4500 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Trastuzumab with trimodality treatment for esophageal adenocarcinoma with HER2 overexpression: NRG Oncology/RTOG 1010.

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Background: Trastuzumab is a monoclonal antibody against human epidermal growth factor receptor 2 (HER2). The primary objective of RTOG 1010 was to determine if trastuzumab increases disease-free survival (DFS) when combined with trimodality treatment for patients with HER2 overexpressing esophageal adenocarcinoma. **Methods:** This open label, randomized phase III trial included patients with newly diagnosed stage T1N1-2, T2-3N0-2 adenocarcinoma of the esophagus involving the mid, distal, or esophagogastric junction and up to 5cm of the stomach. All patients received chemotherapy (C) of paclitaxel, 50mg/m^2 and carboplatin AUC = 2, weekly for 6 weeks, with radiation (XRT: 3D-CRT or IMRT, 50.4 Gy in 28 fractions) followed by surgery. Patients were randomized 1:1 to receive weekly trastuzumab 4mg/kg week 1 then 2mg/kg/weekly x 5 during CXRT then 6 mg/kg for 1 dose prior to surgery and 6mg/kg every 3 weeks for 13 treatments after surgery. HER2 status was determined by IHC and gene amplification by FISH. With a 2-sided alpha of 0.05, 162 DFS events provide 90% power to detect a signal for an increase in median DFS from 15 to 25 months. DFS and overall survival (OS) were estimated by the Kaplan-Meier method. and arms were compared using the log rank test. The Cox proportional hazards model was used to analyze treatment effect. **Results:** 571 patients were entered for assessment of HER2 expression, 203 HER2+ patients randomized. The median follow-up for alive patients is 5.0 years. The estimated 2, 3, and 4-year DFS (95% CI) for the CXRT +trastuzumab arm were 41.8% (31.8%, 51.7%), 34.3% (24.7%, 43.9%), and 33.1% (23.6%, 42.7%), respectively, and for the CXRT arm were 40.0% (30.0%, 49.9%), 33.4% (23.8%, 43.0%), and 30.1% (20.7%, 39.4%), respectively; log-rank p = 0.85. The median DFS time is 19.6 months (13.5-26.2) for the CXRT +trastuzumab arm compared to 14.2 months (10.5-23.0) for the CXRT arm. The hazard ratio (95% CI) comparing the DFS of CXRT+trastuzumab arm to the CXRT arm was 0.97 (0.69, 1.36). The median OS time was 38.5 months (26.2-70.4) for the CXRT+trastuzumab arm compared to 38.9 months (29.0-64.5) for the CXRT arm, hazard ratio (95% CI): 1.01 (0.69, 1.47). There was no statistically significant increase in treatment-related toxicities with the addition of trastuzumab including no increase in cardiac events. **Conclusions:** The addition of trastuzumab to trimodality treatment did not improve DFS for patients with HER2 overexpressing esophageal adenocarcinoma. Supported by NCI grants U10CA180868, UG1CA189867, U10CA180822 and Genentech. Clinical trial information: NCT01196390. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

4501 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Perioperative ramucirumab in combination with FLOT versus FLOT alone for resectable esophagogastric adenocarcinoma (RAMSES/FLOT7): Results of the phase II-portion—A multicenter, randomized phase II/III trial of the German AIO and Italian GOIM.

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Background: Periop. FLOT has become SOC for resectable, esophagogastric adenocarcinoma. However, patient's outcome is still poor. This trial evaluates the addition of the VEGF-R2 inhibitor ramucirumab (RAM) to FLOT for resectable patients (pts). **Methods:** This is a prospective, international, randomized, investigator-initiated phase II/III trial. Pts with resectable, Her2-negative, adenocarcinoma of the stomach and GEJ ($\geq$ cT2 or cN+) were enrolled. Pts were randomized to 4 pre-and post-operative cycles of FLOT (docetaxel 50 mg/m^2; oxaliplatin 85 mg/m^2; leucovorin 200 mg/m^2; 5-FU 2600 mg/m^2, q2w) alone (Arm A) or the same regimen with RAM 8mg/kg q2w, followed by 16 cycles RAM (Arm B, FLOT-RAM). Important endpoints of phase II (exploratory) were major pathological (complete and nearly complete) response, centrally assessed acc. to Becker criteria, R0-resection rate, and safety. GEJ type I tumors and pts requiring trans-thoracic esophagectomy were excluded for safety reasons during the conduct of the study. **Results:** In total, 180 pts were randomized. Baseline characteristics were similar between arms (male, 73%; median age, 60y; cT3/T4, 83%; cN+, 78%; GEJ, 54%; signet-ring cells, 40%). However, the FLOT-RAM arm included more unfavorable pts with T4 (9% vs. 4%), Siewert type I tumors (18% vs. 13%), impaired ECOG PS of 1 (34% vs. 20%), and concomitant disease (87% vs. 79%). 91% of pts with FLOT and 92% with FLOT-RAM completed the 4 pre- cycles. R0-resection (in the full set) could be achieved in 83% of pts with FLOT and 97% of pts with FLOT-RAM ($p = 0.0049$). The rate of major path response was similar in both arms and was 30% for FLOT and 27% for FLOT-RAM. Surgical morbidity was observed in 37% of pts with FLOT and 44% of pts with FLOT-RAM. Mortality was 2.5% with FLOT and 5.9% with FLOT-RAM including GEJ type I tumors and dropped to 2.9% in both arms after excluding type I tumors per amendment. There was bit more G$\geq$3 adverse events with FLOT-RAM (78% vs. 89%). **Conclusions:** In this phase II trial, the addition of ramucirumab to perioperative FLOT significantly improved R0-resection rates without an impact on path response, mainly because more patients could proceed to operation. The FLOT-RAM is safe, when type I tumors are excluded. Clinical trial information: NCT02661971. Research Sponsor: Lilly Deutschland GmbH.

Perioperative trastuzumab and pertuzumab in combination with FLOT versus FLOT alone for HER2-positive resectable esophagogastric adenocarcinoma: Final results of the PETRARCA multicenter randomized phase II trial of the AIO.

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Background: Perioperative FLOT is a standard of care for resectable, esophagogastric adenocarcinoma (EGA). This trial evaluates the addition of trastuzumab (tras) and pertuzumab (per) to FLOT for HER2-positive resectable patients (pts). **Methods:** PETRARCA is a prospective, multicenter, randomized, investigator initiated trial planned as a phase II/III investigation. We report the phase II part of this trial. Pts with HER2+ resectable EGA (≥ cT2 or cN+) were enrolled. Pts were randomized 1:1 to 4 pre- and post-operative cycles of FLOT (Docetaxel 50 mg/m²; Oxaliplatin 85 mg/m²; Leucovorin 200 mg/m²; 5-FU 2600 mg/m², q2w) (Arm A) or the same regimen with tras 8/6 mg/kg and per 840 mg q3w, followed by 9 cycles tras/per (arm B). Primary endpoint for the phase II part was the rate of pathological complete remission (pCR). Main secondary endpoints were DFS, OS and safety. **Results:** The trial closed prematurely and did not proceed to phase III. In total, 81 pts were randomized (A, 41; B, 40). Baseline characteristics were balanced (overall, male 79%; median age 60; cT3/T4 86%; cN+ 85%; GEJ 75%). 93% in arm A and 90% in arm B completed pre-OP treatment as planned. More pts had at least one dose modification in arm B (A, 44%; B, 70%). The pCR rate was significantly improved with tras/per (A, 12%; B, 35%; p = 0.02). Likewise, the rate of pathological lymph node negativity was higher with tras/per (A, 39%; B, 68%). R0-resection rate (A, 90%; B, 93%) and surgical morbidity (A: 43%; B, 44%) were comparable. Moreover, in-house mortality was equal in both arms (overall 2.5%). Median DFS was 26 months in arm A and not yet reached in arm B (HR 0.58, p = 0.14). After a median follow-up of 22 months median OS was not yet reached. DFS and OS rates [with 95% CI] at 24 months were 54% [38-71%] and 77% [63-90%] in arm A and 70% [55-85%] and 84% [72-96%] in arm B, respectively. In terms of toxicity more ≥ grade 3 adverse events were reported with tras/per (75% vs. 85%), especially diarrhea (5% vs. 41%) and leukopenia (13% vs 23%). **Conclusions:** The addition of tras/per to perioperative FLOT significantly improved pCR and nodal negativity rates in pts with Her2+ resectable esophagogastric adenocarcinoma at the price of higher rates of diarrhea and leukopenia. Clinical trial information: NCT02581462. Research Sponsor: Roche.

4503 Oral Abstract Session, Fri, 8:00 AM-11:00 AM

Pembrolizumab versus paclitaxel for previously treated patients with PD-L1–positive advanced gastric or gastroesophageal junction cancer (GC): Update from the phase III KEYNOTE-061 trial.

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Background: KEYNOTE-061 (NCT02370498) is a global phase 3 study of pembrolizumab vs paclitaxel as second-line therapy for GC. At the time of primary analysis (data cutoff: Oct 26, 2017), in patients with PD-L1–positive status (combined positive score [CPS] ≥1), pembrolizumab did not significantly prolong overall survival (OS) vs paclitaxel (9.1 months vs 8.3 months) but did elicit a longer duration of response (DOR) and a favorable safety profile vs paclitaxel. We present results of KEYNOTE-061 in patients with CPS ≥1, ≥5, and ≥10 after 2 additional years of follow-up (cutoff: Oct 7, 2019). **Methods:** Adult patients with GC that progressed after platinum + fluoropyrimidine chemotherapy were randomly assigned 1:1 to pembrolizumab 200 mg Q3W for up to 35 cycles (~2 y) or standard-dose paclitaxel. OS and progression-free survival (PFS) in the CPS ≥1 population were the primary end points. Comparisons were made using stratified log-rank tests. **Results:** At the time of this analysis, 366/395 patients with CPS ≥1 had died (92.6%). Pembrolizumab prolonged OS vs paclitaxel in PD-L1–positive patients (Table). No significant differences appeared between groups in PFS (Table). Objective response rate (ORR) was higher for pembrolizumab in the CPS ≥10 group, and DOR was longer with pembrolizumab using all CPS cutoffs (Table). There were fewer drug-related adverse events (AEs) with pembrolizumab than paclitaxel in the overall population (53% vs 84%). **Conclusions:** This long-term analysis found that second-line pembrolizumab prolonged OS among patients with PD-L1–positive GC and led to fewer drug-related AEs vs paclitaxel. Clinical trial information: NCT02370498. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Efficacy Outcomes.

	Pembrolizumab CPS ≥1 n = 196	Paclitaxel CPS ≥1 n = 199	Pembrolizumab CPS ≥5 n = 95	Paclitaxel CPS ≥5 n = 91	Pembrolizumab CPS ≥10 n = 53	Paclitaxel CPS ≥10 n = 55
OS, deaths, n (%)	176 (89.8)	190 (95.5)	84 (88.4)	86 (94.5)	44 (83.0)	51 (92.7)
OS, months, median (95% CI)	9.1 (6.2-10.7)	8.3 (7.6-9.0)	10.4 (6.7-15.5)	8.3 (6.8-9.4)	10.4 (5.9-18.3)	8.0 (5.1-9.9)
HR (95% CI)	0.81 (0.66-1.00)	—	0.72 (0.53-0.99)	—	0.69 (0.46-1.05)	—
P	0.03	—	0.02	—	0.04	—
PFS, months, median (95% CI)	1.5 (1.4-2.0)	4.1 (3.2-4.3)	1.6 (1.4-2.8)	4.0 (2.8-4.4)	2.7 (1.4-4.3)	4.0 (2.7-4.4)
HR (95% CI)	1.25 (1.02-1.54)	—	0.98 (0.71-1.34)	—	0.79 (0.51-1.21)	—
ORR, % (n)	16.3 (32)	13.6 (27)	20.0 (19)	14.3 (13)	24.5 (13)	9.1 (5)
DOR, months, (range)	19.1 (1.4+ to 47.1+)	5.2 (1.3+ to 16.8)	32.7 (4.1 to 47.1+)	4.8 (1.3+ to 15.3)	NR (4.1 to 47.1+)	6.9 (2.6 to 6.9)

SWOG S1505: Results of perioperative chemotherapy (peri-op CTx) with mfolfirinox versus gemcitabine/nab-paclitaxel (Gem/nabP) for resectable pancreatic ductal adenocarcinoma (PDA).

