2nd dose for NLR was 2.3, for PLR 2.15, for MLR 0.3, for ALB 4.2 and for dNLR 1.48. With a median follow up of 21 months, 14 pts (35%) had died. Median PFS was 27.2 m (95% CI 16.0-38.4m) and OS was not reached (NR). Pts with baseline higher NLR (>2.61 vs. <2.61) had a significantly lower PFS: 15.8 m vs. NR (HR 0.181; 95% CI 0.051-0.638, p=0.03), which was also true for pts with elevated dNLR (>1.71 vs. <1.71): PFS 15.8 m vs. NR (HR 0.174; 0.049-0.614, p=0.03). Baseline PLR, ALB, MLR and NLR, PLR, ALB, dNLR and MLR values after the 2nd dose was not statistically significant for PFS. **Conclusions:** We have identified that baseline NLR and dNRL are significant predictive factors in patients with GEP-NETs treated with PRRT. Research Sponsor: None.

372 Poster Session

Copy number alterations in plasma cell-free DNA from metastatic gastroenteropancreatic neuroendocrine neoplasms. *First Author: Gitta Boons, University of Antwerp, Edegem, Belgium*

Background: Recent studies, including our proof-of-concept study, demonstrated the possibility to detect tumor-derived molecular alterations in cell-free DNA (cfDNA) from plasma of patients with a gastroenteropancreatic neuroendocrine neoplasm (GEP-NEN). More in-depth evaluation of the biomarker potential of cfDNA in GEP-NENs is warranted, since highly sensitive and specific blood-based biomarkers are an important unmet need for this tumor type. The aim of our study was to detect tumor-associated copy number alterations (CNAs) in cfDNA from GEP-NEN patients to molecularly characterize the tumor and to estimate tumor fraction, as a measure of tumor burden, and to evaluate changes in these parameters over time. **Methods:** Metastatic GEP-NEN patients were included within NETwerk, a multi-institutional network of nine hospitals in Belgium. Clinicopathological data were collected to correlate experimental and clinical findings. Plasma samples were collected from all patients and cfDNA was extracted and subjected to shallow whole-genome sequencing (WGS). Detection of CNAs and estimation of tumor fraction, based on the sequencing data, were performed using the R-based tool ichorCNA. **Results:** In total, 80 samples of 29 metastatic GEP-NEN patients were analyzed using shallow WGS. All patients had a well-differentiated GEP-NEN of Grade 1/2 and primary sites were pancreas (N = 15), small intestine (N = 9), colon (N = 1), caecum (N = 1), ileocaecal valve (N = 1), pylorus (N = 1) and unknown (N = 1). Median number of samples per patient was two, with a median time between first and last sampling of six months. In 25 cfDNA samples from nine patients (31%), CNAs with tumor fractions higher than 3% could be detected. The primary tumor site of all CNA-positive patients was pancreas, corresponding to 60% of included pancreatic NEN (PNEN) patients. Six of the CNA-positive patients were included at initiation of everolimus treatment. The detected CNA patterns were similar to the copy number profiles of PNENs described in literature, e.g. whole-chromosome gains of chromosomes 5, 7, 9, 12, 13, 14, 19 and 20. CNA profiles were relatively stable over time, although in two patients new alterations did arise. Tumor fractions changed over time, which could be linked to changes in tumor burden, tumor progression and treatment response according to RECIST1.1 criteria and will be further examined, including in additional samples that are being collected. **Conclusions:** Cell-free DNA of metastatic GEP-NEN patients contains CNAs that correspond to CNA profiles seen in tumor tissue samples. CNAs can be used to quantify the tumor fraction in cfDNA over time, which will be linked to tumor progression in our ongoing study, particularly in the promising subgroup of PNEN patients. Research Sponsor: Kom op tegen Kanker (Stand up to Cancer, the Flemish cancer society), Other Government Agency.

373 Poster Session

Ampullary neuroendocrine tumors: A window into a rare tumor using a national database. *First Author: Samantha M Ruff, Northwell Health, Manhasset, NY*

Background: Ampullary neuroendocrine tumors (NET) make up < 1% of all gastrointestinal NETs. Information about their behavior and prognosis is reliant on small case series. This study set out to describe the population of patients who are diagnosed with ampullary NETs and compare them to patients with duodenal and pancreatic head NETs. **Methods:** The National Cancer Database (2004 – 2016) was queried for patients with ampullary, duodenal, and pancreatic head NETs. Clinicopathologic and treatment characteristics were compared. Subset analysis was performed on patients who underwent surgery. Kaplan Meier (KM) analysis and Cox regression were used to analyze the survival of patients with ampullary NETs. **Results:** Overall, 872 patients were identified with ampullary NET, 9692 with duodenal NET, and 6562 with pancreatic head NET. Patients with ampullary NET had an average age of 60.9 +/- 14.5 years, were evenly split among men and women (N = 437, 50.1% vs N = 435, 49.9%, respectively), and primarily Caucasian (N = 663, 76.0%). 72.1% underwent local tumor destruction or surgery (N = 629). Most did not receive radiation (N = 832, 95.4%), chemotherapy (N = 627, 71.9%), or hormone therapy (N = 788, 90.4%). Patients with ampullary NETs had more poorly differentiated tumors (N = 119, 13.6%) than patients with duodenal (N = 159, 1.6%) or pancreatic head (N = 602, 9.2%) NETs. Patients with ampullary NETs had more positive lymph nodes (N = 288, 33%) than patients with duodenal (N = 915, 9.4%) or pancreatic head (N = 1381, 21%) NETs. At five years, the overall survival for patients with ampullary, duodenal, and pancreatic head NETs was 57%, 68%, and 46%, respectively. Within the surgical population, five-year survival for patients with ampullary (N = 367), duodenal (N = 991), and pancreatic head (N = 1961) NETs was 60%, 74%, and 72%, respectively. When compared, there was a statistically significant difference between the mean overall survival of patients with ampullary (98 +/- 4.7 months), duodenal (112 +/- 2.5 months), and pancreatic head (108 +/- 1.7 months) NETs ($p < 0.001$). In the cox regression analysis, sex, Charlson-Deyo score, lymph node positivity, lymph-vascular invasion, mitotic rate, chromogranin A level, 5-HIAA level, and tumor size did not correlate with survival. Increasing age (HR 1.04, CI 1.01 – 1.07, p = 0.008) and worse tumor differentiation (poorly differentiated HR 3.33, CI 1.38 – 8.04, p = 0.008 and undifferentiated HR 8.31, CI 2.77 – 24.92, $p < 0.001$ compared to well differentiated) were associated with increased mortality. **Conclusions:** This study sheds light on a rare tumor histology. When compared to patients who underwent surgical resection for duodenal or pancreatic head NETs, patients with ampullary NETs had a significantly worse prognosis. Identifying prognostic factors allows us to create more concrete treatment recommendations and provide patients with improved prognostic information. Research Sponsor: None.

374 Poster Session

Incidence and patterns of secondary malignancies in patients with neuroendocrine neoplasms: A SEER database analysis. *First Author: Meena Sadaps, Cleveland Clinic, Cleveland, OH*

Background: Neuroendocrine tumors (NETs) are comprised of a group of biologically and clinically heterogenous malignancies arising from a variety of anatomic sites, the majority of which lie within the gastrointestinal tract. Prior literature has reported on the association between NETs and other primary malignancies (OPM), most of which also end up being within the gastrointestinal tract, but these studies are limited by small sample sizes. We aim to further analyze the association of NETs and OPM on a larger scale using a population-based cancer registry. **Methods:** Malignant primary cancer with NET features were identified from the Surveillance Epidemiology and Ends Results (SEER) registry between 1975 and 2017. The histology/behavior of NET included carcinoid tumor, neuroendocrine carcinoma, pancreatic endocrine tumor, atypical carcinoid tumor, and other including insulinoma, glucagonoma, gastrinoma, VIPoma, somatostatinoma and enterochromaffin cell carcinoid. First NET observation from each patient was examined. Patients with NET were grouped into three categories: only one primary cancer with NET, first primary cancer with NET and first primary cancer without NET based on sequence number of primary cancer recorded in SEER. Distribution of NET between gastrointestinal (GI) and non-GI sites was described. Demographics were compared by NET sequence group and between GI and non-GI sites. **Results:** 45,896 patients with NET were analyzed (77.9% Caucasian, 47.0% male, median age 62.0 years). More than half (65.7%) of the NETs were observed in GI sites. Within the GI tract, 31.3% were in the small intestine, 25.1% in the rectum, 16.6% in pancreatobiliary, and < 11% in other GI locations. Age at NET diagnosis was younger in those with GI NETs (median 60.0 vs 65.0, $p < 0.001$). 71.2% of NET found in only cancer diagnosis, 10.4% of NET in first followed by a second primary malignancy, and 18.4% in a non-NET primary followed by NET. Mean age was 58.9 for NET primary only, 61.0 for NET primary first and 68.3 for non-NET primary first ($p < 0.0001$). More Caucasian patients had non-NET primary first (82.3%) compared to NET primary only (76.9%) and NET primary first (75.5%). No gender differences were observed amongst the three groups. Carcinoid tumor histology was more prevalent in NET primary first (78.6%) compared to NET primary only (67.3%) and non-NET primary first (66.6%), while neuroendocrine carcinoma histology was more prevalent in NET only (27.4%) and non-NET first (29.3%) compared to NET first. **Conclusions:** 28.8% of patients with NETs were found to have OPM, either preceding or following their NET diagnosis. It is imperative that patients with NET undergo age-appropriate cancer screening to help identify any concurrent malignancies. Further research is warranted to identify the location of such additional malignancies and the timeframe in which they occur in relation to the NET. Research Sponsor: None.

TPS375 Trials in Progress Poster Session

A phase I study of safety and immunogenicity of survivin long peptide vaccine (SurVaxM) in patients (pts) with metastatic neuroendocrine tumors (NETs). *First Author: Medhavi Gupta, Roswell Park Cancer Institute, Dept. of Medicine, Buffalo, NY*

Background: Metastatic neuroendocrine tumors (NETs) have a poor prognosis and there are limited options after first-line treatment with somatostatin analogues (SSA)/chemotherapy. Therefore, new therapies are urgently needed. Survivin is an intracellular protein that alters cell division, function of cell death proteases and inhibits apoptosis. It is undetectable in adult cells and expressed in many tumors, making it an ideal target. SurVaxM is a 15 amino acid synthetic peptide vaccine. It stimulates antigen presentation via intracellular cell-surface target recognition and induces CD8+ & CD4+ T cells and IgG production. It was well tolerated in a phase I trial in recurrent glioma pts (Fenstermaker et al., Neurooncol; 2014). Prelim analysis from a phase II study in glioma patients (pts) showed its efficacy (Ahluwalia et al., Neurooncol; 2018). Targeting survivin in NETs is based on our work with tissue microarrays from gastroenteropancreatic (GEP) and lung NETs that showed that its expression correlated with a worse overall survival (Hanif et al., Oncotarget; 2020). We have an ongoing single-arm phase I trial evaluating the safety and immunogenicity of SurVaxM in metastatic NETs. **Methods:** Ten eligible pts with any grade metastatic GEP/lung origin NETs that are survivin positive by immunohistochemistry and have progression on SSA within the last 6 months on two CT scans >4 weeks apart per RECIST v1.1 are being enrolled. Pts receive a fixed dose of 500 mcg of SurVaxM in Montanide ISA 51 subcutaneously along with 100 mcg of GM-CSF q2 weeks X 4 doses. SSA is continued at the same dose as before. Pts free of progression and toxicity at 6 months get extra doses of SurVaxM q12 weeks, up to 1 year. Subjects are assessed continuously for safety per NCI CTCAEv5.0. Response assessment via CT scans per RECIST v1.1 q12 weeks. Primary objective is to assess safety of SurVaxM +/- SSA. Secondary objectives are to assess overall response rate, progression free survival, duration of response and vaccine immunological response (anti-survivin antibody titers and survivin-specific CD8 T-cell responses). Safety analysis is per Pocock stopping boundary with the assumption of true toxicity of 0.2 and unacceptable toxicity of 0.3 at a significance level of 0.05.To this date, eight patients were screened out of which five patients were enrolled. One patient did not meet the eligibility criterion due to negative survivin staining and the other two did not meet the RECIST v1.1 progression criterion. Of the five pts enrolled, two were of lung origin, two of GEP, and the remainder one of thymic origin. Three pts had high grade neuroendocrine carcinoma, one patient had atypical bronchial tumor and one with low-grade NET. Currently, two pts remain on the study. The enrollment is ongoing. The trial is funded by The Neuroendocrine Tumor Research Foundation. Research Sponsor: The Neuroendocrine Tumor Research Foundation (NETRF).

TPS376 Trials in Progress Poster Session

Phase II trial of the CDK4/6 inhibitor abemaciclib in patients (pts) with advanced and refractory well-differentiated gastroenteropancreatic neuroendocrine tumors (GEP NETs). *First Author: Kit Man Wong, University of Washington/Seattle Cancer Care Alliance, Seattle, WA*

Background: Despite advances in the treatment of advanced GEP NETs, long-term disease control remains a challenge. Overexpression and altered regulation of cyclin-dependent kinases (CDK) 4 and 6 have been observed in multiple subtypes of GEP NETs. Preclinical studies have demonstrated that the CDK 4/6 inhibitor palbociclib reduces growth of pancreatic NET cell lines and levels of phosphorylated retinoblastoma protein *in vitro*. Moreover, the drug significantly inhibited tumor growth *in vivo* in pancreatic NET xenograft models. Abemaciclib is a selective small molecule CDK 4/6 inhibitor, approved for the treatment of HR+ HER2– metastatic breast cancer. Clinical activity and central nervous system penetration of the drug have been observed in several tumor types in clinical trials, including partial response in one pt with metastatic small intestinal NET. We have developed a Phase 2 trial of abemaciclib in GEP NETs to evaluate its efficacy and safety in these rare cancers. **Methods:** This is an investigator-initiated non-randomized phase 2 trial using a two-stage design. Eligible pts have metastatic or locally advanced unresectable well-differentiated grade 1-2 GEP NETs, ECOG PS 0-2, and must have progressed on at least one line of systemic therapy. Prior or concurrent treatment with somatostatin analogs is allowed,. Abemaciclib is administered at a dose of 200 mg orally every 12 hours continuously in 28-day cycles. Dose reductions for toxicities are allowed to level -1 (150 mg) and -2 (100 mg). Primary endpoint is objective response rate (ORR) by RECIST v1.1. Secondary endpoints include progression free survival (PFS), overall survival (OS), and toxicity. A two-stage design with 88% power to detect an increase in ORR to 20% with abemaciclib at the 1-sided 0.05 level would require a total of 37 patients. Stage 1 will include 20 patients, and if one response is seen among these patients, the study will continue to enroll another 17 patients. The trial was activated in January 2020, and 3 patients have been enrolled to date. Available archival tumor tissue and molecular profiling data are collected for future correlative studies including assessment of response biomarkers. Research Sponsor: Eli Lilly.

377 Oral Abstract Session

Alliance A021501: Preoperative mFOLFIRINOX or mFOLFIRINOX plus hypofractionated radiation therapy (RT) for borderline resectable (BR) adenocarcinoma of the pancreas. *First Author: Matthew H. G. Katz, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Neoadjuvant therapy has been associated with a median overall survival (OS) of 18 – 23 months (mo) in patients (pts) with BR pancreatic ductal adenocarcinoma (PDAC). To establish reference regimens to which novel treatments can be compared in future studies, we evaluated neoadjuvant mFOLFIRINOX with or without RT in BR PDAC in a phase II National Clinical Trials Network (NCTN) trial. **Methods:** Pts with ECOG PS 0-1 and BR PDAC confirmed by central real-time radiographic review after pre-registration were randomized to either arm A: 8 cycles of neoadjuvant mFOLFIRINOX (oxaliplatin 85 mg/m^2, irinotecan 180 mg/m^2, leucovorin 400 mg/m^2 and infusional 5-fluorouracil 2400 mg/m^2 over 46 hours), or arm B: 7 cycles of mFOLFIRINOX followed by stereotactic body RT (SBRT, 33-40 Gy in 5 fractions [fx]) or hypofractionated image guided RT (HIGRT, 25 Gy in 5 fx). Pts in either arm without disease progression underwent pancreatectomy, then 4 cycles of adjuvant mFOLFOX6 (oxaliplatin 85 mg/m^2, leucovorin 400 mg/m^2 and infusional 5-fluorouracil 2400 mg/m^2 over 46 hours). The primary endpoint, 18-mo OS rate, of each arm was compared to a historical control of 50%. Planned interim analysis mandated closure of either arm in which <11 of first 30 accrued pts underwent R0 resection. **Results:** 155 pts pre-registered and 126 pts were enrolled to arm A (N=70; 54 randomized, 16 following closure of arm B) or arm B (N=56; closed at interim analysis, all pts randomized prior to closure). Median age (A: 63y, B: 67y), median CA 19-9 level (A: 171 U/ml, B: 248 U/ml) and ECOG PS (A: 51% PS 0, B: 57% PS 0) of registered pts were similar between arms (p > 0.05). Treatment detailed in Table. The 18-mo OS rate based on Kaplan Meier estimates was 67.9% (95%CI: 54.6 – 78.0) in arm A and 47.3% (95%CI: 33.7 – 59.7) in arm B. Among pts who underwent pancreatectomy, 18-mo OS rate was 93.1% (95%CI: 84.3 – 100) and 78.9% (95%CI: 62.6 – 99.6) in arm A and B, respectively. With median follow-up of 27 and 31 mo, median OS was 31.0 (95%CI: 22.2 – NE) mo and 17.1 (95%CI: 12.8 – 24.4) mo in arm A and B, respectively. **Conclusions:** Neoadjuvant mFOLFIRINOX was associated with favorable OS relative to historical data in pts with BL PDAC in this phase II NCTN trial. mFOLFIRINOX with hypofractionated RT did not improve OS compared to historical data. mFOLFIRINOX represents a reference regimen in this setting and a backbone on which to add novel agents. Support: U10CA180821, U10CA180882, U24CA196171; https://acknowledgments.alliancefound.org Clinical trial information: NCT02839343. Research Sponsor: U.S. National Institutes of Health.

Therapy by treatment arm (N = 126), (n [%]).

	Arm A (mFOLFIRINOX) n = 70	Arm B (mFOLFIRINOX + RT) n = 56
Initiated preop treatment	66	55
Started cycle 8 ctx or RT*	47 (71)	40 (73)
Surgery	38 (58)	28 (51)
Pancreatectomy	32 (48)	19 (35)
R0 pancreatectomy	28 (42)	14 (25)
Initiated postop ctx	22 (33)	13 (24)
Completed all treatment	20 (30)	10 (18)

Ctx, chemotherapy

*SBRT (n = 35); HIGRT (n = 5)

378 Rapid Abstract Session

Overall survival from the phase 3 POLO trial: Maintenance olaparib for germline BRCA-mutated metastatic pancreatic cancer. *First Author: Talia Golan, The Oncology Institute, Sheba Medical Center at Tel-Hashomer, Tel Aviv University, Tel Aviv, Israel*

Background: POLO is the first phase 3 trial to evaluate maintenance therapy with the poly(ADP-ribose) polymerase inhibitor (PARPi) olaparib (O) in patients with metastatic pancreatic cancer (mPaC) and a germline *BRCA* mutation (*gBRCAm*) whose disease had not progressed on first-line platinum-based chemotherapy (PBC). POLO demonstrated that patients had significantly longer progression-free survival (PFS; primary endpoint) with maintenance O than with placebo (P; hazard ratio [HR], 0.53; 95% confidence interval [CI], 0.35–0.82; *p*= 0.004). Herein, we present final overall survival (OS) data. **Methods:** POLO was a randomized, double-blind, placebo-controlled trial (NCT02184195) conducted at 119 sites in 12 countries. Eligible patients had mPaC without disease progression for ≥16 weeks on PBC and a deleterious or suspected deleterious *gBRCAm*. Patients were randomized 3:2 to O (300 mg tablet twice daily) or P. OS (time from randomization until death) was a key secondary endpoint assessed using a log-rank test. A multiple-testing procedure (MTP) was used, with alpha passed to OS owing to a significant PFS result. Time from randomization to second disease progression or death (PFS2), to discontinuation of treatment (TDT), and to initiation of first (TFST) or second (TSST) subsequent therapies following treatment discontinuation or death were secondary endpoints (log-rank test, not in MTP). Primary analysis of OS after 108 deaths; data cut-off (DCO) July 21 2020. **Results:** Ninety-two and 62 patients were randomized to O and P, respectively; those censored had a median follow-up of 31.3 months (mo) and 23.9 mo, respectively. At DCO, n = 13 remained on O; n = 2 on P. OS was similar for the O and P groups (median 19.0 and 19.2 mo, respectively; HR 0.83 favoring O; 95% CI 0.56–1.22; *p*= 0.3487). OS at 36 mo was 33.9% for O and 17.8% for P. Median PFS2 was 16.9 mo for O vs 9.3 mo for P (HR, 0.66; 95% CI 0.43–1.02; *p*= 0.0613). TFST, TSST and TDT were longer with O than P (Table). TDT at 24 mo was 24.3% for O vs 3.3% for P; at 36 mo was 17.2% for O vs 3.3% for P. Incidence of grade ≥3 adverse events (AEs) was 49% for O (anemia most common [12.2%]); 25% for P (anemia, hyperglycemia, upper abdominal pain most common [3.3%]). Treatment was discontinued owing to AEs for 8.9% patients in the O arm vs 1.6% for P. **Conclusions:** Although HR for OS was in favor of maintenance O vs P among patients with a *gBRCAm* and mPaC whose disease had not progressed during PBC, there was no statistically significant difference. PFS2 showed a clear trend for treatment benefit beyond disease progression in favor of O, but was not alpha protected. Safety data were consistent with the primary analysis. Clinical trial information: NCT02184195. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	Hazard ratio (95% CI)	P-value	Median (mo) olaparib/placebo N = 92/62
OS	0.83 (0.56-1.22)	0.3487	19.0/19.2
PFS2	0.66 (0.43-1.02)	0.0613[a]	16.9/9.3
TFST	0.44 (0.30-0.67)	< 0.0001[a]	9.0/5.4
TSST	0.61 (0.42-0.89)	0.0111[a]	14.9/9.6
TDT	0.43 (0.29-0.63)	< 0.0001[a]	7.5/3.8

[a]Nominal

379 Poster Session

Improved overall survival for patients with early-onset pancreatic ductal adenocarcinoma. *First Author: Kanika G. Nair, George Washington University School of Medicine, Washington, DC*

Background: The median age of diagnosis of pancreatic ductal adenocarcinomas (PDAC) is 70 years. Only about 20% of patients are diagnosed prior to the age of 60. We sought to identify clinical characteristics and outcomes of patients with early-onset PDAC as compared to later-onset PDAC. **Methods:** We identified histologically confirmed cases of pancreatic adenocarcinoma with information about age and overall survival (OS) diagnosed between 2004 and 2016 from the National Cancer Database (NCDB). Differences in demographic, disease and treatment characteristics and socioeconomic factors between younger and older patients were assessed by Chi-square test. The effect of age, race, insurance status, community median income and community educational attainment on overall survival (OS) were assessed using log rank test. **Results:** Of 321,896 patients who met inclusion criteria, 71,263 (22%) were younger than 60 years and 250,633 were 60 years of age or older at diagnosis. Median OS for younger patients was 9.5 months, compared to 5.6 months for older patients ($p< 0.0001$). Younger patients were more likely to be diagnosed with stage IV disease (47.8% vs 43.4%), to be Black (16.1% vs 10.7%) or Hispanic (6.4% vs 4.5%), have a Charlson-Deyo comorbidity index of 0 (73.5% vs 63.3%), have private insurance (65.1% vs 20.5%), and receive treatment at academic centers (45.9% vs 40.9) (all $p< 0.0001$). Younger patients were also more likely to receive surgery (26.2% vs 19.5%), radiation (23.0% vs 15.9%), and chemotherapy (65.9% vs 46.7%) (all $p< 0.0001$). **Conclusions:** Survival for patients with early-onset PDAC is significantly better than older patients despite more patients being diagnosed with stage IV disease. This may be attributable to younger patients having less comorbidities and receiving more treatment. Concerningly, Black and Hispanic patients make up a larger proportion of younger patients with PDAC, and further work is needed to investigate these differences and underlying causes. Research Sponsor: None.

380 Poster Session

Characterization of undiagnosed pancreatic ductal adenocarcinoma on CT scans. *First Author: John Chang, Banner MD Anderson Cancer Center, Gilbert, AZ*

Background: Pancreatic ductal adenocarcinoma (PDAC) is the third leading cause of cancer-related deaths. At present, the best 5-year survival is 25% for resectable PDAC. For small (1 cm) stage 1 PDAC, resection has resulted in much better survival. The goal of this study was to evaluate the appearance and location of early undiagnosed PDAC on computed tomography scans (CT) prior to diagnosis with the goal of minimizing missing early PDAC. We also categorize the errors as either perceptive or cognitive. **Methods:** PDAC cases were retrospectively reviewed from 1/1/2012 through 12/31/2018 from our tumor registry, identifying 81 cases with paired CT scans both at the time of and prior to diagnosis. Among these, 31 contained imaging features considered diagnostic or suspicious for early PDAC(38%). These "errors" were classified by radiologic features and as well as by location. In addition, errors were classified into "perceptive errors" when the first study was read as normal, and as "cognitive errors" when the report noted an abnormality but failed to note suspicion for malignancy. **Results:** Among the 31 undiagnosed PDAC, 18 had features of an identifiable mass (58%), 9 had pancreatic ductal dilatation (29%), and 4 had evidence of perivascular soft tissue (13%). 44% of undiagnosed tumors were located in the head-neck, 39% in the body, and 17% in the tail. Perceptive errors were found in 58% and 42% were cognitive. No significant differences were seen between perceptive and cognitive errors based on suspicious features. **Conclusions:** Radiologic findings of early PDAC was retrospectively evident in more than one third of cases in which prior imaging was performed. These findings are most often masses or ductal dilatation. Location of these undiagnosed tumors were distributed throughout the gland. This study identifies the radiologic features of undiagnosed PDAC which may provide an opportunity for future prospective studies and improved technology which may improve early detection of pancreatic cancer. Research Sponsor: None.

381 Poster Session

Resection rate of locally advanced pancreatic cancer in gemcitabine plus nab-paclitaxel versus FOLFIRINOX. *First Author: Shahriar Sharif, RenovoRx, Los Altos, CA*

Background: There is no established treatment for locally advanced pancreatic cancer (LAPC), but by utilizing the regimens approved for metastatic pancreatic cancer, hope remains for rendering tumors resectable with chemotherapy. In this context, we looked at the resection rate in patients receiving gemcitabine plus nab-paclitaxel (Gem-Nab) in a prospective trial of patients with LAPC. **Methods:** TIGeR-PaC is an ongoing phase III clinical trial, studying the role of intra-arterial Gemcitabine (IA-Gem) in LAPC. The trial is designed with an induction phase where patients receive 3 cycles of Gem-Nab and a cycle of radiation after which they are randomized to IA-Gem or continuing with 4 cycles of Gem-Nab. We studied the resection rate in patients receiving Gem-Nab during induction who had subsequently continued receiving Gem-Nab post-randomization. **Results:** As of July 2020, 80 patients have been enrolled in the study. From this report, 30 patients were excluded because they had not completed induction and/or active treatment or were randomized to IA-Gem at the time of analysis. From the remaining 50 patients, 5 underwent resection for an overall resection rate of 10%. The median age for the total cohort was 67 years (range 47-83). Most of the resections were performed on the younger cohort of patients under 65 years (median age 60, range 47-65) in whom the resection rate was 4 out of 22 (18.2%). **Conclusions:** In the younger cohort of patients, TIGeR-PaC results are in line with the 15% resection rate in the LAPACT trial of patients with median age of 65 years, as reported by *Phillip et al., 2020*. In the TIGeR-PaC study the resection rate for LAPC treated with Gem-Nab was 10% overall, and 18.2% for younger patient population. These resection rates are comparable to the other reports for Gem-Nab and are similar to retrospective reports for the younger patients undergoing resection after treatment with FOLFIRINOX. Clinical trial information: NCT03257033. Research Sponsor: RenovoRx.

382 Poster Session

Efficacy and safety of liposomal irinotecan plus fluorouracil/leucovorin after progression on conventional irinotecan-containing chemotherapy for metastatic pancreatic adenocarcinoma. *First Author: Kyunghye Bang, Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea*

Background: Liposomal irinotecan (nal-IRI) plus fluorouracil/leucovorin (5-FU/LV) has demonstrated its clinical benefit in patients with metastatic pancreatic adenocarcinoma (mPAC) who progressed on prior gemcitabine-based chemotherapy. However, its role in patients who previously treated with conventional irinotecan has not been investigated. We analyzed clinical outcomes of nal-IRI + 5-FU/LV in mPAC patients after progression on conventional irinotecan-containing chemotherapy. **Methods:** In this multicenter retrospective analysis, a total of 35 patients with mPAC who received nal-IRI + 5-FU/LV after progression on irinotecan-containing regimen, between January 2017 and March 2020, were included. The ratio of time-to-progression (TTP) with nal-IRI + 5-FU/LV to TTP with conventional irinotecan (TTPr) was correlated with duration and cumulative dose of prior conventional irinotecan. **Results:** The median age was 58 years (range, 35-73) and 16 patients (46%) were male. All patients received prior irinotecan as the component of FOLFIRINOX. The median duration of prior irinotecan was 4.6 months (range, 0.5-16.8) and median cumulative dose of prior irinotecan was 1230 mg (range, 150-4650). Objective response rate of nal-IRI + 5-FU/LV was 2.9% (1 partial response) and stable disease was achieved in 31.4% (n = 11). With median follow-up duration of 9.2 months [95% CI, 7.8-10.5], the median PFS and OS were 2.0 months [95% CI, 1.4-2.6] and 4.4 months [95% CI, 3.6-5.7], respectively. 6-month PFS rate was 16.3% and OS rate was 37.5%. The median TTPr was 0.41 (range 0.07-2.07) and this showed negative correlation between cumulative dose of prior irinotecan (R = -0.37, p = 0.041). There was a tendency for the negative correlation between TTPr and duration of prior irinotecan (R = -0.35, p = 0.062). Most common grade 3-4 toxicities were neutropenia (20%) and fatigue (8.6%). **Conclusions:** Nal-IRI + 5-FU/LV showed only modest efficacy for mPAC patients who progressed on conventional irinotecan-containing chemotherapy. Cumulative dose of prior conventional irinotecan may be correlated with the efficacy of nal-IRI + 5-FU/LV. Research Sponsor: None.

383 Poster Session

Adjuvant therapy in patients with resected pancreatic adenocarcinoma: Analysis of treatment allocation patterns in a Canadian provincial institution. *First Author: Manik Chahal, BC Cancer Agency, Vancouver, BC, Canada*

Background: In recent years adjuvant therapy (AT) for pancreatic cancer has evolved. Improved overall survival (OS) was demonstrated first in 2017 with gemcitabine and capecitabine (GemCap), and then further improved in 2018 with FOLFIRINOX compared to gemcitabine (gem) alone. Given these options, we retrospectively reviewed the patterns of AT allocation in the province of British Columbia (BC) during these periods of adoption of newer AT regimens. **Methods:** Patients (pts) treated at BC Cancer centers between January 2017 to June 2018 (the GemCap era), and July 2018 to July 2019 (the FOLFIRINOX era), who had undergone curative intent resection and received at least one cycle of AT were included for chart review. Patient and disease characteristics, treatment details, and stated rationale for choice of AT regimen were collected. Analyses were performed with one-way ANOVA for comparison of means between regimens, and Chi-squared or Fisher Exact tests to determine correlation between clinicopathologic factors and likelihood of undergoing a given AT regimen. **Results:** 122 pts were identified: 67 treated in the GemCap era (gem: 25, 37%, and GemCap: 42, 63%) and 55 treated in the FOLFIRINOX era (gem: 18, 33%, GemCap: 18, 33%, FOLFIRINOX: 19, 34%). Examined variables included age, gender, ECOG, T and N stage, margins, lymphovascular invasion and post-operative CA19-9. In the GemCap era, use of GemCap vs Gem was associated with younger average age (p = 0.001) and positive lymph node status (91% vs. 60%, p = 0.005). In the FOLFIRINOX era, use of gem AT was associated with a delayed time from surgery to consultation. (p = 0.036) AT assignment was not influenced by high volume vs low volume centre in the GemCap era; however, pts were more likely to receive GemCap in low-volume centres during the mFOLFIRINOX era (p = 0.045). The most common stated reasons for choice of a less intense AT regimen were pt comorbidities or functional status (GemCap era: 24% and FOLFIRINOX era: 31%). **Conclusions:** Despite improvements in survival with newer AT regimens, the majority of pts in our real-world setting were assigned a less intense AT regimen. Within the limits of a small sample size, significant pt or disease factors predictive of AT assignment were not identified aside from age and lymph node positivity in the GemCap era, and time from surgery to consultation in the FOLFIRINOX era. Efforts to improve adoption of newer AT regimens and optimize pt eligibility for FOLFIRINOX are warranted. Research Sponsor: None.

384 Poster Session

AGIG chemo-immunotherapy in patients with advanced pancreatic cancer: A single-arm, single-center, phase II study. *First Author: Wangshu Dai, The Comprehensive Cancer Center of Drum Tower Hospital, Medical School of Nanjing University & Clinical Cancer Institute of Nanjing University, Nanjing, China*

Background: To date, chemotherapy remains the only effective treatment of unresectable pancreatic adenocarcinoma. In the last few years, the interest in the use of immunological anticancer strategies is greatly increased. AGIG is a novel chemo-immunotherapy regimen that combines nab-paclitaxel + gemcitabine chemotherapy with sequential recombinant interleukin-2 and granulocyte-macrophage colony stimulating factor (GM-CSF) therapy. We conducted a single-arm prospective phase II study to determine the efficacy and safety of the first-line treatment of advanced pancreatic cancer with AGIG regimen. **Methods:** Nab-paclitaxel (120 mg/m^2) and gemcitabine (1000 mg/m^2) were administered intravenously to all patients on days 1 and 8 triweekly, interleukin-2 and GM-CSF (100 μg) were administered subcutaneously on days 3-5 after chemotherapy. The primary end point was ORR by the Response Evaluation Criteria in Solid Tumors, version 1.1. Secondary end points included safety profile, progression-free survival (PFS), overall survival (OS). Patients' conditions and the efficacy and safety were assessed every 4 cycles. **Results:** Between 11/2018 and 01/2020, 64 patients were enrolled. In the 64 evaluable patients, the ORR and DCR were 43.75% and 76.6%, respectively. The median follow-up time was 12.1 (range 7.1-22.4) months, the median PFS was 5.7 (range 1.63-15.8) months, and the median OS was 14.2 (range 2.9-22.0) months. The most common adverse event was fever (75%). The incidence of grade 3/4 neutropenia was 4.69%. In subgroup analyses, we found that eosinophil count in the blood elevated three times higher than baseline level predicted a longer survival. **Conclusions:** The AGIG Chemo-immunotherapy regimen has presented encouraging ORR, OS, and manageable toxicities as first-line therapy for advanced pancreatic cancer. This regimen may be a novel reliable therapeutic option for patients with preserved performance status. The improvement of treatment efficiency may be related to the activation of non-specific immune response. Clinical trial information: NCT0376867. Research Sponsor: The Affiliated Nanjing Drum Tower Hospital of Nanjing University Medical School.

Best Response	Patients No.(%) AGIG (n = 64)
Partial response	28(43.75)
Stable disease	21(32.81)
Progressive disease	15(23.43)
Disease control rate	49(76.6)

385 Poster Session

Treatment patterns and survival outcomes of older patients with advanced pancreatic cancer (APC): A Canadian real-world evidence study. *First Author: Atul Batra, All India Institute of Medical Sciences, New Delhi, India*

Background: We aimed to compare chemotherapy regimens used and overall survival (OS) among geriatric patients (≥ 75 years) with APC as compared to old (65-74 years) and young (< 65 years) patients with APC. **Methods:** In this retrospective population-based analysis, we identified patients with APC (defined as inoperable/metastatic disease) from 5 large provinces in Canada who were diagnosed from 2011 to 2016. Kaplan-Meier curves were plotted to derive OS and multivariable Cox regression models were constructed to determine the associations of different age groups on OS. **Results:** We included 636 patients diagnosed with APC of whom 258 (40.6%), 247 (38.8%) and 131 (20.6%) were young, old and geriatric. Approximately half (45.7%) of all patients were women. Eastern Cooperative Oncology Group performance status (ECOG PS) was known in 508 patients at diagnosis among whom 62.2% were 0-1 and 37.8% were 2+. ECOG PS was more likely to be 2+ in the geriatric group (46.8% vs 41.1% vs 31.3%; P = 0.017). Most patients (95.8%) had metastatic disease while the remaining patients had inoperable locally advanced disease. Within the study cohort, 38.7% received chemotherapy. Treatment rates differed based on age: 41.9% in young patients, 40.9% in old patients and 28.2% in geriatric patients (P = 0.02). Choice of first-line chemotherapy varied and included FOLFIRINOX (F) in 99 (40.2%), gemcitabine and nab-paclitaxel (GN) in 91 (37.0%) and gemcitabine (G) in 56 (22.8%). F, GN and G were administered in 27.0%, 32.4% and 40.5% of geriatric patients, 40.6%, 32.7% and 26.7% of old patients, and 44.4%, 42.6% and 13.0% of young patients, respectively (P = 0.007). After adjusting for baseline factors, both geriatric (odds ratio [OR], 0.70; 95% confidence interval [CI], 0.42-1.17; P = 0.175) and old patients were as likely to receive chemotherapy (OR, 1.04; 95% CI, 0.70-1.56; P = 0.815) as their young counterparts. The median OS was 7.1 (6.3-8.4), 6.7 (5.5-8.9) and 5.3 (4.3-6.8) months in young, old and geriatric patients, respectively. After adjusting for baseline variables, both geriatric (hazard ratio [HR], 1.25; 95% CI, 0.96-1.62; P = 0.101) and old patients (HR, 1.16; 95% CI, 0.94-1.42; P = 0.171) experienced similar OS as young patients. ECOG PS 2+ at presentation was associated with worse OS as was treatment with G. **Conclusions:** Overall treatment rates for APC are low in the real world. The poor OS in geriatric patients with APC is driven by poor PS and use of less intensive chemotherapy. Age alone should not be considered a contraindication for more intensive chemotherapy since treatment benefit is observed across all age groups. Research Sponsor: None.