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Background: Clinical outcomes after curative treatment of resectable PDA remain suboptimal. To assess the potential of early control of systemic disease with multiagent peri-op CTx, we conducted a prospective trial in the National Clinical Trials Network. **Methods:** S1505 was a randomized phase II trial of peri-op CTx (12 weeks pre-, 12 weeks post-op) with either mFOLFIRINOX (Arm 1) or Gem/nabP (Arm 2). Eligibility required confirmed tissue diagnosis of PDA, ECOG PS 0 or 1, and resectable disease per Intergroup criteria. Primary outcome was 2-year overall survival (OS), using a "pick the winner" design; for 100 eligible patients (pts), accrual up to 150 pts was planned to account for cases deemed ineligible at central radiology review. We previously presented data on eligibility (ASCO 2019 abstr 4137). Here we present the final efficacy and toxicity results for the eligible pts. **Results:** From 2015 to 2018, 147 pts were enrolled; there were 102 eligible pts; 55 in Arm 1; 47 in Arm 2. For Arms 1 and 2 respectively: median age, 66 (44-76) and 64 (46-76) years; males, 36 (65%) and 24 (51%); and ECOG PS 0, 34 (62%) and 31 (66%) pts. Treatment details are shown in Table. For Arm 1 and Arm 2, respectively: Two-year OS was 41.6% and 48.8%; median OS was 22.4 months and 23.6 months. Neither arm's 2-year OS estimate was statistically significantly higher than the *a priori* threshold of 40% (p=0.42 in Arm 1 and p=0.12 in Arm 2). Median disease-free survival (DFS) after resection was 10.9 months in Arm 1 and 14.2 months in Arm 2 (p=0.87). **Conclusions:** We have demonstrated: 1) two-year OS of 41.6% (median 22.4 months) with mFOLFIRINOX and 48.8% (median 23.6 months) with Gem/nabP for all eligible pts starting treatment for resectable PDA; 2) post-resection DFS of 10.9 months and 14.2 months, respectively; 3) adequate safety and high resectability rates with peri-op CTx; 4) little evidence that either regimen improves OS compared with the historical standard. Clinical trial information: NCT02562716. Research Sponsor: U.S. National Institutes of Health.

Outcomes by Treatment Arm for Eligible Patients (N=102).

	Arm 1 (mFOLFIRINOX; N=55)	Arm 2 (Gem/nabP; N=47)
Started pre-op CTx	53 (96%)	45 (96%)
Completed pre-op CTx	46 (84%)	40 (85%)
Surgical resection	40 (73%)	33 (70%)
Complete or major pathologic response*	10 (25%)	14 (42%)
Started post-op CTx	33 (60%)	28 (60%)
Completed all treatment	27 (49%)	19 (40%)
Diarrhea^	15%	7%
Neutropenia^	19%	38%
Peripheral neuropathy^	9%	7%

*Denominator is those who underwent resection (40 and 33 for Arm 1 and 2, resepectively). ^Only grade 3 or higher

4505 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

ESPAC-5F: Four-arm, prospective, multicenter, international randomized phase II trial of immediate surgery compared with neoadjuvant gemcitabine plus capecitabine (GEMCAP) or FOLFIRINOX or chemoradiotherapy (CRT) in patients with borderline resectable pancreatic cancer.

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Background: Patients with borderline resectable pancreatic cancer have poor survival and low resection rates. Neoadjuvant therapy may improve the outcome for these patients. The aim of this trial was to determine the feasibility and efficacy of a comparison of immediate surgery versus neoadjuvant GEMCAP or FOLFIRINOX or CRT. **Methods:** Eligible patients with NCCN defined borderline resectable (following central review of the baseline CT scan) and biopsy proven pancreatic cancer were randomised (stratified by centre) to receive immediate surgery, or neoadjuvant therapy of either 2 cycles of GEMCAP, or 4 cycles of FOLFIRINOX or 50.4Gy capecitabine-based CRT in 28 daily fractions over 5 $^{1}/_{2}$ weeks. Patients were restaged at 4-6 weeks and underwent surgical exploration if still borderline resectable. Resected patients received adjuvant therapy. Follow up was 12 months. There was quality assurance of surgery and CRT. Primary endpoints were recruitment rate and resection rate (R1/R0). Secondary endpoints included overall survival and toxicity. A target of 90 patients was set to determine feasibility and resection rates. Rates will be presented as point estimates and survival compared across treatment arms using a log-rank test. Analyses will be on an ITT basis. **Results:** Between August 2014 and December 2018, 90 patients were randomised with 88 included in the full analysis set (32 immediate surgery, 20 GEMCAP, 20 FOLFIRINOX, 16 CRT). Median age was 63 years, 44% were men. WHO performance status was 0 and 1 in 45% and 55% respectively. Median CA19-9 was 603 kU/L at baseline. 44 (79%) patients completed neoadjuvant therapy. Recruitment rate was 21 patients per year. Resection rate was 62% for immediate surgery and 55% for neoadjuvant therapy (p=0.668). R0 resection rate on resected patients was 15% and 23% respectively (p=0.721). One year survival rate was 40% [95% CI, 26% – 62%] for immediate surgery and 77% [95%CI, 66% - 89%] for neoadjuvant therapy. Log-rank analysis showed an HR=0.27 [95% CI, 0.13 – 0.55]; $\chi 2$ (1) = 14.91, P<0.001. 9 out of the 51 neoadjuvant patients included in the safety set reported 12 serious adverse events of grade 3 or above. **Conclusions:** There was no difference in resection rate between arms, however neoadjuvant therapy had a significant survival benefit compared with immediate surgery. Clinical trial information: 89500674. Research Sponsor: Cancer Research UK.

Donafenib versus sorafenib as first-line therapy in advanced hepatocellular carcinoma: An open-label, randomized, multicenter phase II/III trial.

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Background: Sorafenib is still the standard first-line therapy for advanced hepatocellular carcinoma (HCC). Donafenib, a novel multikinase inhibitor, showed potential benefits in a previous phase Ib study in HCC. **Methods:** In this open-label, randomized phase II/III trial (ZGDH3), patients with unresectable or metastatic HCC, a Child-Pugh liver function score ≤ 7, and no prior systemic therapy were enrolled from 37 sites across China and randomized (1:1) to receive oral donafenib (0.2 g) or sorafenib (0.4 g) twice daily until intolerable toxicity or disease progression. The primary endpoint was overall survival (OS). Efficacy analysis was primarily based on the full analysis set (FAS). **Results:** Between March 2016 and April 2018, 668 patients were randomized (donafenib, 334; sorafenib, 334) and included in the intention-to-treat (ITT) set, of whom 659 were analysed by FAS (328 *vs* 331). Donafenib was associated with a significantly longer median OS than sorafenib in both FAS (12.1 months *vs* 10.3 months, hazard ratio 0.831, 95% confidence interval 0.699–0.988, $p = 0.0363$) and ITT (12.0 months *vs* 10.1 months, 0.839, 0.706–0.996, $p = 0.0446$). There were no significant differences in median progression-free survival (3.7 months *vs* 3.6 months, $p = 0.2824$), objective response rate (4.6% *vs* 2.7%, $p = 0.2448$), and disease control rate (30.8% *vs* 28.7%, $p = 0.5532$). Grade 3 or worse adverse events (AEs) occurred in 191 (57.4%) and 224 (67.5%) patients ($p = 0.0082$), respectively, and AEs of special interest and those leading to treatment interruption occurred in 287 (86.2%) *vs* 309 (93.1%, $p = 0.0049$) and 101 (30.3%) *vs* 141 (42.5%, $p = 0.0013$). A numerically lower number of patients reported serious AEs (55 [16.5%] *vs* 67 [20.2%], $p = 0.2307$) with donafenib. Common AEs with donafenib included hand-foot skin reaction (50.5%), aspartate aminotransferase increased (40.5%), blood bilirubin increased (39.0%), platelet count decreased (37.8%), and diarrhea (36.6%). **Conclusions:** Donafenib significantly improves OS over sorafenib with favourable safety and tolerability. Donafenib is a promising superior first-line therapy for advanced HCC. Funding: Zelgen. Clinical trial information: NCT02645981. Research Sponsor: Zelgen.

4507 **Oral Abstract Session, Fri, 8:00 AM-11:00 AM**

Apatinib as second-line therapy in Chinese patients with advanced hepatocellular carcinoma: A randomized, placebo-controlled, double-blind, phase III study.

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Background: Chinese patients (pts) account for more than 50% of hepatocellular carcinoma (HCC) cases in the world and have special features in etiology, biological behavior, treatment strategy and prognosis. The aim of this study was to evaluate the efficacy and safety of apatinib, an inhibitor targeting vascular endothelial growth factor receptor-2, in Chinese pts with pretreated advanced HCC. **Methods:** In this randomized, placebo-controlled, double-blind, phase 3 trial done in 31 sites in China, pts with HCC who had received at least one line of systemic therapy (including sorafenib and oxaliplatin-based chemotherapy, which is another first-line standard-of-care in China) and had Child-Pugh liver function class A or B $\leq$7 points were enrolled. The pts were randomly assigned (2:1) to receive 750 mg apatinib orally once daily or placebo and stratified by ECOG performance status (0 or 1), previous sorafenib treatment (yes or no), and extrahepatic spread and/or macrovascular invasion (yes or no) in 28-day treatment cycles. The primary endpoint was overall survival (OS). **Results:** Between Apr 01, 2014 and May 03, 2017, 393 pts were randomized and received at least one dose of study treatment (261 in apatinib arm and 132 in placebo arm). The median OS was significantly longer with apatinib than that with placebo (8.7 months [95% CI 7.5-9.8] *vs* 6.8 months [95% CI 5.7-9.1]; hazard ratio 0.785 [95% CI 0.617-0.998]; p=0.0476). Pts in the apatinib arm also had prolonged median progression free survival (PFS) compared with those in the placebo arm (4.5 months [95% CI 3.9-4.7] *vs* 1.9 months [95% CI 1.9-2.0]; hazard ratio 0.471 [95% CI 0.369-0.601]; p$<$0.0001). The objective response rate was 10.7% (95% CI 7.2-15.1) with apatinib versus 1.5% (95% CI 0.2-5.4) with placebo. Treatment-related adverse events (TRAEs) were reported in 250 (97.3%) pts in the apatinib arm and 92 (70.8%) pts in the placebo arm. The most common TRAEs of grade 3 and 4 were hypertension (71 [27.6%] pts in the apatinib arm *vs* 3 [2.3%] pts in the placebo arm), hand-foot syndrome (46 [17.9%] *vs* 0), decreased platelet count (34 [13.2%] *vs* 1 [0.8%]), and decreased neutrophil count (27 [10.5%] *vs* 0). 24 (9.3%) pts with apatinib and 13 (10.0%) pts with placebo died due to adverse events, and none were deemed treatment-related by investigators. **Conclusions:** Apatinib significantly prolonged OS and PFS in Chinese pts with pretreated advanced HCC, and was well tolerated with a manageable safety profile. Clinical trial information: NCT02329860. Research Sponsor: Jiangsu Hengrui Medicine Co., Ltd.

Efficacy, tolerability, and biologic activity of a novel regimen of tremelimumab (T) in combination with durvalumab (D) for patients (pts) with advanced hepatocellular carcinoma (aHCC).

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Background: The combination of dual immune checkpoint inhibitors (ICI) T (anti–CTLA-4) and D (anti–PD-L1) showed tolerability with a promising objective response rate (ORR) in the initial cohort of this study (NCT02519348). Subsequent evaluation of pts with solid tumors treated with increasing doses of T suggested priming with a higher dose of T may induce a stronger immune response and enhance antitumor activity. Thus, the randomized expansion cohorts comprised 4 arms evaluating T and D as monotherapies and 2 T+D regimens, including a novel T+D regimen featuring a single, priming dose of T. **Methods:** ICI-naïve pts with aHCC who progressed on, were intolerant to, or refused sorafenib were randomized to one of two T+D combinations: T300+D (T 300 mg + D 1500 mg 1 dose followed by D Q4 weekly [Q4W]) or T75+D (T 75 mg Q4W + D 1500 mg Q4W [4 doses] followed by D Q4W); or single agent D (1500 mg Q4W) or T (750 mg Q4W). Safety was the primary endpoint. ORR by blinded, independent central review using RECIST v1.1, duration of response (DoR), circulating lymphocytes, and overall survival (OS) were assessed. **Results:** At data cut-off (09/02/2019), 332 pts were enrolled. Median follow-ups were 11.7 months (mo) for T300+D, 14.6 (T75+D), 8.9 (D), and 15.8 (T). Treatment-related adverse event (trAE) incidences are shown (Table); no deaths were attributed to trAEs for T300+D or T. The T300+D arm had the highest confirmed ORR (DoR not reached [NR]) and longest OS (Table). A unique proliferative T cell profile was identified for pts in the T300+D arm, suggesting additive biologic activity for the combination, and showed pts with an OR exhibited high cytotoxic (CD8) counts. **Conclusions:** The encouraging clinical activity and tolerable safety profile suggest T300+D provides the best benefit-risk profile as opposed to T75+D or monotherapies. The unique pharmacodynamic activity of the T300+D regimen further supports its use in aHCC. T300+D and D are being evaluated in the ongoing phase III HIMALAYA study (NCT03298451) in first-line HCC vs sorafenib. Funding: AstraZeneca. Clinical trial information: NCT02519348. Research Sponsor: AstraZeneca.

	T300+D (n=75)	T75+D (n=84)	D (n=104)	T (n=69)
Grade 3/4 trAEs, %	35.1	24.4	17.8	42.0
Serious trAEs, %	13.5	11.0	10.9	21.7
Grade 5 trAEs, n	0	1[a]	3[b]	0
Discontinuation due to trAEs, %	10.8	6.1	7.9	11.6
Median OS (95% CI), mo	18.7 (10.8-NR)	11.3 (8.4-14.6)	11.7 (8.5-16.9)	17.1 (10.9-NR)
ORR (95% CI), %	22.7 (13.8-33.8)	9.5 (4.2-17.9)	9.6 (4.7-17.0)	7.2 (2.4-16.1)
Median DoR, mo	NR	13.2	14.8	24.0

[a]hepatic failure
[b]abnormal hepatic function, hepatic failure, pneumonitis

4509 Poster Discussion Session; Displayed in Poster Session (Board #117), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Intrathoracic versus cervical anastomosis after minimally invasive esophagectomy for esophageal cancer: A randomized controlled trial.

Moniek Verstegen, Frans van Workum, Bastiaan Klarenbeek, Suzanne Gisbertz, Gerjon Hannink, Jan Willem Haveman, Joos Heisterkamp, Ewout Kouwenhoven, Jan Van Lanschot, Grard Nieuwenhuijzen, Donald Van der Peet, Fatih Polat, Maroeska Rovers, Camiel Rosman, ICAN Trial Study Group; Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; Radboud University Medical Center, Nijmegen, Netherlands; Amsterdam UMC - AMC, Amsterdam, Netherlands; University Medical Center Groningen, Groningen, Netherlands; St Elizabeth Hospital, Tilburg, Netherlands; ZGT Hospital, Almelo, Netherlands; Erasmus University Medical Center, Rotterdam, Netherlands; Catharina Hospital, Eindhoven, Netherlands; Amsterdam UMC - VUmc, Amsterdam, Netherlands; Canisius Wilhemina Hospital, Nijmegen, Netherlands

Background: Robust evidence is lacking whether Ivor Lewis minimally invasive esophagectomy (MIE) or McKeown MIE should be preferred for patients with mid to distal esophageal or gastro-esophageal junction Siewert I-II (GEJ) cancer. **Methods:** In this multicenter randomized controlled trial, patients with esophageal (below the level of the carina) or GEJ cancer planned for curative resection were recruited. Eligible patients were randomly assigned (1:1) to either Ivor Lewis MIE or McKeown MIE. The primary endpoint was anastomotic leakage (AL) requiring endoscopic, radiologic or surgical intervention. Secondary outcome parameters were overall AL rate, postoperative complications, length of stay and mortality. **Results:** A total of 262 patients were randomly assigned to Ivor Lewis MIE (n = 130) or McKeown MIE (n = 132). Seventeen patients were excluded from the trial due to not meeting inclusion criteria (n = 2), physical unfitness for surgery (n = 3), patients' choice (n = 3), interval metastases (n = 5) or peroperative metastases (n = 4). AL necessitating reintervention occurred in 15 (12.3%) of 122 patients after Ivor Lewis MIE and in 39 (31.7%) of 123 patients after McKeown MIE (relative risk 0.39, 95% CI 0.22-0.65; risk difference 19.4%, 95% CI 7.9%-31.8%). Overall AL rate was 12.3% after Ivor Lewis MIE and 34.1% after McKeown MIE. Severe complications (Clavien-Dindo $\geq$ 3b) were observed in 10.7% after Ivor Lewis MIE and in 22.0% after McKeown MIE. Pleural effusion requiring drainage occurred in 9.8% of patients after Ivor Lewis MIE and 21.1% of patients after McKeown MIE. RLN palsy rate was 0% after Ivor Lewis MIE and 7.3% after McKeown MIE. Median length of hospital stay was 10 days (IQR 8 – 15 days) after Ivor Lewis MIE and 12 days (IQR 9 – 18 days) after McKeown MIE. ICU length of stay and mortality rates were comparable between groups. **Conclusions:** These findings provide evidence for a lower rate of AL requiring reintervention after Ivor Lewis MIE compared to McKeown MIE for patients with mid to distal esophageal or GEJ cancer. Clinical trial information: NTR4333. Research Sponsor: ZonMw.

4510 Poster Discussion Session; Displayed in Poster Session (Board #118), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Laparoscopic sentinel node navigation surgery versus laparoscopic standard gastrectomy with lymph node dissection in early gastric cancer: Final three-year survival results of multicenter randomized controlled phase III trial (SENORITA trial).

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Background: The benefits and hazards of laparoscopic sentinel node navigation surgery (LSNNS), compared with laparoscopic standard gastrectomy (LSG) with lymph node dissection in early gastric cancer (EGC), are unknown. The SENORITA trial investigated the clinical impact of LSNNS in EGC in terms of short-term surgical outcomes, long-term survival and quality of life. **Methods:** This study is a prospective, multicenter, randomized controlled, non-inferiority trial. Patients with preoperatively diagnosed gastric adenocarcinoma with T1N0 of 3 cm or less in diameter, regardless of histology, except absolute indication for endoscopic resection were eligible. Patients were randomized to LSG or LSNNS using dual tracers. The primary endpoint is 3-year disease-free survival (3yDFS). Planned sample size per arm is 290 patients with the non-inferiority margin of 2.737 in hazard ratio (HR) assuming that LSG achieve 97% 3yDFS, 5% of type 1 error and 80% of power. Three-year recurrence-free survival (3yRFS), overall survival (3yOS) and disease specific death rate (3yDSDR) were evaluated as secondary endpoints. **Results:** From March 2013 to December 2016, 580 patients were randomized (LSG arm 292 vs. LSNNS arm 288). After 53 patients dropped out before surgery, operation was performed in 527 patients (269 vs. 258), representing the full analysis set. LSG was performed in 266 according to the protocol excluding 3 open conversion. After exclusion of 13 without LSNNS due to various reasons, LSNNS was performed in 245 patients according to the protocol. After median follow up of 47.5 months, 3yDFS were 95.5% and 91.8% (HR 1.901, CI 0.911 – 3.967), respectively. The 3yRFS was 98.9% and 95.2% (p=0.019), and 3yOS was 99.2% and 97.6% (p=0.166), and 3yDSDR was 99.5% and 99.1% (p=0.591), respectively. **Conclusion:** LSNNS in EGC did not show non-inferiority compared with LSG in terms of 3yDFS. However, 3yOS and 3yDSDR of LSNNS were comparable to LSG by the rescue surgery of recurrence. LSNNS might be an alternative surgical option instead of LSG in selected EGC patients. Clinical trial information: NCT01804998. Research Sponsor: Grant 2010150-1 from National Cancer Center, Korea.

4511 Poster Discussion Session; Displayed in Poster Session (Board #119), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Sintilimab in patients with advanced esophageal squamous cell carcinoma refractory to previous chemotherapy: A randomized, open-label phase II trial (ORIENT-2).

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Background: Patients (pts) with advanced esophageal squamous cell carcinoma (ESCC) refractory to first-line chemotherapy have limited treatment options. The study aims to evaluate the efficacy and safety of sintilimab, a PD-1 inhibitor, versus chemotherapy in these pts, and explore predictive value of PD-L1 and neutrophil-to-lymphocyte ratio (NLR) on efficacy of sintilimab. **Methods:** The open-label, multi-center phase 2 trial (NCT03116152) enrolled advanced ESCC pts refractory to first-line chemotherapy, and randomly assigned (1:1) them to receive sintilimab (200mg, Q3W) or chemotherapy (paclitaxel, 175mg/m^2, Q3W; or irinotecan, 180mg/m^2, Q2W), intravenously. The primary endpoint was overall survival (OS). Explorative endpoint were effects of PD-L1 and NLR on efficacy of sintilimab. **Results:** From May 16, 2017 to Aug 30, 2018, 190 pts were randomly assigned to sintilimab or chemotherapy (n = 95 per group). With the median follow-up of 7.2 months for sintilimab group and 6.2 months for chemotherapy group, the median OS in sintilimab was significantly higher than chemotherapy (7.2m vs. 6.2m, hazard ratio [HR] 0.70, P = 0.034). The objective response rate (ORR) was greater in sintilimab than chemotherapy with 12.6% vs. 6.3%, and the median duration of response was longer (8.3m vs. 6.2m). Incidences of treatment-related adverse events (TRAEs) of any grade (54.3% vs. 90.8%) and of grade 3-5 (20.2% vs. 39.1%) were both numerically less in sintilimab than in chemotherapy. The ORR in sintilimab versus chemotherapy in pts with tumor PD-L1 tumor proportion score (TPS) $\geq$1% and with TPS $\geq$10% were 20.2% vs. 0%, and 35.7% vs. 0%, respectively. In sintilimab group, pts with low NLR ($<$ 3) had a significant longer median OS (HR 0.54, P = 0.019) than with high NLR. **Conclusions:** Sintilimab was superior to chemotherapy with a significantly prolonged survival benefit and a favorable safety profile in pts with advanced ESCC refractory to first-line chemotherapy. High tumor PD-L1 expression (TPS $\geq$1% or $\geq$10%) might indicate more response benefit to sintilimab for these pts, and low NLR might be a positive predictive factor for sintilimab. Clinical trial information: NCT03116152. Research Sponsor: Innovent Biologics, Inc.

4512 Poster Discussion Session; Displayed in Poster Session (Board #120), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

The association of molecular biomarkers with efficacy of pembrolizumab versus paclitaxel in patients with gastric cancer (GC) from KEYNOTE-061.