Characteristic	Hazard ratio	95% CI	P-value
Age	Ref		
Young	1.16	0.94-1.42	0.171
Old	1.25	0.96-1.62	0.101
Geriatric			
Sex	Ref	0.87-1.26	0.627
Female	1.04		
Male			
ECOG PS	Ref	1.06-1.58	0.003
0-1	1.29		
2+			
Chemotherapy			
None	Ref	0.60-1.34	0.594
G	0.89	0.50-0.87	0.003
GN	0.65	0.40-0.76	< 0.001
F	0.58		

386 Poster Session

Investigating real-world treatment sequencing outcomes in advanced pancreatic cancer: A purple translational registry analysis. *First Author: Jordan Santucci, Walter & Eliza Hall Institute of Medical Research, Melbourne, Australia*

Background: Current standard combination first line palliative chemotherapy regimens in advanced pancreatic ductal adenocarcinoma (PDAC) have not been compared in head-to-head trials. Data on optimum treatment sequencing is also lacking. **Methods:** To assess whether first line (1L) treatment with gemcitabine/nab-paclitaxel (Gem/Nab-P)(SEQ1) or FOLFIRINOX (SEQ2) in the palliative treatment setting impacts survival outcomes, data for patients receiving palliative intent combination chemotherapy between 2016 and May 2020 was extracted from PURPLE, a prospective pancreatic cancer registry enrolling consecutive patients across multiple institutions. **Results:** Of 637 patients, 180 (28%) who received 1L single agent therapy and/or palliative radiotherapy were excluded. Of the remaining 449 patients, 132 (29%) had locally advanced disease (LA PDAC), 67 had local recurrence (15%), and 250 (56%) had de novo metastatic disease (mPDAC). Patients receiving 1L Gem/Nab-P (n=376, 84%) were older (median 67 vs 59 years, P<0.001), had a higher Charlson Comorbidity Index (CCI) (CCI ≥2: 18% vs 3%, Odds Ratio [OR] 8.0, P=0.002), and poorer performance status (ECOG≥2: 10% vs 1%, OR 8.4, P=0.01) compared to the 1L FOLFIRINOX group (n=73, 16%). 140 (37%) patients receiving 1L Gem/Nab-P (SEQ1) and 32 (44%) patients receiving 1L FOLFIRINOX (SEQ2) received second line (2L) chemotherapy. SEQ1 2L regimens included FOLFIRINOX (n=14), FOLFIRI (n=49), FOLFOX (n=35) and 5FU alone (n=3). SEQ2 2L regimens included Gem/Nab-P (n=19), Gem/5FU (n=4), Gem/Cisplatin (n=1) and gemcitabine alone (n=5). Median progression free survival (mPFS) did not differ between patients receiving 1L Gem/Nab-P vs 1L FOLFIRINOX (5.7 vs 5.1 months, P=0.54); nor did median overall survival (mOS; 11.3 vs 12.3 months, P=0.37). In the subset of patients who went on to receive 2L chemotherapy, mPFS in 2L was shorter for SEQ1 compared to SEQ2 (2.9 vs 5.2 months, Hazard Ratio [HR] 1.3, P=0.03) but mOS did not differ (15.9 vs 17.3 months P=0.91). In the subset with LA PDAC, mPFS in 2L was comparable (2.9 vs 3.3 months, P=0.55) but mOS was significantly longer with SEQ1 (22.5 vs 13.8 months, HR 0.50, P=0.01). In mPDAC, mPFS in 2L was shorter with SEQ1 (2.3 vs 5.6 months, HR 1.64, P=0.03), but mOS did not differ by sequence (13 vs 17 months, P=0.23). **Conclusions:** There were no significant differences in survival outcomes between 1L choices of chemotherapy, despite patients offered 1L FOLFIRINOX (SEQ2) being younger and fitter. Survival differences observed for LA PDAC versus mPDAC will be further explored. Given the multiple potential confounders, randomised clinical trials are needed to make firmer conclusions regarding the optimal initial treatment for each patient subset. Research Sponsor: Philip Hemstritch Foundation, Pancare Foundation.

387 Poster Session

Real-world outcomes in recurrent versus de novo metastatic pancreatic adenocarcinoma. *First Author: Laura Miotke, University of Utah School of Medicine, Salt Lake City, UT*

Background: Optimal management of patients with recurrent pancreatic ductal adenocarcinoma (PDAC) is unknown. In the clinical trials that established a survival benefit with combination chemotherapy compared to single agent gemcitabine, patients with recurrent PDAC were either excluded (PRODIGE-4) or severely underrepresented (MPACT). In this study, we evaluated clinical outcomes of recurrent PDAC patients who receive systemic therapy and compared outcomes to patients with *de novo* advanced PDAC. **Methods:** Patients diagnosed with advanced PDAC between 2014 and October of 2019 were included using the nationwide Flatiron Health EHR-derived deidentified database. Patients without a clinic visit or initiation of treatment within 90 days of diagnosis were excluded. Patients were characterized as either *de novo* or recurrent PDAC based on stage at diagnosis and history of surgery. Patients with recurrent PDAC were further stratified based on time to recurrent disease. Overall survival (OS) was summarized within groups via Kaplan-Meier survival estimates, and compared between groups in the context of univariable and multivariable Cox proportional hazards models. The covariates adjusted for were gender, age, race, ECOG, smoking status, primary site, CA199, albumin, lymphocytes, neutrophils and monocytes. **Results:** We included 5170 patients with advanced PDAC, of which 1101 (21.3%) met criteria for recurrent disease. Patients with recurrent PDAC were more likely to have tumors in the head of the pancreas (71% vs 40%, $p < 0.001$) and had lower median CA19-9 (92.8 vs 617, $p < 0.001$), compared to the *de novo* PDAC patients. Median OS for the recurrent group was 10.8 m (95% CI = 9.9-11.7) vs. 7.3 m (95% CI = 7.0-7.7) in the *de novo* group ($p < 0.001$, both univariate and multivariable adjusted analyses). The most common first line palliative chemotherapy in patients with recurrent disease was Nab-paclitaxel plus gemcitabine (41%) or FOLFIRINOX (21%). Patients who recurred within six months of surgery (28%) had an OS of 10.0 m (95% CI = 8.7 -11) vs. 11.6 m (95% CI 10-12, p = 0.256) in those who recurred greater than six months from surgery. **Conclusions:** Our data suggest that patients with recurrent disease have significantly better survival outcomes compared to patients with *de novo* metastatic disease. We did not observe a significant difference in survival of patients who recurred within 6 months of resection compared to those who recurred greater than six months after surgery. These data support the inclusion of patients with recurrent PDAC in clinical trials, including those who develop recurrent disease within 6 months of surgery, with appropriate stratification for these variables. Research Sponsor: NCI Cancer Center Support grant (P30CA042014-23.

388 Poster Session

Comparison of first-line (1L) treatment (tx) patterns and overall survival by age at diagnosis among patients with metastatic pancreatic ductal adenocarcinoma (mPDAC). *First Author: Rawad Elias, Hartford Healthcare Cancer Institute, Hartford, CT*

Background: Pancreatic cancer is mostly diagnosed in patients (pts) aged ≥ 65 years and the mortality rate is the highest among older adults. As the population ages, it is expected that there will be a significant rise in the number of older pts with mPDAC but guidance regarding their management is limited as these pts are under-represented in clinical trials. The oncological care of older adults in daily practice is challenged by various age-related conditions. Therefore, a better understanding of the real-world population will help in the development of more effective tx strategies. This study describes the proportion of pts with mPDAC who were treated, the types of regimens received, and the associated survival outcomes by age at diagnosis. **Methods:** Data were extracted for pts diagnosed with mPDAC between Jan 2015 and Mar 2020 from the Flatiron Health database. Pts were stratified into three age groups at diagnosis: <70y, 70-79y, and ≥ 80y. The proportion of pts was evaluated who received 1L tx and the types of regimens received in the metastatic setting. ECOG performance scores (PS) at tx initiation were described. Overall survival (OS) from the start of 1L was estimated using Kaplan-Meier methods. **Results:** Overall, of the 8,382 pts identified, 71.3% (n=5,973) received tx. Among pts who received tx, 55.5% (n=3,313) were aged <70y at diagnosis, 33.0% (n=1,972) were 70-79y, and 11.5% (n=688) were 80y+. Among those with data available, ECOG PS ≥2 was observed in 15.9% (n=381) of pts <70y, 21.0% (n=309) of pts 70-79y, and 29.9% (n=147) of pts 80y+($p < 0.001$). The proportion of pts who received tx decreased with increasing age at diagnosis: 74.9%, 70.9%, and 58.5% for pts aged <70y, 70-79y, and 80y+, respectively. Gemcitabine monotherapy (gem-mono) and gemcitabine + nab-paclitaxel (GNP) accounted for > 70% of regimens prescribed to pts aged 80y+. The median OS (mOS) for patients treated with GNP, gem-mono, FOLFIRINOX, and liposomal irinotecan-based regimens are presented in the table. **Conclusions:** This study of treatment patterns among pts with mPDAC found that older pts were more likely to have a decreased performance status and are less likely to receive treatment. However, older adults who received systemic therapy had comparable survival outcomes to younger pts treated with a similar regimen. The results of this large descriptive analysis suggest that the treatment strategy of mPDAC should not be based on age but rather on an overall assessment of the performance/functional status and geriatric profile of older pts. Research Sponsor: Ipsen.

	<70y		70-79y		80y+		
	mOS	95% CI	mOS	95% CI	mOS	95% CI	p-value
Overall 1L	7.9	7.6 - 8.3	6.8	6.3 - 7.2	6.2	5.5 - 6.8	<0.001
GNP	6.9	6.4 - 7.5	6.5	5.8 - 7.1	6.8	5.9 - 8.7	0.25
FOLFIRINOX	9.8	9.0 - 10.4	9.6	8.1 - 11.2	6.6	2.3 - 13.6	0.064
Gem-mono	3.0	2.2 - 4.1	4.0	3.1 - 5.2	4.4	3.3 - 5.7	0.72
Liposomal irinotecan-based	7.0	4.7 - 12.8	6.9	5.3 - 8.6	6.8	4.5 - NR	0.75

389 Poster Session

Population-based, real-world prognostic factors related to survival among patients with metastatic pancreatic ductal adenocarcinoma (mPDAC). *First Author: Kenneth H. Yu, Memorial Sloan Kettering Cancer Center/Weill Cornell Medical College, New York, NY*

Background: Pancreatic cancer is expected to be the third deadliest cancer in the US in 2020. Many real-world studies of pts with mPDAC are restricted to single centers, limiting the generalizability of the insights they generate. There is a need to understand prognostic factors of survival in a broader setting to aid in tailoring treatment strategies for pts. This study aimed to identify important population-based predictors related to survival among pts diagnosed with mPDAC. **Methods:** Data were extracted for pts diagnosed with mPDAC between Jan 2017 and Dec 2019 from the Flatiron Health database. Predictive models for overall survival from the start of each treatment were developed using multivariable Cox proportional hazards regression. Treatment specific predictive models were generated for pts treated with first line (1L) gemcitabine + nab-paclitaxel (GNP), 1L FOLFIRINOX, 1L gemcitabine monotherapy (gem-mono), and 2L liposomal irinotecan-based regimens. The holdout method was used for cross-validation, splitting the data into 70% training / 30% validation. Age at diagnosis, sex, body mass index, smoking status, and ECOG performance score (PS) were included in all models due to clinical importance. Demographic, clinical characteristics, hematological labs, liver function tests (LFTs), and serum bilirubin levels were assessed for inclusion into the models. Uno's concordance statistic (c-statistic) was used to assess the predictive accuracy of the models. **Results:** Of the 3,572 pts included in the study, 44% (n = 1,557) received 1L GNP, 27% (n = 954) received 1L FOLFIRINOX, 7% (n = 265) received gem-mono, and 22% (n = 796) received other regimens. 38% (n = 1,345) pts received 2L and of those, 17% (n = 222) received liposomal irinotecan-based regimens. Among all 1L pts, the following were included in the final model: prior surgery, white blood cell (WBC) counts, serum albumin, LFTs (ALP and ALT), serum bilirubin, and ascites (c-statistic: 0.65). The model for pts treated with GNP differed from the overall model via the addition of neutrophil counts and removal of serum bilirubin and ascites (c-statistic: 0.67). Stage at initial diagnosis was included in the model only for pts treated with 1L FOLFIRINOX (c-statistic: 0.68). Among pts treated with gem-mono the LFTs were not included in the model (c-statistic: 0.78). ALP, serum albumin, and WBC counts were important predictors of survival among pts treated with 2L liposomal irinotecan-based regimens (c-statistic: 0.70). Across all regimens the strongest predictors of survival were ECOG PS, serum albumin, and ALP. **Conclusions:** In one of the largest contemporary real-world studies of patients with mPDAC to date, important population predictors of survival in pts receiving systemic treatment were identified. Further validation studies are needed to understand the generalizability of these results. Research Sponsor: Ipsen.

390 Poster Session

Real-world safety data and differentiation of second-line (2L) 5-fluorouracil (5-FU) based regimens among patients with metastatic pancreatic ductal adenocarcinoma (mPDAC). *First Author: George P. Kim, George Washington University, Division of Hematology & Oncology, Washington, DC*

Background: Chemotherapy related adverse events (AEs) can impact the treatment of patients, reducing quality of life and leading to dose delays and treatment discontinuation. This study examined the proportion of patients (pts) with mPDAC treated with 5-FU-based regimens in the 2L setting who experienced AEs during treatment. **Methods:** Data were extracted for pts diagnosed with mPDAC who initiated 2L treatment between January 2016 and July 2020 from the Flatiron Health electronic health database. Pts included in the study were treated with FOLFIRINOX (FFX), FOLFOX, FOLFIRI, or a regimen containing liposomal irinotecan. The occurrence of grade 3 (G3) and grade 4 (G4) neutropenia, G3/G4 elevated alanine transaminase (ALT) and anemia where transfusion was indicated were determined using lab results and the grading criteria from the Common Terminology Criteria for Adverse Events v4.03. The occurrence of diarrhea, fatigue, nausea and vomiting (N/V), and neuropathy were identified from structured diagnosis records through ICD-10-CM codes. Duration of therapy (DOT) was assessed for each regimen. Descriptive statistics for AEs and DOT were reported. **Results:** Of the 804 pts included in the study, 28.4% (n=228) received FFX, 39.8% (n=320) received regimens containing liposomal irinotecan, 24.8% (n=199) received FOLFOX, and 7.1% (n=57) received FOLFIRI. The median DOT (IQR) was 86 days (d) (43 – 206), 79d (41 – 169), 72d (43 – 166), and 84d (46 – 148) for pts who received FFX, liposomal irinotecan, FOLFOX, and FOLFIRI, respectively. G3/G4 neutropenia (<1000/mm3) presented in 28.1% (n=64) of pts treated with FFX, 11.9% (n=38) of pts treated with liposomal irinotecan, 17.1% (n=34) of pts treated with FOLFOX, and 36.8% (n=21) of pts treated with FOLFIRI. NV occurred in 14.9% (n=34), 13.1% (n=42), 12.6% (n=25), and 10.5% (n=6), respectively. The full AE results are summarized in the table. **Conclusions:** In this assessment of often dose-limiting AEs among pts with mPDAC treated in 2L, pts who received liposomal irinotecan had the lowest proportion of neutropenia. No clear pattern was noted for N/V, neuropathy, fatigue, anemia, and elevated ALT. Further research is necessary to determine the real-world cost implications of AEs in this patient population. Research Sponsor: Ipsen.

Adverse event	FOLFIRINOX (n=228)	Liposomal irinotecan containing (n=320)	FOLFOX (n=199)	FOLFIRI (n=57)
G3 Neutropenia	42 (18.4%)	31 (9.7%)	24 (12.1%)	10 (17.5%)
G4 Neutropenia	29 (12.7%)	14 (4.4%)	13 (6.5%)	12 (21.1%)
G3/G4 Neutropenia	64 (28.1%)	38 (11.9%)	34 (17.1%)	21 (36.8%)
Anemia: transfusion indicated	30 (13.2%)	33 (10.3%)	24 (12.1%)	9 (15.8%)
G3/G4 Elevated ALT	9 (3.9%)	9 (2.8%)	5 (2.5%)	2 (3.5%)
Diarrhea	25 (11%)	30 (9.4%)	8 (4%)	7 (12.3%)
Fatigue	25 (11%)	25 (7.8%)	19 (9.5%)	6 (10.5%)
Nausea and vomiting	34 (14.9%)	42 (13.1%)	25 (12.6%)	6 (10.5%)
Neuropathy	6 (2.6%)	12 (3.8%)	4 (2%)	3 (5.3%)

391 Poster Session

Real-world study of treatment patterns and outcomes among patients with metastatic pancreatic ductal adenocarcinoma (PDAC) in Europe. *First Author: Julien Taieb, Georges Pompidou European Hospital, Paris, France*

Background: Few data are available regarding real-world treatment patterns and outcomes for metastatic PDAC (mPDAC) in Europe. **Methods:** This retrospective, observational, chart-review study involved medical oncologists and gastroenterologists from France, Germany, Italy, Spain, and the UK. Physicians completed online patient (pt) reports for 20 consecutive pts diagnosed with PDAC between 01 and 10/2016. Here, the analysis is focused on treated pts diagnosed with mPDAC. Reports provided information on general disease and pt characteristics, diagnosis, and treatment of metastatic disease. Outcomes included median PFS and OS according to each line of metastatic therapy. In addition, how baseline performance status (PS) and treatment sequence affected OS and PFS were assessed. **Results:** 304 physicians (France [n=62], Germany [n=60], Italy [n=63], Spain [n=66], UK [n=53]) participated and enrolled 6,000 pts with PAC, of whom 3827 had mPDAC. Of the 3827, 3432 were treated for their metastatic disease. The most common first-line therapies were modified FOLFIRINOX (28.4%), gemcitabine + nab-paclitaxel (28.0%), and gemcitabine monotherapy (23.0%), while the most common second-line therapies were gemcitabine monotherapy (25.0%), 5-FU + oxaliplatin (21.8%), and gemcitabine + nab-paclitaxel (16.7%). The longest median PFS and OS were obtained when using mFOLFIRINOX as first-line therapy, with gemcitabine-based combinations as second-line therapy. However, pt characteristics were more favorable with FOLFIRINOX compared with the other regimens used in first line. The most common treatment in first line for patients with a worse baseline PS (PS >1) was gemcitabine monotherapy (571 patients [46%]); in addition, having a worse baseline PS was predictive of shorter survival in second line. The most common reason for discontinuation of either line was disease progression. The study showed that the choice of first- and second-line treatment among European physicians is in accordance with current ESMO guidelines; in contrast, the choice of subsequent line was more heterogeneous, according to local practices. Additional data concerning first and second line OS and PFS per treatment regimen will be presented at the meeting. **Conclusions:** This large real-life study highlights a clear picture of treatment patterns in European real-world clinical practice and outcomes for metastatic PDAC, which may help in more effectively managing such patients in the future. Further univariate and multivariate analysis will complete this first description. Research Sponsor: Baxalta/Shire and Servier.

392 Poster Session

Real-world one-year overall survival among patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) treated with liposomal irinotecan in the NAPOLI-1 based regimen. *First Author: George P. Kim, George Washington University, Division of Hematology & Oncology, Washington, DC*

Background: Pancreatic cancer remains one of the most lethal cancers in the United States (US) with a 5-year relative survival of 9%. Among patients who received liposomal irinotecan + 5-fluorouracil (5-FU) and leucovorin in the NAPOLI-1 study, a randomized phase 3 study in patients with mPDAC previously treated with gemcitabine-based therapy, 25% (n = 29) were alive at ≥ 1 year. This study examines the real world one-year survival of patients with mPDAC treated with liposomal irinotecan as a doublet with 5-FU in the NAPOLI-1 based regimen. **Methods:** This retrospective observational study utilized the Flatiron Health EHR database from over 280 cancer clinics in the US. Data were analyzed for adult patients with mPDAC treated with liposomal irinotecan-based regimens between November 2015 and July 2020. Patient characteristics and one-year overall survival (OS) based on Kaplan-Meier estimates were assessed. Cycles were defined as unique days with an administration of liposomal irinotecan. **Results:** There were 669 patients (median age: 69y, IQR: 62-75) included in the study. ECOG performance status (PS) of 0-1 and 2+ were reported for 78.3% (n = 396) and 21.7% (n = 110) of patients, respectively. ECOG PS was not captured for 24.4% (n = 163) of patients. 16.3% (n = 109) of patients initiated liposomal irinotecan-based in the first line (1L) metastatic setting, 47.5% (n = 318) in second line (2L), and 36.2% (n = 242) in the third line or later (3L+). The median number of cycles received was 4 (IQR: 2 – 8). Among all patients, one-year OS was 17.2% (95% CI: 14.3% - 20.7%). One-year OS was 31.5% (22.1% – 41.3%) for patients treated in 1L, 16.4% (12.2% - 21.1%) for patients treated in 2L, and 12.2% (7.5% - 18.0%) for patients treated in 3L. The median number of cycles for 1L, 2L, and 3L were 5, 4, and 3, respectively. One-year OS increased as patients were able to receive more cycles of liposomal irinotecan. Patients who received at least 2 cycles of liposomal irinotecan (n = 551) had a one-year OS of 20.4% (16.8% - 24.2%). Among patients who received at least 4 cycles (n = 359) and at least 8 cycles (n = 170), the one-year OS estimates were 29.1% (24.0% - 34.3%) and 47.9% (39.7% - 55.7%), respectively. **Conclusions:** In this real-world cohort of patients with mPDAC treated with liposomal irinotecan, as expected, one-year OS increased as patients remained on therapy. Patients in this cohort were older, had more prior lines of therapy, worse ECOG PS, and similar exposure to treatment compared with patients in the registrational phase 3 NAPOLI-1 study. Among patients who received at least 4 cycles of liposomal irinotecan, one-year OS (29%) was similar to both the intent-to-treat (25%) and per protocol treated patient populations in the NAPOLI-1 trial (34%). Further studies are needed to understand the predictors of long-term survival among patients with mPDAC. Research Sponsor: Ipsen.

393 Poster Session

Reference values for EORTC QLQ-C30, for metastatic pancreatic cancer (mPC): Enhancing the interpretation of HRQoL scores in the POLO trial. *First Author: Hedy L. Kindler, University of Chicago, Chicago, IL*

Background: Metastatic pancreatic cancer (mPC) and its treatments significantly impact patients' (pts) health-related quality of life (HRQoL). POLO, a randomized, double-blind, placebo-controlled phase 3 trial evaluated the efficacy of olaparib as maintenance therapy in mPC pts who had not progressed during ≥16 weeks of first-line platinum-based chemo. HRQoL was assessed in POLO using EORTC QLQ-C30. To enhance the interpretation of HRQoL scores in POLO, we derived EORTC QLQ-C30 reference (ref) values for mPC from the literature, as these had not been previously established. **Methods:** A systematic literature review was conducted to identify existing baseline values in published data. EORTC QLQ-C30 ref values were calculated by deriving mean scores based on studies meeting all inclusion criteria. EORTC QLQ-C30 mean values were calculated for POLO using pooled baseline data from both study arms (olaparib; placebo). **Results:** Out of 186 studies identified, 4 met all inclusion criteria. Depending on respective EORTC QLQ-C30 subscale, the final sample sizes ranged from n=466 to n=639. Compared to the newly derived EORTC QLQ-C30 ref values based on the literature, POLO pts reported markedly better HRQoL scores at baseline across most subscales, with eight subscales showing differences of >15 points (table). **Conclusions:** This is the first study to systematically derive EORTC QLQ-C30 ref values for mPC. We found that mPC pts enrolled in POLO had better HRQoL scores compared with those reported in the literature and often close to or better than general population norm data, possibly due to positive effects of prior platinum-based first-line treatment, resolution of chemotherapy-related symptoms, response shift, or a combination. These newly derived ref values enhance the interpretation of patients' HRQoL trajectory within a maintenance treatment setting. Research Sponsor: AstraZeneca Pharmaceuticals.

Newly derived ref values vs. baseline POLO scores vs. general population normative data.

EORTC QLQ-C30 Scale	*n*	*Newly derived mPC ref values (mean)*	*Baseline POLO scores (n=147; mean)*	*Difference (POLO vs. mPC ref values)*	*General population norm data (n=11,343; mean)*	*Difference (POLO vs. norm data)*
Global health status	629	54.3	71.9	17.6	66.1	5.8
Physical functioning	639	78.2	83.9	5.8	85.1	-1.2
Role functioning	473	62.5	78.1	15.6	84.3	-6.2
Emotional functioning	638	65.9	81.4	15.5	74.2	7.2
Cognitive functioning	473	81.5	85.5	4.0	84.8	0.7
Social functioning	469	70.2	76.8	6.6	86.2	-9.4
Fatigue	639	46.0	29.5	-16.5	29.5	-0.0
Nausea and vomiting	476	16.2	8.3	-7.9	5.9	2.4
Pain	639	41.9	16.6	-24.3	25.3	-7.0
Dyspnoea	475	19.4	10.0	-9.4	15.9	-5.9
Insomnia	476	41.6	23.1	-18.5	26.6	-3.5
Appetite loss	476	44.6	14.7	-29.9	10.0	4.7
Constipation	473	32.7	13.4	-19.3	12.5	0.9
Diarrhoea	469	13.5	15.5	2.0	9.5	6.0
Financial difficulties	466	15.7	19.3	3.6	10.6	8.7

394 Poster Session

Development of a pancreatic cancer prediction model using a multinational medical records database. *First Author: Limor Appelbaum, Beth Israel Deaconess Medical Center, Boston, MA*

Background: Previous work by our group has demonstrated that leveraging Machine Learning on diagnostic codes from Electronic Health Records (EHRs), can identify individuals at high-risk for Pancreatic Duct Adenocarcinoma (PDAC), as early as 1 year before current cancer diagnosis. We aim to improve the performance of our existing PDAC risk stratification model, by using an independent, multi-center dataset, and adding lab test features. **Methods:** EHR data from TriNetX, a federated global health research network, was utilized to develop Logistic Regression (LR) models. Diagnoses and lab test data from 32 different Health Care Organizations in the United States from 2015-2020 was used. PDAC patients ages 60-80 years, were identified using ICD codes, and cross-checked with tumor registry and pathology data to decrease false positives. Only patients with one or more clinical encounter/s, at least 6 months prior to cancer diagnosis, were included. Prediction time cutoffs of 180, 270, and 360 days before PDAC diagnosis were used. Preliminary basic data analysis was initially performed to explore potential lab test features that could be used to improve model performance. The discriminatory capabilities of the LR models were compared using Area Under the Receiver Operating Characteristic Curve (AUC) and 95% Confidence Interval using empirical bootstrap over test data were computed. We used L2-regularized LR, and performed evaluation using cross-validation. We report cross-validation performance. In contrast to prior published work that used predefined feature sets for model development, we incorporated a wide range of indicators, and relied on regularization to address potential overfitting risk. **Results:** The LR models were trained and evaluated on diagnoses and labs for 25,644 patients (cases= 1352; age-sex paired controls). Lab test administration per patient (i.e., for a given patient, what lab tests were administered and how frequently), was found to be the most valuable feature for improving discrimination. For almost every type of lab test, the average number of administrations per patient was higher for PDAC patients than controls. The top lab tests with highest discriminatory coefficients included glucose, potassium, hematocrit, hemoglobin, sodium, chloride and creatinine. With a 365-day lead time, the diagnoses-based LR obtained a test AUC of 0.58, the lab-test based LR obtained a test AUC of 0.72. The combined diagnoses and lab-test model ("concatenated LR model") outperformed both of these models, obtaining a test AUC of 0.73. **Conclusions:** Our findings demonstrate that LR models based on concatenated lab test and diagnoses feature sets ("concatenated LR models"), can outperform both diagnoses-based LR models and lab-test-based LR models, and can be utilized in early prediction of PDAC development. Research Sponsor: None.

395 Poster Session

Circulating tumor DNA methylation as markers for early detection of pancreatic ductal adenocarcinoma (PDAC). *First Author: Xiaoding Liu, Department of Pathology, Peking Union Hospital, Beijing, China*

Background: PDAC is a cancer of high mortality and low survival. Its early detection is critical due to symptoms often occur only at advanced stages. However there is no reliable screening tool to identify high-risk patients. ctDNA methylation has recently emerged as a promising new target to differentiate PDAC plasma from normal plasma for its early detection. **Methods:** Reduced representation bisulfite sequencing libraries were made in 46 PDAC tissues, 30 para-PDAC tissues and 20 PDAC plasmas to screen PDAC-specific markers, which was done by quantifying and comparing methylation levels of genomic regions and individual CpG sites between those groups. Markers were validated in plasma samples from 84 PDAC patients and 64 normal controls to propose a blood classifier. The best-performing markers were developed into a targeted sequencing panel, which was tested on a larger collection of plasma samples from patients of a variety of pancreatic diseases to build and validate a PDAC-predicting model. **Results:** We profiled genome-wide methylation patterns of tissues samples to identify 171 PDAC-specific markers. We reiterated training and cross-validating PDAC classification models using SVM method, and achieved an average sensitivity of 86% and specificity of 88%. To prove the feasibility of a non-invasive detection in plasma, a targeted methylation assay using those markers was tested on PDAC and normal plasmas, and yielded an average sensitivity of 68.4% and a specificity of 85.8%. We refined the panel by selecting the most discriminatory markers and built the version II of the panel, which was named PANcreatic Cancer Detection Assay, or PANDA, for a more efficient target capture, which was validated in an independent cohort of plasma samples that included 94 PDAC cases, 25 chronic pancreatitis (CP) cases and 80 normal samples from multiple centers. The PANDA achieved an AUC of 0.906 when classifying PDAC from normal, and an AUC of 0.882 when separating PDAC from CPs, both of which are more accurate than CA19-9, the conventional blood marker for PDAC. We further integrated test subjects' age and their CA19-9 level as features into the PANDA model, which further elevated their AUC to 0.882 and 0.933 when classifying PDAC plasma from either CP plasma or normal plasma, respectively. **Conclusions:** We have developed PANDA, an NGS based target assay covering PDAC-specific DNA methylation targets by screening and validation on PDAC tissues and plasmas. Combined with age and CA19-9 blood level, PANDA has shown encouraging results to classify PDAC plasma from non-malignant diseases, demonstrating its potential to be optimized into non-invasive diagnostics for blood-based early PDAC screening. Research Sponsor: Intergovernmental Cooperation Fund of China Science and Technology Exchange Center (2017YEFD110300).

396 Poster Session

Genomic characterization of *ATM* alterations in advanced pancreatic ductal adenocarcinoma (PDAC). *First Author: Sheron Perera, Princess Margaret Cancer Centre/University Health Network/University of Toronto, Toronto, ON, Canada*

Background: *BRCA*1/2 and *PALB2* are genes critical to the faithful repair of double strand breaks through the homologous recombination repair (HRR) pathway. Alterations in these genes serve as predictive biomarkers to both platinum and PARP inhibitors. Ataxia-telangiectasia mutated (*ATM)* is also indirectly involved in HRR; however, its role as a predictive biomarker to DNA damage response agents is debated. Herein we evaluated the genomic characteristics and clinical outcomes of patients with *ATM* alterations on the Comprehensive Molecular Characterization of Advanced Ductal Pancreas Adenocarcinoma for Better Treatment Selection (COMPASS) trial. **Methods:** Patients on this study undergo a biopsy for whole genome sequencing (WGS) and RNA sequencing prior to chemotherapy; those with germline variants in *ATM* were reviewed by a genetics counsellor and defined as pathogenic, likely pathogenic, variant of unknown significance (VUS) or benign/likely benign. Genomic characteristics were reviewed and published classifiers of homologous recombination deficiency (HRD) were applied to all cases and included the percentage of substitution base signature (SBS) 3, the HRDetect score, the computed algorithm of large scale transitions, telomeric allelic imbalances and loss of heterozygosity (LOH), otherwise known as the genomic instability score (GIS). **Results:** As of January 2020, 304 patients were enrolled and 245 patients had both WGS and clinical data available. 86 germline variants in *ATM* were present in 70 patients. The majority of these (80%) were classified as benign or likely benign. 10 VUS were detected and 4 patients (2%) had pathogenic/likely pathogenic variants (PV). Of these 4 patients, LOH or a second somatic hit was evident in 1 case. Upon review of the PVs and VUS, SBS were consistent with typical PDAC and tumour mutational burden was low. HRDetect scores were low (< 0.1) for 13/14 cases with either a VUS or PV; one VUS without biallelic loss, had a high HRDetect score, with presence of SBS 3 and a high GIS. This particular case was also found to have a tandem duplicator phenotype. None of the 4 cases with PV had evidence of HRD. Furthermore all four were treated with platinum based regimens without evidence of response. **Conclusions:** In a large series of sequenced pancreatic cancers, the presence of pathogenic germline variants in *ATM* was rare, with none of the cases demonstrating evidence of HRD. This suggests that this population is unlikely to benefit from PARP inhibition. Research Sponsor: Wallace McCain Centre for Pancreatic Cancer/Princess Margaret Cancer Foundation, Terry Fox Research Institute, Canadian Cancer Society Research Institute, and Pancreatic Cancer Canada Foundation. Other Government Agency.

397 Poster Session

The timing and the dose of advanced care planning in patients with resectable pancreatic cancer: Who makes the call? *First Author: Lyudmyla Demyan, Zucker School of Medicine at Hofstra/Northwell Department of Surgery, New Hyda Park, NY*

Background: The timing and the extent of Advanced Care Planning (ACP) in patients with pancreatic ductal adenocarcinoma (PDAC) undergoing curative-intent resection are generally dictated by the surgeon performing the operation. The aim of this study is to evaluate surgeons' insights, perceptions, and biases regarding preoperative ACP. We hypothesize that many surgeons harbor significant reservations about extensive preoperative ACP. **Methods:** A qualitative investigation using 1:1 interviews with 40 open-ended questions were conducted with convenience sample. Data accrual continued until theme saturation was achieved. Grounded theory approach was used for data coding and analysis. **Results:** A total of 10 interviews were conducted with expert pancreatic surgeons from 6 medical centers—6 males and 4 females. The median number of years in practice was 15 (IQR 13-30) and the median number of pancreatic cancer cases performed per year was 52 (IQR 39-75). During preoperative counseling all surgeons discuss the possibility of recurrence and postoperative complications but attempt to motivate patients by emphasizing hope, optimism, and fact that surgery offers the only opportunity for cure. 90% of surgeons report no formal training in ACP. All surgeons report comfort with end of life conversations when death is imminent, but most lack experience with in-depth preoperative ACP. All surgeons emphasized that ACP should be led by a physician that both knows the patient well and understands the complexity of PDAC management. All surgeons recognized potential benefits of ACP, including delivery of goal-concordant care (60%), increased prognostic awareness (40%), and better life planning (40%). 50% report discussing in-depth ACP related to perioperative complications, but not long-term oncologic outcome. 80% of surgeons report that they actively steer away from in-depth ACP during preoperative counseling. Barriers to in-depth ACP reported by surgeons include taking away hope (70%), lack of time (50%) and concern for sending "mixed messages" (50%). Further, 50% of surgeons perceived that extensive preoperative ACP is not appropriate for patients with PDAC undergoing curative-intent resection. Most surgeons (60%) believe that ACP should occur as a process throughout the disease and in-depth discussions were more appropriate during postoperative visits (30%) and/or recurrence (60%). **Conclusions:** Despite recognizing potential benefits, most pancreatic surgeons report actively avoiding in-depth ACP conversations prior to curative-intent surgery. Surgeons had difficulty articulating the best time for ACP and felt that ACP should occur as a continuum throughout the course of treatment, with the depth of the discussion echoing the disease progression and patients' readiness for such conversation. Future studies could evaluate patients' perspective on the timing and the dose of ACP. Research Sponsor: None.