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Background: KEYNOTE-061 (NCT02370498) was a randomized, open-label, phase 3 study of pembrolizumab vs paclitaxel in patients with advanced gastric or gastroesophageal junction adenocarcinoma with tumor progression after first-line therapy (N =592). We explored the association of tissue tumor mutational burden (tTMB) status and clinical outcomes in patients with GC enrolled in KEYNOTE-061, including the relationship with PD-L1 combined positive score (CPS) and microsatellite instability-high (MSI-H) status. **Methods:** In patients from KEYNOTE-061 with evaluable tumor and matched normal whole exome sequencing (WES) data (N = 420; pembrolizumab, 218; paclitaxel, 202), the association of tTMB (continuous $\log_{10}$ scale) with confirmed ORR and PFS by blinded central radiology review per RECIST v1.1, and OS was evaluated within each treatment arm using logistic regression (ORR) and Cox proportional hazards regression (PFS; OS). The clinical utility of tTMB was assessed using the prespecified cutoff of 175 mut/exome. Clinical data cutoff: October 26, 2017. **Results:** tTMB was significantly associated (α=0.05) with ORR, PFS, and OS in patients treated with pembrolizumab (one-sided $P<0.001$) but not paclitaxel (two-sided $P>0.600$). The area under the receiver operating characteristics curve for tTMB and response (pembrolizumab vs paclitaxel) was 0.68 (95% CI, 0.56-0.81) vs 0.51 (95% CI, 0.39-0.63). Patient outcomes by tTMB cutoff are reported in Table. There was low correlation between tTMB and PD-L1 CPS in both treatment arms ($r<0.18$). tTMB remained significantly associated with all clinical end points with pembrolizumab after adjusting for PD-L1 CPS and with PFS and OS after excluding MSI-H patients. **Conclusions:** This exploratory analysis from KEYNOTE-061 is the first to demonstrate a strong association between tTMB and response to pembrolizumab in patients with GC. Data further suggest tTMB is a significant and independent predictor beyond PD-L1 status. Clinical trial information: NCT02370498. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	tTMB <175, pembrolizumab (n=178)	tTMB <175, paclitaxel (n=166)	tTMB ≥175, pembrolizumab (n=40)	tTMB ≥175, paclitaxel (n=36)
ORR, % (95% CI)	8.4 (4.8-13.5)	13.3 (8.5-19.4)	30.0 (16.6-46.5)	11.1 (3.1-26.1)
PFS, mo, median (95% CI)	1.5 (1.5-1.6)	4.1 (3.1-4.3)	4.1 (2.1-8.6)	4.1 (3.0-8.2)
HR (95% CI)	1.78 (1.43-2.22)	–	0.73 (0.44-1.22)	–
OS, mo, median (95% CI)	5.7 (4.7-8.7)	8.8 (8.3-9.9)	16.4 (10.8-NR)	8.1 (6.8-12.1)
HR (95% CI)	1.12 (0.89-1.41)	–	0.46 (0.27-0.81)	–

4513 Poster Discussion Session; Displayed in Poster Session (Board #121), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-positive advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma: A randomized, phase II, multicenter, open-label study (DESTINY-Gastric01).

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Background: T-DXd is an antibody-drug conjugate composed of an anti-HER2 antibody, cleavable tetrapeptide-based linker, and topoisomerase I inhibitor. In a phase 1 trial of T-DXd (5.4 or 6.4 mg/kg), the objective response rate (ORR) was 43.2% (19/44) and median progression-free survival (mPFS) was 5.6 mo in patients with advanced HER2+ gastric cancer (GC). DESTINY-Gastric01 (DS8201-A-J202; NCT03329690) is an open-label, multicenter, randomized, phase 2 study of T-DXd in HER2-expressing advanced GC or GEJ adenocarcinoma; results are from the primary analyses for ORR and interim overall survival (OS) in HER2+ patients. **Methods:** Patients with centrally confirmed HER2+ (IHC 3+ or IHC 2+/ISH+ on archival tissue) GC that progressed on ≥ 2 prior lines were randomized 2:1 (T-DXd 6.4 mg/kg q3w or physician's choice [PC] irinotecan or paclitaxel). All patients received prior HER2 therapy. Stratification factors were region, ECOG PS (0;1), and HER2 status. The primary endpoint was unconfirmed ORR by independent central review. Secondary endpoints were OS (alpha controlled), PFS, disease control rate (DCR), duration of response (DOR), and safety. **Results:** 187 patients received T-DXd (n = 125) or PC (n = 62 [55 irinotecan; 7 paclitaxel]); 79.7% Japan, 20.3% Korea. Patients had a median of 2 prior lines of therapy, and 44.4% had ≥ 3. At data cutoff (8 Nov 2019), 22.4% of T-DXd and 4.8% of PC patients remained on treatment. ORR was 51.3% (61/119; 11 CR and 50 PR) with T-DXd vs 14.3% (8/56; all PR) with PC ($P < .0001$); confirmed ORR, 42.9% vs 12.5% ($P < .0001$); DCR, 85.7% vs 62.5% ($P = .0005$); mDOR, 11.3 vs 3.9 mo; mPFS, 5.6 vs 3.5 mo (HR, 0.47 [95% CI, 0.31-0.71]; $P = .0003$). OS was significantly prolonged with T-DXd (mOS, 12.5 vs 8.4 mo; HR, 0.59 [95% CI, 0.39-0.88]; $P = .0097$; prespecified O'Brien Fleming boundary, $P = .0202$); 12-month OS, 52.1% vs 28.9%. Grade ≥ 3 AEs occurred in 85.6% of patients with T-DXd vs 56.5% with PC; the most common were neutrophil count decreased (51.2%; 24.2%), anemia (37.6%; 22.6%), and white blood cell count decreased (20.8%; 11.3%). 12 patients (9.6%) had T-DXd–related interstitial lung disease (ILD; 2 grade 3, 1 grade 4, no grade 5) vs 0 with PC. 1 drug-related death (pneumonia [non-ILD] in the T-DXd arm) occurred. **Conclusions:** T-DXd demonstrated statistically significant and clinically meaningful improvements in ORR and OS compared with standard chemotherapy (paclitaxel or irinotecan) in patients with HER2+ advanced gastric or GEJ adenocarcinoma. Clinical trial information: NCT03329690. Research Sponsor: Daiichi Sankyo Co., Ltd.

4514 Poster Discussion Session; Displayed in Poster Session (Board #122), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

FOLFIRI plus ramucirumab versus paclitaxel plus ramucirumab as second-line therapy for patients with advanced or metastatic gastroesophageal adenocarcinoma with or without prior docetaxel: Results from the phase II RAMIRIS Study of the AIO.

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Background: Ramucirumab (Ram) as monotherapy or plus paclitaxel is a proven second-line option for advanced gastroesophageal adenocarcinoma (GEA). More and more patients (pts) are pretreated with docetaxel in the perioperative or first-line setting. These pts may benefit more from another, non-cross resistant chemotherapy backbone regimen. This trial evaluates the addition of Ram to FOLFIRI as second line treatment. **Methods:** This is a multicenter, randomized, investigator initiated, phase II trial. Pts with GEA who have progressed after treatment with a fluoropyrimidine/platinum-containing regimen were randomized 2:1 to either FOLFIRI plus Ram every two weeks (Arm A) or paclitaxel (days 1, 8, 15 of a 28-day cycle) plus Ram every two weeks (Arm B). Major endpoints were overall survival (OS), objective response rate (ORR), disease control rate (DCR), progression free survival (PFS) and toxicity. **Results:** 111 pts (median age 61 years, 65% of pts had prior docetaxel therapy) were enrolled and 110 analyzed within intention to treat population (ITT, Arm A, 72; Arm B, 38). In the ITT, there was no significant difference in median OS (A, 6.8 vs. B, 7.6 months, HR 0.94, p = 0.77) and median PFS (A, 4.6 vs. B, 3.6 months, HR 0.72, p = 0.12). For pts with prior docetaxel use (71/110), median PFS was A, 4.3 vs. B, 2.0 months, HR 0.49, p = 0.008 and median OS was A, 7.5 vs. B, 6.4 months, HR 0.71, p = 0.25. In 101 pts with tumor assessment and included in the response analysis, ORR and DCR was 23% and 65% in Arm A and 11% and 60% in Arm B, respectively. 67 pts assessable for response were pre-treated with docetaxel. In these pts, ORR was 24% in Arm A and 9% in Arm B. Disease control rate (DCR) was 67% and 41% for Arm A and B respectively. Both therapies were similarly tolerable, final safety results will be shown. **Conclusions:** The RAMIRIS trial demonstrated feasibility of the combination of FOLFIRI and Ram. With a response rate of 24% and a median PFS of 4.3 months, docetaxel pre-treated pts seemed to derive pronounced benefit from FOLFIRI-Ram, providing a rationale for a phase III trial, which is currently ongoing. Clinical trial information: NCT03081143. Research Sponsor: Lilly.

4515 Poster Discussion Session; Displayed in Poster Session (Board #123), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase III APACT trial of adjuvant *nab*-paclitaxel plus gemcitabine (*nab*-P + Gem) versus gemcitabine (Gem) alone for patients with resected pancreatic cancer (PC): Outcomes by geographic region.

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Background: The APACT trial was one of the largest and most geographically diverse trials of adjuvant chemotherapy for resected PC, allowing for comparison of outcomes by geographic region. In this analysis, we report updated overall survival (OS) results for the intent-to-treat (ITT) population and examine outcomes by geographic region. **Methods:** Treatment-naive patients with histologically confirmed PC, macroscopic complete resection, Eastern Cooperative Oncology Group performance status 0 or 1, and carbohydrate antigen 19-9 $<$ 100 U/mL were eligible. Stratification factors were resection status (R0/R1) and lymph node status (positive/negative). Treatment was initiated $\leq$ 12 weeks postsurgery. Patients received *nab*-P 125 mg/m^2 + Gem 1000 mg/m^2 or Gem 1000 mg/m^2 on days 1, 8, and 15 of six 28-day cycles. The primary endpoint was disease-free survival by independent review. Secondary endpoints were OS and safety. **Results:** The updated OS analysis (data cutoff date, January 2020) revealed a median OS of 41.8 months with *nab*-P + Gem compared with 37.7 months with Gem alone (hazard ratio [HR] 0.81; 95% CI, 0.68 - 0.97; nominal $P = 0.047$; Table). In each geographic region, the median OS with *nab*-P + Gem was numerically longer than with Gem alone. **Conclusions:** The updated OS analysis of the ITT population supports the previously reported trend favoring *nab*-P + Gem. The geographic regional analyses reveal numerically longer OS with *nab*-P + Gem vs Gem alone and variable outcomes by region; however, the differences do not support the trend observed in the ITT population, potentially due to limited sample sizes. Registration: EudraCT (2013-003398-91). Clinical trial information: NCT01964430. Research Sponsor: Bristol-Myers Squibb.

Survival Outcomes by Geographic Region.

	nab-P + Gem		Gem			
Group	n	Median (95% CI) OS, mo	n	Median (95% CI) OS, mo	HR (95% CI)	*P* value
ITT population	432	41.8 (35.55 - 46.75)	434	37.7 (31.11 - 40.51)	0.81 (0.68 - 0.97)	0.047
North America	144	38.5 (32.56 - 53.13)	156	35.0 (28.25 - 41.33)	0.73 (0.54 - 0.99)	0.11
Europe	203	41.8 (32.82 - 48.03)	205	38.1 (30.72 - 43.40)	0.88 (0.68 - 1.13)	0.40
Australia	30	31.5 (19.06 - NA)	20	28.1 (17.05 - 43.01)	0.65 (0.30 - 1.38)	0.39
Asia Pacific	55	45.5 (27.01 - NA)	53	40.6 (24.21 - NA)	0.83 (0.50 - 1.39)	0.43

NA, not applicable

4516 Poster Discussion Session; Displayed in Poster Session (Board #124), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

ESPAC-4: A multicenter, international, open-label randomized controlled phase III trial of adjuvant combination chemotherapy of gemcitabine (GEM) and capecitabine (CAP) versus monotherapy gemcitabine in patients with resected pancreatic ductal adenocarcinoma: Five year follow-up.