398 Poster Session

Opportunity costs of undergoing surgical resection and perioperative chemotherapy for pancreatic adenocarcinoma. *First Author: Szu-Aun Lim, Department of Surgery, Brody School of Medicine at East Carolina University, Greenville, NC*

Background: Treatment of early stage pancreatic ductal adenocarcinoma (PDAC) includes surgical resection and either neoadjuvant or adjuvant chemotherapy. Due to the intensity of treatment and perioperative morbidity rates of pancreatic resection, patients may spend a significant portion of their survival time in receipt of clinical care. However, time spent in receipt of care has not been previously described in patients with early stage PDAC. The primary aim of this study was to determine the total time spent in receipt of surgical and perioperative chemotherapy in patients with resectable PDAC. **Methods:** A retrospective cohort study was performed of patients diagnosed with PDAC who underwent curative-intent resection at a single institution tertiary care center between January 2015 and October 2019. Patients who died within 30 days of surgery were excluded. Total care time, including all relevant clinician visits, laboratory, radiologic and procedural studies, and treatment visits, was abstracted from the primary medical record. Care time included estimated travel time based on patient address. Care time was divided into preoperative, surgical, and systemic therapy phases of care. Time spent in surgical care included the hospital length of stay, postoperative follow-up visits, and admissions for postoperative complications. **Results:** A total of 86 patients were identified. Median total preoperative care time was 29 hours (IQR 11-135; 0.4% of survival time, range 0% - 72.7%). Median total time spent in surgical care was 216 hours (IQR 164-371; 2% of survival time, range 0.3% - 68.4%). Among the patients who received systemic chemotherapy care within the same institutional health system (N = 41), median total time spent in receipt of systemic therapy was 447 hours (IQR 194-647; 3% of survival time, range 0.1% - 55.4%). 10.5% of patients (N = 9) spent more than 10% of total survival time in surgical care and 5.8% (N = 5) patients spent more than 10% of survival time in receipt of systemic care. Median cumulative travel time for patients was 19 hours (IQR 10.2-37.6). **Conclusions:** For the majority of patients undergoing resection for PDAC, time spent in receipt of surgical care does not appear to represent a substantial time burden relative to survival time. However, for a subset of patients, the time burden is considerable. Further research to determine predictors of increased time spent in receipt of multimodality cancer care is warranted to better inform patient and surgeon communication and decision-making. Research Sponsor: None.

399 Poster Session

Sepsis and pancreatic cancer: Biliary stents a significant risk factor in patients undergoing chemotherapy. *First Author: Charles Charles Li, RenovoRx, Los Altos, CA*

Background: For patients with pancreatic cancer, tumor growth causing obstruction of the bile duct is a common, yet troubling occurrence, leading to potential serious complications including severe infections. A common technique to correct such an occurrence is the placement of a biliary stent. However, a biliary stent can cause a separate series of complications, especially for patients receiving chemotherapy. A current standard of care treatment for locally advanced pancreatic cancer is intravenous (IV) infusion of gemcitabine and nab-paclitaxel, with the prescribing information for these drugs noting that 5% of patients have experienced sepsis, with those having biliary stents potentially becoming fatal. **Methods:** In an on-going phase III clinical trial comparing standard of care IV gemcitabine and nab-paclitaxel versus intra-arterial delivery of gemcitabine directly to the tumor via a novel dual-occlusion balloon catheter, data from the cohort of 78 patients (total enrolled as of 1 June 2020) were analyzed for the incidence rate of sepsis among patients with and without biliary stents present. Data analyzed were limited to the initial four-month induction phase, in which patients were to receive two cycles of IV gemcitabine and nab-paclitaxel, one cycle of either IMRT or SBRT, and then one more cycle of IV gemcitabine and nab-paclitaxel. **Results:** Among the 78 patients, 12 had one episode of sepsis for an incidence rate of 15%. Of the 78 patients, 39 had a biliary stent placed and 9 experienced sepsis during induction (23%) compared to 2 patients among the 39 without a biliary stent present (5%; Chi-square = 4.99, p = 0.02). One additional patient with a biliary stent experienced urosepsis due to urinary tract infection, unrelated to the biliary stent. The majority of the septic events occurred after placement of the stent during the first cycle of chemotherapy (5 of 9 patients), with an average of 8.2 days passed after a dose of chemotherapy was infused to the septic event (range: 2 to 20 days). There was no relationship between ANC and the risk of sepsis. Among other covariates analyzed, age, gender, BMI, and a history of diabetes were not factors shown to affect the likelihood of a septic event. Among the 9 patients who had a septic event with a biliary stent, 2 were fatal, and 3 were withdrawn from the study due to complications from the septic event. **Conclusions:** These data suggest while the placement of a biliary stent may alleviate certain complications with biliary obstruction, combined with the immunosuppressive qualities of chemotherapy, the likelihood of sepsis increases, with incidence rates significantly greater than those previously reported in the drugs' prescribing information or previous studies. The current practice of the insertion of the biliary stent potentially introduces flora during the procedure, resulting in potential infection later with administration of chemotherapy. Clinical trial information: NCT03257033. Research Sponsor: RenovoRx.

400 Poster Session

Impact of pancreatic enzyme replacement therapy (PERT) on clinical outcomes in nonresected pancreatic cancer (PC): Initial results. *First Author: Vincent J. Picozzi, Virginia Mason Hospital and Medical Center, Seattle, WA*

Background: Current NCCN guidelines recommend PERT use in PC patients (pts) with symptoms of EPI. However, little evidence exists regarding clinical outcomes following PERT use in PC pts, especially those with nonresected disease. We present initial results from PERT use in this pt group regarding disease control and symptom improvement. **Methods:** Pts with initially nonresected PC were obtained for this study from the Virginia Mason PC Database. Eligibility criteria included:1) pathologically diagnosed nonresected adeno PC from January 2014-December 2019 ; 2) no prior PC anticancer therapy (PCRx) of any kind; 3) ≥2 PGSGA (Patient Generated Global Subjective Assessment) forms completed with initial PGSGA reporting before 30 days following first PCRx. Pts were stratified by PERT vs non-PERT prescription as validated by the EHR. Clinicians tended to prescribe PERT based on either abnormal fecal elastase and/or clinical symptoms (e.g. diarrhea) as in the PGSGA; no formal criteria for PERT usage existed. Pts were considered to have received PERT if prescribed for the majority of time during the assessment period (i.e. > 30 days) and were analyzed based on an "intent to treat" basis without compliance validation. **Results:** 344 pts were identified via this method ; 207 (60%)/137 (40%) did/did not receive PERT. > 95% received Creon as PERT. Median time from 1st day PCRx to 1st reassessment was 60 days. 79% pts completed PGSGA prior to and 97% within 2 weeks of 1st day PCRx. Pt characteristics were balanced between PERT/ non PERT groups including race (90% white), age (median 68 yrs), sex (M/F 53%/47%), non-metastatic/ metastatic disease 24%/76% . BMI distribution (< 18.5 3%, 18.5-25 40%, 25-30 34%, and >30 23%),and albumin distribution (<3 g/dL 6%, 3-3.4 g/dL 12% and ≥3.5 g/dL 82%). However, mean baseline PGSGA score was higher in the PERT vs non PERT group (9.9 overall, 10.9 (95% CI 10.1-11.7) vs 8.2 (95% CI 7.3 - 9.1), p< 0.01). At 1st reassessment, disease control (PR+SD) (83% overall) was greater in the PERT (87%) vs. non PERT (79%) group (p=0.04).Change from baseline PGSGA was favorable overall (Δ-5.0, 95% CI-5.7--4.3), and in all pt subsets, but with greater improvement in the PERT (Δ-6.0) vs. non PERT (Δ -3.4) group (p< 0.001) and in disease controlled (Δ-5.3) vs. non-disease controlled (Δ- 3.2) pts (p=0.033). Disease controlled vs. non-disease controlled PERT pts did not differ in their PGSGA response (Δ-6.2/-4.8, p=0.98) **Conclusions:** 1) PERT vs non-PERT pts were similar with respect to basic clinical or nutritional parameters (e.g. BMI, albumin) in this pt cohort. 2) Despite having more adverse baseline PGSGA scores, PERT pts were statistically superior to non PERT pts with respect to both frequency of disease control and magnitude of PGSGA response during initial Rx 3) Further investigation of the detail involving PERT usage and clinical outcomes in nonresected PC is warranted from these data. Research Sponsor: Abbvie.

401 Poster Session

Projected 30-day out-of-pocket and total spending on pancreatic enzyme replacement therapy under Medicare Part D. *First Author: Arjun Gupta, University of Texas Southwestern Medical Center, Dallas, TX*

Background: Pancreatic enzyme replacement therapy (PERT) can reduce symptoms of indigestion and improve nutrition in patients with exocrine pancreatic insufficiency. PERT is under-prescribed, and this may be related to actual costs and prescriber sensitivity to these costs. Thus, we aimed to assess PERT costs. **Methods:** We used Medicare Part D formulary and pricing files for the first quarter of 2020 to conduct a patient-level modeling study to describe point-of-sale and out-of-pocket costs for each PERT formulation among Part D stand-alone and Medicare Advantage prescription drug plans. We calculated costs across nationwide plans under three scenarios: (1) standard benefit design ($435 deductible and 25% coinsurance after the deductible is met); (2) 25% coinsurance (for fills after the deductible and in the coverage gap until the patient spends $6,350 out-of-pocket); and (3) 5% coinsurance (once catastrophic coverage is reached). PERT doses are identified by the lipase content per capsule (in United States Pharmacopeia, USP, units). We calculated the number of units for each PERT formulation/ dose form that would provide optimally dosed PERT for the average US adult (250,000 USP units of lipase per day), based on guidelines and consensus. We first calculated costs for a single unit of PERT. Next, we calculated the number of units needed daily for each formulation/ dose form to provide optimally dosed PERT, and multiplied it by 30 to generate 30-day requirements and costs. **Results:** Across 3,974 plans nationwide, five PERT formulations in seventeen different doses were covered by Medicare plans in 2020. The range of lipase content in a single unit ranged from 3,000 to 40,000 USP units, and the per-unit list price ranged from $1.44 to $13.89. The point-of-sale price for a 30-day supply of optimally dosed PERT ranged from $2,109 to $4,840. For patients, the expected out-of-pocket costs for a 30-day supply of optimally dosed PERT averaged $999 across formulations (range, $853 to $1536) for those paying a deductible and coinsurance, $673 (range, $527 to $1210) for fills made after meeting the deductible until reaching catastrophic coverage, and $135 (range, $105 to $242) after reaching catastrophic coverage. **Conclusions:** In this analysis of 2020 Medicare Part D plans, the estimated out-of-pocket cost for just a 30-day supply of optimally dosed PERT was high— at least $100 in the catastrophic phase and approximately $1,000 in the initial phase. In the setting of pancreas cancer, already associated with heavy symptom burden and distress, the financial burden from a supportive care intervention (such as PERT) has been underappreciated. These costs may serve as a barrier to Medicare beneficiary drug access and contribute to financial toxicity. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology.

402 Poster Session

Nanoliposomal irinotecan-based chemotherapy after regular irinotecan-based chemotherapy in patients with pancreas cancer. *First Author: Caleb J Smith, Department of Internal Medicine, Mayo Clinic, Rochester, MN*

Background: Pancreas cancer is an aggressive malignancy with limited therapeutic options. Nanoliposomal irinotecan (Nal-IRI) is a preferred second-line treatment, and current guidelines recommend its use in the absence of prior irinotecan. This study aimed to assess whether patients who had received regular irinotecan derive benefit from Nal-IRI. **Methods:** Medical records of metastatic pancreas cancer patients who had received regular irinotecan and then Nal-IRI were reviewed. The following information was extracted from each medical record: patient demographics, confirmation of a diagnosis of exocrine pancreas cancer, initial cancer stage, dates of administration of the drugs of interest, adverse events that occurred with Nal-IRI treatment, reasons for stopping regular irinotecan, and reasons for starting and stopping Nal-IRI. The primary endpoint was overall survival after the initiation of Nal-IRI (an *a priori* threshold of $>$ 4 months defined success). Survival data were censored based on date of last follow up. Direct quotes from the medical record were documented to provide insight on prescribing Nal-IRI when guidelines advised the contrary. **Results:** Sixty four patients met eligibility criteria with a median age of 65 years (range: 36, 80 years). Prior to Nal-IRI, 61 patients had received FOLFIRINOX, and 3 FOLFIRI. Of these, 32 patients manifested progressive disease on regular irinotecan-based therapy. Nal-IRI was prescribed with a fluoropyrimidine; only one patient received monotherapy. At time of analysis, 54 patients had died. Median overall survival from initiation of Nal-IRI was 5.1 months (95% confidence interval (CI): 5.6, 4.3, months). An exploratory comparison, based on no cancer progression with regular irinotecan versus progression, showed improved survival with Nal-IRI in the former group: 6.1 months (95% CI: 9.3, 5.1 months) versus 4.3 months (95% CI: 4.8, 2.3 months); p=0.0006. Nal-IRI adverse events occurred as expected. Qualitative data illustrated several themes, including "limited treatment options," which appeared to drive the decision to prescribe Nal-IRI. **Conclusions:** Nal-IRI might be considered in pancreas cancer patients who had received regular irinotecan, particularly in the absence of disease progression with the latter. Research Sponsor: None.

403 Poster Session

Comparative efficacy of commonly used first-line chemotherapy regimens in advanced pancreatic cancer: A network meta-analysis. *First Author: Philip A. Haddad, Feist-Weiller Cancer Center at LSUHSC-Shreveport, Overton Brooks VAMC, Shreveport, LA*

Background: Pancreatic adenocarcinoma is one of the deadliest cancers, ranking fourth in mortality and accounting for up to 7% of all cancer related deaths in the United States. For many years, Gemcitabine and its combinations have been the standard first-line treatments for patients with unresectable locally advanced or metastatic pancreatic cancer (aPC). Recently, FOLFIRINOX was shown to be associated with a survival advantage as well. These chemotherapy combinations have not been compared to each other. We conducted this network meta-analysis to evaluate the relative efficacy of the commonly used chemotherapy regimens in patients with aPC. **Methods:** A review of the medical literature was conducted using online databases. Inclusion criteria consisted of English language; diagnosis of aPC; treatment with Gemcitabine (GEM) combined with Capecitabine (CAPE), Erlotinib (ERLO), or nab-Paclitaxel (NABPAC) and treatments with FOLFIRINOX; and randomized studies reporting survival and response rates. A frequentists network meta-analysis was conducted using netmeta package and random-effects model. **Results:** Six studies comprising a total of 2,717 participants were included. FOLFIRINOX demonstrated a significantly better relative risk (RR) of progression and death (P&D) followed by GEM+NABPAC, GEM+ERLO, GEM+CAPE, and GEM in a decreasing order. When compared to GEM-based combination as a group, FOLFIRINOX maintained its superior RR for P&D. Moreover, FOLFIRINOX and GEM+NABPAC had significantly better response rates than GEM+CAPE and GEM+ERLO. Inconsistency analysis did not reveal any significant differences between direct and indirect estimates. **Conclusions:** This network meta-analysis is the first to compare and rank commonly used treatment regimens in aPC. It indicates that FOLFIRINOX combination seems to be superior to GEM-based combinations with respect to P&D as well as response rates. Nevertheless, among GEM-based combinations, GEM+NABPAC seems to have the best profile given its lower RR for P&D and higher response rates. Research Sponsor: None.

404 Poster Session

ARC-8: Phase I/Ib study to evaluate safety and tolerability of AB680 + chemotherapy + zimberelimab (AB122) in patients with treatment-naive metastatic pancreatic adenocarcinoma (mPDAC). *First Author: Gulam Abbas Manji, Columbia University Herbert Irving Comprehensive Cancer Center, New York, NY*

Background: AB680, a potent, selective small-molecule inhibitor of soluble and membrane-bound CD73, targets a major pathway of extracellular adenosine production with the aim of eliminating adenosine-mediated immunosuppression within the tumor microenvironment. In mPDAC, programmed cell death protein-1 (PD-1) axis inhibitors have limited clinical activity as monotherapies or combined with standard-of-care (SOC) chemotherapy. *KRAS* mutations, present in $>$90% of invasive PDACs, are associated with significantly elevated CD73 expression and poor clinical outcomes. Thus, mPDAC may be particularly sensitive to CD73 inhibition combined with SOC chemotherapy + anti-PD-1 antibody (zimberelimab [Zim]) treatment. **Methods:** ARC-8 (NCT04104672) is an ongoing phase 1b, dose escalation and expansion study in patients (pts) with treatment-naive mPDAC. In the dose escalation, AB680 (25, 50, 75, or 100 mg) is administered intravenously once every 2 weeks (Q2W) with standard doses of nab-paclitaxel/gemcitabine (NP/Gem) + Zim (240 mg) in a 3+3 design to determine the recommended dose for expansion (RDE). In the dose expansion, AB680 will be administered at the RDE with NP/Gem + Zim. Adverse events (AEs) and dose-limiting toxicities (DLTs) are recorded and graded per NCI CTCAE 5.0. AB680 pharmacokinetics, pharmacodynamics, and biomarker evaluations are also being performed throughout the study. Clinical activity is assessed every 8 weeks per RECIST v1.1. **Results:** As of 04SEPT2020, enrolled patients include 4 in Cohort 1 (25 mg AB680), 6 in Cohort 2 (50 mg AB680), and 3 in Cohort 3 (75 mg AB680). Initial AE profiles were similar to those observed for NP/Gem. The most common treatment-related AEs were fatigue (n=6, 43%), anemia (n=4, 29%), and neutrophil count decrease (n=4, 29%); anemia (n=2, 14%) was the most common treatment-related grade 3/4 AE. Initial pharmacodynamic data (50 mg dose) indicated excellent peripheral target coverage at AB680 trough concentrations. Best overall responses for 9 evaluable pts were 3 with partial response (1 in Cohort 1; 2 in Cohort 2), including a complete response of a target lesion, and 5 with stable disease (1 in Cohort 1; 4 in Cohort 2). One pt in Cohort 1 discontinued the study due to progressive disease. As of the cutoff date, 1 DLT (Grade 2 autoimmune hepatitis) occurred in Cohort 2; the event completely resolved with steroids and the pt was able to resume study treatment. No DLTs were reported in Cohort 3. **Conclusions:** Preliminary results from ARC-8 indicate that AB680, the first clinical-stage small-molecule CD73 inhibitor, in combination with SOC chemotherapy + Zim has a manageable safety profile consistent with that expected for each agent alone and demonstrates early signals of clinical activity. Dose escalation to 100 mg AB680 (Cohort 4) is ongoing to inform RDE selection. Clinical trial information: NCT04104672. Research Sponsor: Arcus Biosciences, Inc.

405 Poster Session

Efficacy and preclinical safety of ARB202, a potential first-in-class anti-CDH17/CD3 bispecific T-cell engager, for treatment of pancreatic and colorectal cancers. *First Author: Dennis A Wong, Arbele Corporation, Redmond, WA*

Background: Globally, gastrointestinal (GI) cancers, which account for around 28% of all cancers, has increased constantly at a CAGR of 2% (2014-2019), while the treatment options remain limited and often ineffective. This is largely due to late diagnosis and lack of new tumor associated antigens for most of the GI malignancies. Cadherin-17, CDH17 (aka CA17), is being evaluated as a potential therapeutic target and molecular marker for GI cancers, of which aberrant expression of CDH17 was reported in 50-90% in tumor samples (including stomach, pancreas, liver/bile duct and colon) by multiple groups. The present study aims to develop a humanized CDH17-CD3 bispecific T-cell engager antibody, ARB202, to treat advanced pancreatic and metastatic colon cancers. **Methods:** The ARB202 bispecific was generated from anti-CDH17 monoclonal ARB102 as previously described (Lum Y et al, Mol. Pharm. 2020) by linking a CD3-binding scFv in the format of IgG4-scFv. Biophysical properties, efficacy and safety were evaluated. Efficacy was addressed in cytotoxicity assays, IL2-release assays and subcutaneous xenograft models using multiple GI tumor target lines. Preclinical safety profiles include Tissue cross-reactivity assays and GLP repeat-dose toxicity studies in NHP. **Results:** The ARB202 bispecific antibody was efficiently produced (yield ~1 g/L) and remained stable for at least 3 months under accelerated stress tests. Binding affinity (Kd [M]) of ARB202 to CDH17 and CD3 was at 10^{-10} and 10^{-9} respectively, with cellular affinities of 10^{-9} and 10^{-8}. In vitro cytotoxicity assays demonstrate that ARB202-mediated tumor cell killing is CDH17-dependent and requires immune synapse formation with effector T cells. By contrast, normal cells and CDH17-negative cancer cells are resistant. Pancreatic AsPC1 xenograft model revealed an ARB202 (co-inoculated with human PBMC) dose-dependent inhibition of tumor growth. Human IL-2 release in mice blood samples was consistent with functional CDH17 and CD3 engagement. ARB202 PK profile in rodents and NHP was found to be excellent relative to other bispecifics and GLP toxicity studies showed no significant findings nor adverse effects. **Conclusions:** ARB202 bispecific antibody promises to be a first-in-class biologic, which may tackle approximately 50% of GI cancers that which have been reported CDH17 positive. First-in-human clinical study with advanced GI cancers is scheduled to start in Q1 2021. Research Sponsor: None.

406 Poster Session

Randomized multicenter phase II/III study with adjuvant gemcitabine versus neoadjuvant/adjuvant FOLFIRINOX in resectable pancreatic cancer: The NEPAFOX trial. *First Author: Salah-Eddin Al-Batran, University Cancer Center Frankfurt, Institut für Klinisch-Onkologische Forschung am Krankenhaus Nordwest, Frankfurt, Germany*

Background: The outcome of pancreatic cancer remains poor. Few patients (pts) can be assigned to surgery and 80% of resected pts experience a relapse. Currently, adjuvant ctx is standard, but prognosis remains poor. FOLFIRINOX (FFX) is a SOC in metastatic and meanwhile in the adjuvant setting and may represent a valuable neoadjuvant option in resectable and borderline resectable stages. We initiated the NEPAFOX- trial in Germany to explore the efficacy of perioperative FFX. **Methods:** This is a multicenter randomized phase II/III trial. Recruitment of the trial was stopped after 40 patients (pts) due to poor accrual. Pts with resectable or borderline resectable adenocarcinoma of the pancreas without metastases were eligible. Eligible pts were randomized to (arm A) upfront surgery followed by adjuvant gemcitabine (1000 mg/m^2) for 6 months or (arm B) perioperative FFX (irinotecan 180 mg/m^2, oxaliplatin 85 mg/m^2, 5-FU 400mg/m^2 bolus, 5-FU 2400 mg/m^2, sodium folinate 400 mg/m^2) 4-6 cycles (8-12 weeks) pre and further 4-6 cycles post surgery. The primary endpoint is OS. Secondary endpoints include PFS, perioperative morbidity, mortality, and others. **Results:** 40 pts (42.5% female) were randomized over 3 years (05.03.2015 FPI - 23.03.2018 LPI), 21 in arm A, 19 in arm B. Age range was 46-84y, median age 64y.Before randomization, 76.2% of the pts in Arm A and 78.9% in Arm B were classified as primarily resectable the remaining pts as borderline resectable. Patients received in median 3 cycles in Arm A (range: 0-6) and 6 in Arm B (range: 1-12). Surgery was performed in 18 pts (85.7%) in Arm A and 11 (57.9%) in Arm B. Reasons for not conducting surgery were for Arm A patient´s wish (1 pt) and inoperability (2 pts), for Arm B early progressive disease (4 pts), death (1 pt), pneumonia (1 pt), and toxicities (1 pt). 13 (Arm A) and 5 (Arm B) pts had a R0-Resection. Perioperative morbidity occurred in 72.2% of operated pts in Arm A and 45.5% in Arm B. Median OS was 25.68 months in Arm A (6 events of death) and 10.03 months in Arm B (14 events) with HR 0.366 and p = 0.0337. Median PFS was 9.8 months in Arm A (12 events) and 6.64 months in Arm B (16 events) with HR 0.722 and p = 0.4099. **Conclusions:** Due to low pt numbers, the analyses for primary and secondary endpoints are not robust and only descriptive. Median OS for Gemcitabine- arm was in the line with literature data and better than for FFX, but pt/event numbers are too for conclusion. Only 11 out of 19 FFX pts underwent surgery, only 9 pts had pancreatic resection, indicating that pts should be extremely good selected before starting a neoadjuvant approach. According to CT or MRI pts of arm B were not more advanced regarding tumor staging. Nevertheless, there were no safety issues in the FFX arm regarding surgical complications, so neoadjuvant/ perioperative treatment approach seems to be feasible, subjected to the small number of pts in the study. Clinical trial information: NCT02172976. Research Sponsor: medac, Vifor, Pfizer.

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Efficacy and safety of 5-fluorouracil (5-FU) / levofolinate / irinotecan (FOLFIRI) for previously treated advanced pancreatic cancer (APC). *First Author: Hiromichi Shirasu, Division of Clinical Oncology, Shizuoka Cancer Center, Shizuoka, Japan*

Background: 5-fluorouracil (5-FU) / levofolinate / irinotecan (FOLFIRI) is one of the preferred regimens for patients (pts) with advanced pancreatic cancer (APC) who received prior gemcitabine-based therapy in the National Comprehensive Cancer Network Guidelines. However, its survival benefit or safety in clinical practice is unclear. **Methods:** We retrospectively assessed the data of consecutive pts with APC who received FOLFIRI as a second or later-line treatment after gemcitabine-based therapy at Shizuoka Cancer Center between May 2014 and March 2020. **Results:** The characteristics of 102 pts included in this analysis were as follows: median age (range), 67 (39-78) y; male/female, 55/47; ECOG PS0/1/2, 21/72/9; the number of metastatic sites 0/1/2/3/4, 7/48/35/8/4; unresectable/recurrent, 84/18; UGT1A1 status wild/*6 or*28 heterozygous/homo or double-heterozygous/unknown, 40/40/5/17; treatment line of FOLFIRI 2nd/3rd/4th, 64/32/6. Previous treatment history according to the treatment line of FOLFIRI was as follows: 2nd-line, all patients received GEM-based regimen, GEM plus nanoparticle albumin bound paclitaxel in 63 pts (98.4%) and GEM in 1 (1.6%); 3rd, GEM-based and S1 in 20 (62.5%), GEM-based and 5-FU/levofolinate/oxaliplatin (FOLFOX) in 12 (37.5%); 4th, GEM-based, FOLFOX and S-1 or other agent in 5 (83.3%), 2 GEM-based regimens and S1 in 1 (16.7%). The median treatment cycle was 5 (range 1-55). The median treatment cycle according to the treatment line was as follows: 2nd-line, 7(1-55); 3rd, 4(1-14); 4th, 3.5(1-10). The initial dosage for each cytotoxic agent was as follows: bolus 5-FU injected/omited 72/30; continuous 5-FU 2400/2000/1200 mg/m^2, 88/13/1; irinotecan 180/150/120/less than or equal to 100mg/m^2, 27/59/13/3. The overall response rate (ORR) and disease control rate (DCR) were 5.9% and 52.9%, respectively. ORR and DCR according to the treatment line were as follows: 2nd-line, 9.3/64.1%; 3rd, 0/68.8%; 4th, 0/50.0%. At the median follow up 6.5 M, the median overall survival (OS) and progression free survival (PFS) were 6.6M and 3.1M, respectively. The median OS and PFS according to the treatment line were as follows: 2nd-line, 8.1/3.6M; 3rd, 5.1/2.1M; 4th, 6.6/2.0M. Adverse events (AEs) were observed in 70.8% pts. Grade 3 or higher AEs occurred in 27.2% pts [neutropenia in 26 (25.2%) pts, febrile neutropenia in 4 (3.9%) pts, nausea in 4 (3.9%) pts, decreased appetite in 3 (2.9%) pts]. No treatment related deaths were observed. **Conclusions:** FOLFIRI is well tolerated and effective especially in the second-line treatment for pts with gemcitabine-refractory APC. Research Sponsor: None.

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Irreversible electroporation versus chemotherapy with or without radiation for locally advanced pancreatic adenocarcinoma: A systematic review and meta-analysis. *First Author: Kavin Sugumar, University Hospitals, Seidman Cancer Center and Department of Surgery, Cleveland, OH*

Background: Multi-agent chemotherapy (CT) with or without radiotherapy (RT) is the standard of care for non-metastatic Type B locally advanced pancreatic cancer (LAPC). Irreversible electroporation (IRE) has been described as a treatment modality in patients with LAPC but published post-operative morbidity and mortality rates are high for a non-curative procedure. There have been few studies that have compared directly IRE with standard of care CT ± RT. We performed a meta-analysis of the available literature to compare the outcomes between these treatment groups in LAPC. **Methods:** A systematic literature search was performed in Medline, Embase, and the Cochrane Library in September 2020. Studies that focused on comparing outcomes between IRE and CT ± RT for LAPC were selected for further study. The impact of IRE versus CT ± RT was evaluated using forest plot analysis. Overall survival (OS) and progression free survival (PFS) served as the primary endpoints. As a secondary objective, short term morbidity and mortality data in both groups was evaluated. **Results:** Our search yielded 326 papers. After excluding duplicates, 3 studies met inclusion criteria. All were retrospective. Combined, these studies included clinical data on 3,862 patients. The meta-analysis indicated that patients with LAPC who underwent IRE had better OS (HR = 0.46, 95% CI: 0.28-0.74) and PFS (HR = 0.38, 95% CI: 0.24-0.60) compared to patients who received CT ± RT. Due to incomplete morbidity, 30-, and 90- day mortality information reported in the included studies, further analysis was not performed for the same. **Conclusions:** There is a striking paucity of studies comparing IRE with the standard of care treatment approaches for LAPC. Our meta-analysis reveals that IRE has been associated with longer OS and PFS compared to CT ± RT. However, these studies are limited by retrospective study design, heterogeneity of population and chemotherapy regimens, and incomplete morbidity data, precluding any conclusions. Until higher quality, comparative retrospective studies, or more importantly, prospective studies with standardized indications are conducted, IRE should be used with caution and remains experimental in the treatment of PDAC. Research Sponsor: None.

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Efficacy observation of albumin-bound paclitaxel combined with S1, sequential and alternate gemcitabine combined with oxaliplatin in the first-line treatment of metastatic pancreatic ductal adenocarcinoma (mPDAC): A single-arm, prospective study. *First Author: Zhiwei Li, Cancer Hospital Affiliated to Harbin Medical University, Harbin, China*

Background: Chemotherapy is effective in mPDAC but the effect is not satisfactory. Alternate sequential treatment appears to be feasible and effective, with manageable toxicities and decreased neurotoxicity. Similar studies have not been carried out in China. Therefore, we evaluated the efficacy and safety of albumin-bound paclitaxel combined with S1, sequential and alternate gemcitabine combined with oxaliplatin in the first-line treatment of patients with mPDAC. **Methods:** Based on an expected 6-month PFS rate of 45% and a threshold 6-month PFS rate of 25%, a one-sided exact test is applied setting α = 0.025. The number of patients required for a power of 80% was calculated to be 24. Considering the drop rate of 15%, 30 patients need to be enrolled in the experiment. This open-label, single-arm, prospective study enrolled patients with locally advanced and metastatic pancreatic cancer, who have not received prior chemotherapy regimens and radiation therapy between Jan, 2019 and Dec, 2020. The patient receives the NS regimen first: albumin-bound paclitaxel(125mg/m^2) was administered for the first and eighth day by intravenous drip and S1 (40-60 mg)was administered orally twice a day for 2 cycles with 3-week cycle. Then the GEMOX regimen is applied sequentially and alternately: Gemcitabine (1000mg/m^2, intravenous infusion for 30 minutes, administration on the first and eighth days) and oxaliplatin (130mg/m^2, intravenous injection for 2 hours, administration on the second day) were given for 2 cycles with 3-week cycle. After that, the NS and GEMOX regimen were alternately used again. The treatment was continued until disease progression or unacceptable toxic effects. **Results:** In this study, 36 eligible patients received the sequential treatment of the above regimen with a median age of 59 years (range 35 to 67 years). 24 patients were eligible for efficacy analysis. Median follow up time was 8.8 months. 45.8% (11/24) of patients completed 3 alternating (8 cycles) treatment, and 33.3% (8/24) of patients completed 2 alternating (6 cycles) treatment, other patients only completed 1 alternate treatment. 6-month PFS rate was 70.8% (17/24) , The median PFS of 24 patients was 8.9 months. The final OS and PFS was not yet achieved. The most common grade 3/4 treatment related AEs were thrombocytopenia (13.33%), granulopenia (8.3%), peripheral nerve toxicity (5.6%), and all adverse reactions could be recovered to less than grade 2 after suspension of medication or reduction of dose. **Conclusions:** The treatment of albumin-bound paclitaxel combined with S1, sequential and alternate gemcitabine combined with oxaliplatin showed promising efficacy and manageable toxicities in patients with mPDAC, and required more prospective patients to be enrolled. Clinical trial information: ChiCTR1900024867. Research Sponsor: None.

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Early outcomes of irreversible electroporation after stereotactic body radiation therapy for the treatment of locally advanced pancreatic adenocarcinoma (LAPC): A matched pair analysis. *First Author: Emanuel Boyer, University of South Florida Morsani College of Medicine, Tampa, FL*

Background: Outcomes remain poor for those diagnosed with unresectable pancreatic cancer. SBRT and IRE have independently demonstrated high rates of local control and minimal toxicity for patients with locally advanced pancreatic cancer (LAPC). Data is limited regarding safety and efficacy in the sequential use of both therapies. **Materials and Methods:** A single institution retrospective matched cohort analysis was performed for patients with non-metastatic pancreatic cancer treated with induction chemotherapy and SBRT followed by IRE, compared with patients of the same cohort who did not receive IRE. Patients were paired based on age, tumor stage, GTV D95, CA19-9 prior to SBRT, and chemotherapy type to mitigate selection bias in surgical candidates. Overall survival (OS), progression free survival (PFS), freedom from local failure (FFLF) and freedom from distant failure (FFDF) were the primary outcomes compared via Kaplan-Meier survival analysis with log-rank methods. **Results:** From July, 2014 to February, 2020 17 patients received SBRT followed by IRE. These patients were matched with 17 patients who received SBRT from January, 2012 to March, 2019. Most patients received neoadjuvant FOLFIRINOX (82.4%) and were AJCC 8 stage III (79.4%). Median age of the overall cohort was 65.5 years and 50% were male. Median dose delivered to 95% of gross tumor volume was 32.61 Gy, and median pre SBRT CA19-9 value was 70.5 U/mL. There were no statistically significant differences in matched characteristics between the two cohorts. Among the SBRT+IRE, the median time between IRE and SBRT was 66 days (range:49-467 days). The median OS, PFS, FFLF, and FFDF for IRE+SBRT vs. SBRT alone from SBRT was 10.8 vs 15.1 months, 9.6 vs. 15.3 months, 15.7 vs. 15.3 months, 15.9 vs. 14.4 months respectively (all $P > .10$). 11 patients in the entire cohort experienced toxicity as a result of their radiation therapy (35%), with one G3 GIB and one patient experiencing G3 abdominal pain. Among the 17 patients who underwent IRE, nine patients experienced toxicity (53%). Most of these events were G3, with two G4 intestinal bleeds. There was zero mortality in the 90 day period post operatively. **Conclusions:** In a retrospective cohort,non-selective delivery ofIRE afterSBRT demonstrated no oncological benefit for patients with unresectable pancreatic adenocarcinoma compared to only SBRT. Compared to historical experiences of IRE alone, there was no increase in overall toxicity with the combination of SBRT and IRE. The optimal timing, sequencing, and indications for IRE and SBRT in LAPC remain unknown and are best assessed prospectively. Research Sponsor: Research, Innovation & Scholarly Endeavors at USF Health, Morsani College of Medicine.

	Total N = 34	IRE+SBRT N = 17	SBRT Alone N = 17
Age (median)	65.5	65	67
Chemotherapy			
FOLFIRINOX	28	14	14
Gem/Abraxane	6	3	3
Tumor Stage			
III	27	12	15
IIB	3	3	0
IIA	2	1	1
IB	2	1	1
CA19-9 (median)	70.5	84.2	56.7
GTV D95 (median)	32.61	32.38	32.92

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Predictive value of plasma tumor mutation burden (TMB) in the CCTG PA.7 trial: Gemcitabine (GEM) and nab-paclitaxel (Nab-P) vs. GEM, nab-P, durvalumab (D) and tremelimumab (T) as first line therapy in metastatic pancreatic ductal adenocarcinoma (mPDAC). *First Author: Daniel John Renouf, BC Cancer Agency, Vancouver, BC, Canada*

Background: PA.7 evaluated whether combining PD-L1 and CTLA-4 inhibition with GEM and Nab-P increases efficacy as first line therapy in mPDAC. High TMB is associated with immunotherapy sensitivity, with a threshold of ≥10 mut/Mb receiving FDA accelerated approved for pembrolizumab in a tissue agnostic setting. We assessed the predictive value of plasma TMB in the PA.7 trial. **Methods:** This randomized phase II study (ClinicalTrials.gov NCT02879318) assessed the efficacy and safety of GEM, Nab-P, D, and T (arm A) vs. GEM and Nab-P (arm B) in patients (pts) with mPDAC (n = 180). The primary endpoint was overall survival (OS). Pretreatment plasma was sequenced with the CLIA-certified PredicineATLAS cfDNA next generation assay (600 genes, 2.4 Mb panel). A pre-specified cut point of 5 mut/MB was selected based on distribution of TMB in the trial. 2-sided alpha set at 0.1. **Results:** 180 pts were randomized (119 to arm A and 61 to arm B). There was no significant difference in OS (9.8 months in arm A vs. 8.8 months in arm B, p-value 0.72) or PFS (5.5 months and 5.4 months respectively, HR 0.98, p-value 0.91). Plasma TMB analysis was performed on 174/180 pts with available samples, and tumor derived variants were detected in 173/174 pts (99.4%). 172 pts were microsatellite stable and 1 pt was microsatellite high (MSI-H) (plasma TMB 52.9 muts/Mb). Using the pre-specified cut-point of 5 mut/Mb there was no significant predictive value from plasma TMB (interaction p = 0.91). Using a minimum p-value approach, a cut-point of 9 mut/MB appeared predictive (p-interaction = 0.064; significant at pre-specified p = 0.1). 8/174 (4.6%) pts had a plasma TMB ≥9 mut/Mb (5/115 (4.4%) in arm A and 3/59 (5%) in arm B). GEM, Nab-P, D+T was associated with improved OS in patients with plasma TMB ≥9 mut/Mb (HR 0.30, 90% CI 0.06-1.37) while no activity was seen in pts with < 9 mut/Mb, (HR 0.97, 90% CI 0.73-1.29). TMB cut-point analysis revealed a clear trend for a decreasing HR favoring the GEM, Nab-P, D and T arm above the selected cut point, with no benefit in the low TMB group. **Conclusions:** Plasma TMB analysis was successful in over 99% of pts with available samples. Plasma TMB ≥9 mut/Mb was predictive of benefit from the addition of dual immune checkpoint inhibitors (D and T) to Gem and Nab-P, with a significant interaction p-value. While only present in a subgroup of pts (4.6%), this data defines a group beyond MSI-H PDAC that may benefit from immunotherapy. The optimal cut-point for high TMB in this setting requires validation. A clinical trial specifically assessing the role of chemotherapy combined with immune checkpoint inhibition in high TMB mPDAC is warranted. Clinical trial information: NCT02879318. Research Sponsor: Canadian Cancer Trials Group, Pharmaceutical/Biotech Company.

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POLO: Radiologic assessment of the impact of maintenance olaparib in patients (pts) with metastatic pancreatic cancer (mPaC). *First Author: Lawrence Howard Schwartz, Department of Radiology, Columbia University College of Physicians and Surgeons, New York, NY*

Background: The phase III POLO study (NCT02184195) demonstrated a benefit of maintenance olaparib over placebo in the radiologically assessed primary endpoint of progression-free survival (PFS) in pts with mPaC (median 7.4 vs 3.8 months [mo]; 12-mo rate 34% vs 15%). The impact of radiologic assessment of pancreatic lesions, which is considered challenging, was explored. **Methods:** Tumors were assessed using Response Evaluation Criteria in Solid Tumors version 1.1 by blinded independent central review (BICR) in pts with mPaC treated with maintenance olaparib or placebo. PFS was analyzed in subsets of pts based on various event criteria. **Results:** All 154 randomized pts had mPaC prior to chemotherapy, of whom 122 had disease in the pancreas at POLO baseline (BL); 34% (53/154) had pancreas-only target lesions (TL), 26% (40/154) also had ≥1 TL outside of the pancreas, and in 19% (29/154) pancreatic disease was recorded as non-TL. Sensitivity analyses were consistent with the primary PFS analysis (Table), including when all pancreas lesion assessments were discounted (median PFS 7.4 vs 4.7 mo; 12-mo rate 38% vs 22%). Of 53 pts with pancreas-only TLs at BL, 34 had disease progression (PD); in 20 pts this was not solely based on TL measurements (16 had new lesions; 4 had multiple-cause PD). Confirmed objective responses occurred during study maintenance treatment in 20% of olaparib pts (18/92) and 10% of placebo pts (6/62). In pts with pancreas-only TLs at BL there were 7 responses in the olaparib arm (1 complete response [CR], 6 partial responses [PR]) and 2 (2 PR) in the placebo arm. In pts who had ≥1 TL outside of the pancreas at BL there were 11 (1 CR, 10 PR) and 4 (4 PR) responses, respectively. Responses were generally durable irrespective of TL location. **Conclusions:** The significant PFS benefit with maintenance olaparib over placebo shown in the primary analysis was consistent across all sensitivity analyses and was not impacted by radiologic assessment of pancreatic TLs. Taken together, these findings suggest that contrary to historically held belief, primary pancreas TLs may be appropriate for inclusion as sites of RECIST-evaluable disease and for assessment of treatment outcome. Clinical trial information: NCT02184195. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	Events/Pts		
PFS Analyses	**Olaparib**	**Placebo**	**HR (95% CI)**
Primary			
By BICR	**60/92**	**44/62**	**0.53 (0.35–0.82)**
Sensitivity			
Excluding all pancreas assessments	56/92	39/62	0.62 (0.40–0.97)
Excluding pts with TL in pancreas only	41/63	27/38	0.46 (0.26–0.80)
Excluding pts with PD in pancreas only	52/84	37/55	0.51 (0.32–0.82)
By investigator assessment	54/92	48/62	0.51 (0.34–0.78)

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Phase II randomized, double-blind study of mFOLFIRINOX plus ramucirumab versus mFOLFIRINOX plus placebo in advanced pancreatic cancer patients (HCRN GI14-198). *First Author: Walid Labib Shaib, Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA*

Background: Vascular endothelial growth factor (VEGF) and VEGF receptor (VEGFR)-mediated signaling and angiogenesis contribute to the pathogenesis and progression of pancreatic adenocarcinoma (PCA).VEGF is expressed in all PCA tumors. VEGF-A/VEGFR-2 signaling plays an important role in inducing invasion and migration of PCA cells. The pVEGFR-2 is significantly associated with invasion of the anterior capsule of pancreas and arteries. In preclinical studies, the anti-tumor activity of fluoropyrimidines, but not that of gemcitabine, caused the release of bone marrow derived circulating endothelial progenitor cells (CEPs) and Tie-2 expressing monocytes (TEMs) as well as the induction of pro-angiogenic growth factors. **Methods:** This phase II randomized, multi-center, and double-blinded trial was designed to compare the efficacy and safety of mFOLFIRINOX/ramucirumab (Arm A) versus mFOLFIRINOX/ placebo (Arm B) as front-line therapy in recurrent or metastatic PCA patients. The primary endpoint was progression free survival (PFS) at 9 months, and the secondary endpoints included overall survival (OS) and response rate. **Results:** A total of 86 subjects were enrolled, 82 were eligible (42 in Arm A v. 40 in Arm B). The mean age of the subjects in the two arms were comparable (61.7 v. 63.0, respectively); 43 male, 69 Caucasian. On the univariate analysis, there was no difference in distribution between the 2 arms for age, gender, race and ethnicity. The median PFS was 5.6 in Arm A compared to 6.7 months in Arm B (one-sided log-rank, p = 0.322). At 9 months, the progression free rates were 25.1% v. 35% for Arms A and B, respectively. The mFOLFIRINOX/ramucirumab combination was well tolerated. Patients in Arm A reported a slightly higher number of adverse events (AEs) encounters, most commonly diarrhea (29 vs 28), fatigue (25 v. 25), vomiting (24 v. 14), weight loss (23 v. 17), and abdominal pain (20 v. 15). Arm A had more SAEs than Arm B (43 v. 25), with sepsis most commonly reported in both arms (3 in each), vomiting (3 v. 2), diarrhea (3 v.1) and duodenal obstruction (3 v. 0). Arm B had a slightly higher response rate (22.58%) compared to Arm A (17.65%) that was not statistically significant. The median OS in Arm A was 10.3 compared to 9.7 months for Arm B (one-sided log-rank, p = 0.094). **Conclusions:** In this randomized phase 2 study, the addition of ramucirumab to mFOLFIRINOX did not improve PFS, response rate, or OS as initial therapy for metastatic pancreatic cancer. FOLFIRINOX/ Ramucirumab combination was well tolerated in the treatment of PCA. Clinical trial information: NCT02581215. Research Sponsor: Eli Lilly.

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Type of fiducial marker and clinical outcomes in stereotactic body radiation therapy for pancreatic cancer. *First Author: J Richelcyn Baclay, Stanford University, Stanford, CA*

Background: Stereotactic body radiation therapy (SBRT) for pancreatic cancers has been shown to improve local control, and is an important option for treatment, especially for unresectable disease. Verifying the tumor location prior to delivery of SBRT is challenging, so fiducial markers are used to track tumor location. There is currently no standard of which fiducials to use in treatment. This study would like to compare outcomes of patients treated with SBRT using different fiducial markers. **Methods:** Records of patients diagnosed with primary pancreas cancer who were treated with chemotherapy and SBRT were reviewed from 2006-2019. Patients were excluded if they were treated with Cyberknife, were metastatic at presentation, recurrence /persistent disease after Whipple/radiation therapy, were secondary metastatic disease (from another primary), and if they were resected after SBRT. Patients were categorized according to the fiducial used for tumor tracking during SBRT treatment: gold seeds, intrabiliary stent, or both. Cumulative incidence of local recurrence (CIR) was analyzed with death as competing event, and time to over-all survival was estimated using Kaplan-Meier curves. **Results:** A total of 129 patients with available fiducial information were included in this study, of which 64 (49.6%) were treated with SBRT using gold seeds, 23 (17.8%) using intrabiliary stent, and 42 (32.6%) using both the seeds and stent. There were no difference between groups in terms of baseline characteristics such as age (p = 0.169), sex (p = 0.293), and stage grouping (p = 0.293). Median follow-up time was 15 months (range: 0.3-37.3 months). The 6- and 12-month CIR were 1.5% (95%CI, 0.1%-7.4%) and 11% (95%CI, 4.8%-20.2%) for patients treated with seeds, 4.3% (95%CI, 0.2%-18.6%) and 30.4% (95%CI, 13.1%-49.8%) for patients treated with stent, and 4.8% (95%CI, 0.8%-14.6%) and 19.5% (95%CI, 9.0%-32.9%) for patients treated with both (p = 0.007). Median time to overall survival was 15.3 months (95%CI, 13-17.8 months) for patients treated with seeds, 21.3 months (95%CI, 14.7-29.6 months) for patients treated with stent, and 15.7 months (95%CI, 11.5-19.7 months) for patients treated with both (p = 0.307). Univariate analysis for predictors of local failure did not show significance for age (p = 0.812), or advanced stage (p = 0.483), but was significant for the presence of seeds (p = 0.006). **Conclusions:** The type of fiducial marker used for tracking during pancreas SBRT treatment was associated with local failure but no difference in overall survival. Further analysis is warranted to see which clinical factors contribute to this difference. Research Sponsor: None.

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Investigate the efficacy of immunotherapy for treatment of pancreatic adenocarcinoma (PDAC) with mismatch repair deficiency (dMMR). *First Author: Arish Noor, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL*

Background: Immune checkpoint inhibitors (ICI) have been approved in solid tumors with dMMR. However, only limited data are available for PDAC with dMMR given the rarity of dMMR in PDAC. We evaluated efficacy of ICIs in PDAC with dMMR. **Methods:** Retrospective clinical and pathologic data were collected for patients (pts) with pancreatic adenocarcinoma from May 2017 to June 2020 at Moffitt cancer center. **Results:** We identified 10 pts with dMMR PDAC. The median age was 64.5 years (range: 42-86) and 4 pts were male. 4 pts had resectable disease, 3 had locally advanced and 3 had metastatic disease at initial diagnosis. MSH6 deficiency (def) was found in 2 cases, PMS2 def in 2, MLH/PMS2 def in 5, and MSH2/MSH6 in 1. 7 pts were treated with ICIs. 3 pts had locally advanced and 4 had metastatic disease when they started ICIs. 5 received Pembrolizumab (pem), 1 received ipilimumab/ nivolumab (ipi/ nivo), and 1 received pem then ipi/nivo after progressive disease (PD) on pem. The median number of prior lines of chemotherapy was 1 (range 0-2). 6 pts were evaluable, and 1 had rapid disease progression after 1 dose of pem. Among 6 evaluable pts, 3 had an objective response (1: complete response and 2: partial response), and 2 had stable disease (SD). Median progression-free survival was 8.2 mo, and median overall survival was not reached with median follow-up (FU) of 6.8 mo. The median duration of response was not reached with a median FU of 22.6 mo. The pt with CR remained disease-free for up to 22 months. The pt whose treatment was switched to ipi/nivo after PD on pem achieved SD > 4mo on ipi/nivo. While on immunotherapy, one patient with ipi/nivo developed immunotherapy associated rash requiring systemic steroids, and another on pem developed hypothyroidism requiring levothyroxine. **Conclusions:** This series suggest ICIs can provide durable clinical efficacy in pts with dMMR PDAC. Research Sponsor: None.

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The impact of multi-agent chemotherapy in metastatic pancreatic adenocarcinoma: A population-based study utilizing the SEER database. *First Author: Kavin Sugumar, University Hospitals, Seidman Cancer Center and Department of Surgery, Cleveland, OH*

Background: Over the last decade, various landmark trials have demonstrated the impact of multi-agent chemotherapy in the treatment of PDAC. However, the impact in the 'real world' has been less clear. The ACCORD trial (2011) was a phase III trial comparing combination chemotherapy (FOLFIRINOX) and single agent (gemcitabine) for advanced disease. The MPACT trial introduced another beneficial regimen (nab-paclitaxel and gemcitabine) in 2013. Subsequently, multi-agent chemotherapy became standard of care for medically appropriate patients. **Methods:** We used the Surveillance, Epidemiology, and End Results (SEER) database to identify patients diagnosed with PDAC between 1998 and 2017. The cohort was divided into two groups: 1998-2011 (pre-ACCORD) and 2012-2017 (post-ACCORD). We analyzed all patients with metastatic PDAC for overall survival and compared results in the two groups using Kaplan Meier analysis and multivariate Cox proportional hazards models. An interrupted time series analysis was also used to compare the temporal trends in 2-year survival between 1998 and 2017. **Results:** A total of 47,134 patients were diagnosed with PDAC between 1998 and 2017. Nearly two-third of patients (26,438; 57%) had distant disease. On univariate survival analysis, there was a significant increased overall survival probability in the 2012-17 group compared to the 1998-2011 group ($p<0.05$). The one- and two-year survival rates were 11% and 3% in the pre-ACCORD period compared to 14% and 4 % after the ACCORD trial respectively. This difference remained significant on multivariate analysis while adjusting for covariates (HR=0.08, 0.78-0.92, p=0.05). On interrupted time series analysis, we observed a steady rise in 2- year survival between 1998 and 2017. There was a significant jump in the two-year survival probability from 16% at 2011 to 20% at 2012 in metastatic PDAC (β=0.02, 0.009-0.03, $p<0.0001$, Table). **Conclusions:** Beyond the randomized clinical trial arena, overall survival has increased over time, with a statistically significant jump around the time of the ACCORD trial. However, the absolute increase in the 'real world' is smaller than the gains observed in prospective clinical trials. Research Sponsor: None.

Interrupted time series analysis two-year survival rates between 1998-2015 using Newey-West regression analysis.

Parameter	Regression coefficient	95% confidence interval	p-value
Year of diagnosis: 1998-2011	0.001	0.0005, 0.002	0.007
Year of diagnosis: 2012	0.02	0.14, 0.03	**<0.0001**
Year of diagnosis: 2012-2015	-0.0005	-0.002, 0.001	0.607

417 Poster Session

Microbiomic profiles of bile in patients with benign and malignant pancreaticobiliary disease. *First Author: Shyam K. Poudel, Western Reserve Health Education, Warren, OH*

Background: In pancreaticobiliary (PB) cancers, there is a paucity of data on predictive and pathophysiologic role of the biliary microbiome. We analyzed bile collected from patients with benign and malignant PB diseases to identify microbiomic signatures associated with malignancy. **Methods:** We collected bile samples from consenting patients during routine endoscopic retrograde cholangiopancreatography at the Cleveland Clinic, approved by the Institutional Review Board. DNA was extracted from bile specimens using PowerViral RNA/DNA Isolation kit. Bacterial 16S rRNA gene amplification and library construction were performed according to the 16S Metagenomic Sequencing Library Preparation guide from Illumina. Post-sequencing analysis was done using QIIME (Quantitative Insights Into Microbial Ecology), Bioconductor phyloseq, microbiomeSeq and mixMC packages. **Results:** Of 46 enrolled patients, 32 had PB cancers including pancreatic (N = 25), cholangiocarcinoma (N = 6), and gallbladder (N = 1). The rest (N = 14) had benign PB diseases including acute and chronic pancreatitis, and gallstones. Using multivariate approach in mixMC to classify Operational Taxonomic Units (OTUs), we found a predominance of genera *Dicekeya* (p = 0.0002), [*Eubacterium*] *hallii group* (p = 0.0007), *Bacteroides* (p = 0.00099), *Faecalibacterium* (p = 0.007), *Facklamia* (p = 0.013), *Peptococcus* (p = 0.013), *Bergeyella* (p = 0.0024), *Lachnospira* (p = 0.026), and *Lactobacillus* (p = 0.025) in bile samples from PB cancers as compared to benign PB diseases. Furthermore, bile samples from patients with pancreatic cancer showed an increased abundance of genera *Enterobacter, Parabacteroides, Atopobium, Alloprevotella, Prevotella 7, Acinetobacter, Bergeyella, Clostridium sensu stricto, Lactobacillus,* and *Rothia*; and a decreased abundance of genera *Tannerella, Peptococcus, Colinsella, Capnocytophaga, Achromobacter, Ruminococcus 2, Bacteroides, Alistipes, Barnesiella,, Lachnoclostridium, Lautropia, Akkermansia,* and *Christensenellaceae R-7 group* as compared to bile samples from patients with cholangiocarcinoma. **Conclusions:** Distinct microbiome signatures are associated with benign and malignant PB diseases. There is a difference in the relative abundance of OTUs in bile samples between patients with benign PB diseases vs PB cancers, and between pancreatic cancer vs cholangiocarcinoma. Our findings raise the possibility that either these OTUs have a role in carcinogenesis, or that changes in the microenvironment of benign PB diseases differ from PB cancers leading to distinct separation of the OTU clusters. Further studies to explore and validate our findings are needed. Research Sponsor: Sondra and Stephen Hardis Endowed Chair.

418 Poster Session

Evaluating the intratumor microbiome of pancreatic ductal adenocarcinoma (PDAC) by analyzing the fresh frozen tissues obtained by endoscopic ultrasound-guided fine needle aspiration (EUS-FNA). *First Author: Shintaro Nakano, Division of Cancer Center, Hokkaido University Hospital, Sapporo, Japan*

Background: Recent studies implied that intratumor microbiome was associated with carciniogenesis, development, prognosis and chemoresistance of pancreatic cancer (PC). There was more abundant bacteria in tumor tissue of pancreatic cancer than that of healthy controls. In clinical setting, diversity of intratumor bacteria was associated with good outcome of patients with resected pancreatic cancer. Specific intratumor bacteria could inactivate gemcitabine, which is crucial drug for PDAC, and may contribute to the resistance of gemcitabine.While most previous studies analyzed intratumor bacteria in PC by using resected tumor tissues, it was often impossible to obtain tumor sample from unresectable advanced PC. In addition, it is unclear whether tiny tissue obtained by endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is useful for analyzing intratumor microbiome.Therefore, we planned to evaluate the intratumor microbiome by analyzing the sample from EUS-FNA. **Methods:** This study was carried out as a single center, prospective observational study. The patients with PC were eligible for this study. PC tissues were collected from patients who undergo EUS-FNA. Biopsy tissues from the duodenal and gastric mucosa were also collected from the same patients. All samples were immediately stored at -80°C until use. Bacterial DNA was extracted from these specimens and 16S rRNA sequencing was performed. The endpoints of this study were success rate of detecting intratumor bacteria and association between intratumor bacteria and bacteria on the duodenal or gastric mucosa. **Results:** A total of 90 tissue samples from 30 patients were collected. The median age was 70 years (range 54-86 years), 19/5/6 patients had pancreatic head/body/tail tumor, 16s rRNA sequencing analyses showed that 24 samples (80%) of FNA from pancreatic tumor, 30 samples (100%) of gastric mucosa and 29 samples (97%) of duodenum mucosa could be analyzed. In diversity analyses, PC showed a lower alpha diversity compared to gastric or duodenum tissue. There was a significant difference in microbial structure between PC and duodenum tissue. In PC, dominant phylum was Proteobacteria and dominant genus was Acinetobacter. **Conclusions:** PC tissues obtained by EUS-FNA were useful for analyzing intratumor microbiome. Research Sponsor: Grant-in-Aid for Scientific Research, Division of Cancer Center, Hokkaido University Hospital.

419 Poster Session

Immunologic predictors of therapeutic response to neoadjuvant chemotherapy for pancreatic ductal adenocarcinoma (PDA) in SWOG S1505. *First Author: Davendra Sohal, University of Cincinnati, Cincinnati, OH*

Background: A role for the immune system in predicting treatment outcomes in PDA has not been well-studied prospectively, especially in the curative setting. Here, we investigated the capacity of two established chemotherapy regimens to trigger an immune response against PDA when administered as neoadjuvant therapy. **Methods:** We used available PDA surgical specimens from SWOG S1505 (a randomized phase II trial of perioperative chemotherapy with either mFOLFIRINOX [FFX] or gemcitabine/nab-paclitaxel [GA] for resectable PDA; ASCO 2020 abstr 4504) resected after 3 months of neoadjuvant chemotherapy, and matched untreated controls from the biorepository at the University of Utah. Multiplex immunohistochemistry (IHC) for CD8, CD68, CK19, FOXP3, PDL1, CD3, and Ki67 was performed; regions of interest (ROIs) were transcribed by a central pathologist. ROIs were digitally quantified using custom image analysis algorithms created using Visiopharm Integrator System software to detect and classify cells within superimposed grids for quantification; medians and coefficients of variation (CV) were calculated. Wilcoxon signed-rank test and Cox regression models were used to analyze associations between IHC cell counts and pathologic response (pR) and overall survival (OS), respectively. **Results:** IHC cell counts varied between treated (Rx) (n = 57; FFX = 34, GA = 23) and control (C) (n = 61) specimens for: CK19 percent area was 7.9 vs 15.6 ($p < 0.001$); total Ki67/mm^2 was 211 vs 400 ($p < 0.001$); total CD3/mm^2 was 376 vs 676 ($p < 0.001$); Foxp3/mm^2 was 81.5 vs 152.8 ($p < 0.001$); CD8/mm^2 was 313 vs 477 ($p < 0.001$); CD68/mm^2 was 507 vs 741 (p = 0.015). PDL1 expression was undetectable in the majority of specimens, both Rx and C. FFX (vs GA) was associated with fewer CK19$^+$Ki67$^+$ cells (459 vs 1026, p = 0.017) but more CD68$^+$ cells (33,241 vs 13,334, p = 0.007) and slightly more CD8$^+$ cells (19,809 vs 14,344, p = 0.049). In all Rx patients, complete/major (n = 19) vs poor/no (n = 36) pR was associated with total CD3/mm^2: 461 vs 308 (p = 0.019); the other parameters showed no notable differences. OS showed no remarkable associations with the tested parameters. **Conclusions:** We have demonstrated: 1) Decreased tumor cells and proliferating cells in Rx vs C samples, as expected. This decrease is more pronounced with FFX compared with GA; 2) Decreased total CD3$^+$ T cells as well as regulatory Foxp3$^+$ T cells in Rx vs C samples, which is unexpected; 3) A reduction in CD68$^+$ myeloid cells in Rx vs C samples, which is expected but more pronounced with GA compared with FFX; 4) Rx samples did not show an increased expression of PDL1, compared with C; and 5) Improved pR was associated with increased T cell infiltrate, pointing toward a possible mechanism. Together, these data support the capacity of neoadjuvant chemotherapy to modulate the immune response to PDA. Therapeutic implications of such changes merit further investigation. Clinical trial information: NCT02562716. Research Sponsor: U.S. National Institutes of HealthPharmaceutical/Biotech Company.

420 Poster Session

Olaparib sensitivity observed in metastatic pancreatic cancer (mPaC) with a wide spectrum of germline *BRCA1* and *BRCA2* mutations (gBRCAm). *First Author: Talia Golan, The Oncology Institute, Sheba Medical Center at Tel-Hashomer, Tel Aviv University, Tel Aviv, Israel*

Background: The POLO study (NCT02184195) showed that mPaC patients (pts) with a deleterious or suspected deleterious gBRCAm, and whose disease had not progressed during ≥16 weeks of first-line platinum-based chemotherapy, had significantly longer progression-free survival (PFS, primary endpoint) with maintenance olaparib vs placebo: median 7.4 vs 3.8 months, hazard ratio (HR) 0.53; *P*= 0.004. PFS benefit was observed in pts with g*BRCA1*m (HR 0.40) and g*BRCA2*m (HR 0.63). The POLO study represents the largest BRCAm prevalence study in pancreatic cancer. We report additional exploratory analysis to further characterize patient gBRCAm profiles, including the relationship with efficacy. **Methods:** Pts were enrolled based on either a previously identified gBRCAm status from a local test result and subsequently confirmed by central testing, or a prospectively identified gBRCAm. Pts received maintenance olaparib 300 mg twice daily (tablet) or placebo. PFS was assessed by blinded independent central review (modified RECIST v1.1). **Results:** Of 3194 prospectively screened pts, a valid BRCA test result was obtained for 3175 (99%) from 12 countries; gBRCAm prevalence was 6.2% in pts not previously known to harbor a gBRCAm (196/3175; 1.6% g*BRCA1*m, 4.5% g*BRCA2*m). In countries (n = 8) with > 100 pts prospectively tested, highest gBRCAm prevalence was 9.2% (USA) and lowest 4.0% (Spain). Prevalence by race (> 100 pts); 6.4% Caucasian, 4.6% Asian. In total, 154 pts with a gBRCAm satisfied all eligibility criteria and were randomized (106 prospectively tested and 48 by local test [44/48 subsequently confirmed by Myriad testing]). 37/154 (24%) randomized pts carried a common Ashkenazi Jewish founder mutation, the majority being from Israel (21 pts). From a total of 151 variants, frameshift mutations were most frequent (g*BRCA1*m 69.6%, g*BRCA2*m 71.4%) followed by nonsense mutations (g*BRCA1*m 6.5%, g*BRCA2*m 17.1%). The efficacy (PFS) of olaparib vs placebo in the different subgroups are shown in the table. **Conclusions:** In pts with mPaC enrolled in POLO, g*BRCA2*m were more prevalent than g*BRCA1*m and mutation type was predominantly frameshift. PFS benefit was consistent across a heterogenous spectrum of gBRCAm and with the previously reported full analysis set. Clinical trial information: NCT02184195. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

gBRCAm profile	n	HR	95% CI
Deleterious	151	0.55	0.36-0.84
Frameshift	106	0.67	0.43-1.06
Non-founder	93	0.51	0.30-0.88
Founder*	61	0.65	0.36-1.18

*Common Ashkenazi Jewish and other founder mutations

421 Poster Session

Comprehensive genomic profiling (CGP) utilizing cell-free DNA (cfDNA) in patients (pts) with pancreatic ductal adenocarcinoma (PDAC). *First Author: Ben George, Froedtert & The Medical College of Wisconsin, Milwaukee, WI*

Background: PDAC has a propensity for early systemic dissemination and most pts with primary tumors radiographically confined to the pancreas harbor micro-metastases. cfDNA based CGP offers a non-invasive mechanism to identify actionable genomic targets in PDAC and account for serial clonal evolution in response to therapeutic selection pressure. We interrogated the Foundation Medicine database to characterize cfDNA based CGP in pts with PDAC. **Methods:** We performed a retrospective analysis of pts with PDAC who underwent cfDNA based CGP between May 2016 and February 2020. cfDNA based CGP was done utilizing either the FoundationOne Liquid (F1-Liquid) or the Foundation-ACT (F-ACT) testing platform. Samples were interrogated for exonic and select intronic regions of cancer-related genes for both F1-Liquid (Exons: 70 genes; Select Introns: 7 genes) and F-ACT (Exons: 59 genes; Select Introns: 6 genes). Variant zygosity and somatic/germline status (SGZ) for short variant mutations was computationally predicted without matched normal tissue using an investigational method. A Gaussian Mixture Model (GMM) was used to identify latent molecular classes in samples harboring somatic, pathogenic variants (n=613); the Bayesian Information Criteria (BIC) was used for model selection. **Results:** We identified 1,009 pts with cfDNA based CGP - median age was 65, 55% were male, and median cfDNA concentration was 24 ng/μL. cfDNA yield had an influence on the detection of somatic alterations ($p < 0.001$). 613/1009 (60.8%) of pts had at least one somatic alteration detected on cfDNA based CGP. *TP53* (53.7%), *KRAS* (40.3%) and *CDKN2A* (6.5%) were the most frequently altered genes (Table1). Homologous Recombination DNA Damage Repair (HR-DDR) gene alterations [somatic and/or germline *BRCA2*, *ATM*, and *CHEK2* alterations], were detected in 12.3% (124/1009) pts – 11.4% (46/403) in *KRAS* mutated pts and 12.9% (78/606) in *KRAS* wildtype (WT) pts. Fusions were detected only in *KRAS* WT pts (1.5%, 6/403). Pts with cfDNA based CGP could be classified into 4 latent classes – class 1 (*KRAS* - 100%, *TP53* - 100% and *CDKN2A* – 33.3%), class 2 (*KRAS* - 65.7%), class 3 (*KRAS* – 68.2%, *CDKN2A/B* – 7.7%) and class 4 (*KRAS* – 38.5%, *TP53* - 26.7%). **Conclusions:** The putative role of cfDNA based CGP in monitoring therapeutic response and clonal evolution in pts with PDAC may be predicated on cfDNA yield. In clinical scenarios where pre-treatment tissue availability is limited, cfDNA based CGP may be have utility in leveraging the predictive value of somatic and/or germline HR-DDR gene alterations. The prognostic and/or predictive relevance of the four latent classes needs validation in clinically annotated data sets. Research Sponsor: None.

10 Most frequently altered genes in cfDNA samples (N=1,009).

Gene	cfDNA CGP (N=1009)	
TP53	542	53.7%
KRAS	407	40.3%
CDKN2A	66	6.5%
ATM	23	2.3%
PIK3CA	22	2.2%
TERT	14	1.4%
PTEN	14	1.4%
NF1	14	1.4%
JAK2	13	1.3%
GNAS	11	1.1%

422 Poster Session

Correlation between comprehensive genomic profiling (CGP) utilizing tissue-based testing (T-CGP) and cell-free DNA (cfDNA) in patients (pts) with pancreatic ductal adenocarcinoma (PDAC). *First Author: Ben George, Froedtert & The Medical College of Wisconsin, Milwaukee, WI*

Background: Early systemic dissemination is a salient feature of PDAC and the ability to reliably detect as well as monitor cfDNA based alterations may have predictive and/or prognostic value. However, a clear correlation between the clonality of the primary tumor and micro-metastatic disease has not been established in PDAC. We examined the correlation between T-CGP and cfDNA based CGP in pts with PDAC. **Methods:** We performed a retrospective analysis of PDAC pts who had both T-CGP (October 2010 – March 2020) and cfDNA based CGP (May 2016 – March 2020), with an average of 645 days between tests (Range: 21 – 2101 days) For T-CGP, exonic regions and select intronic regions of cancer related genes were sequenced to a high uniform depth (>500X median coverage) using FoundationOne Heme (Exons: 315 genes; Select Introns: 28 genes) and FoundationOne CDx (Exons: 310 genes; Select Introns: 34 genes). cfDNA based CGP, was performed using either FoundationOne Liquid (Exons: 70 genes; Select Introns: 7 genes) or Foundation-ACT (Exons: 59 genes; Select Introns: 6 genes) platform. **Results:** Eighty-one pts were identified with both T-CGP and cfDNA based CGP - median age was 61 years, 59.3% (48/81) were male and 66.2% (49/74) had reported metastatic disease. The median tumor DNA content available for T-CGP analysis was 112.3 ng. The median cfDNA concentration was 1.7 ng/μL, and the number of reported ct-DNA based somatic alterations correlated significantly with the concentration of ct-DNA (Spearman's $R = 0.19$, $p < 10^{-8}$). 75/81 (92.6%) and 41/81 (50.6%) of pts had at least one pathogenic somatic alteration detected by T-CGP and cfDNA based CGP, respectively. *KRAS*, *TP53* and *CDKN2A* were the most frequently altered genes in both T-CGP and cfDNA based CGP (Table1). Homologous Recombination DNA Damage Repair (HR-DDR) gene alterations [*BRCA2, ATM,* and *CHEK2* alterations] were detected in 7.4% (6/81) of T-CGP and 7.4% (6/81) cfDNA based CGP, respectively. Two *BRAF* fusions were detected from samples tested with T-CGP, however these were not detected with the cfDNA assay. Conversely, an *ALK-EML4* fusion was detected using both platforms. **Conclusions:** The concordance between T-CGP and cfDNA based CGP in HR-DDR gene alterations may be indicative of the germline status of some of these alterations; nevertheless, it suggests the predictive utility of cfDNA based CGP in PDAC. The differential prevalence of other gene alterations between the two modalities is likely reflective of the cfDNA yield available for CGP and to a lesser extent, clonal evolution. cfDNA based CGP holds promise as a complimentary predictive tool to T-CGP. Research Sponsor: None.

Most frequently altered genes in both T-CGP and cfDNA based CGP.

Gene	Solid (N=81)		Liquid (N=81)	
KRAS	70	86.4%	34	42.0%
TP53	55	67.9%	6	7.4%
CDKN2A	44	54.3%	2	2.5%

423 Poster Session

Serial cell-free DNA (cfDNA) sampling in advanced pancreatic ductal adenocarcinoma (PDAC) patients may predict therapeutic outcome. *First Author: Gehan Botrus, Mayo Clinic Arizona, Phoenix, AZ*

Background: Advanced PDAC remains a deadly disease with a 5-year survival rate of less than 10%. cfDNA - based next generation sequencing (NGS) may identify actionable alterations in patients with PDAC. In this study, we aim to determine the feasibility of utilizing serial cfDNA NGS testing and its potential relevance in predicting therapeutics outcomes. **Methods:** A total of 23 PDAC patients with PDAC cfDNA isolated from plasma collected at diagnosis and upon disease progression to first line SOC therapy and were analyzed on a 73-74 gene NGS panel (Guardant Health). Changes in molecular profiles from baseline to progression were analyzed for overall survival, progression free survival (PFS), and treatment response. PFS and OS were analyzed using the Kaplan-Meier method and the log-rank test was used to compare the survival of different groups of patients. All p-values were two-sided. Analyses were performed using R (version 3.5.1, R Foundation, Vienna, Austria). **Results:** In this retrospective study, the 1-year probability of survival was 71% (median 473 days) and the 1-year PFS was 14% (median 212 days). *TP53* and *KRAS* were the most frequently mutated genes identified in baseline samples, with 78% prevalence for each. Patients with clearance of *TP53* 17% (3/18) patients and/or *KRAS* 33% (6/18) patients clones after first line therapy significantly increases PFS (p=0.0056 and p=0.037, with HR of 0.087 and 0.32, respectively). However, appearance of *TP53* or *KRAS* alterations upon progression does not significantly affect overall survival or PFS. **Conclusions:** The preliminary results from this study suggest that cfDNA clearance of TP53 and/or KRAS alterations may predict for improved PFS in PDAC. Confirmation of these findings in larger studies is warranted. Research Sponsor: None.

424 Poster Session

Prognostic value of KRAS and PI3K pathway mutations for advanced pancreatic ductal adenocarcinoma (PDAC) patients (pts). *First Author: Adam Diehl, University of Washington School of Medicine, HEMONC-Hematology/Medical Oncology, Seattle, WA*

Background: KRAS mutation (MUT) variants (var) have been associated with differential clinical outcomes in advanced PDAC pts (Hendifar, 2020). Recent data from PDAC cell lines suggests that, unlike KRAS G12D/V, the KRAS G12R var is unable to interact with p110α PI3Kα and relies on KRAS-independent p110γ PI3K activity to support macropinocytosis, a nutrient uptake process necessary for tumor growth (Hobbs, 2020). **Methods:** We retrospectively reviewed advanced PDAC pts who received at least first-line (1L) systemic therapy and underwent next generation sequencing (NGS) at University of Washington between 2013 and 2020. We analyzed, using Fisher's exact test, whether KRAS var were associated with PI3K pathway mutations (PI3K MUT). Using multivariate (Cox proportional hazards) analysis, we compared overall survival (OS) and progression-free survival (PFS) from start of 1L therapy for pts whose tumors harbored any KRAS var with and without stratification by PI3K MUT status. **Results:** 127 pts had NGS (96% tissue, 4% ctDNA). Median OS (mOS) and PFS were 16.8 months (mos) and 8.6 mos, respectively. 111 PDAC were KRAS MUT (87%): 43 (39%) G12D, 35 (32%) G12V, 23 (21%) G12R, 1 (0.9%) G12C, 6 (5%) Q61. 15 PDAC (12%) had 16 PI3K MUT, including 7 PIK3CA, 3 AKT2, 3 RICTOR, 1 PTEN, 1 PIK3C2B, and 1 PIK3R1. PI3K MUT occurred in 26% of tumors with KRAS G12R vs 8% in other KRAS var (p=0.0265). In multivariate analysis controlling for age, performance status, stage at diagnosis, type of 1L chemotherapy, TP53 MUT and GATA6 amplification status, pts with KRAS G12R var PDAC vs other variants had longer mOS (20.4 vs 14.5 mos, HR 0.67 (95% CI 0.47 – 0.93), p=0.0215) and mPFS on 1L therapy (12.2 vs 6.8mos, HR 0.60 (95% CI 0.40 – 0.85), p=0.0040). In pts with KRAS G12R var PDAC, concurrent PI3K MUT vs PI3K WT associated with shorter mOS (19.4 vs 24.2mos, HR 2.79 (95% CI 0.97 – 10.6), p=0.0570). In pts with non-G12R KRAS var tumors, PI3K MUT vs WT did not confer shorter OS (mOS 17.6 vs 14.5 mos, HR 1.20 (95% CI 0.72 – 2.0), p=0.55). **Conclusions:** KRAS G12R PDAC have a higher incidence of PI3K MUT than other KRAS var. KRAS G12R status may confer improved prognosis vs other KRAS variants, albeit this benefit is offset by the presence of concurrent PI3K MUT. Research Sponsor: Jacob Green Charitable Foundation.