John P. Neoptolemos, Daniel H. Palmer, Paula Ghaneh, Juan W. Valle, David Cunningham, Jonathan Wadsley, Tim Meyer, Alan Anthoney, Bengt Glimelius, Stephen Falk, Ralf Segersvard, Gary William Middleton, Paul J. Ross, Harpreet Singh Wasan, Alec McDonald, Tom David Lewis Crosby, Eftychia Eirini Psarelli, Pascal Hammel, Thilo Hackert, Markus W. Buchler, European Study Group for Pancreatic Cancer (ESPAC); University of Heidelberg, Heidelberg, Germany; Liverpool Experimental Cancer Medicine Centre, Liverpool, United Kingdom; University of Liverpool, Liverpool, United Kingdom; The Christie NHS Foundation Trust, Manchester, United Kingdom; Royal Marsden Hospital, Sutton, United Kingdom; Weston Park Hospital, Sheffield, United Kingdom; University College London Cancer Institute, London, United Kingdom; St James's Institute of Oncology, St. James's University Hospital, West Yorkshire, United Kingdom; Uppsala University, Department of Immunology, Genetics and Pathology, Uppsala, Sweden; Bristol Haematology and Oncology Centre, Bristol, United Kingdom; Karolinska Institute, Stockholm, Sweden; University of Birmingham, Birmingham, United Kingdom; Guy's Hospital, London, United Kingdom; Hammersmith Hospital, Imperial College Health Care Trust, London, United Kingdom; Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom; Velindre Cancer Centre, Cardiff, United Kingdom; Hôpital Beaujon (AP-HP), Clichy, and University Paris VII, Paris, France

Background: The ESPAC-4 trial demonstrated that adjuvant GEM/CAP for pancreatic cancer significantly improved survival compared to GEM monotherapy. The aim of this study is to evaluate the long-term outcomes in the ESPAC-4 trial. **Methods:** Patients with pancreatic ductal adenocarcinoma were randomized within 12 weeks of surgery (stratified for R0/R1 resection margin status and country) to have either six 4-week cycles of IV GEM alone or GEM with oral CAP. The primary endpoint was five-year survival; secondary endpoints were toxicity and relapse free survival. 722 patients (480 expected events), 361 in each arm, were needed to detect a 10% difference in 2-year survival rates with 90% power (log-rank test with 5% two-sided alpha). **Results:** Between Nov 10 2008 and Sep 11 2014, 732 patients were randomized with 730 included in the full analysis set (366 GEM, 364 GEM/CAP). Median age was 65 years, 57% were men. WHO performance status was 0, 1 or 2 in 42% 55% and 3% respectively. Postoperative median CA19-9 was 19 kU/L. Median maximum tumor size was 30 mm, 61% were R1 resections, 80% were node positive and 40% were poorly differentiated. The data freeze was on 24 February 2020; median follow up was 60 months with 531 overall deaths, 280 in GEM, and 251 in GEM/CAP. Median (95% CI) survival (months) for patients treated with GEM/CAP was 27.7 23.3 – 31.2) and 26.0 (22.7 – 28.4) for GEM. Five-year (95% CI) survival rates were 20 (16 – 25) % for GEM and 28 (23 – 33) % for GEM/CAP. Stratified log-rank analysis revealed an HR=0.84 [95% CI, 0.70 – 0.99]; χ^2 (1) = 3.87, P=0.049. 70 out of 366 GEM patients in the safety set reported 101 grade 3/4 serious adverse events, while 65 out of 359 GEM/CAP patients reported 97 grade 3/4 serious adverse events (P=0.724). **Conclusions:** Adjuvant GEM/CAP for pancreatic cancer had a statistically significant improvement in survival compared to GEM monotherapy. Clinical trial information: 96397434. Research Sponsor: Cancer Research UK.

4518 Poster Discussion Session; Displayed in Poster Session (Board #126), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A prospective randomized controlled trial of selective transarterial chemoembolization using drug-eluting beads loaded with epirubicin versus selective conventional transarterial chemoembolization using epirubicin-lipiodol for hepatocellular carcinoma: The JIVROSG-1302 PRESIDENT study.

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Background: Transarterial chemoembolization (TACE) with selective catheterization into the segmental or subsegmental hepatic arteries supplying HCC is often performed to achieve the complete local control of HCC in the patients with a limited number of small sized nodules. To clarify which of TACE with drug-eluting beads loaded with epirubicin (DEB-TACE) or conventional TACE with epirubicin-lipiodol (cTACE) can achieve the complete response (CR) more frequently, we performed a randomized controlled trial of DEB-TACE vs. cTACE. **Methods:** Between March 2016 and May 2019, unresectable HCC patients with Child-Pugh class A or B who were scheduled to receive selective TACE were randomly assigned 1:1 to the DEB-TACE group and the cTACE group. The primary endpoint was the CR rate at 3 months, and the secondary endpoints were the CR rate at 1 month and rate of adverse events (AEs). The response and AEs were assessed according to the modified RECIST by an independent review committee and the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0., respectively. **Results:** A total of 200 patients (DEB-TACE, 99 patients; cTACE 101 patients) were enrolled from 22 Japanese institutions. The patient characteristics were well-balanced between the two groups. The median number of tumors was one in both groups and the median tumor size was 20.0 mm in the DEB-TACE group and 20.5 mm in the cTACE group. The table shows the CR rates and frequencies of AEs. The CR rates of cTACE at 3 and 1 months were significantly higher than those of DEB-TACE. The frequency of AEs (all grades), including pyrexia, malaise, increased serum total bilirubin (T-Bil) and increased serum alanine transaminase (ALT), was significantly higher in the cTACE group than in the DEB-TACE group. **Conclusions:** Selective cTACE appeared to have greater efficacy for local tumor control as compared to selective DEB-TACE, however, the frequencies of post-embolization syndromes were higher in the cTACE group than in the DEB-TACE group. Clinical trial information: UMIN000021250. Research Sponsor: National Cancer Center Research and Development Fund (26-A-27).

	DEB-TACE N = 99	cTACE N = 101	*p*-value
CR rate at 3 months	27.6%	75.2%	< 0.0001
CR rate at 1 month	35.7%	84.2%	< 0.0001
Any grade of AE: pyrexia	19%	46%	< 0.0001
Any grade of AE: malaise	11%	26%	0.0103
Any grade of AE: increased serum T-Bil	22%	49%	0.0001
Any grade of AE: increased serum ALT	35%	78%	< 0.0001

4519 Poster Discussion Session; Displayed in Poster Session (Board #127), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

A phase Ib study of lenvatinib (LEN) plus pembrolizumab (PEMBRO) in unresectable hepatocellular carcinoma (uHCC).

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Background: LEN is a multikinase inhibitor of VEGFR 1–3, FGFR 1–4, PDGFRα, RET, and KIT, approved for first line (1L) treatment of uHCC. PEMBRO, an anti-PD-1 monoclonal antibody, was granted accelerated approval for the treatment of patients (pts) with HCC after sorafenib therapy. We assessed the safety and efficacy of LEN + PEMBRO in uHCC. **Methods:** In this phase 1b trial (NCT03006926), pts received LEN 12 mg/day (bodyweight [BW] ≥60 kg) or 8 mg/day (BW <60 kg) orally + PEMBRO 200 mg IV on Day 1 of a 21-day cycle. Primary endpoints were safety and tolerability for Part 1 and objective response rate (ORR) and duration of response (DOR) by mRECIST and RECIST v1.1 per independent imaging review (IIR) in the 1L setting for Part 2. **Results:** 104 pts (part 1, n=6; part 2, n=98) were enrolled. No DLTs were reported in Part 1; 100 pts were included in the 1L analysis of LEN + PEMBRO–4 pts (part 1) excluded due to prior sorafenib. At data cutoff (October 31, 2019) and median follow-up of 10.6 months, 37 pts continued treatment (LEN only, n=3; both drugs, n=34); median duration of treatment was 7.9 months (LEN, 7.6 months; PEMBRO, 7.4 months). Median OS was 22.0 months (95% CI 20.4–not estimable [NE]), median PFS was 8.6 months (95% CI 7.1–9.7), and ORR was 36% (95% CI 26.6–46.2) (RECIST v1.1 per IIR). Additional efficacy outcomes are shown in the table. Treatment-emergent adverse events (TEAEs) occurred in 99% of pts (grade ≥3, 85%; grade ≥4, 23%). The most common grade ≥3 TEAE was hypertension (18% of pts). Treatment-related AEs (TRAEs) occurred in 95% of pts (grade ≥3, 67%; grade ≥4, 4%). The most common grade ≥3 TRAE was hypertension (17% of pts). 36% of pts had serious TRAEs and 3 pts died from a TRAE (acute respiratory failure/acute respiratory distress syndrome, n=1; intestinal perforation, n=1; abnormal hepatic function, n=1). **Conclusions:** LEN + PEMBRO has promising antitumor activity with a tolerable safety profile. An ongoing phase 3 trial (NCT03713593) is assessing LEN + PEMBRO vs LEN alone as 1L therapy for uHCC. Clinical trial information: NCT03006926. Research Sponsor: This study was sponsored by Eisai Inc., Woodcliff Lake, NJ, USA, and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Inc., Kenilworth, NJ, USA.

	mRECIST per IIR*	RECIST v1.1 per IIR*	mRECIST per investigator review*
ORR, n (%)	46 (46)	36 (36)	41 (41)
95% CI	36.0–56.3	26.6–46.2	31.3–51.3
Complete response (CR)	11 (11)	1 (1)	5 (5)
Partial response (PR)	35 (35)	35 (35)	36 (36)
Median DOR, months (95% CI)	8.6 (6.9–NE)	12.6 (6.9–NE)	12.6 (6.2–18.7)
Median time to response, months (range)	1.9 (1.2–5.5)	2.8 (1.2–7.7)	2.7 (1.2–11.8)
Disease control rate†, n (%)	88 (88)	88 (88)	86 (86)
95% CI	80.0–93.6	80.0–93.6	77.6–92.1
Median PFS, months (95% CI)	9.3 (5.6–9.7)	8.6 (7.1–9.7)	8.2 (7.4–9.7)

*n=100 †CR + PR + stable disease (≥5 weeks)

4520 Poster Discussion Session; Displayed in Poster Session (Board #128), Fri, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Fri, 8:00 AM-11:00 AM

Phase II study assessing tolerability, efficacy, and biomarkers for durvalumab (D) ± tremelimumab (T) and gemcitabine/cisplatin (GemCis) in chemo-naïve advanced biliary tract cancer (aBTC).

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Background: In aBTC, GemCis is the standard of care as 1st-line treatment. Immunotherapies have shown early promising efficacy in some BTC patients (pts). We assessed D (anti-PD-L1) ± T (anti-CTLA-4) and GemCis in 1L BTC pts, including an extensive biomarker analysis (NCT03046862). **Methods:** Pts were first enrolled in the biomarker cohort (BMC) to receive 1 cycle of Gem 1000 mg/m^2 + Cis 25 mg/m^2 on D1 & D8, followed by GemCis + D 1120 mg and T 75 mg, Q3W until disease progression (PD). Subsequent pts were allocated to GemCis + D (3 combo cohort [3C]) or GemCis + D+T (4 combo cohort [4C]) until PD. In all cohorts, tumor biopsies were obtained pre-treatment, after 1 cycle, and at PD. Blood samples for ctDNA were obtained every cycle. **Results:** 121 pts were enrolled. Median follow-up durations were 28.5 months (m; 95% CI, 26.5-30.5), 11.3 m (95% CI, 9.1-13.5), and 11.9m (95% CI, 8.4-15.4) in the BMC, 3C, and 4C arms, respectively. Efficacy data are shown (Table). The most common adverse events (AEs, any grade) were neutropenia (54.5%), nausea (59.5%), and pruritus (55.44%). The most common grade 3/4 AEs were neutropenia (50.4%), anemia (35.5%), and thrombocytopenia (16.5%). In the BMC cohort, frequent mutations were found in DNA damage repair, cell cycle regulation, and genome instability genes (eg, *ATM*, *BRCA2*, *POLE*, *MSH2*, *CDKN2A*). Distinct somatic variants were detected in responders vs non-responders. Baseline tissue TMB did not correlate with PFS or OS. Reductions in ctDNA variant allele frequency (VAF) were more prominent among responders during early D+T cycles. ctDNA VAF on C3, D1 was significantly correlated with ORR ($P < 0.015$). Pretreatment PD-L1 expression was not associated with efficacy, but PD-L1 expression after 1st GemCis cycle trended with improved PFS. **Conclusions:** These are the first clinical data of D±T plus chemotherapy in chemo-naïve aBTC pts. The addition of immunotherapy to chemotherapy was tolerable and showed very promising efficacy. Biomarker analyses show early signs of markers associated with response. The combination of GemCis + D is being investigated in the Phase 3 TOPAZ-1 trial (NCT03875235). Clinical trial information: NCT03046862. Research Sponsor: AstraZeneca.