425 Poster Session

Molecular profiling of advanced pancreatic ductal adenocarcinoma (PDAC): Role of ctDNA. *First Author: Angela Lamarca, Department of Medical Oncology, The Christie NHS Foundation Trust/Institute of Cancer Sciences, University of Manchester, Manchester, United Kingdom*

Background: Molecular profiling of tumour samples and circulating tumour DNA (ctDNA) may inform treatment of advanced cancer; the role of ctDNA to predict progression-free-survival (PFS) and overall survival (OS) in advanced PDAC is not fully understood. **Methods:** Eligible patients: those diagnosed with advanced PDAC undergoing molecular profiling [tumour (Foundation Medicine CDx/Caris) or ctDNA (FoundationMedicine Liquid (72 cancer-related genes))]. Baseline patient characteristics and molecular profiling outcomes, including mutant allele frequency (MAF) for pathological alterations were extracted. The primary aim was to assess the impact of presence of ctDNA at time of systemic chemotherapy initiation on PFS and OS. **Results:** Total of 26 samples (ctDNA 18 samples and 8 tumour samples) from 25 patients diagnosed with advanced PDAC underwent molecular profiling. When the whole population was analysed, the rate of sample analysis failure seemed to be higher when tumour tissue was tested (37.5%) compared to ctDNA (5.56%); p-value 0.072. The overall rate of identification of pathological findings was 72.73%, with 18.18% of patients having targetable findings [EGFRmut (1 patient), KRAS G12C mut (1 patient), FGFR2 fusion (1 patient), RNF43 mut (1 patient)]; these findings impacted treatment management in one patient only (RNF43 mutation; Wnt inhibitor). Variants of unknown significance were identified in 63.64% of samples. Patients with ctDNA analysis at time of palliative chemotherapy initiation (16 samples; 15 patients) were analysed [6 female (40.00%), median age 69.57 years (range 51.61-81.49), metastatic disease (66.67%), 80% first-line (80%), 20% second-line]. Pathological mutations were identified in 9/15 (60.00%) of these patients (KRAS mutation identified in 6/9). After median follow-up of 8.33 months from sample acquisition, 80% and 53.33% of patients had progressed and died, respectively. Median estimated PFS and OS were 5.65 months (95% CI 1.59-8.17) and 7.80 months (95% CI 4.13-not reached). Presence (vs absence) of pathological alterations in ctDNA showed a trend towards shorter PFS (2.91 vs 6.51 months; HR 1.38 (95% CI 0.40-4.77)) and OS (6.12 vs 9.72 months; HR 2.03 (95% CI 0.60-6.82)). **Conclusions:** This pilot study demonstrates the feasibility of ctDNA analysis in patients with advanced PDAC prior to initiation of palliative therapy. The presence of pathological alterations in ctDNA may prognosticate for worse PFS and OS. Larger studies are required to confirm these findings. Research Sponsor: None.

426 Poster Session

Clinical and molecular features of adenosquamous pancreatic cancer (ASQ): A distinct histological subtype. *First Author: Christopher Jakubowski, Department of Oncology, Johns Hopkins Sidney Kimmel Cancer Center, Baltimore, MD*

Background: Adenosquamous pancreatic cancers (ASQ) constitute 1-5% of all pancreatic cancers. The clinical and molecular understanding of this aggressive variant, along with potential differential response to systemic therapies, is an understudied yet important topic. **Methods:** After obtaining Institutional Review Board approvals, the Johns Hopkins cancer registry and electronic medical record was interrogated for histopathological and clinical characteristics of ASQ. Archived pathological slides were re-examined to quantify the squamous component, response to neoadjuvant therapy and immune infiltrate. **Results:** Of 8,908 patients from 2003 to 2018, a total of 155 had histology consistent with ASQ. 52% presented with resectable disease, 12% with borderline resectable, 12% with locally advanced, 17% with metastatic, and 8% of cases had an unknown presentation status. Primary FNA diagnosis was available for 103 patients and 57% (n = 59) reported squamous findings on FNA. 53 patients received radiation therapy (19 neoadjuvant, 22 adjuvant, 15 palliative). Systemic therapy was received by 104 patients (32 neoadjuvant, 52 adjuvant, 67 palliative therapy for advanced/metastatic disease). The most common neoadjuvant regimens used were FOLFIRINOX (n = 9) and gemcitabine/nab-paclitaxel (n = 7). Reported responses in the neoadjuvant setting (n = 26) included 10 with stable disease (SD), 11 partial response (PR) and 5 progressive disease (PD). The most common regimens used in the first line advanced setting were FOLFIRINOX (n = 18), gemcitabine/nab-paclitaxel (n = 9), and gemcitabine (n = 8). Of 55 responses recorded there were 13 SD, 15 PR, 25 PD and 2 complete responses (CR). Of the patients who received first line therapy, 54% (n = 36), 15% (n = 10) and 6% (n = 4) went on to receive second, third or fourth line therapy, respectively. 118 patients (76.13%) had a reported date of death. Of the 98 patients who received definitive surgical resection the median recurrence free survival (mRFS) and overall survival (mOS) was 7.36 and 14.17 months, respectively. Of the 44 patients that presented with de novo unresectable or metastatic disease, mOS was 7.53 months. The mOS of advanced disease patients from the time of receipt of first line palliative chemotherapy was 8.45 months. Molecular panels revealed mutation frequencies of common somatic and DNA repair genes in similar frequency to pancreatic adenocarcinoma. The mean tumor mutation burden of 18 patients was 4.7 with a max of 27. Of 27 patients who received MMR/MSI testing 100% were pMMR/MSS. **Conclusions:** This is one of the largest single center series of ASQ patients reported and describes unique findings related to neoadjuvant and advanced disease treatment experience. Overall this study confirms the continued poor survival and poor response to standard regimens in this disease suggesting we should consider alternative treatment paradigms. Research Sponsor: Conquer Cancer Foundation of the American Society of Clinical Oncology.

427 Poster Session

Mutational profile analysis and related outcomes in primary and metastatic pancreatic cancer (PC). *First Author: Abhinav Rohatgi, Winthrop Oncology Hematology Associates, Mineola, NY*

Background: PC has not been well molecularly characterized and there is an unmet need in our understanding of the biological properties of PC. One previous study has found that the presence of *CDKN2A* mutations is an independent negative prognostic OS indicator. We evaluated molecular analysis on tumor specimens to determine whether increased mutational burden affects survival. **Methods:** PDAC samples from patients seen at the NYU Perlmutter Cancer Center at Winthrop Oncology Hematology Associates between 2015-2020 were profiled using next generation sequencing through Foundation Cdx. Genomic data was correlated with mined clinical data. Pt outcomes were correlated with the presence of mutations defined in 3 categories: 3 or less mutations, 4 mutations, 5 or more mutations. **Results:** Our cohort (N = 81) included 42% men and 58% women. 55% percent had primary (localized and locally advanced) disease and 44% had stage IV disease. Genetic mutations were most commonly found in KRAS, CDKN2A, TP53, NOTCH, SMAD4. Mutations seen less frequently were BRAF, HER2, RB1, ARID1A, MTAP, MLL, BRCA2. 43% of pts had 3 or less mutations, 15% 4 mutations, 42% had 5 or more mutations. There was no difference in number of mutations present between primary vs metastatic cancers. Median PFS was 13.5 months and overall survival (OS) for all pts was 20.0 months. The OS in primary group was 26.1 mos while it was 12.4 mos in the metastatic group. Patients with 5+ mutations had a 1.5 mos decreased OS and a 10% decreased 24-mos OS%. When stratified by primary (localized) disease, there was an 8.3 mos decrease in the 5+ mutation group vs 3 mutation group. When stratified by metastatic disease at diagnosis, there was no appreciable difference in OS between mutational groups. **Conclusions:** In the primary PC cohort, increasing burden of gene alteration patterns from 3 to 5+ mutations is correlated with decreased overall survival. The effect did not extend to the metastatic group likely due to disease burden driving survival whereas in primary PC group, survival reflected the tumor biology. This suggests that as additional carcinogenic pathways (DNA repair, growth, apoptosis) are mutated, tumor biology becomes more aggressive. This study provides an impetus for mutational profiling in early stage pancreatic cancer. These findings can contribute to the use of molecular profiles for prognostication and further development of targeted therapies. Research Sponsor: None.

Outcomes in each mutational profile among primary and metastatic pancreatic cancers.

	Whole Cohort		Primary Disease		Metastatic Disease	
Mutational Group	Overall Survival (mos)	24 mos OS (%)	12 mos PFS%	Overall Survival (mos)	12 mos PFS%	Overall Survival (mos)
3 (or less) Mutations	19.9	32.3%	50.0%	26.7	21.4%	10.1
4 Mutations	25.8	50.0 %	66.6%	28.6	50.0%	23.1
5+ Mutations	18.4	22.5%	70.5%	18.4	21.4%	10.4
Whole Cohort	20.0	29.6%	61.3%	26.1	25.7%	12.4

428 Poster Session

Evaluating the clinical impact of primary tumor location in pancreatic adenocarcinoma. *First Author: Randi Zukas Carhart, Thomas Jefferson University Hospital, Philadelphia, PA*

Background: Pancreatic adenocarcinoma is the fourth most common cause of cancer-related death in the US. The location of the primary lesion has long been thought to influence survival due to differences in time to presentation and ability to undergo cancer directed surgery. We hypothesized that patients with tumors arising in the body or tail (distal) would have poorer survival than patients who presented with lesions in the head of the pancreas (proximal) and that this difference would be true regardless of stage at diagnosis due in part to other factors such as intrinsic differences in the biology of these tumor types. A retrospective chart review at a single center with a high volume of pancreatic cancer directed surgery was carried out to address this question. **Methods:** Institution database was queried to identify patients with the ICD9 diagnosis of pancreatic adenocarcinoma of the head, body, and tail between 2014-2017; the inclusion criteria were 18 years or older, biopsy proven adenocarcinoma and a single mass in the pancreas at presentation. A total of 907 entries were screened with 324 patients being analyzed (236 proximal and 88 distal). CDC National Death Index registry and obituary reports were utilized to determine official dates of death. **Results:** Overall median survival was statistically higher in the proximal group than the distal group 16.0 vs 11.2 months (p=0.015). However, there was no significant difference in survival by stage of the proximal group over the distal group with stage I/II in the proximal group surviving 21 months versus distal 25.7 months, p=0.436; stage III, proximal surviving 11.7 months versus distal 18.0 months, p=0.393; stage IV, proximal surviving 6.5 months versus distal 4.9 months, p=0.675. The distal group was more likely to be metastatic on diagnosis (59% versus 18%) and was less likely to undergo surgery (34% vs 50%). In the surgical group, there was similar survival of 24.6 months in the proximal group versus 19.4 distal (p=0.795). **Conclusions:** Patients in the proximal group had a higher overall survival than the distal group as expected. Overall, however, when broken down by stage or surgery, the difference in survival between the proximal and distal groups was minimal with Hazard Ratio 0.96 (95%, CI=0.7, 1.30). Therefore, early stage diagnosis or surgery strongly account for the survival benefit in the proximal population rather than other factors like an intrinsic difference in the nature of the tumors themselves. Research Sponsor: None.

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The use of elevated circulating hepatocyte growth factor (HGF) level as a potential prognostic biomarker in locally advanced pancreatic cancer. *First Author: Hannah Johnson Roberts, Massachusetts General Hospital, Boston, MA*

Background: The hepatocyte growth factor (HGF)/c-MET pathway has pleiotropic functions in tumor progression including invasion and cancer cell survival. The potential use of circulating plasma HGF as a prognostic biomarker is not known. **Methods:** This was an analysis of plasma HGF in patients enrolled in a single arm phase II study (NCT01821729) of patients with previously untreated locally advanced pancreatic ductal adenocarcinoma (PDAC) treated with FOLFIRINOX and losartan followed by chemoradiotherapy before resection was attempted (Murphy JE et al., 2019). Eligible patients from the trial included those who had undergone baseline research labs including HGF. Circulating HGF was measured in the plasma on day 1 of treatment using ELISA, and the median value was used to define high vs low levels for the purpose of analysis. The association of elevated HGF with overall survival (OS) was analyzed by univariable and multivariable Cox regression, adjusting for tumor size ($\leq$ versus $>$ 40 mm) and serum CA19-9 ($\leq$ versus $>$ 37 U/mL). **Results:** There were 46 eligible patients with a median follow up of 31 months. The median age was 63 (range 42-78) and 52% were female (24/46). Median tumor size was 41.4 mm (range 18–68 mm). There were 41/46 patients (89.1%) with elevated baseline CA19-9. Median baseline HGF was 1,250.55 pg/mL (range 650.9–6,459.1). Median OS was 38.4 months for patients with baseline HGF at or below the median, and 19.3 months for those with elevated HGF. On univariate analysis, elevated HGF was associated with poorer OS (HR 2.28, 95% CI 1.06–4.87, p = 0.03). On multivariate analysis, after controlling for tumor size and baseline CA19-9, elevated plasma HGF remained significantly associated with poorer OS (HR 2.58, 95% CI 1.16–5.70, p = 0.02). **Conclusions:** In conclusion, elevated baseline circulating plasma HGF is an independent biomarker of poorer OS in patients with locally advanced PDAC treated with neoadjuvant therapy. Further randomized studies are needed to define the negative predictive biomarker value for high plasma HGF and identify the optimal HGF range as well as determine applicability to other stages of disease. These results support the continued investigation of plasma HGF in ongoing clinical trials with PDAC patients. Research Sponsor: U.S. National Institutes of HealthOther Foundation.

430 Poster Session

Familial pancreatic cancer (FPC) status as a clinical biomarker in patients receiving platinum-based systemic therapy: A case-control analysis. *First Author: Deirdre Kelly, Princess Margaret Cancer Center, Toronto, ON, Canada*

Background: Familial pancreatic cancer (FPC) is broadly defined as kindreds with at least a pair of first-degree relatives with pancreatic ductal adenocarcinoma (PDA). The role of DNA damage response agents, including platinum has not been well studied in this patient population. **Methods:** In this retrospective analysis, treatment details and clinical outcomes were analyzed in pts with FPC with advanced, unresectable or recurrent disease enrolled in the Ontario Pancreatic Cancer Study database. The primary outcome, overall survival (OS) was calculated from the initial diagnosis of advanced disease until death. 179 non-FPC patients from the COMPASS trial [NCT02750657] served as a control cohort all of whom had full molecular profiling and family history documented. OS between pts that received platinum-based therapy, and those that did not was compared using multivariable Cox proportional hazards model adjusting for age, sex, diagnosis year and FPC status. Interaction between FPC status and platinum was evaluated. **Results:** A total of 205 FPC pts were identified, 71% of pts had full germline testing and 16 (8%) had germline pathogenic variants in BRCA1/2. 104 (51%) were female and 101 (49%) male. Median age was 63 years (20-93) and 58 (28%) received platinum-based chemotherapy. Within the control arm (n=179), 71 (40%) were female, and 108 (60%) male; the median age was 64 years (29-84) and 106 (59%) received platinum-based therapy. In univariable analysis, median OS in pts with FPC was 16.9 months compared to 9.6 months (HR 0.46 [95% CI 0.37-0.58]). FPC patients receiving platinum had a superior median OS of 19 months compared to 15.5 months without platinum. In a multivariable analysis, both FPC (HR 0.33 [95% CI 0.21-0.51]) and receipt of platinum HR 0.53 [95% CI 0.38-0.73]) were prognostic. No interaction was seen with FPC and receipt of platinum (p=0.15). **Conclusions:** FPC status is prognostic but not predictive of platinum response in this study. Further molecular profiling of this unique cohort of patients will provide insights into putative predisposing germline alterations, and novel treatment strategies. Research Sponsor: None.

431 Poster Session

Impact of *KRAS* alterations in localized pancreatic cancer (PC). *First Author: Aditya Varnam Shreenivas, Medical College of Wisconsin, Milwaukee, WI*

Background: Patients (pts) with localized PC do not routinely undergo comprehensive genomic profiling (CGP) unless they develop recurrent or metastatic disease. *KRAS* is the most frequently mutated gene in PC, however, the impact of different *KRAS* mutations in localized PC has not been well characterized. We interrogated our genomic database to analyze the *KRAS* status in PC pts who presented with localized disease at diagnosis (Dx). **Methods:** We identified PC pts at our institution who underwent CGP utilizing the Foundation One CDx assay and had localized disease at initial Dx; these pts were categorized into resectable/borderline resectable PC (LPC) and locally advanced PC (LAPC). All pts with LPC and LAPC underwent neoadjuvant chemotherapy and chemoradiation prior to possible surgery (all intended therapy - AIT). Tissue from metastatic sites was used for CGP in pts who developed recurrent/metastatic disease before or after completion of AIT. The primary tumor was used for CGP in pts who completed AIT without subsequent relapse or in the absence of adequate metastatic tissue. Effect of each gene on response and survival outcomes was estimated using proportional odds and Cox regression analysis, respectively, adjusting for stage. **Results:** 75 pts were identified, median age at Dx was 65 years, 59% were male, 65% had a primary tumor in the pancreatic head. 38 (86%) pts with LPC completed AIT compared to 21 (68%) pts with LAPC ($p<0.001$). *KRAS* mutation was detected in 95% (71/75) of pts- 94% (67/71) in codon 12 and 6% (4/71) in codon 61. The various *KRAS* mutations and their association with completion of AIT is summarized in the table. The likelihood of completing AIT did not differ based on *KRAS* wildtype (WT) vs mutated status (p =1.00), the mutated codon (codon 12 vs. codon 61; p =1.00) or the individual *KRAS* point mutations (p = 0.7); however, all patients with G12A (N= 1), G12C (N=1), G12L (N=1) and G12R (N=11) mutations completed AIT. *KRAS* status (mutated vs. WT) and the individual *KRAS* mutations were not associated with overall survival (OS) after adjusting for stage (p= 0.13 and p = 0.26 respectively). Median OS for patients with LPC and LAPC, was 39 months (mos) and 29 mos respectively. **Conclusions:** *KRAS* status and individual *KRAS* mutations did not have an impact on completing AIT or mOS; however, these findings need to be interpreted with caution due to the inherent biases involved in such analyses. The clinical significance and functional relevance of *KRAS* G12A, G12C, G12L and G12R mutations, though relatively rare, needs further characterization as well as mechanistic elucidation. Research Sponsor: None.

***KRAS* mutations and completion of AIT.**

KRAS mutations	Total N=75(row %)	AIT -No N=16 (row %)	AIT -Yes N=59(row%)	P value
G12A	1 (100.0)	0 (0.0)	1 (100.0)	*P=0.705* [C, +]
G12C	1 (100.0)	0 (0.0)	1 (100.0)	
G12D	32 (100.0)	9 (28.1)	23 (71.9)	
G12L	1 (100.0)	0 (0.0)	1 (100.0)	
G12R	11 (100.0)	0 (0.0)	11 (100.0)	
G12V	21 (100.0)	5 (23.8)	16 (76.2)	
Q61H	4 (100.0)	1 (25.0)	3 (75.0)	
WT	4 (100.0)	1 (25.0)	3 (75.0)	

432 Poster Session

Number of nonsynonymous genomic variants may correlate with prognosis in advanced pancreatic cancer. *First Author: Suneel Deepak Kamath, Cleveland Clinic Taussig Cancer Institute, Cleveland, OH*

Background: Pancreatic cancer is associated with poor outcomes at any stage. A very small number of patients - approximately 3% of those with metastatic disease - experience long-term survival through 5 years but the biologic mechanisms underlying the benefit observed with these "exceptional responders" are incompletely understood. We explored potential genomic differences between exceptional responders and typical responders to treatment for advanced pancreatic cancer that could confer a more favorable biology. **Methods:** We included consecutive exceptional responders and matched controls (MCs) with advanced pancreatic cancer in a 1:3 ratio from the Cleveland Clinic from April, 2013 – August, 2017. ERs were defined as patients with overall survival (OS) $>$ 18 months for metastatic disease and $>$ 24 months for locally advanced disease. Controls were matched by age, gender, stage and type of chemotherapy given and experienced OS at or below median survival for their stages. Clinical variables including demographics, comorbidities, stage, histology and treatment history were collected. Next generation sequencing (NGS) was performed for DNA sequencing of 648 genes and tumor mutation burden (TMB) on available tissue. The study population initially comprised of 14 exceptional responders and 42 MCs. However, only 4 exceptional responders and 6 MCs were included for analysis due to insufficient tissue for NGS for the remaining patients. Descriptive statistics were used for statistical analysis. Differences in survival outcomes were assessed using the Kaplan-Meier method and log-rank test. **Results:** The median ages for the exceptional responders and MCs were 69 and 67.5 years, respectively. Both groups were at least 75% male and white. Of the exceptional responders, 50% had pancreatic tail primaries compared to 0% of the MCs. There were no differences between groups in first-line chemotherapy used. Exceptional responders had significantly fewer non-synonymous mutations compared to MCs (2.25 vs. 5.17, p = 0.014). Mutation count $<$ 3 was associated with significantly better progression-free survival (PFS) and OS as shown in the Table. TMB did not differ between exceptional responders and MCs (4.88 vs. 5.70 Muts/Mb, p = 0.39). Of the exceptional responders, 50% had alterations in BAGE2 versus 0% of MCs. Conversely, 50% of MCs had alterations in LRP1B, CUL4B or APC vs. 0% of exceptional responders. **Conclusions:** Having a lower number of non-synonymous mutations may correlate with exceptional response to systemic therapy and therefore with improved survival in pancreatic cancer. Pancreatic tail primary may also be associated with improved outcomes. These findings, though limited by small sample size, should encourage future study into genomic signatures of exceptional response. Research Sponsor: None.

	Mutation Count < 3	Mutation Count > 3	P value
PFS (months)	17.2	2.3	0.002
OS (months)	29.4	4.6	0.013

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Molecular characterization of pancreatic cancers as seen in the *SLUG* gene revealing cancer progression. *First Author: Natsuko Kawanishi, Division of Medical Oncology, USC Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, CA*

Background: The *SLUG* gene plays an important role in EMT by repressing E-cadherin and promotes metastasis. Previous data suggest that overexpressed *SLUG* gene in pancreatic cancer (PC) showing a high frequency of metastasis and poor prognosis. As *SLUG* contribution to characteristics or metastatic features remains elusive, we clarified its functional roles in PC progression. **Methods:** A total of 2958 pancreatic tumors were analyzed using Whole Transcriptome sequencing, NextGen Sequencing (NGS) (NextSeq, 592 gene panel) or Whole Exome Sequencing (WES) (NovaSeq) (Caris Life Sciences, Phoenix, AZ). Microsatellite instability (MSI) status was tested by fragment analysis, immunohistochemistry (IHC) and NGS. PD-L1 expression was tested by IHC. Tumor mutational burden (TMB) was measured by counting all mutations found per tumor (a universal cutoff point of ≧10 mutations per MB). Immune cell fraction was calculated by quanTIseq (Finotello 2019, Genome Medicine). **Results:** A total of 1274 primary and 1684 metastatic pancreatic tumors were included for this study. They were divided equally into four classes in each group, according to their *SLUG* expression levels. Tumors in the highest quartile of *SLUG* expression (QH) showed significantly higher frequency in peritoneal-retroperitoneal-omentum metastasis (15.0%) compared to the lowest quartile (QL) (4.8%) ($p = .0001$). Similar trends were seen in the abdomen (6% vs 1%, $p = .001$) and bone (2.8% vs 0.0%, $p = .005$). However, liver (55.0% in QH vs 63.1% in QL) and lung (2.8% vs 14.1%) metastasis occurred most frequently in QL and the least frequently in QH ($p = .0197$ and $p = .001$, respectively). This data indicated that tumors with high *SLUG* gene expression levels tend to lead to disseminated metastasis, and with low expression levels, they tend to spread intravascularly. We detected significant differences among genetic mutations in *ATM* (5.7% in QL vs 1.8% in QH, $p < 0.001$) and *APC* (2.9% vs 0.5%, $p < 0.001$), and Wnt signaling expressions were higher in QL (4.6%) than QH (0.7%) ($p < 0.001$). Binary TMB-H and MSI-H tumors had higher frequencies in QL (2.7% and 2.1%) compared to QH (0.3% and 0.1%) ($p < 0.001$ in both). Contrastingly, PD-L1 expression levels were higher in QH (23.4%) compared to QL (11.0%) ($p < 0.001$) and had a linear relationship with the expression levels. The median values of the population of B cells, M1 and M2 macrophages were significantly higher in QH compared to QL, but those of myeloid dendritic and CD8+T cells conversely decrease as the *SLUG* expression increases. **Conclusions:** Our data indicated the *SLUG* expression level could determine the tumor characteristics in progression, especially the pattern of metastasis in PC, and it could possibly predict the prognosis and/or therapeutic effects. We also showed immune oncologic markers which have some relationships with *SLUG* expressions. Further investigation is warranted to better understand *SLUG* gene functions. Research Sponsor: None.

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Shared DNA-based copy number with divided methylation changes differentiate and clinically associate early stage pancreatic cancer tumors. *First Author: Hsueh-Ping Chao, Livestrong Cancer Institutes, University of Texas at Austin Dell Medical School, Austin, TX*

Background: There is no known molecular taxonomy of pancreatic cancer that can guide therapeutic strategies. Understanding the fundamental molecular mechanism underlying pancreatic cancer biology remains an unmet need. We explore the extent to which combinations of DNA-based molecular changes in copy number (CN) and methylation separate early stage PAAD tumors and associated with survival outcomes. **Methods:** We performed genome-wide combined cluster analyses on DNA-based CN and methylation changes using TCGA data. We examined cluster associations with clinical outcomes by comparing in months (mos), Kaplan--Meier estimated overall survival (OS) and disease-free interval (DFI) using a log-rank test. We performed additional comparisons among CN-Methylation derived clusters with respect to PAAD phenotypes. **Results:** Using 78 early stage pancreatic cancer tumors from TCGA with CN, methylation and clinical outcomes data, we identified two patient clusters with distinct gene copy number signatures that when combined with three methylation signatures, resulted in three additional clusters. Thus, the same gene CN signature, when combined with different methylation signatures, further differentiated tumors into sub-clusters with varying levels of associations with clinical outcome. Among them, analogous to current gene-expression based subtypes, we also identified an immune-rich subtype that was associated with improved overall survival (n=21, median OS=16mos; DFI=16mos), and an extracellular matrix (ECM)-rich with worse survival (n=19, median OS=12mos; DFI=8mos). Unlike previous expression subtypes, we identified another metabolic-enriched subtype with the same worse median OS and DFI, differentiated by methylation with the ECM-rich subtype. The improved OS cluster had a signature of CN neutral and increased methylation, while the poor cluster had a signature of CN gains and increased methylation among a set of genes distinct from the improved cluster. No significant differences in age, site, microsatellite instability and KRAS status among clusters were noted. Notably, in a multivariable model that included gene expression-based subtypes, only our DNA-level subtypes remained significantly associated with overall survival. **Conclusions:** While RNA-level changes often display large variations, DNA-level changes are more robust. Copy number changes appear to separate tumors into poor and improved prognosis clusters, while methylation appears to inform on the further separation of poor prognosis into various levels. A DNA-based molecular taxonomy for early stage pancreatic cancer could prove invaluable when used in combination with methylation-based circulating tumor DNA assays for clinical trial monitoring of tumor responses. Research Sponsor: None.

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Development and validation of a radiomics nomogram to discriminate advanced pancreatic cancer patients with liver metastases or other metastatic patterns. *First Author: Junjie Hang, Changzhou No. 2 People's Hospital, the Affiliated Hospital of Nanjing Medical U, Changzhou, China*

Background: Pancreatic cancer patients with liver metastases had much poorer prognosis than those with other metastatic patterns. This study aimed to develop and validate a radiomics model to discriminate pancreatic cancer patients with liver metastases from patients with other metastatic patterns. **Methods:** We evaluated 77 patients advanced pancreatic cancer (APC) with different metastatic patterns and performed texture analysis on the region of interest (ROI). 58 patients and 19 patients were allocated randomly into the training cohort and the validation cohort with almost the same proportion of patients with liver metastases. An independent samples *t*-test was used for initial feature selection in the training cohort. Random Forest Classifier (RFC) was used to construct models based on these features in both cohorts and a radiomics signature (RS) was derived from the model. Then a nomogram was constructed based on RS and CA19-9, and validated with calibration plot and decision curve. The prognostic value of RS was evaluated by Kaplan-Meier methods. **Results:** A nomogram based on the RS and CA19-9 was constructed and it demonstrated good discrimination in the training cohort (AUC = 0.93) and validation cohort (AUC = 0.81). Kaplan-meier methods showed that patients with RS>0.61 had much poorer OS than patients with RS < 0.61 in both cohorts. **Conclusions:** This study presents a radiomics nomogram incorporating both RS and CA19-9, which can be used to discriminate advanced pancreatic cancer patients with liver metastases from patients with other metastatic patterns. Research Sponsor: National Natural Science Foundation of China (81902955), Other Foundation.

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Genomic biomarker discovery of first-line gemcitabine/nabpaclitaxel treatment in Chinese advanced pancreatic carcinoma patients. *First Author: Juan Du, The Comprehensive Cancer Center of Drum Tower Hospital, Medical School of Nanjing University & Clinical Cancer Institute of Nanjing University, Nanjing, China*

Background: Pancreatic carcinoma is one of the most lethal malignancies worldwide and is characterized by extremely poor prognosis. Gemcitabine plus Nab-paclitaxel (GNp) has been recommended by international guidelines for first-line treatment of locally advanced or metastatic pancreatic carcinoma. However, exploration into molecular biomarkers of GNp treatment is still limited. This study aims to observe and evaluate the efficacy and safety of first-line GNp treatment of pancreatic carcinoma, and to explore potential predictive and prognostic biomarkers to screen advantageous population. **Methods:** From December 20, 2018 to July 6, 2020, patients with metastatic pancreatic carcinoma, who received first-line GNp treatment, were enrolled. The primary endpoint was progression-free survival (PFS), and the secondary endpoints were overall survival (OS), overall response rate (ORR), disease control rate (DCR), and adverse events (AE). Patients were collected formalin fixed paraffin embedded (FFPE) samples and sequenced by a next-generation sequencing (NGS)-based 450 gene panel carried out by OrigiMed, a College of American Pathologists (CAP) accredited and Clinical Laboratory Improvement Amendments (CLIA) certified laboratory. **Results:** In this study, tissue samples from 101 patients were assessed by NGS, including 58 (57.4%) primary tissues and 43 (42.6%) metastasis tissues. So far, 72 patients were available for efficacy analysis, the ORR and DCR were 38.2% and 77.9%, respectively, and were similar between patients sampled from primary lesions and metastasis lesions. The PFS and OS were 176 days and 308 days, respectively. The most frequently mutated genes were *KRAS* (91.9%), *TP53* (76.8%), *CDKN2A* (32.3%) and *SMAD4* (26.3%). Germline pathogenic *BRCA2* mutations were detected in 3 (3.0%) patients, while somatic mutations of *BRCA2* were found in 2 (2.0%) patients. For *KRAS*, missense mutations resulted in single amino acid substitutions primarily at G12 (88.1%), and lower frequencies at Q61 (4.0%) and V14 (1.0%). At G12, five different amino acid substitutions have been identified, with G12D (37.6%) the predominant mutation, G12V (32.7%), G12R (11.9%), G12C (3.0%) and G12A (1.0%). The ORR to AG treatment was significantly higher in *TP53*-alteration (-alt, 47.1%) than in *TP53*-wild-type (-WT, 11.1%) subgroups (p=0.01). Median OS times in *CDKN2B*-alt and *CDKN2B*-WT patients were 180 days and 323 days (p=0.029), respectively. **Conclusions:** Current evidence indicates that GNp is a valuable option for the first-line treatment of metastatic pancreatic cancer. *TP53* may serve as a novel response-predictive gene for GNp treatment in pancreatic carcinoma. Overall survival was significantly prolonged in *CDKN2B*-WT patients compared with *CDKN2B*-alt patients. This study provided insights in identifying patients who might potentially benefit from GNp therapy. Clinical trial information: NCT03768687. Research Sponsor: Chen Xiao-Ping Foundation for the Development of Science and Technology of Hubei Province.

437 Poster Session

Phase II/III study of SM-88 in patients with metastatic pancreatic cancer. *First Author: Vincent Chung, City of Hope, Duarte, CA*

Background: SM-88 (racemetyrosine, Tyme Inc) is a dysfunctional tyrosine derivative used with MPS (methoxsalen 10mg, phenytoin 50mg and sirolimus 0.5mg). SM-88 was well tolerated with improvement in survival among select heavily pretreated PDAC patients who achieved stable disease (HR 0.08, p = 0.02) (Noel et al. *Annal Oncol* 2019). Circulating tumor cells (CTCs) were prognostic in identifying a PDAC subgroup that may be more likely to benefit from SM-88. Preliminary radiomic analysis of the largest metastases at baseline correlated with baseline CTCs (Ocean et al, *Annal Oncol* 2019). Here we describe the subsequent randomized portion of the trial in third-line patients only, of SM-88 vs physician/patient choice chemotherapy, to evaluate the potential role of SM-88 in metastatic PDAC through analysis of CTCs and passively acquired biometrics data from a wearable device. **Methods:** Prospective open-label RCT (Tyme 88 Panc Part 2, NCT03512756) after 2 prior lines for metastatic PDAC. A cell adhesion matrix (CAM) was used to enrich solitary CTCs and cells in clusters floating in the medium after 24 hour culture. Isolated CTCs were collected each cycle on day 1, isolated, and enumerated by flow cytometry using the epithelial cell surface marker Epi+ and cellular uptake of green fluorescent labeled CAM (GCAM+). **Results:** As of Sept 15, 67 subjects were consented. Randomized and evaluable subjects (n=38) included: mean age 65y (45-86); BMI 24.6 (18.8-38.7); female 39.5%; White 76.3%. Of treated subjects 65.8% (25/38) had 166 AEs, with 25.7% (26/101) being at least possibly SM-88-related, with 1 Grade 3. Four CTC subpopulations defined by GCAM, Epi+ and cluster status, were enumerated and correlated to each other (r=0.03-0.71). At least one CTC subpopulation was detected at baseline (mean 33.8 cells/2mL) in all subjects (n=27). The longest metastatic lesion diameter at baseline correlated with baseline CTCs (r=0.55 for Epi+ cluster; r=0.52 for GCAM+ cluster). CTCs were successfully separated and enumerated at each cycle for correlation with survival, response and other parameters. The median baseline daily step count during the first two weeks on treatment was 3993.8 (IQR: 2745.6 - 5078) for those alive vs. 689.3 (IQR: 630.0-2083.6) among deaths in evaluable subjects (p = NS). Passively acquired mean heart rate during week 3 on trial was 89.3 (SD 10.5) among those who died vs. 78.0 (SD 9.2) among those living; medians are 87.0 for deaths vs. 79.2 for alive (p= NS). **Conclusions:** In a preliminary exploratory analysis, passively acquired biometrics from a wearable device can be collected for correlation with other clinical outcomes. CTC collection and enumeration is also feasible for correlation with traditional trial outcomes. Given that the longest lesion diameter is correlated with CTCs at baseline, additional radiologic feature analysis (eg radiomics) may be important predictor of CTCs. SM-88 was well tolerated with no treatment-related Grade 4 or 5 events. Clinical trial information: NCT03512756. Research Sponsor: Tyme Inc.

438 Poster Session

Significant lipid and neutrophil accumulation and active inflammasome in high BMI tumor regions of human pancreatic ductal adenocarcinoma. *First Author: Ahmed Khattab, Allegheny Health Network, Pittsburgh, PA*

Background: Obesity is an established risk factor for cancer and cancer-related mortality. Adipocytes may act as a "damage" signal resulting in the accumulation of innate immune cells, fueling an inflammatory microenvironment. Among the innate immune cells, tumor-associated neutrophils (TANs) are confirmed to accumulate inside the tumor. As obesity is a significant risk factor for a poorer prognosis in pancreatic ductal adenocarcinoma (PDAC), we hypothesize that obesity-driven adipose fuels the progression of PDAC in a TAN and inflammasome-facilitated manner. This may happen through several mechanisms, including genomic instability of aggressive PDAC clonal populations. **Methods:** Tissue from resected tumors of PDAC patients (n = 44) with a body-mass index (BMI) $>$ 27 (obese [n = 21]) and BMI $<$ 22 (normal [n = 23]) were incubated with anti-human CD66b antibodies and detected using standard immunofluorescent microscopy techniques. Images were acquired in a Zeiss Axioplan microscope workstation and analyzed by ZEN and Metamorph software. **Results:** We identified the presence of adipocytes in all tissue sections and CD66b+ neutrophils in all tissue sections of normal BMI patients and in 81% of high BMI patients. There is a significantly greater density of adipocytes in the tumor environment when compared to adjacent normal areas, suggesting that these cells are acting as a damage signal. Our novel data also shows that high BMI results in a significantly higher neutrophil count in tumor specific tissue when compared to patients with a low BMI. These data suggest an association between BMI and inflammasome accumulation in the tumor environment. **Conclusions:** Our data uniquely shows that CD66b+ neutrophils tend to accumulate inside PDAC in high BMI patients and this is associated with intra-tumoral active inflammasomes. The higher concentrations of these inflammasomes in higher BMI patients may be of mechanistic relevance in understanding how inflammation induces progression of PDAC. A larger cohort of tissues from PDAC obtained from low and high BMI individuals will be needed to test our hypothesis and to begin to decipher the role of obesity on inflammation and PDAC progression. Research Sponsor: Johns Hopkins University Grant.