	BMC (n = 30)	3C (n = 45)	4C (n = 46)
ORR (95% CI), %	50.0 (32.1-67.9)	73.4 (60.5-86.3)	73.3 (60.4-86.2)
DCR (95% CI), %	96.7 (90.3-100)	100 (100-100)	97.8 (93.5-100)
mDOR (95% CI), m	11.0 (3.9-11.8)	9.8 (8.1-11.4)	9.1 (4.5-15.0)
mPFS (95% CI), m	13.0 (10.1-15.9)	11.0 (7.0-15.0)	11.9 (10.1-13.7)
mOS (95% CI), m	15.0 (10.7-19.3)	18.1 (11.3-24.9)	20.7 (13.8-27.6)

4521 **Poster Session (Board #129), Fri, 8:00 AM-11:00 AM**

Neoadjuvant chemotherapy plus surgery for high-risk advanced gastric cancer: Long-term results of KDOG1001 trial.

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Background: In the phase 2, open-label, KDOG1001 (UMIN000003642) study, neoadjuvant chemotherapy (NAC) with docetaxel, cisplatin, and S-1 (DCS), followed by gastrectomy with D2 lymph node dissection for high-risk advanced gastric cancer showed feasibility of DCS therapy with an enough R0 resection rate of 90%. Here we present long-term results after a minimum follow-up of 3 years. **Methods:** Patients with bulky node metastasis (bulky N), linitis plastica (type 4), or large ulcero-invasive-type tumors (type 3) received up to four 28-day cycles of DCS neoadjuvant chemotherapy (docetaxel at 40 mg/m^2, cisplatin at 60 mg/m^2 on day 1, and S-1 at 40 mg/m^2 twice daily for 2 weeks) followed by gastrectomy with D2 lymphadenectomy. This analysis presents the final preplanned assessment of outcomes after 3 years. Primary endpoint was R0 resection rate. Secondary endpoints included overall survival (OS), progression free survival (PFS), completion rate of the protocol treatment, and pathological response rate (pRR) of DCS NAC. **Results:** Of 40 patients enrolled from May 2010 through January 2017, 7 (17.5%) had bulky N, 18 (45.0%) had type 4, and 16 (40%) had large type 3 with 1 (2.5%) having both large type 3 and bulky N2. All included patients underwent preoperative DCS chemotherapy followed by surgery with D2 lymphadenectomy with 32 (80%) completed postoperative S-1 therapy for 1 year. After a median follow-up for surviving patients of 67 mo (range, 36 mo to 110 mo) at the last follow-up in January 2020, 3-year OS was 78% [95% confidence interval (CI) 62–88%], while 3-year PFS was 63% (95% CI 47–76%). Completion rate of the protocol treatment was 62.5% (25/40) with pRR of 57.5% (23/40). In bulky N2, 3-y OS was 86% and 3-y PFS was 71% with pRR of 100%. In type 4, 3-y OS was 67% and 3-y PFS was 50% with pRR of 44%. In large type 3, 3-y OS was 88% and 3-y PFS was 75% with pRR of 56%. Patients with type 4 had significantly worse OS and PFS than those with the other types [HR 7.20 (95% CI 2.23–32.21) and HR 3.00 (95% CI 1.21–8.19)]. **Conclusions:** Preoperative chemotherapy with up to four cycles of DCS followed by gastrectomy plus adjuvant S-1 therapy is a promising treatment strategy for patients with bulky node metastasis, type 4 and large type 3 gastric cancers. For type 4 cancer, further improvement of treatment strategy is needed. Clinical trial information: 000003642. Research Sponsor: None.

4522 **Poster Session (Board #130), Fri, 8:00 AM-11:00 AM**

A phase II study of rh-endostatin combined with paclitaxel and nedaplatin in treating patients with recurrent or metastatic esophageal squamous cell carcinoma (ESCC).

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Background: For patients (pts) with metastatic ESCC, the prognosis is poor. Rh-endostatin (endostar), a potent inhibitor of angiogenesis, has shown clinical activity when combined with chemoradiotherapy in treating locally advanced ESCC. This single-arm phase 2 study was designed to assess the efficacy and safety of endostar combined with paclitaxel and nedaplatin in treating pts with recurrent or metastatic ESCC. **Methods:** Eligible pts had recurrent or metastatic ESCC and Karnofsky score ≥70. Endostar (30 mg/day, continuous infusion, day 1-14) plus paclitaxel (150 mg/m^2, day 4) and nedaplatin (80 mg/m^2, day 4) were administered every 3 weeks for 6 cycles followed by maintenance therapy with endostar. Primary endpoint was progression-free survival (PFS). Secondary endpoints included objective response rate (ORR), disease control rate (DCR), overall survival (OS) and adverse events (AEs). **Results:** From January 2015 to August 2019, 53 pts were enrolled. 44 (83%) pts were male. The median age was 59 years. 43 (81%) pts had pathology of poor or moderate differentiated ESCC. The middle and lower thirds of the esophagus (81%) were the most common primary tumor sites. 11 (21%) patients had undergone esophagectomy. At the time of treatment, 49 (93%) pts were diagnosed with clinical stage IVB. The most common metastatic sites were lymph node (91%), lung (32%) and liver (26%). 50 pts were assessable for response. No complete response was observed. 21 pts achieved a best response of partial response and 14 pts had stable disease. ORR was 42% and DCR was 70%. The median PFS and OS was 5.1 months (95% CI 3.7-6.6 months) and 13.2 months (95% CI 8.0-18.4 months) respectively. The most common AEs observed during this study were anemia (49.1%), neutropenia (34%), fatigue (28.3%) and anorexia (26.4%). The most common Grade 3/4 AE observed was neutropenia (17%). **Conclusions:** The combination of endostar plus paclitaxel and nedaplatin is a well tolerated treatment modality with promising activity in previously untreated recurrent or metastatic ESCC. Its efficacy and safety could be further studied in randomized trials. Clinical trial information: NCT02350517. Research Sponsor: Simcere.

4523 **Poster Session (Board #131), Fri, 8:00 AM-11:00 AM**

Pembrolizumab (pembro) versus standard of care chemotherapy (chemo) in patients with advanced gastric or gastroesophageal junction adenocarcinoma: Asian subgroup analysis of KEYNOTE-062.

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Background: First-line treatment with pembro or pembro + chemo vs chemo alone was evaluated in patients with PD-L1 combined positive score (CPS) ≥1, HER2-negative advanced gastric cancer in the randomized, active-controlled, phase 3 KEYNOTE-062 study (NCT02494583). We present results from the Asian subpopulation receiving pembro monotherapy or chemo. **Methods:** Eligible patients were randomly assigned 1:1:1 to pembro 200 mg, pembro + chemo (cisplatin + 5-FU or capecitabine), or placebo + chemo every 3 weeks for ≤35 cycles (~2 years). Randomization was stratified by region, disease status, and fluoropyrimidine treatment. Primary end points for this analysis were overall survival (OS) in patients with CPS ≥1 and patients with CPS ≥10; progression-free survival (PFS) and objective response rate (ORR) were exploratory end points. Data cutoff was March 26, 2019. **Results:** Globally, 256 patients received pembro monotherapy and 250 received chemo. Pembro was noninferior to chemo for OS in CPS ≥1 per prespecified margins (median OS, 10.6 vs 11.1 months, respectively; HR [99.2% CI], 0.91 [0.69-1.18]). In the Asian population 62 patients received pembro and 61 received chemo; 26 and 22 had CPS ≥10 (Table). Compared with the global population, Asian patients had a higher proportion of ECOG performance status 0, more diagnoses of stomach cancer, and a greater proportion with 0-2 metastatic sites. Median OS was longer with pembro than chemo using both CPS cutoffs (HR [95% CI]: CPS ≥1, 0.54 [0.35-0.82]; CPS ≥10, 0.43 [0.21-0.89]); 12- and 24-month OS rates were higher for pembro using both CPS cutoffs (12-month OS: CPS ≥1, 69% vs 54%; CPS ≥10, 81% vs 68%; 24-month OS: CPS ≥1, 45% vs 23%; CPS ≥10, 54% vs 27%). The HR (95% CI) for PFS was 1.11 (0.76-1.64) for CPS ≥1 and 0.71 (0.36-1.39) for CPS ≥10. **Conclusions:** In Asian patients with advanced gastric cancer, OS favored pembro in patients with CPS ≥1 and CPS ≥10. Clinical trial information: NCT02494583. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	CPS ≥1		CPS ≥10	
	Pembrolizumab n = 62	Chemotherapy n = 61	Pembrolizumab n = 26	Chemotherapy n = 22
Median OS, months	22.7	13.8	28.5	14.8
HR (95% CI)	0.54 (0.35-0.82)	—	0.43 (0.21-0.89)	—
12-month OS, %	69.4	54.1	80.8	68.2
24-month OS, %	44.8	23.0	53.6	27.3
Median PFS, months	4.1	6.5	7.2	6.9
HR (95% CI)	1.11 (0.76-1.64)	—	0.71 (0.36-1.39)	—
12-month PFS, %	26.9	21.3	25.1	18.3
ORR, %	22.6	37.7	26.9	31.8

4524 **Poster Session (Board #132), Fri, 8:00 AM-11:00 AM**

HX008, an anti-PD1 antibody, plus irinotecan as second-line treatment for advanced gastric adenocarcinoma: A phase II clinical trial.

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Background: Patients with advanced gastric or gastro-oesophageal junction cancer that progresses on chemotherapy have poor outcomes. We investigated HX008, an Anti-PD1 Antibody, with irinotecan in patients with advanced gastric or gastro-oesophageal junction cancer that progressed on first-line chemotherapy with a platinum and/or fluoropyrimidine. **Methods:** This study is a multicenter, open, phase II clinical study of recombinant humanized anti-pd-1 monoclonal antibody HX008 injection plus Irinotecan that was conducted at 11 hospitals in China. Eligible patients are adults with histologically confirmed advanced gastric or gastro-oesophageal junction cancer. Subjects participating in this study are required to submit a archived tumor tissue specimen or newly obtained biopsy of tumor lesions at the site of no previous radiotherapy and peripheral blood (2mL) for detection of PD-L1 and MSI/MMR expression. The samples will be tested for expression of PD-L1 and MMR by immunohistochemistry (IHC) in the central laboratory, and MSI levels will be determined by polymerase chain reaction (PCR) and gel electrophoresis. Subjects received PD-1 monoclonal antibody HX008 at 200mg (d1, intravenous drip, once every 3 weeks) plus irinotecan at 160mg/m2 (d1, intravenous drip, 60 ~ 120min, once every 2 weeks). Response was assessed every 6 weeks in accordance with Response Evaluation Criteria in Solid Tumors version 1.1. Primary endpoints was objective remission rate (ORR). **Results:** Between October 2018 and September 2019, a total of 58 patients with advanced gastric or gastro-oesophageal junction cancer were enrolled in this study. Median (range) age was 61 (27-71) years, and most patients were male (72.4%). Among 53 patients who were evaluated, 15 (28.3%) experienced objective response and 22 (41.5%) experienced stable disease (SD). The median progression free survival (PFS) was 5.4 months, the one-year survival rate was 71.3%. The most common treatment-related adverse events of grade 3 or 4 included neutropenia(31.0%), anemia(15.5%), loss of appetite (6.9%), vomiting(5.2%), nausea(3.4%), diarrhea (1.7%) and fatigue (1.7%). There were no treatment-related deaths. **Conclusions:** HX008 injection plus Irinotecan demonstrated promising activity and manageable safety in patients with advanced gastric or gastro-oesophageal junction cancer that progressed on first-line chemotherapy with a platinum and fluoropyrimidine. Clinical trial information: NCT03704246. Research Sponsor: None.

4525 **Poster Session (Board #133), Fri, 8:00 AM-11:00 AM**

A phase Ib study of nivolumab plus trastuzumab with S-1/capecitabine plus oxaliplatin for HER2-positive advanced gastric cancer (Ni-HIGH study): Safety evaluation.

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Background: Addition of an anti-PD-1 antibody to trastuzumab (Tmab) reportedly enhances ADCC activity of Tmab, leading to an additive antitumor effect. We investigated the safety and tolerability of nivolumab (Nivo) plus Tmab combined with S-1 or capecitabine (Cape) and oxaliplatin (Ox) for pts with HER2-positive (+) advanced gastric cancer (AGC). Here, we report the safety evaluation results. **Methods:** This open-label, phase 1b study was conducted at four centers in Japan. The study consisted of safety (n = 12) and expansion (n = 24–30) parts. Chemotherapy-naïve pts aged ≥ 20 years with histopathologically confirmed HER2+ AGC and measurable lesions were eligible. In the safety evaluation, pts were assigned to cohort 1 or 2 in sequence. Pts received Nivo (360 mg, day 1), Tmab (course 1: 8 mg/kg; course 2–: 6 mg/kg, day 1), Ox (130 mg/m^2, day 1) and either S-1 (40 mg/m^2 bid, days 1–14; cohort 1) or Cape (1000 mg/m^2 bid, days 1–14; cohort 2) every 3 weeks until disease progression or unacceptable toxicity. The primary purpose of the safety evaluation was to determine the toxicity and tolerability of this combination therapy. An independent data and safety monitoring committee assessed the tolerability of the study treatments before starting the second treatment course. A preliminary evaluation of tumor response on the cut-off date (December 16, 2019) was also performed. **Results:** From November 2018 to August 2019, 12 pts with HER2+ AGC were enrolled in the safety part (six pts each in cohorts 1 and 2). During the 1st course, all 12 pts experienced at least one adverse event (AE). The most common AEs were peripheral sensory neuropathy (PSN) (n = 4) and leukocytopenia (n = 3) in cohort 1 and PSN (n = 5) and anorexia (n = 4) in cohort 2. AEs of grade ≥ 3 were observed in only one pt in cohort 1 (grade 3 neutropenia). No pt suspended or discontinued study treatments due to AEs. One pt in cohort 1 reduced dose of S-1 due to grade 2 erythema and continued the subsequent courses with the dose. After a median follow-up of 6.1 (range, 3.1–13.3) months, one pt from cohort 1 achieved a complete response, eight pts (four in each cohort) achieved a partial response, and three pts (one in cohort 1 and two in cohort 2) showed stable disease. No progressive disease was observed. **Conclusions:** Both Nivo plus Tmab and either S-1 or Cape plus Ox are tolerable in pts with HER2+ AGC. Both cohorts 1 and 2 have progressed to the expansion part of the study. Clinical trial information: 000034222. Research Sponsor: ONO pharmaceutical co.

4526 **Poster Session (Board #134), Fri, 8:00 AM-11:00 AM**

Assessment of FcgRIIIA single nucleotide polymorphisms (SNPs) on the efficacy of IgG1 monoclonal antibodies (mAbs) in PANGEA study patients (pts) with advanced gastro-esophageal adenocarcinoma (aGEA).

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Background: Targeted therapies (Ttx) have had limited efficacy in aGEA. The phase IIa PANGEA trial assessed the outcomes of pts treated with IgG1 mAbs targeting receptor tyrosine kinases (RTKs) or PD-1 based on predefined molecular groups. The fragment C (Fc) portion of mAbs binds to IgG receptors (FcgR) of immunologic effector cells such as natural killer (NK) cells, leading to antibody-dependent cell-mediated cytotoxicity (ADCC). The FcgR subclass, FcgRIIIA, has genetic variants with different Fc binding affinities. A single nucleotide polymorphism (SNP) in FcgRIIIA substitutes phenylalanine (F) with valine (V) at amino acid position 158, enhancing FcgR's affinity for the IgG1 Fc domain. Pts with V/V or V/F FcgRIIIA allotypes have enhanced NK cell binding affinity compared to the homozygous F/F allotype. We evaluated the association of FcgRIIIA SNPs on Ttx outcomes amongst PANGEA pts and another cohort of aGEA pts treated with IgG1 mAbs. **Methods:** Whole-blood samples were identified from aGEA pts (N = 104), including 70/80 available PANGEA pts, who were treated with an IgG1 mAb (trastuzumab 24, anti-EGFR 21, anti-PD1 30, ramucirumab 48) in at least 1 Ttx line. After lymphocyte DNA extraction, FcgRIIIA genotyping was performed. The Cox proportional hazard model and log-rank tests, adjusted for pt age, were used to assess for an association of genotype with overall survival (OS). **Results:** Of 104 genotyped pts, the F/F, F/V & V/V genotypes were observed at a frequency of 32%, 51% and 17% respectively. There was no significant difference in median OS (mOS) between the F/F, F/V or V/V or comparing F/F vs V/F+V/V overall, nor in the PANGEA-only cohort. A trend of increased mOS was seen in 20 non-PANGEA pts harboring F/V or V/V compared to 14 F/F pts (mOS 43.4 vs 23.1 months, HR 0.41 [0.15-1.14] p = 0.09). However, 3-year OS rates trended higher in V/F+V/V pts (22%, 16/71) compared to F/F pts (7%, 2/33) (p = 0.09). At 3 years, 50% of V/V+V/F non-PANGEA pts were alive versus 13% of F/F pts (p = 0.04), while 13% of V/V+V/F PANGEA pts were alive versus 0% of F/F pts (p = 0.32). **Conclusions:** Amongst pts receiving IgG1 mAbs, the high affinity V FcgRIIIA SNP enriched for a subgroup of 'extreme responders' alive 3 years from diagnosis. Multivariate analyses accounting for baseline characteristics in a larger number of pts are ongoing to further elucidate the role of FcgRIIIA SNPs as predictive biomarkers. These findings may have implications on IgG1 mAb ADCC optimization. Research Sponsor: K23 award CA178203-01A1 from the National Cancer Institute, the University of Chicago Comprehensive Cancer Center Award in Precision Oncology-Cancer Center Support Grant P30CA014599, the Castle Foundation, Live Like Katie Foundation Award, Other Foundation.

4527 **Poster Session (Board #135), Fri, 8:00 AM-11:00 AM**

Tumor response and growth rate of nivolumab treatment in advanced gastric cancer: Real-world data from a large observational/translational study, JACCRO GC-08 (deliver trial).

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Background: Nivolumab (Nivo) demonstrated survival benefit in previously treated gastric cancer (GC) patients (pts), with a response rate (RR) of 11% and a disease control rate (DCR) of 40% (Kang YK, et al. *Lancet* 2017). There are few real-world data of Nivo and its predictive markers are needed in GC. It has been demonstrated that some tumors grow rapidly after Nivo treatment, but the proportion is uncertain. **Methods:** DELIVER trial was a prospective, multicenter, observational/translational study which assessed pts with advanced GC treated with Nivo alone and ECOG Performance Status (PS) 0-2 (UMIN000030850). The aims were to evaluate the efficacy and safety of Nivo in real world, and to discover novel host-related immune-biomarkers (gut microbiome, genetic polymorphism, gene expression, and metabolome) using fecal and blood samples which were collected before and after Nivo treatment. The RR, DCR, progression-free survival, overall survival, and tumor growth rate (TGR) were estimated as the efficacy. The response was evaluated by first imaging based on RECIST version 1.1. The TGR was calculated as a percentage increase in tumor volume during 1 month (Champiat et al. *Clin Cancer Res* 2017). **Results:** A total of 501 pts was enrolled in this study from Mar 2018 to Aug 2019, and 487 pts were evaluable for analysis (median age 70-y, 71% male, ECOG PS0/1/2 42%/44%/14%, tub/por/sig 45%/41%/5%, 21% HER2-pos, 42% pts with ascites). The DCR was 39.2% (95%CI 34.9-43.7) in evaluable pts. In 282 pts with measurable lesions, the RR was 6.7% (95%CI 4.1-10.3) and DCR was 36.5%. Sub-analysis by patient background indicated that DCR was 41% for PS0, 42% for PS1, and 24% for PS2. In addition, the DCR was lower in pts with ascites compared to those without ascites (28.6% vs. 47.0%, $p = 0.005$). The TGR decreased after introduction of Nivo in 124 (56.6%) of 219 evaluable pts for TGR; however, 20.5% pts were identified as experiencing hyper-progressive disease (HPD) which was defined as a $\geq$2-fold increase of the TGR before and after Nivo. When defining HPD as a $\geq$2-fold increase of tumor growth kinetics ratio and 50% increase of tumor burden, 9.6% pts experienced it. **Conclusions:** The real-word data of the large observational trial showed a comparable DCR to that of clinical trial in advanced GC treated with Nivo. This trial revealed the tumor behavior and some pts who experienced rapid tumor growth after Nivo treatment in clinical practice; biomarkers for HPD and the definition should be established. Clinical trial information: UMIN000030850. Research Sponsor: Ono Pharmaceutical and Bristol-Myers Squibb.

4528 **Poster Session (Board #136), Fri, 8:00 AM-11:00 AM**

Evaluation of spatiotemporal heterogeneity of PDL1 expression in gastroesophageal adenocarcinoma (GEA) at baseline diagnosis and after chemotherapy.

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Background: PDL1 expression is a predictive marker for response to anti-PD1/PDL1 agents (IO) for GEA. As a prognostic biomarker, data are conflicting. Molecular heterogeneity of various biomarkers for GEA has been established. To characterize heterogeneity of PDL1 expression and its clinical relevance, we compared PDL1 expression in primary (1^O) and metastatic (met) tumors of newly diagnosed stage IV advanced GEA (aGEA), and before and after chemotherapy treatment (tx) for stage II–IV GEA. We assessed the prognostic relevance of PDL1 expression in aGEA. **Methods:** We retrospectively reviewed a cohort of 130 patients (pts) diagnosed with GEA in 2013–2019, with a total of 328 tumor samples with PDL1 expression data. PDL1 was defined as positive if combined positive score (CPS) was ≥ 1 using the 22C3 pharmDx assay. Analysis was performed by McNemar's test for paired PDL1 and univariate Cox proportional-hazards model for overall survival (OS). **Results:** Of 328 tumors, 45% were PDL1+ and 55% PDL1-. CPS ranged 0–100 (median 1, IQR 0–5), and CPS was ≥ 10 for 19% of tumors. Concordance between PDL1 status of paired baseline 1^O and baseline met tumors was 63% (32/51) (Table). Of 31 PDL1+ baseline 1^O tumors, 52% (16/31) had PDL1- paired baseline met tumors, while of 20 PDL1- baseline 1^O tumors, only 15% (3/20) had PDL1+ paired baseline met tumors. Only 35% (18/51) of met tumors were PDL1+, compared to 61% (31/51) PDL1+ 1^O tumors ($p < 0.003$). Post-tx tumors exhibited 62% (46/74) concordance of PDL1 status compared to pre-tx 1^O tumors. Of 43 PDL1+ baseline tumors, 35% (15/43) were PDL1- post-tx; of 31 PDL1- baseline tumors, 42% (13/31) were PDL1+ post-tx ($p = 0.71$). In pts with aGEA at diagnosis, OS did not significantly differ depending on baseline 1^O tumor PDL1 status (median OS of 17.9 [95% CI 14.6–26.5] months for PDL1- and 16.7 [12.0–26.3] months for PDL1+; $p = 0.6$), nor depending on baseline met PDL1 status. **Conclusions:** PDL1 expression demonstrated notable baseline discordance between 1^O and met tumors, particularly directional from PDL1+ 1^O tumor to PDL1- met. Discordance before and after chemotherapy was also observed, but with similar proportions of PDL1+ pre-tx and post-tx tumors. These findings may have predictive IO therapeutic implications if confirmed in larger independent analyses. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

	Baseline met PDL1-	Baseline met PDL1+	Post-tx PDL1-	Post-tx PDL1+
Baseline 1^O PDL1-	17	3	18	13
Baseline 1^O PDL1+	16	15	15	28

4529 **Poster Session (Board #137), Fri, 8:00 AM-11:00 AM**

Phase II study of intraperitoneal paclitaxel combined with S-1 plus cisplatin for gastric cancer with peritoneal metastasis: SP + IP PTX trial.