439 Poster Session

Prognostic impact of chemoradiation-related lymphopenia in patients with locally advanced pancreatic cancer. *First Author: Daniel W Kim, Massachusetts General Hospital, Boston, MA*

Background: Chemoradiation (CRT) induced lymphopenia is common and associated with poorer survival in multiple solid malignancies. The objective of this study was to evaluate the prognostic impact of lymphopenia in patients with nonmetastatic, unresectable pancreatic ductal adenocarcinoma (PDAC) treated by neoadjuvant FOLFIRINOX (5-fluorouracil [5FU]/leucovorin/irinotecan/oxaliplatin) followed by CRT. We hypothesized that severe lymphopenia would correlate with worse survival. **Methods:** The inclusion criteria for this single-institution retrospective study were: 1) biopsy-proven diagnosis of unresectable PDAC, 2) absence of distant metastasis, 3) receipt of neoadjuvant FOLFIRINOX followed by CRT, and 4) absolute lymphocyte count (ALC) available prior to and two months after initiating CRT. In general, CRT consisted of 5FU or capecitabine and RT with 58.8 Gy over 28 fractions. Lymphopenia was graded according to CTCAE v5.0. The primary variable of interest was lymphopenia at two months, dichotomized by ALC of $<$ 0.5/μl (Grade 3 lymphopenia). The primary endpoint was overall survival (OS). Cox modeling and Kaplan-Meier methods were used to perform survival analyses. **Results:** A total of 138 patients were identified. Median follow-up for the entire cohort was 16 months. Median age was 65. Fifty-six percent were female, 86% were Caucasian, and 97% had ECOG $\leq$1. Median tumor size was 3.8 cm. Tumor location was pancreatic head in 63%, body in 22%, tail in 8%, and neck in 7%. Median baseline ALC for the entire cohort was 1.5 k/ul. Two months after initiating CRT, 106 (77%) had severe (Grade 3 or worse) lymphopenia. While there were no significant differences in baseline patient or disease characteristics, patients with severe lymphopenia received higher doses of RT with longer duration of treatment compared to those without severe lymphopenia. On multivariable Cox model, severe lymphopenia at two months was significantly associated with increased hazards of death (HR = 4.00 [95% CI 2.03-7.89], p $<$ 0.001). Greater number of neoadjuvant FOLFIRINOX cycles received prior to CRT was associated with lower hazards of death (HR = 0.84 [95% CI 0.77-0.92], p $<$ 0.001). The 12-month OS was 73% vs. 90% in the cohort with vs. without severe lymphopenia, respectively (log-rank p $<$ 0.001). **Conclusions:** Treatment-related lymphopenia is common and severe lymphopenia may be a prognostic marker of poorer survival in locally advanced pancreatic cancer. Closer observation in high-risk patients and minimization of RT dose and duration are potential approaches to mitigating CRT-related lymphopenia. Our findings also suggest an important role of the host immunity in pancreatic cancer outcomes, supporting the ongoing efforts of immunotherapy trials in pancreatic cancer. Research Sponsor: None.

440 Poster Session

Long-term outcomes of a prospective single institution study with multi-agent chemotherapy and stereotactic body radiation therapy in locally advanced or recurrent pancreatic adenocarcinoma. *First Author: Colin Hill, Department of Radiation Oncology and Molecular Radiation Sciences, Johns Hopkins University School of Medicine, Baltimore, MD*

Background: We previously reported a multi-center study in which gemcitabine and stereotactic body radiation therapy (SBRT) were shown to be safe with outcomes comparable to chemoradiation in locally advanced pancreatic cancer (LAPC). This prospective clinical trial was developed to evaluate the efficacy of adding SBRT to multi-agent chemotherapy in LAPC. Herein, we report on the long-term survival outcomes. **Methods:** From 2012 to 2015, 48 patients (pts) were prospectively enrolled after multidisciplinary evaluation at a single high-volume pancreatic center. Pts received multi-agent chemotherapy (CTX) with modified mFOLFIRINOX (mFFX) or gemcitabine/abraxane followed by 5 fractions of SBRT (median 33 Gy; range, 25-33 Gy). At the time of fiducial placement, biopsies were obtained and DNA extracted for targeted sequencing using MSK-IMPACT. Kaplan-Meier curves were generated to compare survival outcomes by sub-group. Multivariate analysis (MVA) was performed to identify factors prognostic for survival. **Results:** 44 pts (91.7%) had LAPC disease and 4 (8.3%) had locally recurrent disease. The median follow-up interval was 21.5 months (mo) from diagnosis. CTX consisted of mFFX in 25 pts (52.1%) with 24 pts (50.0%) receiving therapy for a duration $\geq$4 mo. Of 44 pts with LAPC, 15 (34.1%) were surgically explored, and 11 (73.3%) achieved a margin-negative resection. From diagnosis and after completion of SBRT, respectively, the median overall survival (OS) was 21.6 (95% CI 16-29.7 mo) and 14.6 mo (95% CI: 11.6-23.0 mo); median progression free survival (PFS) was 13.2 (95% CI 11.9-18.1mo) and 6.4 mo (95% CI: 5-12.7 mo); median local PFS (LPFS) was 23.9 (95% CI 18.9-56.9 mo) and 15.8 mo (95% CI: 12.9-27.6 mo); and median distant metastasis free survival (DMFS) was 18.4 (95% CI 12.6-29.3 mo) and 8.5 mo (95% CI: 6.3-17.2 mo). Resected pts experienced better DMFS at 1-year (78% *vs.* 34%, *p*= 0.004) with an improved trend for 1-year OS (73% *vs.* 52%, *p*= 0.331). If CTX duration was $\geq$4 mo, 1-year OS (75% *vs.* 42%, *p*= 0.018), PFS (50% *vs.* 21%, *p*= 0.022), and DMFS (72% *vs.* 29%, *p*= 0.031) were significantly improved. In 44 LAPC pts, MVA confirmed $\geq$4 mo duration of CTX was associated with OS, PFS, and DMFS. Surgical resection was associated with improved DMFS, and CA19-9 level prior to SBRT was associated with PFS and LPFS. The most common mutations detected from biopsy specimens were *KRAS* (64.3%), *TP53* (50%), and *SMAD4* (16.7%). **Conclusions:** In a prospective trial of pts with LAPC receiving multiagent CTX and SBRT, clinical outcomes were improved with longer durations of CT ($>$ 4 mo). A high proportion of LAPC pts underwent margin negative resection with favorable outcomes. Future studies should focus on which pts are most likely to benefit from SBRT and surgery following multiagent CTX. In pts who cannot undergo resection, escalated doses of SBRT may be indicated. Clinical trial information: NCT01781728. Research Sponsor: None.

441 Poster Session

Cost efficiency and budget-neutral expanded access to antineoplastic therapy from cost-savings derived from conversion to biosimilar pegfilgrastim-cbqv for the prophylaxis of chemotherapy-induced (febrile) neutropenia (CIN/FN): Simulation modeling in metastatic pancreatic cancer. *First Author: Ali McBride, University of Arizona Cancer Center, Tucson, AZ*

Background: Biosimilars have contributed to the reduction in the cost of prophylaxis of CIN/FN in recent years. Savings generated from conversion to biosimilars could be reallocated on a budget-neutral basis to provide expanded access to additional prophylaxis or to anti-neoplastic treatment. To demonstrate this, we simulated: 1) the savings that could be realized from CIN/FN prophylaxis with biosimilar pegfilgrastim-cbqv (BIOSIM-PEG) over reference pegfilgrastim with or without on-body injector (PEG/PEG-OBI), 2) a model of expanded access to BIOSIM-PEG from cost-savings achieved from conversion from PEG/PEG-OBI, 3) a model of expanded access to chemotherapy with oxaliplatin, leucovorin, irinotecan, and fluorouracil (FOLFIRINOX) for metastatic pancreatic cancer (mPC), 4) the number-needed-to-convert (NNC) to BIOSIM-PEG to purchase one additional treatment of BIOSIM-PEG, and 5) the NNC to purchase one cycle of FOLFIRINOX. **Methods:** This simulation modeling from the US payer perspective utilized: 1) a blended rate of average selling price (ASP; derived from CMS Q4 2020 reimbursement) and wholesale acquisition cost (WAC; Redbook) for PEG/PEG-OBI, BIOSIM-PEG, and all FOLFIRINOX agents proportionate to the estimated 2020 incident pancreatic cancer age distribution per Surveillance, Epidemiology, and End Results Program (67.6% Medicare-insured patients ≥65 years of age; 32.4% commercially insured patients <65 years); 2) between one and twelve cycles of prophylaxis in a panel of 2,500 mPC patients treated with FOLFIRINOX; and 3) conversion rates from PEG/PEG-OBI to BIOSIM-PEG ranging from 10%–100%. **Results:** Using a current blended ASP/WAC rate, cost-savings of BIOSIM-PEG over PEG/PEG-OBI in a panel of 2,500 mPC patients range from $188,780 (for 1 cycle of prophylaxis at 10% conversion) to $22,653,609 (12 cycles at 100%). In a single cycle of chemotherapy, these savings translate into expanded access to additional BIOSIM-PEG prophylaxis ranging from 53 cycles at 10% conversion from PEG/PEG-OBI to 528 cycles at 100% or to between 321 to 3,214 cycles of FOLFIRINOX, respectively. The savings over twelve cycles could provide up to 6,330 additional cycles of BIOSIM-PEG or 38,571 cycles of FOLFIRINOX (at 100% conversion). The NNC from PEG/PEG-OBI to purchase one additional cycle of BIOSIM-PEG is 4.74; the NNC to purchase once cycle of FOLFIRINOX is 0.78. **Conclusions:** These simulated models demonstrate the magnitude of the cost savings for CIN/FN prophylaxis that can be generated by conversion to biosimilar pegfilgrastim-cbqv. Further, these savings could be reallocated to provide access to anti-neoplastic treatment on a budget-neutral basis, thus enhancing the value of cancer care to both payers and patients. Research Sponsor: Coherus BioSciences.

442 Poster Session

Characteristics and growth rate of lung metastases in patients with primary gastrointestinal malignancies: A retrospective cohort analysis. *First Author: Shohei Burns, University of California San Francisco Helen Diller Family Comprehensive Cancer Center, San Francisco, CA*

Background: There are no formal guidelines for the management of GI cancer pts with lung-exclusive or lung-predominant metastases (LM), which generally take a more indolent course than metastatic disease occurring at other anatomic sites. We performed a retrospective analysis at a high-volume tertiary care center to evaluate host and tumor characteristics of this pt population, describe treatment approaches, and model patterns and rates of growth. **Methods:** Eligible pts were identified through Cancer Center registry data, provider recall, and electronic record review. Criteria included LM occurring either synchronously (SLM) or metachronously (MLM) w/primary cancer diagnosis; nodal, but not visceral or peritoneal, mets allowed. Data re: demographics, tumor characteristics, and rx modalities were collected. We reviewed all eligible CT +/- PET scan reports to gather data on #, location, and size of pulm mets, with all images subsequently reviewed by an independent radiologist. Up to 5 pulm mets were tracked through each pt's clinical course. Growth rate was estimated using a linear mixed model analysis considering patients as the random. **Results:** Forty pts were identified between 9/2009 - 12/2019 (23 F/17 M; 28 white/7 Asian/5 other/multi; median age 62 y.o.; n = 15 w/tobacco hx). Tumor types: pancreatic (n = 18), colorectal (n = 12), hepatobiliary (n = 7), other (n = 3). SLM vs MLM: 13/27; intact vs resected primary = 16/24. Median time from orig cancer dx to onset of MLM = 16 mos (range, 1 to 60 mos). No. of pulm mets at 1st appearance: 1 (n = 7); 2-5 (n = 17); 6-10 (n = 16). Median size of largest pulm met at 1st appearance = 6 mm (range, 0-39 mm); avg growth rate of largest pulm met = 0.18 mm/month (95% CI, 0.08-0.27). Avg growth rate of up to 5 largest lesions (sum) = 0.35 mm/month (95% CI, 0.07-0.64). Median f/u time prior to rx initiation for MLM = 172 days (range, 25-1547 days); 18 pts developed additional mets during their observation period. Rx modalities for LM: surg (n = 6), radiation (n = 18), systemic rx (n = 32). Addn details specific to cancer type, progression patterns, and pt outcomes will be presented at the meeting. **Conclusions:** The natural hx of LM varies across the spectrum of GI malignancies. Further larger-scale efforts to define patterns of growth of LM for different GI cancers, informed by size, #, and clinical/molecular features, are needed to guide appropriate timing and selection of rx as well as surveillance strategies. Research Sponsor: UCSF School of Medicine.

443 Poster Session

Long-term outcomes with neoadjuvant chemotherapy with or without stereotactic body radiation therapy in patients with borderline resectable and locally advanced pancreatic adenocarcinoma. *First Author: Colin Hill, Department of Radiation Oncology and Molecular Radiation Sciences, Johns Hopkins University School of Medicine, Baltimore, MD*

Background: Patients (pts) withborderline resectable pancreatic cancer (BRPC) or locally advanced pancreatic cancer (LAPC) are at high risk of margin positive resection with upfront surgery. Pre-operative stereotactic body radiation therapy (SBRT) may help sterilize vascular margins, but its additive benefit beyond multiagent chemotherapy (CTX) is unclear. We report on long-term outcomes from a high-volume institution of BRPC/LAPC pts who were reviewed by a multidisciplinary team and explored after either multi-agent CTX alone or multi-agent CTX followed by SBRT. **Methods:** Consecutive BRPC/LAPC pts diagnosed 2011-2016 who underwent resection following CTX alone or CTX followed by 5-fraction SBRT (CTX-SBRT) were retrospectively reviewed. Baseline demographic, clinical, and treatment factors were compared between cohorts, and survival analysis was conducted to compare pathologic and survival outcomes. **Results:** Of 199 pts, 77 received CTX alone and 122 received CTX-SBRT. There was no significant difference between cohorts in age, gender, performance status, tumor location, CA19-9 at diagnosis, or post-CTX CA19-9 values (all $p > 0.05$). The CTX-SBRT cohort had a higher proportion of pts with LAPC as compared to the CTX cohort (53% vs 22%, $p< 0.001$). Modified FOLFIRINOX (mFFX) was administered to 55% of pts, while 70% of pts received either mFFX or gemcitabine/abraxane, with no difference between cohorts. Duration of CTX was longer in the CTX-SBRT cohort as compared to the CTX cohort (median 4.6 vs. 2.9 mos, $p= 0.03$), but adjuvant CTX was not given as often in the CTX-SBRT arm (60.4% vs. 86.4%, $p= < 0.001$). Notably, 30% of the CTX cohort also received adjuvant chemoradiation. Pathologic response was significantly improved in the CTX-SBRT cohort vs the CTX cohort, specifically negative margins (92% vs 70%, $p< 0.001$), node negative (59% vs. 42%, $p< 0.001$), and pathologic complete response (7% vs. 0%, $p= 0.02$). On multivariable analysis, after controlling for prognostic factors, CTX-SBRT remained significantly associated with margin negative resection ($p< 0.001$). Despite having more advanced stage and less adjuvant therapy administration in the CTX-SBRT cohort, there was no significant difference in overall survival after surgery (median OS: 24.6 vs. 22.2 mo, $p= 0.79$), local progression free survival (14.0 vs. 13.6 mo, $p= 0.33$), or distant metastasis free survival (16.4 vs. 11.8 mo, $p= 0.33$). **Conclusions:** Despite more advanced disease at presentation, BRPC/LAPC pts treated with CTX-SBRT were more likely to undergo margin negative resection and experienced similar survival outcomes, as compared to CTX alone. More data are needed to refine which patients benefit from neoadjuvant SBRT and how RT administration can be optimized to impact survival outcomes. Research Sponsor: None.

444 Poster Session

Survival outcomes in the modern era for localized pancreatic cancer with multi-agent chemotherapy and stereotactic body radiation therapy. *First Author: Shuchi Sehgal, Philadelphia College of Osteopathic Medicine, Philadelphia, PA*

Background: The benefit of stereotactic body radiation therapy (SBRT) in the neoadjuvant setting for patients with localized pancreatic adenocarcinoma (PDAC) remains an area of active investigation. Herein, we report on surgical, pathologic, and survival outcomes in a modern cohort of borderline resectable pancreatic cancer (BRPC) and locally advanced pancreatic cancer (LAPC) patients (pts) who were treated at a high-volume institution with upfront chemotherapy (CTX) followed by SBRT. **Methods:** A prospectively collected institutional IRB-approved database was reviewed to identify PDAC pts diagnosed between 2015-2018. All pts were seen in our multidisciplinary clinic and treated with multiagent induction CTX followed by 5-fraction SBRT. In general, it was our institutional preference that ECOG 0-1 pts were recommended modified FOLFIRINOX (mFFX), whereas others were recommended gemcitabine/abraxane. Pathological outcomes by stage were characterized. Kaplan-Meier analysis was used to generate survival curves, and factors prognostic for survival were identified. **Results:** Our cohort consisted of 156 pts, including 92 LAPC pts (59%) and 63 BRPC pts (41%). Median follow-up from diagnosis was 21.0 months (range 4-49 mos). Of the entire cohort, 117 (75%) received mFFX and 37 (24%) received gemcitabine/abraxane. Median duration of upfront CTX before SBRT was 4.0 months, with 126 pts (80.8%) receiving greater than 4 months. After SBRT, 130 pts (84%) were surgically explored with 106 pts (68%) successfully resected. Of 106 pts who were resected, 97 pts (92%) achieved negative margins, 63 pts (59%) were node-negative, and eight pts (8%) achieved a pathological complete response (pCR). Among 63 BRPC pts, 49 pts (78%) underwent resection, of whom 47 pts (96%) achieved margin negative resection. Among 92 LAPC pts, 57 pts (62%) underwent resection, of whom 50 pts (88%) achieved margin negative resection. For the entire cohort, median overall survival (mOS) from diagnosis was 25.4 mos (95% CI: 22.2 to NR) and 17.6 mos from SBRT (95% CI: 16.1 to NR). ECOG 0-1, initial biopsy grade (well-to-moderately differentiated), duration of neaodjuvant CTX (≥ 4 mos), surgical resection, and receipt of adjuvant CTX were all associated with improved survival from diagnosis (all $p < 0.05$), but stage (BR vs. LAPC) was not ($p = 0.43$). **Conclusions:** In a modern cohort of patients receiving mFFX (75%) followed by SBRT, a high proportion of pts were successfully resected with favorable pathologic outcomes. Interestingly, OS was not significantly different for BRPC vs LAPC. Factors that proved to be important with respect to OS included duration of neoaduvant CTX, performance status, initial biopsy grade, and receipt of adjuvant CTX, After maximal multiagent CTX, factors other than stage should be considered in determining which pts will benefit from SBRT and/or subsequent surgery. Research Sponsor: None.

TPS445 Trials in Progress Poster Session

Systemic therapy with a loco-regional treatment in patients with locally advanced pancreatic cancer: The SMART study. *First Author: Shahid Ahmed, University of Saskatchewan, Saskatoon, SK, Canada*

Background: Pancreatic cancer is a major cause of cancer-related death. About 40% of patients with pancreatic cancer present with locally advanced disease and are not candidates for curative surgery. Most patients are treated with chemotherapy with a limited life expectancy. The role of local treatment such as radiation is not well defined. Other conventional ablative therapies, such as thermal or cryoablation have limited role due to the risk of collateral damage to the adjacent structures. Irreversible electroporation (IRE) is a novel non-thermal ablation technology that does not cause injury to nearby blood vessels, ducts, and bowel and has the potential to provide longer disease control and thereby better overall survival. We hypothesized that addition of IRE to combination chemotherapy in patients with locally advanced pancreatic cancer will improve their outcomes, and patients with undetectable 12-week post IRE circulating tumor cell DNA will have better prognoses. **Methods:** It is a prospective, multicenter, single-arm phase II study. The primary objective is to determine 12-month PFS rate of patients with locally advanced pancreatic cancer who are treated with combination chemotherapy and IRE. Secondary objectives include identification of prognostic and predictive biomarkers, 24-months survival rate, quality of life of subjects, as well as cost-effectiveness and complication rates of IRE. Based on the assumption that treatment with IRE and chemotherapy would result in doubling of PFS versus chemotherapy alone a sample of n = 27 of patients with locally advanced pancreatic adenocarcinoma is estimated. Eligible patients will be recruited at the two major cancer centers in Saskatchewan. All IRE-eligible patients will receive 12 weeks of induction combination chemotherapy and will undergo IRE if there is no disease progression. An additional 12 weeks of chemotherapy will be recommended. Patients who are not eligible for IRE will receive chemotherapy at the discretion of treating oncologist until disease progression or until they become eligible for IRE. Circulating tumor DNA and a panel of genes will be examined using next-generation sequencing for their correlation with prognosis. Quality of life will be assessed, and cost-effectiveness analysis of IRE will be performed.The results of this study will be used to develop a future multicenter, national phase III trial. Clinical trial information: NCT04276857. Research Sponsor: Saskatchewan Cancer Agency.

TPS446 Trials in Progress Poster Session

A phase II, open-label pilot study evaluating the safety and activity of liposomal irinotecan (Nal-IRI) in combination with 5-FU and oxaliplatin (NALIRIFOX) in preoperative treatment of pancreatic adenocarcinoma (NEO-Nal-IRI Study). *First Author: Brian Hemendra Ramnaraign, University of Florida Health Cancer Center, Gainesville, FL*

Background: Neoadjuvant treatment for potentially curable pancreatic cancer (PDAC) 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 dose modifications, delays and growth factor support due to excessive toxicity which can complicate care delivery when given neoadjuvantly. Liposomal irinotecan injection (Nal-IRI) is FDA approved with a well-tolerated safety profile in relapsed, refractory metastatic PDAC. The current study aims to substitute Nal-IRI for traditional irinotecan in the standard FOLFIRINOX regimen (NALIRIFOX) and to demonstrate safe and effective neoadjuvant delivery. **Methods:** This phase II, open-label, multicenter single-arm study focuses on patients (pts) with operable PDAC without metastatic disease. Other key eligibility criteria include age ≥18 years, resectability confirmed by multiD GI tumor board (resectable vs. borderline), adequate cardiac, renal, hepatic function and ECOG performance status of 0 to 1. Pts receive NALIRIFOX regimen as per the table below every 2 weeks for four months followed by disease reassessment. Pts who remain surgical candidates will undergo surgical resection within 4 to 8 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 during treatment as measured by the NCI validated FACT-G scale. Enrollment continues to a maximum of 28 evaluable pts to demonstrate a reduction in historical 30 day postoperative complication rate. Clinical trial information: NCT03483038. Research Sponsor: Ipsen, University of Florida Health Cancer Center.

NALIRIFOX regimen components given intravenously (IV) every 14 days.

Agent	Dose	Route/Duration
Nal-IRI	50 mg/m^2	IV over 90 minutes
Oxaliplatin	60 mg/m^2	IV over 120 minutes
Leucovorin	400 mg/m^2	IV over 120 minutes
5-fluorouracil infusion	2400 mg/m^2	IV continuous infusion for 46 hours

TPS447 Trials in Progress Poster Session

Randomized phase II trial of olaparib + pembrolizumab versus olaparib alone as maintenance therapy in metastatic pancreatic cancer patients with germline BRCA1 or BRCA2 (g*BRCA*1/2+) mutations: SWOG S2001. *First Author: Vincent Chung, City of Hope, Duarte, CA*

Background: Olaparib was approved in 2019 as maintenance therapy for g*BRCA*1/2+ metastatic pancreatic cancer (mPDA) patients (pts). The POLO trial showed an improvement in median progression free survival (mPFS) with olaparib compared to placebo (7.4 versus 3.8 months) for g*BRCA*1/2+ mPDA pts following either stable disease/response on first-line platinum chemotherapy. Preclinical studies have demonstrated that PARP inhibitors modulate the immune microenvironment by increasing genomic instability, PD-L1 expression and activating the immune inflammatory stimulator of interferon genes (STING) pathway. Several clinical studies in solid tumors have shown preliminary efficacy with the combination of PARP plus immune checkpoint inhibitors. Based upon these data, SWOG S2001 aims to further improve the PFS of g*BRCA*1/2+ mPDA pts. **Methods:** S2001 was developed in collaboration with the Alliance and was activated in SWOG in October 2020. mPDA pts with gBRCA1/2 mutations identified with standard of care germline genetic testing will be eligibleif no progression after receiving 4 to 6 months of platinum chemotherapy (FOLFIRINOX, FOLFOX or gemcitabine/cisplatin). Zubrod performance status (PS) 0 or 1 pts are eligible. Pts will be stratified according to first line chemotherapy, PS 0 versus 1, and disease status after first-line treatment. The primary objective of this study is to evaluate the PFS of mPDA pts treated with olaparib + pembrolizumab compared to olaparib alone as maintenance therapy. Based upon the POLO trial, we expect a mPFS of 7 months in the control arm. Targeting a mPFS of 11.7 months in the experimental arm (hazard ratio 0.6) and assuming 15 months follow-up, 80% power and a 1-sided alpha=0.10, this design requires 78 evaluable pts to be accrued over 3 years. Prospective serial blood samples will be collected to bank DNA and RNA for future correlative studies. Support: NIH/NCI grants U10CA180888 and U10CA180819. Clinical trial information: TBD. Research Sponsor: U.S. National Institutes of Health.

TPS448 Trials in Progress Poster Session

A phase III trial of tumor-treating fields with nab-paclitaxel and gemcitabine for front-line treatment of locally-advanced pancreatic adenocarcinoma (LAPC): PANOVA-3. *First Author: Vincent J. Picozzi, Virginia Mason Hospital and Medical Center, Seattle, WA*

Background: Tumor Treating Fields (TTFields) are a non-invasive, regional antimitotic treatment modality, which has been approved for the treatment of glioblastoma. TTFields at specific frequency (150-200 kHz) are delivered via transducer arrays placed on the skin in proximity to the tumor site. TTFields predominantly act by disrupting the formation of the mitotic spindle during metaphase. TTFields were effective in multiple preclinical models of pancreatic cancer. The phase 2 PANOVA study, the first trial testing TTFields in pancreatic cancer patients, demonstrated the safety and preliminary efficacy of TTFields when combined with nab-paclitaxel and gemcitabine in both metastatic and LAPC. The Phase 3 PANOVA-3 trial (NCT03377491) is designed to test the efficacy and safety of adding TTFields to nab-paclitaxel and gemcitabine combination in LAPC. **Methods:** Patients (N = 556) with unresectable, LAPC (per NCCN guidelines) will be enrolled in this prospective, randomized trial. Patients should have an ECOG score of 0-2 and no prior progression or treatment. Patients will be stratified based on their performance status and geographical region, and will be randomized 1:1 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/m^2) 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 q8w, 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 0.75 in overall survival. Type I error is set to 0.05 (two-sided) and power to 80%. Clinical trial information: NCT03377491. Research Sponsor: Novocure.

TPS449 Trials in Progress Poster Session

CRESTONE: Clinical study of response to seribantumab in tumors with neuregulin-1 (NRG1) fusions—A phase II study of the anti-HER3 mAb for advanced or metastatic solid tumors (NCT04383210). *First Author: Johanna C. Bendell, Sarah Cannon, Nashville, TN*

Background: NRG1 (Neuregulin-1) gene fusions are rare oncogenic drivers found in 0.2% of solid tumors, including lung, pancreatic, gallbladder, breast, ovarian, colorectal, neuroendocrine, and sarcomas. NRG1 is the predominant ligand of HER3 and to a lesser extent HER4. NRG1 fusion proteins retaining an active EGF-like domain drive tumorigenesis and proliferation through aberrant HER3 activation. Importantly, NRG1 fusions are often mutually exclusive with other known driver alterations. NRG1 fusions have been correlated with worse overall and disease-free survival and poor response to treatment with standard therapies including chemotherapy, PD-(L)1 checkpoint inhibitors and combinations of these agents. Inhibition of HER3 and its dimerization partners represents a rational and novel therapeutic approach for tumors harboring an NRG1 fusion supported by case studies of clinical responses to anti-HER3 antibodies or pan-ERBB (tyrosine kinase inhibitors) TKIs like afatinib. Seribantumab is a fully human IgG2 mAb against HER3 uniquely able to inhibit NRG1-dependent activation of HER3, HER3-HER2 dimerization, and downstream signaling through the PI3K/AKT and MAPK pathways. The clinical safety profile of seribantumab has been well characterized through prior monotherapy and combination studies in over 800 patients. **Methods:** CRESTONE is an open label, multicenter phase 2 basket trial of seribantumab in adult patients with NRG1 fusion-positive locally advanced or metastatic solid tumors who have progressed on or are nonresponsive to available therapies. The trial will enroll at least 75 previously treated patients across three cohorts. Cohort 1 (N=55) will include patients who have not received prior treatment with any ERBB targeted therapy. Cohort 2 (up to N=10) will include patients who have progressed after prior treatment which includes ERBB targeted therapy. Cohort 3 (up to N=10) will include patients harboring NRG1 fusions without an EGF-like binding domain. NRG1 fusion status for enrollment will be determined through a local CLIA or similarly accredited molecular assay. NRG1 fusion status for patients in Cohort 1 will be centrally confirmed using an RNA-based NGS assay. This study will evaluate a novel dosing regimen of weekly induction, biweekly consolidation, and Q3W maintenance designed to rapidly achieve steady state levels, optimize exposure, and deliver maximal NRG1 inhibition. The primary endpoint is ORR per RECIST v1.1 by independent radiologic review. Secondary endpoints include duration of response (DoR), safety, PFS, OS, and overall clinical benefit rate. An interim analysis is planned following enrollment of 20 patients in Cohort 1. CRESTONE is open and accruing patients in the United States. Clinical trial information: NCT04383210. Clinical trial information: NCT04383210. Research Sponsor: Elevation Oncology, Inc.

TPS450 Trials in Progress Poster Session

MEKiAUTO: A phase I/II open-label study of combination therapy with the MEK inhibitor cobimetinib, immune-checkpoint blockade with atezolizumab, and the AUTOphagy inhibitor hydroxychloroquine in *KRAS*-mutated advanced malignancies. *First Author: Alexander Raufi, Brown University/ Lifespan Cancer Institute, Providence, RI*

Background: Pancreatic ductal adenocarcinoma (PDAC) and colorectal carcinoma (CRC) are aggressive diseases which account for the third and second leading causes of cancer-related death, respectively. Limited progress has been made towards effective treatments or cure. *KRAS* is mutated or amplified in nearly 30% of all cancers, including up to 95% of PDAC and 45% of CRC. Although no successful KRAS directed therapy has been approved to date, data has emerged demonstrating that inhibition of downstream targets of KRAS, namely MEK/ERK, increases autophagic flux in *KRAS*-mutated tumors. This catabolic process is used by many tumors to maintain viability and recent preclinical studies have shown that combining MEK/ERK and autophagy inhibitors in *KRAS*-mutated tumors can synergistically suppress cancer cell proliferation. Inhibition of autophagy has demonstrated an increase in antigen presentation which sensitize tumors to immune checkpoint inhibitors. Presented here is a trial-in-progress that will evaluate combination of cobimetinib (MEK inhibitor), atezolizumab (anti-PDL1), and hydroxychloroquine (autophagy inhibitor) in *KRAS*-mutated advanced malignancies. **Methods:** This is a phase 1/2 multicenter, open-label study of combination cobimetinib (40-60mg) orally once daily on days 1-21, hydroxychloroquine (600mg) orally twice daily on days 1-28, and atezolizumab 840 mg IV on days 1 and 15 of each 28 day cycle. Patients with histologically confirmed metastatic or unresectable *KRAS*-mutant adenocarcinoma for which standard curative or meaningful life-prolonging treatment options do not exist or are no longer effective will be enrolled. The primary objective of the phase I portion of this trial, which seeks to enroll 18 patients, is to estimate the maximum tolerated dose (MTD) of these agents using a two-stage time-to-event continual reassessment method (TITE-CRM). The primary objective of the phase II portion of this trial, which seeks to enroll approximately 66-157 patients, is to evaluate the preliminary efficacy of this combination, based on the objective response by 16 weeks. Secondary endpoints include PFS, OS, and safety. Correlative aims include analyses of pre- and on-treatment biopsies with quantitative multiplex immunofluorescence, RNA-sequencing, reverse phase protein array for association with clinical benefit and to determine mechanisms of action/resistance. An interim analysis will be performed at the conclusion of the phase I portion of the study. This study is open with 4 patients enrolled at the time of submission. Clinical trial information: NCT04214418. This trial is being conducted as part of the imCORE collaboration. Clinical trial information: NCT04214418. Research Sponsor: genentech/ f. hoffmann-la roche ltd.

TPS451 Trials in Progress Poster Session

Phase I study of SEA-CD40, gemcitabine, nab-paclitaxel, and pembrolizumab in patients (pts) with metastatic pancreatic ductal adenocarcinoma (PDAC) (trial in progress). *First Author: David Lawrence Bajor, Case Western Reserve University/University Hospitals Cleveland Medical Center, Cleveland, OH*

Background: SEA-CD40 is an investigational non-fucosylated, humanized IgG1 monoclonal antibody directed against CD40, a co-stimulatory receptor expressed on antigen-presenting cells (APCs). Activation of CD40 on APCs upregulates cytokine production and co-stimulatory receptors, enhancing tumor antigen presentation to T cells. Preclinical data indicate that treatment of PDAC with chemotherapy in conjunction with a CD40 agonist could enhance antigen presentation and initiate an antitumor immune response (Byrne KT and Vonderheide RH, Cell Rep 2016;15, 2719–2732). A Phase 1 study (SGNS40-001) is evaluating SEA-CD40 monotherapy and in combination with other agents in pts with advanced solid or hematologic malignancies. A cohort is enrolling to evaluate the combination of SEA-CD40, gemcitabine, nab-paclitaxel, and pembrolizumab in PDAC. **Methods:** The cohort consists of pts with metastatic PDAC who have had no prior therapy for metastatic disease. Pts must be ≥18 years old, with (neo)adjuvant therapy completed > 4 months prior to enrollment; ECOG status ≤1; adequate renal, hepatic, and hematologic function; and measurable disease per RECIST v 1.1 criteria. A standard regimen of gemcitabine and nab-paclitaxel on Days 1, 8, and 15 of each 28-day cycle is administered with SEA-CD40 IV on Day 3. Pembrolizumab is administered every 42 days starting on Day 8. The primary objective is to evaluate antitumor activity; secondary objectives are to evaluate safety and tolerability and SEA-CD40 and pembrolizumab pharmacokinetics. Efficacy endpoints are confirmed RECIST objective response rate per investigator (primary), disease control rate (response or stable disease ≥16 weeks), duration of response, progression-free survival, and overall survival. Disease is assessed every 8 weeks using RECIST and immune-based RECIST (iRECIST). Treatment continues until unacceptable toxicity, progressive disease per iRECIST, consent withdrawal, or study closure, whichever occurs first. Assessment of dose-limiting toxicity will occur initially in groups of 6 pts to identify the recommended phase 2 dose of SEA-CD40 for the cohort. Enrollment to this cohort began in November 2019. Clinical trial information: NCT02376699. Research Sponsor: Seattle Genetics, Inc.

TPS452 Trials in Progress Poster Session

Phase I study of mesothelin-targeted immunotoxin LMB-100 in combination with tofacitinib in persons with pancreatobiliary cancer or other mesothelin expressing solid tumors. *First Author: Guillaume Joe Pegna, National Cancer Institute Center for Cancer Research, Bethesda, MD*

Background: LMB-100 recombinant immunotoxin consists of a mesothelin-binding Fab for targeting with a modified *Pseudomonas* exotoxin A payload. Formation of anti-drug antibodies (ADAs) is thought to contribute significantly to limited clinical efficacy of LMB-100 seen in prior clinical trials. Most patients develop clinically meaningful ADAs after 1-2 cycles of LMB-100, resulting in rapid neutralization of LMB-100 during subsequent cycles and undetectable plasma drug levels. Tofacitinib is an oral Janus Kinase-1 and -3 (JAK) inhibitor approved by the FDA for the treatment of rheumatoid arthritis and ulcerative colitis. Pre-clinical studies have shown that tofacitinib can prevent the formation of ADAs against recombinant immunotoxin (Onda et al. *Journal of Immunology* 2014), and that co-administration of tofacitinib with LMB-100 increases immunotoxin serum half- life in mice and anti-tumor efficacy (Simon et al. *JCI Insight* 2019). We hypothesize that co-administration of tofacitinib with LMB-100 will prevent or delay the formation of high titer ADAs to LMB-100, such that 2 effective cycles of immunotoxin can be administered to patients. **Methods:** This phase I clinical trial consists of a dose escalation phase using 3+3 design to determine the maximum tolerated dose (MTD) of LMB-100 that can be administered with tofacitinib in participants (n = 18 max) with mesothelin-expressing solid tumors, followed by a dose expansion phase at the MTD for participants (n = 15) with pancreatic adenocarcinoma or extrahepatic cholangiocarcinoma. The primary objective of the expansion phase is to determine whether co-administration of tofacitinib delays formation of neutralizing anti-LMB-100 ADAs for cycle 2 of treatment as measured by LMB-100 plasma drug levels. A positive outcome will be reached if percent of participants achieving threshold LMB-100 drug levels during cycle 2 increases from 50% to 80% (83.6% probability if >10 of 15 evaluable participants meet this milestone). Plasma drug levels during cycle 3 will also be analyzed as a secondary endpoint. Key inclusion criteria include adults with histologically confirmed previously treated solid tumor malignancies. Participants will receive tofacitinib 10 mg twice daily on days 1-10 and LMB-100 at 65, 100, or 140 mcg/kg on days 4, 6 and 8 of a 21-day cycle. The dose escalation phase has been completed and enrollment onto dose expansion phase is ongoing. Clinical trial information: NCT04034238. Research Sponsor: U.S. National Institutes of Health.

TPS453 Trials in Progress Poster Session

A phase I dose escalation study of eryaspase in combination with modified FOLFIRINOX in locally advanced and metastatic pancreatic ductal adenocarcinoma. *First Author: Marcus Smith Noel, MedStar Georgetown University Hospital, Washington, DC*

Background: FOLFIRINOX remains the standard of care for the first line treatment of patients with locally advanced and metastatic pancreatic adenocarcinoma, however the prognosis remains poor, thus novel treatment options are indicated. Eryaspase, asparaginase (ASNase) encapsulated in red blood cells (RBCs) is an investigational product under development. Following infusion, asparagine and glutamine are actively transported into RBCs where they are hydrolyzed by the encapsulated ASNase. A randomized phase IIb study in patients with advanced pancreatic cancer whose disease progressed following first-line treatment (NCT02195180) was previously conducted. Eryaspase in combination with gemcitabine monotherapy or FOLFOX combination therapy improved overall survival (OS) and progression free survival (PFS). The safety profile of eryaspase was acceptable. A second line pivotal randomized phase III trial (Trybeca-1) is currently enrolling (NCT03665441). We design this phase I study to determine the safety of mFOLFIRINOX combined with Eryaspase in the first line of treatment. **Methods:** Patients with locally or metastatic biopsy proven pancreatic adenocarcinoma will be treated with the combination of mFOLFIRINOX plus Eryaspase. This will be a standard 3+3 design with 4 possible doing levels. mFOLFIRINOX dosing will include 5-Fluorouracil 2400 mg/m2 over 46 hours, Oxaliplatin 85 mg/m2, Irinotecan 150 mg/m2 plus Eryaspase 75 Units/kg at dose level 0. Eryaspase will be dose escalated up to 100 Units/kg. The study will enroll at three academic centers. Key eligibility criteria include performance status 0 or 1; locally advanced or metastatic tumor disease; adequate organ function. The primary objective is to determine the maximum tolerated dose and safety of this novel combination. Key secondary objectives include objective response rate, progression-free survival, overall survival, pharmacokinetics, pharmacodynamics, and biomarker research. A data safety monitoring committee will review data every 3 months. Clinical trial information: 04292743. Research Sponsor: Erytech.

TPS454 Trials in Progress Poster Session

Chemo4MetPanc: A phase II study with combination chemotherapy (gemcitabine and nab-paclitaxel), chemokine (C-X-C) motif receptor 4 inhibitor (motixafortide), and immune checkpoint blockade (cemiplimab) in metastatic treatment naïve pancreas adenocarcinoma (PDAC). *First Author: Ilenia Pellicciotta, Columbia University, New York, NY*

Background: Pancreas adenocarcinoma (PDAC) is an aggressive cancer projected to be the second leading cause of cancer-related death in the United States by 2030 for which improved treatment options are desperately needed. Immune checkpoint blockade (ICB) for PDAC has failed as monotherapy in early phase clinical trials likely due to a highly immunosuppressive tumor microenvironment. The CXCR4/CXCL12 axis is a key immune evasion mechanism thought to deter CD8+ T-cells (CTLs) from infiltrating the tumor. We performed a large seven arm survival and biopsy/necropsy study in KPC mice ($Kras^{LSL.G12D/+}$;$p53^{R172H/+}$;$Pdx1Cre^{tg/+}$) where we demonstrate that addition of gemcitabine to CXCR4 inhibition in combination with ICB, enhanced tumor stabilization and neoplastic cell death, and improved survival by 50 percent. Multiplex immunofluorescence indicated an increased CTL to regulatory T-cell ratio and clustering of CTLs around neoplastic cells. Presented here is a trial-in progress that will evaluate combination of a CXCR4 inhibitor, ICB, and chemotherapy in treatment naïve patients with PDAC. **Methods:** This is a multicenter, single arm, open-label phase 2 study of combination motixafortide 1.25mg/kg SC monotherapy for 5 days during priming followed by twice weekly, cemiplimab 350mg IV once every 21 days, gemcitabine 1000mg/m2 IV with nab-paclitaxel 125mg/m2 IV on days 1, 8, and 15 every 28 days. Patients with histologically confirmed metastatic PDAC who have not received prior therapy will be enrolled. The primary endpoint is overall response rate by 16 weeks. A response rate greater than 45% by 16 weeks is considered promising, whereas a response rate of less than 23% is considered not promising. We will use a Simon optimal 2-stage design, where we will enroll 10 patients in the first stage. If 3 or more patients meet the endpoint in the first stage, the study will be expanded to a total of 40 patients. If a total of 14 or more patients achieve CR or PR by 16 weeks, the agent will be considered promising and worthy of further study. Secondary endpoints include safety, mPFS, disease control rate (DCR), and mOS. Correlative aims include analyses of pre- and on-treatment biopsies with quantitative multiplex immunofluorescence, RNA-sequencing, and generation of patient derived organoids for association with clinical benefit and to determine mechanisms of action/resistance. An interim analysis will be performed at the conclusion of the stage I portion of the study. Clinical trial information: NCT04543071. Research Sponsor: Regeneron Inc and BioLineRxVelocity - Herbert Irving Cancer Center.

455 Rapid Abstract Session

COVID-19 infection in gastrointestinal (GI) cancer patients receiving systemic anticancer treatment (SACT) during the outbreak of the pandemic: The Guy's Cancer Centre experience. *First Author: Eirini Tsotra, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom*

Background: The COVID-19 pandemic has prompted difficult decisions around the use of SACT. These were based on limited early data suggesting cancer patients receiving SACT were at an increased risk of COVID-19 severe infection and death. Our study aim was to identify the COVID-19 infection and mortality rates of GI cancer patients receiving SACT. **Methods:** All GI patients receiving SACT at Guy's Cancer Centre between March, and May 31, 2020 were included. Demographic data (age, ethnicity, socio-economic status (SES)) and cancer characteristics (stage, SACT type, intent and treatment-line) were collected. COVID-19 infection was confirmed by PCR and severity defined by the World Health Organisation (WHO) classification. Patients with clinical or radiological diagnosis alone were excluded. **Results:** Of 417 GI patients receiving SACT during the study period, 345 (82.7%) received chemotherapy (alone or combined with targeted/biological treatment), 68 (16.3%) targeted/biological treatment alone and 4 (1%) immunotherapy. 14 (3.4%) patients were diagnosed with COVID-19, 13 were on chemotherapy and 1 on targeted/biological treatment. Commonest cancers in the COVID-19 positive group were colorectal (57.1%) and hepatobiliary (21.4%), followed by oesophago-gastric (14.3%) and neuroendocrine tumours (7.1%); 57.1% had stage IV disease. 64.3% of the positive patients were male (compared to 57.3% in the COVID-19 negative population), mean age was 57.7 years (63.1 years) and 85.7% had low SES (79.7%). 8 (57.1%) patients had severe infection and there were 3 (21.4%) COVID-19 related deaths. All the patients who died from COVID-19 were male and were receiving palliative chemotherapy. Only one patient was neutropenic (grade 1) when diagnosed with COVID-19. **Conclusions:** The rate of COVID-19 infection in our population was relatively low (3.4%). Of the 14 COVID-19 positive patients, 57.1% had severe infection, 21.4% died (compared to 3.7% mortality in the non-infected group) and all but one were on chemotherapy. This prospective data, from a large UK comprehensive Cancer Centre, provides some evidence that continuing SACT through the pandemic is relatively safe. The risk of COVID-19 related infection and death must be off-set against the cancer-related morbidity and mortality associated with treatment delays.
Research Sponsor: None.

456 Poster Session

Deploying an AI-based online search tool to increase patients' access to and understanding of solid tumor GI clinical trials. *First Author: Pashtoon Murtaza Kasi, University Of Iowa, Iowa City, IA*

Background: The number and complexity of clinical trials has been growing, making finding and accessing trials increasingly challenging. Additionally, the goal of representative trial populations remains elusive with sometimes devastating medical consequences. A key barrier to increasing recruitment efficiency is patients' low awareness of clinical trials as an option. They rarely hear about trials from their oncologists, unless they are based at a research center, which introduces trial population biases by including only patients with good healthcare access. And even if patients decide to search for information on trials themselves, the information is difficult to understand. There are existing trial search tools, but they have multiple shortcomings: complex navigation, limited search functionality, clinical trial data is too complex for non-specialists to understand, and lack of clarity on next steps. **Methods:** Access to trials via a novel trial search tool (www.ancora.ai) which uses AI to restructure trial information was the main focus of this study. For increased GI cancer specificity, 6 key GI cancers were included into the AI model and information was restructured based on key eligibility differentiators identified (see data structure table). Research participants (xx GI oncology patients) were recruited with the support of patient associations (e.g. The Colon Club) leveraging social media. They were asked to complete a 20 minute survey evaluating both an established tool (clinicaltrials.gov) and the novel tool to find trials relevant for them. They had to assess different aspects of the tools' usability on a 5-level Likert scale. Survey results were analyzed in MS Excel, using built-in statistical functions (mean, standard deviation, student's t-test). **Results:** Please note the survey is ongoing and results will be updated. Current survey respondents had a base level of awareness of clinical trials (3.1±1.2), with patient associations and the internet as leading information sources. The novel tool seemed to make it easier to find trials (3.7±0.9 vs. 2.7±1.3), showed an improvement in ease of understanding information presented (3.8±1.1 vs. 2.6±1.3) and directionally provided more clarity on what next steps towards trial enrollment would be (4.2±0.8 vs. 3.7±1.4). Overall, this led to higher patient satisfaction (3.4±1.1 vs. 2.3±0.5). **Conclusions:** Novel patient-focused, AI-driven clinical trial support tools can unlock trial access for all patients. Democratizing trial information will not only increase trial accrual, but also patient satisfaction while reducing disparities. Research Sponsor: None.

Current data structure in trial search tools.

Trial Search Tool	By Sponsor	By Trial Phase	By Tumor	By Cancer Stage	Across Solid Tumors	By Genetic Mutations	By Previous Treatments
Clinicaltrials.gov	x	x	x		x		
Ancora.ai	x	x	x	x	x	x	x
Research Centers			x				
Patient Support Sites		x	x				(x)

457 Poster Session

Gastrointestinal cancer mortality rate global trends over the last century. *First Author: Ravina Sidhu, California Northstate University, Elk Grove, CA*

Gastrointestinal Cancer Mortality Rate Global Trends Over the Last Century
Background: Global gastroenterology cancer mortality trends have drastically changed over past decades due to alterations in risk factors such as diet, populations, exposures, and medical advancements. This study investigates specifically how meat consumption, the biggest evolving risk factor for GI cancer mortality, has influenced various gastrointestinal incidence rates globally. Although the correlation between meat consumption and cancer risk has been investigated, a global temporal study investigating the national mortality rates of gastrointestinal cancers relating to meat production remains unexplored. We researched causes for the trends between meat production and GI cancer mortality in the USA, Canada, Japan, France, and Singapore. **Methods:** Cancer mortality data was collected from the WHO Cancer Mortality Database, specifically the IARC database. Meat consumption data was unavailable between the 1960s-2010, so meat production data was used and obtained from the FAOSTAT. **Results:** The pancreatic cancer mortality rate increased in each country except Canada. This spike is due to increased meat consumption, obesity, lack of screening modalities, poor prognosis, and late diagnosis of the disease. Canada's 1% drop in mortality rate can be attributed to a decreased smoking rate amongst men (62% to 16% from 1965-2017) as well as a decline in meat consumption. The mortality rates of gastric and colorectal cancer (CRC) have decreased despite a meat production increase. Decreased *H. pylori* prevalence (Europe: 48.8% to 39.8%, North America: 42.4% to 26.6%, and Western Asia: 53.6% to 54.3%), better food preservation, and improvement in environmental conditions have lowered gastric cancer incidence. The CRC mortality rate in the USA, Canada, Japan, and France decreased mostly due to colonoscopy screening measures, better treatment, and decreased red meat consumption. In Singapore, increased obesity and high caloric diets account for an increased CRC mortality rate despite decreased meat production. This rate is exacerbated by lower screening rates due to decreased CRC risk awareness. **Conclusions:** Gastric and CRC mortality rates decreased despite increased meat production, while pancreatic cancer incidence rates have increased. These trends are further investigated and necessary to understand to lower the mortality rates of GI cancers on a global scale. Research Sponsor: None.

458 Poster Session

Socioeconomic status (SES) and survival outcomes in patients with gastrointestinal (GI) cancers: An analysis of 1.4 million patients in the National Cancer Database (NCDB). *First Author: Mohamed E. Salem, Levine Cancer Institute, Atrium Health, Charlotte, NC*

Background: SES and access to care are factors that may impact patient outcomes. We examined the impact of SES on survival in patients (pts) with GI cancers. **Methods:** Data obtained from the NCDB were used to examine the association between SES and outcomes of GI cancer pts. Pts were categorized by income and education levels. Logistic regression, Cox proportional hazards models, and chi-square tests were used to examine the differences between the groups. **Results:** A total of 1,409,177 pts diagnosed with GI cancers between 2004 and 2016 were retrospectively studied (table). The majority of pts were male (54.3%), and 83.7% were white, 11.5% black, and 4.7% of other races. Of the entire cohort, 31% of pts lived in the highest income areas, whereas 18.3% were in the lowest and 50.6% in middle-income areas; 23% lived in the highest high school graduation rate (>93%) areas, whereas 17.4% lived in the lowest graduation rate (< 79%) areas; and 82.4% resided in metropolitan areas. Pts in the lowest compared to highest income areas were more likely to be black (OR: 6.5, 6.4-6.6), uninsured (2.9, 2.8-3.0), or have Medicaid (4.13, 4.04-4.22), and have a Charlson-Deyo score ≥ 1 (1.35, 1.33-1.36). In the multivariate analysis, cancer type, stage, tumor differentiation, income, education, insurance status, gender, race, Charlson-Deyo score, and type of treatment center were independent predictors for survival. After controlling for other factors, black pts had a 3% increased risk of death (HR_{adj} = 1.03; 1.02-1.03; $p < 0.001$). Pts from lowest vs highest education areas had a 2% increased risk of death (HR_{adj} = 1.02; 1.01-1.03; $p < 0.001$). Pts from the lowest income vs highest income areas had a 13% increased risk of death (HR_{adj} = 1.13; 1.12-1.14; $p < 0.001$). Pts with Medicaid insurance had a 33% (HR_{adj}: 1.33, CI 1.32-1.34, $p < 0.001$) and uninsured pts had 22% (HR_{adj}: 1.22 (1.20-1.23, $p < 0.001$) increased risk of death compared to pts with private insurance. Pts from urban or rural areas vs metropolitan areas had a 1% increased risk of death (HR_{adj} = 1.01; 1.00-1.02; $p < 0.001$). **Conclusions:** Low SES is associated with worse survival in pts with any GI cancer. Pts with low-income status and Medicaid or no health insurance had the highest risk of mortality. These stark inequities must be addressed with renewed efforts to identify, treat, and better support pts at highest risk for poor outcomes. Research Sponsor: None.

Pts with GI cancers in low and high income areas.

	Income area			
Cancer site (number)	Lowest (ref) Median income <$38,000 (n)	Highest Median income ≥ $68,000 (n)	Adjusted Hazard Ratio (95% CI)	*P*-value
Colorectal 890,867	161,667	266,491	1.12 (1.11-1.14)	< 0.001
Pancreatic 241,397	41,709	75,157	1.14 (1.12-1.16)	
Esophageal 103,634	18,637	30,901	1.10 (1.08-1.14)	
Gastric 120,586	22,059	35,306	1.13 (1.10-1.16)	
Anal 36,202	6,715	10,427	1.23 (1.15-1.31)	
Small bowel 16,491	2,944	5,138	1.17(1.11-1.24)	

ABSTRACT WITHDRAWN

460 Poster Session

Comparison of clinical characteristics and survival outcomes in patients with malignant peritoneal and pleural mesothelioma. *First Author: Vatsala Katiyar, University of Louisville Hospital, Louisville, KY*

Background: Malignant peritoneal mesothelioma (MPeM) is an aggressive tumor strongly associated with asbestos exposure. We analyzed a large nationwide database to better understand the differences in the demographic and clinical patterns of MPeM and pleural mesothelioma (MPlM). **Methods:** The National Cancer Database (NCDB) 2010-15 was queried to identify all patients diagnosed with MpeM and MPlM. The demographic and clinical characteristics were compared using Pearson's chi-square test. Kaplan-Meier method and associated log-rank test were used to compare the unadjusted overall survival of the two malignant mesothelioma (MM) sites. A multivariate Cox regression analysis was done to determine survival difference between the 2 groups. **Results:** Of the 8,668 patients included in the study**,** 1,081 (12.5%) had MPeM and 7,587 (87.5%) had MPlM. The MPeM cohort was younger (median age at diagnosis 61 vs 73 years), predominantly females (45.7% vs 23.5%), had a lower Charlson Deyo Comorbidity Score (> = 1: 24.5% vs 32.1%), had higher percentage of uninsured patients (4% vs 2.2%), was less likely to be treated at a community or comprehensive community center (36.1% vs 47.3%) and had lower proportion of sarcomatous or biphasic histology (9.3% vs 22.4%) compared to MPlM cohort. The MPeM cohort was more likely to receive surgery (56.5% vs 28%) and chemotherapy (68.4% vs 54.5%) but less likely to receive radiation (0.8% vs 11%). The p-value was < 0.001 for all comparisons. The median OS was 19.7 and 9.7 months for patients with MPeM and MPlM, respectively (log-rank p value < 0.001). On multivariate Cox proportional hazards analysis, OS was significantly worse for MPlP compared to MPeP [HR adj: 1.19, 95% confidence interval (CI): 1.09-1.30 ($p < 0.001$)]. **Conclusions:** There is paucity of data about clinical characteristics and outcomes of MPeM. Much of our current knowledge about MPeM is extrapolated from MPlM. Our study suggests significant differences in prognostic factors and survival outcomes between the two sites. Research Sponsor: None.

461 Poster Session

Exploring cancer clinical trial participation in the new normal of COVID-19: The patient perspective. *First Author: Martha Ann Raymond, GI Cancers Alliance, Central Square, NY*

Background: The impact of coronavirus (COVID-19) has significantly affected cancer patients seeking to enroll in a clinical trial. The pandemic has led to an unprecedented disruption across the cancer research community pausing trial operations. Data from the National Institute of Health and the National Library of Medicine indicates 988 cancer clinical trials were suspended from March September 1, 2020, with 60% of institutions enrolling patients at a lower rate. Our research underscores the patient perspective of clinical trial participation amid COVID-19. **Methods:** July September 2020 Nationwide eight-week online survey and interviews. Research goals: gain a better understanding of barriers and cultural attitudes of ethnically diverse communities regarding trial participation; learn the enhanced safety measures needed for patients to feel comfortable returning to the clinic; better understand the importance of effective patient-clinician communication. **Results:** 511 patient participants reported the following insights: 86% reported their healthcare team had not discussed trial participation; 99% reported being comfortable with telehealth visits for pre-screening and monitoring; 82% receive care at community-based hospitals. Barriers to enrollment and additional safety considerations include gaps in outreach and education services for ethnically diverse communities; absence of cultural sensitivity and disregard of historical perspective; financial insecurity and travel; and the need for increased COVID-19 testing, enhanced safety protocols and a proven vaccine. Participants identified their ethnicity as 38% Caucasian; 24% Black/African American; 19% Hispanic/Latino; 16% Asian; 2% Native American/Pacific Islander. **Conclusions:** Clinical trials provide patients access to the newest treatments, and yet only 2%-3% of adult cancer patients enroll in a trial. Common barriers to trial participation have been widely researched, but now amongst the coronavirus pandemic, additional barriers are evident. Based on our research, our call to action is clear: work with key opinion leaders in ethnically diverse populations to help build trust and mutual respect when discussing research studies; and engage patients and clinicians to openly discuss clinical trial enrollment working toward patient-centered communication. The coronavirus pandemic is a devastating public health threat, and it will take a collective effort from the entire cancer community to minimize the effect of COVID-19 on cancer clinical trial participation. Research Sponsor: GI Cancers Alliance, Inc.

462 Poster Session

Stage IV gastrointestinal stromal tumors: Epidemiology, treatment and outcomes in adult US patients. *First Author: Johannes Uhlig, University Medical Center Goettingen, Goettingen, Germany*

Background: To evaluate epidemiology, treatment and outcomes of stage 4 gastrointestinal stromal tumors (GIST). **Methods:** The 2010-2016 United States National Cancer Database was queried for adult patients diagnosed with invasive GIST (ICD code 8936) at AJCC stage 4, without prior malignant disease. Overall survival (OS) was evaluated using Cox proportional hazards regression, accounting for potential confounders in multivariable models. **Results:** A total of 1,578 stage 4 GIST were included (13.3% of all GIST) with a male:female ratio of 1.38:1. The most common cancer site was the stomach (55.4%) and small intestine (40% of stage 4 GIST). At diagnosis, median age was 62 years and median tumor diameter 10 cm. Distant organ metastases were reported in 58.7%, the most frequent being hepatic (n = 801, 50.8% of stage 4 GIST). The majority of stage 4 GIST patients received systemic therapy (78.6%), either alone (35.4%) or combined surgery+systemic therapy (43.3%). Systemic therapy was administered neoadjuvant in 6.9%, adjuvant in 32%, and neoadjuvant+adjuvant in 5.1% of surgically resected patients. Another n = 204 patients (12.9% of all stage 4 GIST) were treated with surgical resection alone. GIST overall survival rates were 88%, 77%, 67% and 51% at 1, 2, 3, and 5 years, respectively. On multivariable Cox proportional hazard models, primary GIST treatment independently affected OS: compared to combined surgery+systemic therapy, OS was shorter for patients receiving systemic therapy alone (HR = 2.77 (95% CI: 2.12-3.61, $p < 0.001$)) and no treatment (HR = 4.2 (95% CI: 2.75-6.43, $p < 0.001$)). No significant OS difference was evident comparing surgery+systemic therapy and surgery alone (HR = 1.23 (95% CI: 0.88-1.72, p = 0.227)). In subgroup analyses of patients undergoing surgical resection, no statistically significant OS difference was evident comparing neoadjuvant, adjuvant and combined neoadjuvant+adjuvant systemic therapy on multivariable analyses. Treatment at non-academic vs. academic centers was associated with shorter OS (multivariable HR = 1.36 (95% CI: 1.1-1.69, p = 0.005)). Further independent OS predictors were male sex (vs. female HR = 1.28 (95% CI: 1.03-1.59, p = 0.023)), older age, higher comorbidities, higher cancer grade, and larger cancer diameter. **Conclusions:** Stage 4 GIST is a rare gastrointestinal malignancy that most commonly manifests in the stomach and small intestine in male patients, with frequent hepatic metastases and excellent 5-year OS rates of up to 51%. Combined surgery+systemic therapy demonstrates best outcomes, although surgical resection alone might yield comparable results in selected patients. Research Sponsor: None.

463 Poster Session

Frequency and distribution of gastrointestinal oncology patient-reported symptomatic adverse events (SAEs) at a comprehensive cancer center. *First Author: Nadine Jackson McCleary, Dana-Farber Cancer Institute, Boston, MA*

Background: In clinical trials, the systematic collection of patient (pt) reported outcomes has been shown to improve quality of life & overall survival. To develop predictive care models for symptom management, we explored the frequency & distribution of SAEs reported by pts who reported electronic patient reported outcomes (ePRO) prior to outpatient visits to the Gastrointestinal Cancer Center (GCC) at Dana Farber Cancer Institute (DFCI). **Methods:** ePRO is a modified NCI Patient Reported Outcomes – Common Terminology Criteria for Adverse Events instrument distributed weekly to GCC pts with a medical/surgical/radiation oncology encounter. Responses are available to the care team in the electronic health record. ePRO consists of presence/frequency/severity/interference of 15 core SAEs (fatigue, insomnia, general pain, decreased appetite, nausea, vomiting, constipation, diarrhea, shortness of breath, numbness and tingling, rash, concentration, fever, anxiety, sadness). Responses are scored 0 to 3 (with 2 and 3 indicating moderate and severe SAEs, respectively). We examined the frequency & distribution of grade 2 and 3 SAEs in ePRO responders by age, gender, race/ethnicity. All pts had gastrointestinal cancer and an outpatient visit for treatment, symptom management, follow-up care. **Results:** From 9/1/2018 to 8/31/2020, 1912 unique pts responded (response rate 23%). Most respondents were age 50-69 years (58% compared to 15% age <50, 27% age ≥70; range 18-95), male (53%), white (75%). Grade 3 SAE frequencies were pain (12%), fatigue (11%), anxiety/constipation/insomnia/decreased appetite (5%), sadness/numbness and tingling/diarrhea (3%), concentration/shortness of breath (2%), nausea/rash (1%), fever/vomiting (0%). Across pts, fatigue, general pain, insomnia, anxiety were the most common grade 2 and 3 SAEs. Shortness of breath, vomiting, rash, fever were least common (Table). **Conclusions:** In GCC pts responding to ePRO, the most frequent SAEs were pain, fatigue, insomnia, anxiety. Shortness of breath, nausea, vomiting, diarrhea were less often severe. Pts <50 were more likely to report severe anxiety but there were no other major differences based on age, sex, race/ethnicity. Ongoing efforts will increase pt/provider engagement and develop predictive models & symptom management interventions from ePRO responses. Research Sponsor: Dana-Farber Cancer Institute funding.

Percent with grade 2 or 3 severe SAE, displaying highest & lowest frequency.

		General pain	Fatigue	Insomnia	Anxiety	Shortness of breath	Vomiting	Rash	Fever
Age	< 50	35.8	33.6	22.2	30.9	5.3	5.4	1.9	1.3
	50-70	32.4	34.7	21.1	18.4	7.5	5.0	1.3	0.9
	70+	29.7	38.5	21.7	18.4	11.8	3.2	3.4	0.9
Sex	Female	32.3	35.5	21.6	24.4	6.9	4.1	1.7	1.0
	Male	32.2	35.7	21.3	16.7	9.6	5.0	2.1	0.9
Race/ Ethnicity	Black	40.2	30.7	16.5	15.3	8.1	7.3	0.0	1.6
	Latinx	36.4	36.4	27.3	9.1	0.0	0.0	0.0	0.0
	Other	37.0	36.0	24.4	17.3	9.9	5.0	1.7	2.0
	White	32.2	38.6	22.5	22.5	7.6	3.8	1.9	0.9

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Association of perioperative red blood cell transfusions with all-cause and cancer-specific death in patients undergoing surgery for gastrointestinal cancer. *First Author: Jesse Zuckerman, Division of General Surgery, Department of Surgery, University of Toronto, Toronto, ON, Canada*

Background: Perioperative anemia and red blood cell (RBC) transfusions are common in patients undergoing gastrointestinal cancer surgery. To adequately balance the risks and benefits of transfusion, clinicians must understand the potential effect of transfusions on long-term outcomes. Methodologic issues have limited previous studies exploring the association between RBC transfusion and survival in this specific patient population. Our objective was to determine, among patients who have undergone gastrointestinal cancer resection, if perioperative RBC transfusions are associated with higher risk of all-cause and cancer-specific death. **Methods:** In this population-based retrospective cohort study, we used administrative datasets containing routinely collected data from Ontario, Canada. Patients who underwent gastrointestinal cancer resection between January 1, 2007 and March 31, 2019 and survived at least 90 days postoperatively were eligible for inclusion. All-cause death from the ninetieth post-operative day was compared between groups using Kaplan-Meier methods and Cox proportional hazards models. Cancer-specific death was compared using competing risk methods. Regression adjusted for potential confounders. Sensitivity analyses, including the E-value, evaluated the robustness of estimates. **Results:** We identified 74,962 patients (mean age, 67.7 years; 55.4% male; 79.7% colorectal cancer) who underwent resection for gastrointestinal cancer and survived at least 90 days after surgery. Over a median follow-up of 4.1 years (interquartile range 1.9-5.0 years), patients who received RBC transfusions demonstrated increased hazards of all-cause and cancer-specific death relative to patients who were not transfused (hazard ratio: 1.39, 95% confidence interval 1.34 to 1.44; cause-specific hazards ratio: 1.36, 1.30 to 1.43). The adjusted risk of all-cause death was higher in early follow-up intervals (3-6 months post-operatively) but remained elevated in each subsequent interval over 5 years. **Conclusions:** RBC transfusion among patients with gastrointestinal cancer is associated with increased all-cause death; this persisted over time suggesting a long-term effect of perioperative transfusion. These findings should help clinicians balance the risks and benefits of transfusion and highlight the need for well-designed, multicenter randomized trials to determine if aggressive transfusion avoidance protocols could improve patient survival after gastrointestinal cancer surgery. Research Sponsor: New Investigator AwardSunnybrook Alternative Funding Plan, Ontario Ministry of Health and Long-Term Care Clinician Investigator Program.

465 Poster Session

Feasibility of using a computerized food frequency questionnaire (FFQ) to assess dietary patterns in patients with advanced gastrointestinal (GI) malignancies. *First Author: Rishi Jain, Fox Chase Cancer Center, Philadelphia, PA*

Background: Identification of poor dietary patterns is important for the optimal management of patients with metastatic GI malignancies who suffer from high rates of malnutrition and sarcopenia which are associated with increased rates of treatment-related toxicity and worsened survival. Dietary records or recall methods and FFQs are available but have high patient burden and are seldom utilized in oncology settings outside of formal nutritional consultations. Thus, we evaluated the feasibility of conducting serial assessments of dietary patterns using a novel computerized FFQ technology. **Methods:** Assessments of diet using the computerized FFQ, nutritional status (NUTRISCORE), QOL and anorexia/cachexia burden (FAACT), anxiety/depression (HADS) and taste burden were done at the time of initiation of first-line chemotherapy (baseline) and 3 months later. The FFQ was done independently either at home on personal computer after visit or via iPad in infusion room. Dietary quality was defined by the Healthy Eating Index 2010 (HEI) score, which was automatically calculated by the computerized FFQ software. Feasibility was defined as at least 70% of patients completing baseline and 3-month assessments. Spearman's correlations were used to determine associations between measures. **Results:** 29 patients with advanced (metastatic or unresectable) GI cancers were enrolled and 23 completed the baseline FFQ (8 colorectal, 5 pancreas, 5 gastroesophageal, 5 other). Median age was 58 (20-78) with M:F ratio of 10:13. The overall completion rate of baseline and 3-month assessments was 81.8%, meeting the pre-defined feasibility criteria. The mean baseline HEI score was 65 (range 38-88). Of patients who completed both baseline and 3-month assessments, the mean HEI score remained stable at 58 with changes in specific HEI components including a 20% decline in the seafood and plant protein score and a 13% decline in the whole grain score and small improvements in other areas (e.g. empty calories, dairy). There were no significant correlations between baseline HEI score and other assessments. **Conclusions:** It is feasible to use a computerized FFQ to assess for longitudinal changes in eating patterns and dietary quality in patients with advanced GI cancers, particularly when patients can complete the assessments during chemotherapy infusions. Preliminary findings also suggest that the FFQ can be helpful for highlighting areas in which diet quality could be improved. Additional analysis of other computerized FFQ data (e.g. macro/micronutrient consumption) is ongoing. Research Sponsor: Supported by grant #15-175-23 from the American Cancer Society TREC Training Workshop R25CA203650 (PI: Melinda Irwin).

466 Poster Session

Incidence, mortality and hospital resource utilization in patients with gastrointestinal cancer and malnutrition: A nationwide analysis. *First Author: Vatsala Katiyar, University of Louisville Hospital, Louisville, KY*

Background: Malignancies are associated with a high prevalence of cachexia, protein energy malnutrition (PEM) and failure to thrive. We analyzed the National inpatient Sample database (NIS) to understand the temporal trends and differences between gastrointestinal cancers (GIC) patients with and without malnutrition. **Methods:** All adults admitted with GIC including esophageal, gastric, pancreatic, hepatic, gall bladder, small and large intestine and anal cancers from 2012-2016 were identified from the NIS using the ICD 9 and ICD 10 codes. We analyzed the temporal trends of mortality and resource utilization. Multivariable logistic regression was used to evaluate the risk factors for malnutrition in patients with GIC. **Results:** There were 2,645,285 GIC inpatient admissions between 2012-2016, out of which 6.1% patients died. 11.1% (±0.22) patients had PEM and three most common GIC associated with PEM were Esophageal (19.7±0.24%), gastric (16.5±0.22%) and small intestine (15.2±0.41%). On multivariate analysis, PEM was more common in male gender (OR: 1.07, 95% CI:1.05-1.08, P<0.01), African- American race (OR:1.14, 95% CI: 1.10-1.17, P<0.01) and Charlson comorbidity index >=2(OR:1.5, 95% 1.42-1.51, P<0.01). Malnourished patients were often terminally ill (48.8% vs 39.8%), in intensive care unit (7.89% vs 3.75%), were more likely to be seen by palliative care team (17.6 % vs 9.8%) and were more likely to die (9.6% vs 5.70%, OR-1.76; p <0.01). The incidence, mortality, and total charge of PEM in patients with GIC significantly increased from 2012 to 2016 as shown in the table below. **Conclusions:** Malnourished patients with GIC tend to have more advanced disease and have an increased mortality as compared to patients with adequate nutritional status. Optimization of their nutritional status can greatly improve outcomes and curb healthcare costs. Research Sponsor: None.

	2012	2016	P value
Incidence, %	9.9(±0.12)	14.5(±0.14)	<0.01
Mortality, %	9 (±0.01)	11.3(±0.03)	<0.01
Length of stay (mean, in days)	6.9(±0.81)	6.6(±0.72)	0.312
Hospital charges (mean, in $)	60312	71709	<0.01

467 Poster Session

Clinical activity of the RET inhibitor pralsetinib (BLU-667) in patients with *RET* fusion–positive solid tumors. *First Author: Vivek Subbiah, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Recent tumor-agnostic drug approvals have resulted in a paradigm shift in cancer treatment away from organ/histology specific indications to biomarker-guided tumor-agnostic approaches. Pralsetinib is a potent and selective RET inhibitor, which has recently been approved by the U.S. Food and Drug Administration (FDA) for the treatment of adults with metastatic *RET* fusion-positive non-small cell lung cancer (NSCLC) and is under New Drug Application review for *RET* mutant thyroid cancers by the FDA. *RET* fusions occur in up to approximately 7–8% of patients with gastrointestinal malignancies, including pancreatic, liver, and colorectal cancers. There are currently no approved selective RET inhibitors for patients with *RET* fusion-positive solid tumors other than NSCLC and thyroid cancer. Here, we present data on the clinical activity of pralsetinib in patients with *RET* fusion–positive solid tumor types other than NSCLC enrolled in the Phase I/II ARROW study (NCT03037385). **Methods:** ARROW consists of a phase I dose escalation (30–600 mg once [QD] or twice daily) followed by a phase II expansion (400 mg QD) in patients with advanced *RET*-altered solid tumors. Primary objectives are overall response rate (ORR), per RECICT v1.1 and safety. **Results:** A total of 13 patients with *RET* fusion–positive thyroid cancer (12 papillary, 1 poorly differentiated; enrollment cutoff July 11, 2019) and 14 patients with *RET* fusion–positive solid tumors other than NSCLC and thyroid (3 pancreatic, 3 colon, 2 cholangiocarcinoma, 6 other; enrollment cutoff November 19, 2019) were enrolled in ARROW and received pralsetinib. At the February 13, 2020, data cutoff, the ORR (blinded central review) in response-evaluable patients with *RET* fusion–positive thyroid cancer was 91% (10/11; 95% CI: 59–100) and disease control rate was 100% (95% CI: 72–100). Treatment was ongoing in 7 of 11 patients. In *RET* fusion–positive solid tumors other than NSCLC and thyroid, ORR (investigator's assessment) was 50% (6/12; 95% CI: 21–79) and responses were observed in all patients with pancreatic cancer (3/3) and cholangiocarcinoma (2/2). Treatment was ongoing in 6 of 12 patients, including 2 of 3 patients with pancreatic cancer and 1 of 2 patients with cholangiocarcinoma. Responses were observed across multiple fusion genotypes. In the 27 patients with *RET* fusion-positive tumors other than NSCLC, most frequent treatment-related adverse events (TRAEs) were grade 1–2, and included anemia (33%), increased aspartate aminotransferase (33%), decreased white blood cell count (33%), hypertension (30%), increased alanine aminotransferase (26%), hyperphosphatemia (19%), and neutropenia (19%). No patients discontinued due to TRAEs. **Conclusions:** Pralsetinib demonstrated broad and durable antitumor activity across multiple advanced solid tumor types, regardless of *RET* fusion genotype, and was well tolerated. The study is ongoing. Clinical trial information: NCT03037385. Research Sponsor: Blueprint Medicines Inc.

468 Poster Session

The gastrointestinal clinical trial landscape: A cross-sectional analysis of clinicaltrials.gov from 2007-2019. *First Author: Nirosha Perera, Mayo Clinic, Rochester, MN*

Background: The burden of gastrointestinal (GI) disease is high, costing over $97 billion annually in the United States (U.S.) alone. Yet the methodological rigor and characteristics of trials leading to guideline development are rarely explored. In 2007, the U.S. mandated that all interventional studies (Phase II-IV) register with ClinicalTrials.gov, the largest international clinical trial database. We characterized registered GI trials to identify features associated with early discontinuation, results reporting and increased methodological rigor. **Methods:** We employed a cross-sectional study design with descriptive, logistic regression, cox regression, time series and survival analyses. We downloaded data for 327 075 studies registered on the Aggregate Analysis of the ClinicalTrials.gov database from October 1, 2007 to December 31, 2019. Trials were excluded if registered prior to 2007 (n=38 111) or for non-interventional study design (n=69 233). After applying GI specific Medical Subject Heading terms to the remaining 219 731 trials, 22 339 trials were identified for manual review. 20 548 trials were found to contain true GI content, representing over seven million patients. Primary exposure variables were trial focus (disease process, anatomical location) and funding (industry, U.S. government, academic). **Results:** Of the 20 548 GI trials, 6.1% were funded by the U.S. government, 35.6% by industry, and 58.3% by academic institutions. The most studied disease process was neoplasia (42.6% of trials), followed by viral hepatitis (10.8%). The majority of neoplasia trials were funded by academic institutions (60.3%) and studied colorectal neoplasms (31.5%), followed by hepatic (17.9%), pancreatic (15.5%), gastric (12.8%), esophageal (10.6%) and biliary tract (4.9%) neoplasms. U.S. government funded trials had the lowest risk of early discontinuation (adjusted Hazard Ratio 0.63, 95% CI: 0.48-0.83, $p<0.001$) and the highest rates of results reporting (25%, X^2 $p<0.001$). Among all trials, the majority did not report Data Monitoring Committee (DMC) oversight (58.6%). Only 12% of phase III trials employed a rigorous methodology, which we defined as being randomized, double blinded, multi-site, overseen by a DMC, and having enrolled ≥50 patients. Government sponsored trials had the highest proportion of trials meeting this definition (19%). Academic sponsored trials, constituting the majority of trials overall, had the lowest proportion (5.3%), in part due to not meeting the multi-site criteria. **Conclusions:** Despite constituting the minority of trials overall, U.S. government funded trials displayed the highest methodological rigor. Stakeholders can look to U.S. government funded trials as a model of improvement, but nevertheless must commit to increasing methodological rigor and results dissemination to strengthen trial findings that guide GI clinical recommendations. Research Sponsor: None.

469 Poster Session

Access to innovative cancer medicines in gastrointestinal oncology: 2010 through 2020. *First Author: David Edward O Reilly, Cork University Hospital, Cork, Ireland*

Background: There are significant disparities in patient access to innovative cancer medicines internationally. We sought to describe global drug licensing developments in gastrointestinal (GI) oncology from 2010 – 2020. We compared US, European, UK and Irish patient access to these drugs, their cost and associated efficacy. **Methods:** Data was collected from public sources online including the FDA, European Medicines Agency (EMA), the UK National Institute of Clinical Excellence (NICE) and the Irish National Cancer Control Programme (NCCP). Anti-cancer compounds approved for GI malignancies between January 1, 2010 and September 1, 2020 were recorded. Approval publications and updated survival analysis outcomes were included to assess for demonstrable overall survival (OS) and/or progression free survival (PFS) benefit. **Results:** There were 26 regimens approved by the FDA for GI malignancies between 2010 and 2020. Slightly over half (n=15, 57.7%) of these regimens were approved by the EMA. The median time from FDA to EMA approval was 3 months (mo) +/- 5 mo. Only a small minority of these regimens were funded for patients in the UK (including the Cancer Drugs Fund, 9 regimens, 31%) or Ireland (IRL) (7 regimens, 27%). The median time from EMA approval to patient access was short in both of these countries (3.5 mo (UK) and 0.5 m (IRL)). However, the range in these countries was large (2 - 73 mo (UK) & 0-24 mo (IRL)). More than half of regimens (15, 57.7%) demonstrated an OS benefit. Of the remaining 11 regimens, a further 6 drugs (23%) demonstrated a PFS benefit. The median OS benefit (if present) was 2.3 mo +/- 3 mo. The median price of these regimens in the USA (list price) was $13,758 per month +/- $5,152. Regimens which demonstrated an OS benefit were not more expensive than those that did not (median $13,065 versus $13,758 respectively, $p < 0.05$). For regimens with an OS benefit, there was no statistically significant correlation between the length of OS benefit and drug cost (Pearson's correlation = 0.32, p = 0.07). **Conclusions:** Less than one third of patients in the UK and Ireland have access to medicines approved by the FDA for GI malignancies between 2010 – 2020. Overall survival benefits are often modest, or absent. The cost of regimens in the USA commonly exceeds $100,000/year irrespective of OS benefit. Our work highlights the necessity to develop a value based-pricing system in GI oncology. Research Sponsor: None.

470 Poster Session

Targeting *GNAS* mutant appendiceal adenocarcinoma. *First Author: Valsala Haridas, University of Texas MD Anderson Cancer Center, Houston, TX*

Background: Appendiceal cancers are rare, comprising just 0.5% of all intestinal neoplasia, preventing the systematic study of these tumors in randomized clinical trials. Given this absence of clinical data, no evidence-based guidelines exist regarding the best management of this disease and no drugs have been developed to specifically target appendiceal adenocarcinoma (AA). The G protein *GNAS* is the second most frequently mutated gene after *KRAS* in low-grade (49%) mucinous AA (52%), making it an attractive drug target in this orphan disease. **Methods:** Using CRISPR, *GNAS* was knocked out in KM12, SNU175 and SKCO1 gastric cell lines that harbor $GNAS^{R201C}$ mutation. The mutant and KO pairs of cells were evaluated for their proliferation rate and ability to form colonies in a clonogenic assay. RNA sequencing of the mutant and knock out cells was performed to determine pathways potentially associated with the GNAS signaling pathway. The Sanger GDSC was used to identify drugs selectively lethal to GNAS mutant tumors. **Results:** KM12 cells knocked out for *GNAS* showed a 40% decrease in proliferation compared to the parent cells with mutant *GNAS* ($p < 0.0001$). *GNAS* knockout significantly reduced colony formation of all three mutant cell lines (KM12: 397 vs. 94, SNU175: 512 vs. 134, and SKCO1: 36 vs. 5, p = 0.0022). Analysis of four $GNAS^{R201C}$ cell lines relative to matched controls identified IGF-1R, MEK and PKC as potential vulnerabilities. *In vivo* validation experiments are currently ongoing. **Conclusions:** Our findings suggest preliminarily that $GNAS^{R201C}$ mutant cell lines are oncogene addicted to GNAS growth signal and could be targeted with inhibitor of GNAS or one of its downstream effectors. Research Sponsor: Cancer Prevention Research Institute of Texas.

471 Poster Session

Adjuvant therapy in the treatment of resected nonmetastatic gallbladder cancer of stage II-IV: A generalized propensity score analysis. *First Author: Wenze Wan, Zhongshan Hospital, Fudan University, Shanghai, China*

Background: The benefit of adjuvant therapy for gallbladder cancer (GBC) remains controversial due to the limited evidence. The current study was aimed to explore the efficacy of adjuvant therapy in patients with resected non-metastatic GBC and to establish a prognosis model to predict the survival benefit of GCB patients with different adjuvant therapies. **Methods:** Patients with resected non-metastatic GBC of stage II-IV were selected from the Surveillance, Epidemiology, and End Results database and divided into non-radiotherapy and chemotherapy (NCRT) group, chemotherapy (CT) group, and chemoradiotherapy (CRT) group. Generalized propensity score (GPS) and inverse probability of treatment weighting (IPTW) was used to reduce the imbalances between groups. Nomogram was constructed based on Cox proportional hazard model, and the model was validated for discrimination and calibration. **Results:** Among the 2689 enrolled patients, 1193 (44.4%) patients were classified as stage II, 1371 (51.0%) as stage III, and 125 (4.6%) as stage IV according to the 8th American Joint Commotion Cancer staging manual. Patients in NCRT, CT, and CRT groups were 1703, 444, and 542 respectively. After the IPTW, absolute standardized differences of baseline characteristics were less than 0.1 both in patients with stage II tumors and with stage III-IV tumors. In patients with GBC of stage II, no significant difference in OS was observed between the three treatment groups ($P > 0.05$). In patients with GBC of stage III-IV, CT group has a superior OS compared with the NCRT group ($P < 0.001$), and CRT group has a superior OS compared with the CT($P < 0.001$) and NCRT ($P < 0.001$) group. Sensitivity analysis showed consistent results. A nomogram was constructed for patients with stage III-IV tumors to predict the survival benefit of adjuvant therapies. The C-index was 0.673 (95% CI: 0.654-0.692) in the validation using the training set (diagnosed at 2004-2012) and was 0.707 (95% CI: 0.677-0·739) in the internal validation using the validation set (diagnosed at 2013-2015). The calibration curves indicated that the predicted probability closely corresponded to the actual observation OS. **Conclusions:** Patients with GBC of stage II could not benefit from adjuvant therapy. Patients with GBC of stage III-IV could benefit from chemotherapy and chemoradiotherapy while chemoradiotherapy provide a superior OS. A nomogram was built to predict the survival benefit of different adjuvant therapies in patients with GBC of stage III-IV. Research Sponsor: the National Natural Science Foundation of China (81702586 and 81872352).

472 Poster Session

Beyond *BRCA*? clinical utility of homologous recombination deficiency in gastrointestinal cancers. *First Author: Erica S Tsang, BC Cancer, Vancouver, BC, Canada*

Background: There is emerging evidence about the predictive role of homologous recombination deficiency (HRD) in multiple cancers. The clinical utility of HRD is less well defined in gastrointestinal (GI) malignancies. **Methods:** We reviewed the whole genome (WGS) and transcriptomic (RNA-Seq) data of patients with advanced GI cancers between 2012-2018 in the Personalized Oncogenomics trial (NCT02155621). Scores were calculated as the sum of loss of heterozygosity, telomeric allelic imbalance, and large-scale state transitions scores. HRD was defined as a score ≥34. Mutational analysis was performed to determine the presence of mutational signature 3, which is usually strongly associated with *BRCA* status. Retrospective chart review was conducted to extract treatment and survival outcomes. Overall survival (OS) from initiation of first-line systemic therapy and time to progression on platinum therapy (TTPp) were calculated. Linear and multivariable regression analyses were conducted. **Results:** Of 154 patients with GI primaries, 56% were male and 105 (68%) were exposed to a platinum agent in the metastatic setting. Primary sites included upper GI (N=20, 9%), pancreas (N=35, 16%), colorectal (N=74, 33%), and other GI primary (N=25, 11%). Ten patients (6%) had a *BRCA1/2* mutation, 20 (13%) had a high HRD score, and 11 (7%) had a high signature 3 score (>0.05). Six patients had both high HRD and high signature 3 scores (Table). On linear regression, high HRD scores and mutational signature 3 were independently associated with longer TTPp (β=4.17, 95% CI 0.15-8.19, p=0.04; β=8.03, 95% CI 2.87-13.18, $p<0.05$, respectively). On multivariable linear regression, after adjusting for HRD score, *BRCA1/2* status, and tumor site, only cases with a mutational signature 3 retained significance ($p<0.05$). HRD status was not prognostic for OS (HR 1.02, 95% CI 0.65-1.62, p=0.92). **Conclusions:** Within a cohort of patients with GI malignancies characterized by WGS and RNA-Seq, mutational signature 3 was more strongly associated with TTPp compared to HRD score. These data highlight potential predictive implications of Signature 3 to complement HRD and *BRCA* status in identifying patients who may benefit from exposure to platinum therapy. Research Sponsor: None.

Patients with both high HRD and high Signature 3 scores.

Patient	HRD Score	Signature 3 Score	DNA Repair Mutations
1	52	0.223	*BRCA2, BLM*
2	43	0.0534	*RECQL5, RIF1*
3	40	0.126	*BRCA2*
4	38	0.0722	*BRCA1*
5	36	0.0782	
6	35	0.0827	

473 Poster Session

Patient characteristics and survival outcomes in gastrointestinal cancers harboring *RNF43* mutations or *RSPO3* fusions: a retrospective analysis. *First Author: Paul Sackstein, Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC*

Background: The growth of intestinal epithelium is dependent on the Wnt/β-catenin signaling pathway. The R-Spondin (RSPO) family of proteins form complexes with Wnt ligand and RNF43 protein, which promote ubiquitination and degradation of Wnt receptors. Patients with gastrointestinal cancers harboring *RSPO3* gene fusions or *RNF43* gene mutations may benefit from Wnt pathway inhibitors. **Methods:** We retrospectively studied 51 patients at our institution diagnosed with gastrointestinal cancers with *RSPO3* gene fusions or *RNF43* gene mutations identified using Caris Life Sciences next-generation sequencing (NGS). Microsatellite-instability (MSI) was evaluated using NGS. Tumor mutational burden (TMB) was estimated from 592 genes by counting all nonsynonymous missense mutations not previously defined as germline mutations, expressed as mutations per megabase. First-line median progression-free survival (PFS) and median overall survival (mOS) were estimated using the Kaplan-Meier method. **Results:** Of the 51 patients in our study, 44 (86.3%) had *RNF43* mutations and 7 (13.7%) had *RSPO3* fusions, 6 of whom had colorectal cancer (CRC) and had *PTPRK* as the fusion partner, 1 case of small bowel cancer had a *RSPO3:IFNGR1* fusion. Median age at diagnosis was 64.0 ± 12.0 years. The most common primary tumors were CRC in 23 patients (45.1%) and pancreas in 12 patients (23.5%). Co-occurring mutations in CRC patients with *RSPO3* fusions included *KRAS* (50%, Q61H, G12C, and G12V), *BRAF* V600E (50%), and *TP53* (100%), none were MSI-H, median TMB (mTMB) was 9.5 (range 7-11). Sixty-seven percent of *RNF43*-mutated CRC patients had the G659fs mutation. Co-occurring findings in *RNF43*-mutated CRC patients included 67% MSI-H, median TMB 27 (range 6-123), *KRAS* (28%), *BRAF* V600E (28%), and *TP53* mutations (33%). Twenty-two patients (43.1%) had stage IV disease, 18 (35.3%) had stage III disease and 11 (21.6%) had stage II disease. Thirty *RNF43*-mutated patients (58.8%) underwent definitive surgical resection, with a mean time to recurrence of 22.2 months and mOS of 43.0 months (95% CI, 15.6-70.4). Among *RNF43*-mutated stage IV CRC (mCRC) patients, median PFS was 8.0 months (95% CI, 5.9-10.1). Stratified by stage, mOS was 111.0 months for stage II disease, 72.0 months for stage III disease, and 37.0 months for stage IV disease (95% CI, 14.7-59.3). **Conclusions:** *RNF43* correlates with overall favorable mOS in patients with mCRC. mOS in *RNF43*-mutated mCRC is similar to those of *RAS* and *BRAF* wild-type subgroups as reported in the TRIBE study (Cremolini et al. 2015). Therefore, *RNF43* mutational status appears to be useful in predicting clinical outcomes for patients with stage IV CRC and overlaps significantly with MSI-H. *RSPO3* fusions are rare events and the clinical outcomes of this subset of patients with tumors with *RSPO3* fusions remains largely unknown. Research Sponsor: None.

474 Poster Session

Increased T-cell receptor repertoire diversity to predict better overall survival in gastrointestinal malignancies. *First Author: Daniel W Kim, Massachusetts General Hospital, Boston, MA*

Background: Severe treatment-induced lymphopenia is a poor prognostic factor for multiple solid malignancies. Emerging data suggests that increased TCR repertoire is associated with improved survival. We hypothesized that increased TCR repertoire following severe treatment-induced lymphopenia would be associated with better survival after accounting for known prognostic factors. **Methods:** Patients within a prospective cohort were retrospectively analyzed for severe (grade 4) lymphopenia during radiotherapy (RT) at a single institution between 2007-2016. Peripheral blood samples were collected weekly. TCR repertoire at 3 time points were evaluated: pre-RT, during or immediately post-RT at absolute lymphocyte count (ALC) nadir, and ~2 months post-RT. Peripheral blood was analyzed via multiparametric flow cytometry. TCR beta sequencing was performed on immunoSEQ platform from Adaptive Biotechnologies. A Gini diversity index reflecting TCR repertoire was calculated as well as percentage change between ALC nadir and ALC 2 months post-RT. Primary endpoint was overall survival (OS). Cox modeling and Kaplan Meier estimates were used for survival analyses. **Results:** 109 patients were enrolled. 20 patients were evaluable with complete data. Median follow up was 40 months. Primary malignancy was pancreatic adenocarcinoma in 40%, gastric adenocarcinoma in 30%, and cholangiocarcinoma in 30%. Clinical stage was I-II in 29%, III in 50%, and IV in 21%. 80% underwent chemotherapy (CTX) pre-RT and none received CTX post-RT. 80% had concurrent CTX during RT. Median RT dose was 56 Gy. Among those with pathology available (n = 12), 17% had a pathologic complete response (pCR) and 83% had R0 resection. Median ALC at each of the three study timepoints was 1.26 k/ul, 0.32 k/ul, and 1.02 k/ul, respectively. 4 (20%) patients had increased TCR repertoire as defined by the change in Gini diversity index while 16 (80%) had decreased TCR repertoire post-RT. There were no significant differences in baseline characteristics between the two cohorts. On univariable analysis, increased TCR repertoire from ALC nadir to 2 months post-RT significantly correlated with better OS (HR = 0.20 [95% CI 0.04-0.93]; p = 0.041). Other variables including ECOG, stage, RT dose, CTX use, pCR, R0 resection, baseline WBC, and ALC at three study time points did not correlate with OS. Patients with increased vs decreased TCR repertoire post-RT had a 3-year OS of 75% vs 22%, respectively (log rank p = 0.026). **Conclusions:** Increased TCR repertoire post-RT was an independent prognostic factor for better OS in our cohort of GI malignancies. Our findings provide biologic insight and refine the association between ALC and cancer outcomes. TCR repertoire warrants further study as a predictive and prognostic biomarker in GI malignancies. Therapeutic approaches to limit severe lymphopenia are ongoing and should include TCR assessment. Research Sponsor: None.

475 Poster Session

Role of DNA polymerases family members in cancer: The pan-cancer perspective. *First Author: Zhiwen Luo, Department of Hepatobiliary Surgery, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China*

Background: DNA polymerases family (DNA pols) has a lengthy reported significant influence on the initiation, development, and progress of cancer. However, the pan-cancer value of whole family members was poorly done. Our study intends to demonstrate the expression pattern and clinical cancer value of DNA pols members as prognostic biomarkers and a therapeutic target of pan-cancer. **Methods:** Comprehensive bioinformatics analyses were done using data from TCGA and CCLE. MultiCox regression was done to select tumor prognosis-related members. Nomogram was constructed to predict the overall survival (OS) across cancer patients. Transcription factor, GO, IPA, and GSEA enrichments were done to explore regulatory mechanisms and functions. **Results:** A total of 22 DNA pols were identified to have a potential to diagnostic value, and 10 DNA pols have a pan-cancer prognostic value under various stages, and cancer type, among which overexpression of 6 DNA-pols (POLA2, POLD1, POLD2, POLE2, POLE4, and POLQ) was found to be significantly related to worse outcomes regarding OS, while 4 DNA-pols (POLH, POLL, POLN, and REV1) significantly related to better outcomes. A 5-DNA pols based risk score (POLQ, POLD2, POLL, POLH, and REV1) was generated by MultiCox regression with a nomogram validated an accurate predictive efficacy. MYB Proto-Oncogene Like 2 (MYBL2) was identified as transcription factors of prognostic DNA pols in pan-cancer, and IPA mimic experiment reveals inhibiting MYBL2 could be a drug target to recover and balance the dysregulated expression pattern of DNA pols in pan-cancer. GO, IPA, and GSEA enrichments revealed functions and pathways altered by DNA pols in cancer, and the results were supported by pan-cancer cell sequencing data. **Conclusions:** DNA pols have a pan-cancer clinical value and can work as potential prognostic biomarkers. Furthermore, MYBL2 could be a drug target for pan-cancer. Research Sponsor: None.

476 Poster Session

Body weight loss (BWL) as a prognostic/predictive factor in previously treated patients (pts) with metastatic gastric or gastroesophageal junction cancer (mGC/GEJC): Post-hoc analyses of the phase III tags trial. *First Author: Michele Ghidini, Azienda Ospedaliera di Cremona, Cremona, Italy*

Background: Nutritional status is closely linked to cancer mortality, and BWL has been shown to be prognostic for survival in curative, first-, and second-line settings in mGC/GEJC. In the phase III TAGS trial, trifluridine/tipiracil (FTD/TPI) showed clinical benefit versus placebo (PBO) and manageable safety in pts with mGC/GEJC who had received ≥2 prior chemotherapy regimens. The association of early BWL with survival outcomes in TAGS was examined in retrospective analyses. **Methods:** The TAGS intent-to-treat (ITT) population was categorized into pts who experienced <3% or ≥3% BWL from the start of treatment until day 1 of cycle 2 (each cycle: 28 days). Overall survival (OS), and progression-free survival (PFS) were compared between subgroups within each treatment arm due to significant imbalances of early BWL between treatment arms. The effect of early BWL on OS was assessed by a univariate Cox proportional hazards (PH) model as well as a multivariate Cox PH model that adjusted for baseline prognostic factors identified in the original ITT analysis. **Results:** Body weight data were available for 451 of 507 (89%) pts in the study (n=304, FTD/TPI; n=147, PBO). In the FTD/TPI and PBO arms, respectively, 74% (224/304 pts) and 65% (95/147) experienced <3% BWL, whereas 26% (80/304) and 35% (52/147) experienced ≥3% BWL at the end of cycle 1. Pts with <3% BWL had longer OS than those with ≥3% BWL in both FTD/TPI (median [m] OS: 6.5 vs 4.9 months [mo]; hazard ratio [HR], 0.75; 95% CI, 0.55–1.02) and PBO arms (mOS: 6.0 vs 2.5 mo; HR, 0.32; 95% CI, 0.21–0.49). The PFS HR for pts with <3% BWL vs ≥3% BWL was 0.95 (95% CI, 0.71–1.25; mPFS, 2.1 vs 1.9 mo) in the FTD/TPI group and 0.49 (95% CI, 0.34–0.72; mPFS, 1.9 vs 1.7 mo) in the PBO group. In the pooled ITT population, the unadjusted HR for the <3% vs ≥3% BWL group calculated using a univariate Cox model was 0.58 (95% CI, 0.46–0.73), indicating a strong prognostic effect of early BWL. Results of multivariate analyses were consistent with univariate analyses and suggested that early BWL was both a prognostic (P<0.0001) and predictive (interaction P=0.0003) factor for OS in pts with mGC/GEJC. Grade ≥3 adverse events (AEs) of any cause were reported in 77% and 82% of FTD/TPI-treated pts in the <3% and ≥3% BWL subgroups, respectively, and in 45% and 67% of placebo-treated pts in the <3% and ≥3% BWL subgroups. **Conclusions:** To our knowledge, this is the first analysis to show that BWL is negatively associated with survival in pts with mGC/GEJC receiving third- or later-line treatment. In TAGS, early BWL (≥3% BWL at the end of cycle 1) was a strong negative prognostic factor for OS regardless of FTD/TPI or PBO treatment. Grade ≥3 AE frequencies were similar in FTD/TPI-treated pts with <3% or ≥3% BWL. The relationship of BWL to other prognostic factors will be explored further. Clinical trial information: NCT02500043. Research Sponsor: Taiho Oncology, Inc.

477 Poster Session

Effect of food on exposure to napabucasin: Data from two phase I studies. *First Author: Xiaoshu Dai, Sumitomo Dainippon Pharma Oncology, Inc., Cambridge, MA*

Background: Napabucasin is an orally-administered NAD(P)H quinone dehydrogenase 1–bioactivatable investigational agent hypothesized to affect multiple oncogenic cellular pathways including STAT3. **Methods:** Food effects on napabucasin pharmacokinetics were evaluated in two studies: one at two sites in Japan (Study 1; JapicCTI-205447) and the other at two sites in the US and three in Canada (Study 2; NCT01775423). Study 1 enrolled healthy Japanese male volunteers (HJMV) who received napabucasin 480 mg (formula 2) per sequential design – fasting on Day (D) 1 followed by a Japanese diet (JD) on D8 – with a 6-D intervening washout. In Study 2, patients (pts) with advanced malignancies received napabucasin 500 mg (formula 1) on D1 in the fasted state, then napabucasin 500 mg (formula 2) on D4 and D8 with a high-fat breakfast [HFB] or in the fasted state per the randomized sequence per crossover design. **Results:** In Study 1, mean plasma napabucasin levels 6–10 h after napabucasin 480 mg administration were higher in fed (JD) vs fasted states; in the fed state, C_{max} increased by 15% and AUC_{last} by ~60% (Table), while t_{max} decreased by ~1.4 hours. Adverse events (AEs) in Study 1 occurred in 5/6 (83.3%) HJMVs (fasted, n=3; fed, n=5; all grade [gr] 1). In Study 2, mean concentration profiles were comparable in fasted and fed (HFB) states for napabucasin 500 mg. When comparing fasted and fed states, C_{max} increased by 21% and AUC_{last} by 39% in the fed state (Table). Interpatient variability was high: geometric CV% for CL/F was 75.9% (fed) and 141% (fasted). AEs in Study 2 occurred in 68% (17/25) of fasted pts (gr 1: n=7; gr 2: n=8; gr 3, n=2) and 50% (7/14) of pts fed an HFB (gr 1: n=2; gr 2: n=3; gr 3, n=2). **Conclusions:** In HJMVs, napabucasin 480 mg administered with a JD increased exposure (C_{max}; AUC_{last}; AUC_{inf}) and decreased t_{max} vs the fasted state. In pts with advanced malignancies, napabucasin 500 mg administered with an HFB increased exposure (C_{max}; AUC_{last}) vs the fasted state. These exposure increases are not considered to be of clinical relevance. Clinical trial information: JapicCTI-205447; NCT01775423. Research Sponsor: These studies were funded by Sumitomo Dainippon Pharma Oncology, Inc.

	C_{max}, ng/mL		AUC_{last}, h*ng/mL		AUC_{inf}, h*ng/mL		CL/F, L/h	
	Fasted	Fed	Fasted	Fed	Fasted	Fed	Fasted	Fed
Study 1 (Japan) (N=6)								
Geometric LS mean	396.7	455.7	2244.4	3668.2	2358.3	3762.9		
Fed/fasted, % [90% CI]	114.9 [94.52, 139.60]		163.4 [112.81, 236.77]		159.6 [110.56, 230.30]			
Study 2 (US), n	16	14	16	14	11	9[a]	11	9
Geometric mean	857	1070	5830	8570	7030	13900	71.2	36.0
Geometric CV %	109	92.9	114	130	141	75.9	141	75.9
Fed/fasted, % [90% CI]	121.46 [101.52, 145.32]		138.77 [108.49, 177.50]		187.33 [114.25, 307.13]			

[a]Due to small sample size (n=9), statistical comparisons should be interpreted with caution.

AUC_{inf}, area under the curve from 0-infinity; AUC_{last}, AUC from 0-last measured concentration; CI, confidence interval; CL/F, apparent total clearance; C_{max}, maximum concentration; CV, coefficient of variation; LS, least squares.

478 Poster Session

Education on reactive oxygen species to lay the foundation for understanding therapeutic advances in anticancer therapy. *First Author: Kinjal Parikh, Medscape Oncology, New York, NY*

Background: The disruption of redox balance is increasingly thought to be one of the most important underlying factors contributing to the development, progression, and metastasis of cancers in human cells. This imbalance in redox homeostasis has been shown to be induced by the generation of free radicals, predominantly reactive oxygen species (ROS). Emerging data have established ROS as a new potential therapeutic target. Understanding the mechanisms associated with tumorigenesis is important to integrate novel potential therapeutic targets and understand which tumors or patient populations may benefit from ongoing research. Shortcomings in oncologists' knowledge and confidence can hamper the integration of new treatments into the care of patients with cancer. **Methods:** An online continuing education (CME) activity consisted of a multi-media 30-minute video panel of two panelists discussing the mechanism, pathophysiology, and the premises for novel anti-cancer therapies. Educational effect was assessed using a repeated paired pre-/post-assessment study design. A McNemar's test was used to identify differences between pre- and post-assessment responses. Effect size was calculated using Cohen's d test by determining the strength of the association between the activity and the outcomes (d < .20 is modest and d ≥ .80 is large). P values were calculated and those < .05 were considered statistically significant. The activity launched 5/14/2020 and data are represented through 8/6/2020. **Results:** A total of 1,033 learners, of which there are 656 physicians, participated in the activity. Participating in education resulted in statistically significant improvements and noticeable educational effect and data for oncologists that answered all pre- and post-assessment questions are represented below (n = 45, p < .001, Cohen's d = .454). Percentages represent relative rates of improvement The role of ROS on cancer cell proliferation, cancer cell toxicity, and the tumor microenvironment (67%, p < .05) The interplay of antioxidants to aid in the development of therapies to induce DNA-damaged cell death (100%; p < .001) The potential biomarkers to aid in the development of therapies to induce DNA-damaged cell death (34%; p < .05). **Conclusions:** This online, interactive, expert-led, CME-certified educational activity resulted in significant gains in oncologist knowledge and confidence regarding the ROS pathway and associated clinical pipeline developments Upon completion of the initiative, only 11% of oncologists were able to answer all 3 matched pre/post questions correctly, signifying the need for further education The novelty of the information to many learners demonstrate the need to continue highlighting clinical advances and molecular pathways that may have potential implications in cancer therapy progress. Research Sponsor: Boston Biomedical, Inc.

479 Poster Session

The impact of immunotherapy education on GI cancers. *First Author: Kinjal Parikh, Medscape Oncology, New York, NY*

Background: Gastrointestinal (GI) cancers are a heterogeneous group of cancers with varying underlying pathophysiology and distinct treatment paradigms. Immunotherapy (IO) is unique in each of the subtypes and biomarkers utility varies. With the expansion of IO in each cancer subtypes, education remains essential to optimize patient outcomes through integration of the latest evidence-based data at point of care. Through the partnership between Medscape Oncology and the Society for Immunotherapy of Cancer, 2 educational activities were designed to increase the knowledge and competence of oncologists surrounding the role of IO in patients with advanced GI cancers. **Methods:** The 2 educational activities included a text based online activity with 3 chapters focused on gastroesophageal cancers, colorectal cancers, and hepatocellular carcinoma (HCC) and a 30-minute online, video discussion with 3 faculty and synchronized slides on HCC. Educational effectiveness was assessed with repeated paired pre/post assessment where learners served as their own controls. A chi-square test was used to identify statistical significance in proportion of correct responses. The first activity launched 11/27/2019 and the second activity launched on 5/8/20. Data were collected and reported through 8/25/2020. **Results:** A total of 8433 learners, including 1543 oncologists, participated from 11/2019 through 8/2020. Participation in education resulted in significant relative improvements among oncologist learners on IO in GI cancers in (n = 641): 110%: role or eligibility of immune checkpoint inhibitors (ICIs) (p < .001) 38%: clinical trial data of ICIs (p < .001) Subsequent education on unresectable HCC demonstrated a significant relative improvement in both knowledge and competence for oncologist learners (n = 902): 19%: regarding clinical trial data in unresectable HCC (p = .073) 19%; competence identifying role of ICIs in unresectable HCC (p < .05) 59%: competence managing irAEs in unresectable HCC (p < .001). **Conclusions:** These 2 online CME-certified educational activities resulted in statistically significant gains in oncologist knowledge surrounding the use of IO in advanced GI cancers Follow-up education on HCC demonstrated the value and benefit of multi-modal and sequential activities on improving competence among oncologists caring for patients with unresectable HCC There remains a need for continuous education as more oncologists utilize IO in their practice while the understanding and availability of clinical data continues to expand and evolve in the varying GI cancer subtypes. More than 50% of learners continued to demonstrate a need in understanding the clinical trial data or role of IO in metastatic GI cancers with more than 40% of the learners demonstrating continued need on clinical trial data or role of IO in HCC specifically. Research Sponsor: Bristol Myers Squibb Company and Merck & Co, Inc.

TPS480 Trials in Progress Poster Session

A phase II open-label study in adult and adolescent patients (pts) with advanced solid tumors harboring fibroblast growth factor receptor (*FGFR*) gene alterations. *First Author: Shubham Pant, The University of Texas MD Anderson Cancer Center, Houston, TX*

Background: The pan-*FGFR* tyrosine kinase inhibitor erdafitinib is approved by the US Food and Drug Administration for adults with locally advanced or metastatic urothelial carcinoma and susceptible *FGFR3/2* genetic alterations who have progressed during or after ≥ 1 line of prior platinum-containing chemotherapy. *FGFR* gene alterations are potential oncogenic drivers that have been reported in many solid tumors in adult and pediatric pts. Because of limited response to standard of care options in pts failing systemic therapy, there is strong rationale to assess the safety and efficacy of erdafitinib in adolescent and adult pts with advanced solid tumors and *FGFR* alterations. **Methods:** This phase 2, open-label study (RAGNAR/42756493CAN2002; NCT04083976) will include pts aged ≥ 12 years with histologically confirmed unresectable, locally advanced, or metastatic solid tumors (except urothelial tumors) harboring predefined *FGFR* mutations or fusions. Eligibility screening includes molecular screening for *FGFR* alterations by central or local next-generation sequencing assays, and other clinical criteria. Pts will enroll into either a broad panel cohort (BPC) of target *FGFR* alterations or an exploratory cohort (EC) for *FGFR* alterations that do not meet criteria for BPC. Approximately 280 pts (BPC, n = 240; EC, n = 40) will be enrolled. The primary efficacy end point is overall response rate (ORR) as assessed by the independent review committee. Secondary end points include investigator-assessed ORR, duration of response, disease control rate, progression-free survival, overall survival, safety, pharmacokinetics, and health-related quality of life. Safety assessments include adverse events, vital signs, electrocardiograms, physical examinations, laboratory tests, performance status assessment, growth assessments in adolescents, and ophthalmologic examination. As of December 2019, pts are being enrolled at ~158 sites in 15 countries. Results of this study will provide efficacy and safety data for erdafitinib across multiple solid tumors with *FGFR* alterations and evaluate the potential benefit of targeting the underlying altered biology of *FGFR* irrespective of tumor histology in adult and adolescent pts. Clinical trial information: NCT04083976. Research Sponsor: Janssen Research & Development, LLC.

TPS481 Trials in Progress Poster Session

A translational study to evaluate genomic markers and concordance with circulating-tumor DNA and circulating tumor cells to predict clinical outcomes in gastrointestinal and pancreatobiliary cancers: Valor trial. *First Author: Ayako Doi, Department of Clinical Oncology, St. Marianna University School of Medicine, Kawasaki, Japan*

Background: Circulating tumor cells (CTCs) are cells that have shed into the vasculature or lymphatics from a primary tumor and are carried around the body in the blood circulation. The CTCs constitute seeds for the subsequent growth of additional tumors (metastases) in distant organs, a mechanism that is responsible for the vast majority of cancer-related deaths. Circulating-tumor DNA (ctDNA) includes DNA which derives from tumor necrosis or apoptosis; therefore, CTCs may potentially represent more precise tumor status compared to ctDNA. There have been few reports to assess the genomic concordance between ctDNA and CTCs in cancer patients. In addition, genomic analysis of ctDNA would find novel mechanism of resistance to anti-EGFR monoclonal antibody (mAb) in metastatic colorectal cancer (mCRC). *RAS* mutations in ctDNA are considered to be one of mechanism of resistance to anti-EGFR mAb in *RAS* wild-type mCRC. However, there is no data regarding CTCs when mCRC patients acquires resistance to anti-EGFR mAb. **Methods:** This translational study prospectively recruits patients with advanced/metastatic gastrointestinal and pancreatobiliary cancers (esophageal, gastric, pancreatic, biliary tract and colorectal cancers) who receive systemic chemotherapy in first- or second-line and mCRC with *RAS* wild-type tumors treated with anti-EGFR mAb in any lines, at St. Marianna University School of Medicine Hospital. We accumulate the clinical data regarding patients' characteristics, treatment, and survival time. The primary objective is to evaluate genomic markers and concordance with ctDNA and CTCs in patients with advanced/metastatic gastrointestinal and pancreatobiliary cancers. Then, this study approaches to assess which biomarkers can predict clinical outcome more accurately. Secondary objectives include evaluating association between genomic status in ctDNA and clinical outcomes; association between genomic status in CTCs and clinical outcomes; comparing genomic change between ctDNA and CTCs in *RAS* wild-type mCRC patients treated with anti-EGFR mAb. Blood draw of total 10mL is performed for analyses of ctDNA and CTCs at 3 time points, pre-treatment of chemotherapy, 4 weeks after treatment start, and disease progression. Blood of 5mL is processed with CTCs enrichment using the CD-PRIME system (Clinomics Inc.) and remaining 5mL is used for the plasma preparation. Genomic alterations are measured using the customized cancer panel which allows the detection of mutations in 51 actionable genes. This study will enroll 70 patients with willing to undergo blood draws. Accrual is starting in May 2019. Clinical trial information: UMIN000036681. Research Sponsor: None.

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