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Background: Intraperitoneal (IP) chemotherapy is a promising treatment option for gastric cancer with peritoneal metastasis. Although a phase III study failed to show a statistically significant superiority of IP paclitaxel (PTX) combined with S-1 and intravenous PTX over S-1/cisplatin (SP), the standard of care as a first-line treatment in Japan, the sensitivity analysis suggested clinical efficacy of the IP PTX. Thus, attempts to combine IP PTX with other systemic therapies with higher efficacy have been warranted. After a dose-finding study, we sought to explore efficacy of a new regimen that combined IP PTX with SP. **Methods:** Gastric cancer patients with peritoneal metastasis confirmed by diagnostic imaging, laparoscopy or laparotomy were enrolled in the phase II multi-institutional prospective trial. In addition to the established SP regimen (S-1 administered orally at a dose of 80 mg/m^2 bid for 21 days followed by a 14-day rest and cisplatin administered intravenously at a dose of 60 mg/m^2 on day 8), IP PTX was administered on days 1, 8 and 22 at a dose of 20 mg/m^2. The primary endpoint is overall survival (OS) rate at one year after treatment initiation. Secondary endpoints are progression free survival (PFS), response rate and toxicity. **Results:** Fifty-three patients were enrolled and fully evaluated for OS and toxicity. The median number of courses was 7 (range 1-20). The 1-year OS rate was 74% (95% CI, 60-83%). The median survival time was 19.4 months (95% CI, 16.7 months-). The 1-year PFS rate was 57% (95% CI, 42-69%). The overall response rate was 20% (95% CI, 1-72%) in 5 patients with target lesions. Cancer cells ceased to be detected by peritoneal cytology in 23 (64%) of 36 patients. Fourteen (26%) patients underwent gastrectomy after response to chemotherapy. The incidences of grade 3/4 hematological and non-hematological toxicities were 43% and 47%, respectively. The frequent grade 3/4 toxicities included neutropenia (23%), anemia (29%), diarrhea (13%) and anorexia (17%). Intraperitoneal catheter and implanted port-related complications were observed in 4 patients. There was 1 treatment-related death. **Conclusions:** IP PTX combined with SP is well tolerated and active in gastric cancer patients with peritoneal metastasis. Clinical trial information: UMIN000023000. Research Sponsor: Japan Society of Clinical Oncology.

4530 **Poster Session (Board #138), Fri, 8:00 AM-11:00 AM**

Gastric inflammatory prognostic index (GIPI) to predict efficacy of PD-1/PD-L1 immune checkpoint inhibitors in metastatic gastroesophageal junction (GOJ)/gastric cancer (GC) patients.

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Background: ICIs demonstrated improved overall survival (OS) in heavily pre-treated mGOJ/GC pts. Pts selection exclusively based on PD-L1 tissue expression appears to be suboptimal, despite data from subgroup analyses of KEYNOTE trials. Strong rationale suggests a potential predictive role of inflammatory biomarkers in ICIs treated mGOJ/GC pts. **Methods:** Ten systemic inflammatory markers [platelets, monocytes, neutrophil/lymphocyte ratio (NLR), platelets-lymphocyte ratio, lymphocytes, sum of mononuclear cells, albumin, lactate dehydrogenase, c-reactive protein (CRP) and serum globulin] were retrospectively analyzed at baseline in 57 mGOJ/GC pts with unknown PD-L1 status treated in second-line with ICIs, and correlated with OS. Least Absolute Shrinkage and Selection Operator (LASSO) method was used to select variables (preliminarily subject to optimal coding using HR smoothed curves for OS) with the highest prognostic value. Selected variables were then analyzed in a multivariate Cox Regression Model and used to build a GIPI nomogram. **Results:** NLR and CRP taken as continuous variables and albumin categorized as $<$ vs $>$ 30 g/dL were found as the most meaningful independent predictors of OS and used to build the GIPI nomogram. Nomogram-based lowest (l), mid-low, mid-high and highest (h) risk quartiles were associated with median(m)OS of 14.9, 7.1, 5.6 and 2.1 months (mos), respectively [HR of l vs h 4.94, p 0.0002]. By optimally dichotomizing CRP and NLR, pts with one or more of the following risk factors: NLR $>$6, CRP $>$15 mg/L, albumin $<$30 g/dL (n: 29) had a mOS of 3.9 mos vs 14.2 mos of pts with no risk factor (n: 28) (HR 2.48, p 0.001). **Conclusions:** GIPI, combining NLR, CRP and Albumin, is the first inflammatory index with a significant prognostic value in mOGJ/GC pts receiving second-line ICIs. Its implementation in correlation with PD-L1 expression in the present cohort is ongoing. GIPI merits validation in independent cohorts and prospective clinical trials.
Research Sponsor: None.

4531 **Poster Session (Board #139), Fri, 8:00 AM-11:00 AM**

X versus XELOX versus PF in definitive concurrent chemoradiotherapy (DCRT) for local advanced squamous esophageal cancer (ESCC): Update from a multicenter, open-label, randomized III trial, CRTCOESC trial.

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Background: PF (5-fluorouracil plus cisplatin) is the standard regimen for local advanced ESCC with DCRT. CRTCOESC aims to evaluate the effect and safety of X (capecitabine) regimen versus XELOX (capecitabine plus oxaliplatin) and PF in Chinese local advanced ESCC with DCRT by randomized, open-label, multicenter designed. **Methods:** Patients with ESCC (T2-4N0-2M0) were randomized to 3 groups as X (capecitabine 625mg/m^2, bid d1-5, 6 weeks), XELOX (oxaliplatin: 65mg/m^2, d1, 8, 22, 29; capecitabine: 625mg/m^2, bid d1-5; 6 weeks), or PF (cisplatin: 75mg/m^2 d1, 29, 5-Fu: 750mg/m^2 CIV24h d1-4, d29-32), Intensity Modulated Radiation Therapy (IMRT) was delivered by 50Gy/2Gy currently. In addition, quadratic randomize were done within all groups to decide whether 2 cycles chemotherapy adding or not after DCRT. 2-year OS and Grade 3-5 AEs were the primary endpoints, 2-year PFS and short-term efficacy (STE) as rates of CR and ORR (CR+PR+SD) (confirmed by gastroscopy biopsy at 16 weeks) were the secondary endpoints. **Results:** 244 pts successfully were accrued from 13 centers during 2014.10-2020.1. 209 pts were finished DCRT and 193 were evaluated STE at 16 weeks. 192 and 147 pts were followed up for 1- and 2- years respectively. There were no differences between 3 groups on patients' baseline characters including age, gender, ECGO score, clinical stage, pathology grade and smoking. In X, XELOX and PF groups, the 2-year OS were 63.8% (30/46), 61.5% (32/52) and 62.5% (30/49) (P = 0.973), the median OS were 39.7 (6.567), 40 (5.195) and 34 (5.736) (months, P = 0.703); the incidences of AEs (grade 3-5) were 26.5% (18/68), 33.8% (25/74) and 49.3% (33/67) (P = 0.0193); the 2-year PFS were 54.3% (25/46), 53.8% (28/52) and 51% (25/49) (P = 0.939), the median PFS were 29.06 (6.124), 17.4 (8.745) and 24.833 (6.777) (months, P = 0.811); the CR rate were 43.8% (28/64), 41.4% (29/70), and 42.4% (25/59) (P = 0.964), and the ORR were 85.6%, 88.6%, and 96.6% (P = 0.119), respectively. There were no differences on OS, PFS and rates of CR and ORR between 3 groups but the incidence of AEs in X group was the lowest significantly. Subgroup analysis results shown adding 2 cycles chemotherapy after CRT had both OS and PFS advantages but lacked statistically significance. **Conclusions:** Compared with PF, DCRT with X or XELOX shown lower incidence of AEs and similar OS, PFS and STE. X regimen carried out the lowest AEs incidence. Adding 2 cycles chemotherapy after DCRT seemly had advantages on OS and PFS. Clinical trial information: NCT02025036. Research Sponsor: National Natural Science Foundation of China.

4532 **Poster Session (Board #140), Fri, 8:00 AM-11:00 AM**

Final results of a phase II trial of first-line FOLFIRINOX for advanced gastroesophageal cancers.

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Background: Standard first-line regimens for patients with metastatic gastroesophageal adenocarcinomas have moderate clinical benefit with objective response rates (ORR) of approximately 40-50%. FOLFIRINOX has been shown to be an effective and well-tolerated first line therapy in other GI cancers. In this open-label, single-arm phase II study of patients with advanced gastroesophageal adenocarcinomas, we sought to evaluate the safety and clinical activity of FOLFIRINOX. **Methods:** The primary endpoint was ORR, and secondary endpoints included safety profile, progression free survival (PFS), overall survival (OS), time to progression (TTP), clinical benefit rate (CBR), and duration of response. Estimated sample size included 41 patients with HER2 negative disease with 90% power to detect an ORR$\geq$60% with alpha of 0.10. No enrollment goal was planned for HER2 positive patients, but they were allowed participation to receive study treatment in combination with trastuzumab. Treatment consisted of 400mg/m2 5-FU bolus, 400 mg/m2 leucovorin, 2400 mg/m2 5-FU infusion over 46 hours, 180 mg/m2 irinotecan, and 85 mg/m2 oxaliplatin. Trastuzumab was administered intravenously as a 6 mg/kg loading dose then given 4 mg/kg every 14 days for HER2 positive patients. This trial is registered with ClinicalTrials.gov, NCT01928290. **Results:** From November 2013 to May 2019, 67 patients were enrolled, of which 26 (39%) had HER2 positive disease. Median follow-up was 16.1 months. ORR was 61% (25/41) for HER2 negative and 85% (22/26) for HER2 positive groups. Overall, one patient (2%) had a complete response, 36 patients (69%) had partial responses, and 13 patients (19%) had stable disease for $>$6 months; therefore, CBR was 96%. Median PFS was 11.9 months, median OS was 17.4 months. 41 patients (83.7%) had dose modification or treatment delay with the most common toxicities being neutropenia, diarrhea, peripheral sensory neuropathy, and nausea with no unexpected toxicities. **Conclusions:** FOLFIRINOX is a highly effective three-drug regimen for first-line treatment of advanced gastroesophageal cancer with expected, tolerable toxicities. Clinical trial information: NCT01928290. Research Sponsor: Washington University School of Medicine Internal Funding.

4533 **Poster Session (Board #141), Fri, 8:00 AM-11:00 AM**

Disease-free survival as a surrogate for overall survival in neoadjuvant trials of gastroesophageal adenocarcinoma: Pooled analysis of individual patient data from randomized controlled trials.

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Background: Disease-free survival (DFS) is an appealing surrogate endpoint for overall survival (OS) in trials on neoadjuvant or adjuvant cancer therapy, because it is available faster and with less follow-up effort. The aim of this study was to assess if DFS can be a valid surrogate endpoint for OS when comparing neoadjuvant treatment followed by surgery to surgery alone for gastroesophageal adenocarcinoma. **Methods:** Individual patient data (IPD) from eight randomized controlled trials (n = 1,126 patients) which compared neoadjuvant therapy followed by surgery with surgery alone for gastroesophageal adenocarcinoma were used for the analysis. Correlation between OS-time and DFS-time was calculated. Kaplan-Meier survival curves and corresponding hazard ratios (HRs) for treatment effects were separately determined for each trial. Subsequently, HRs were pooled in a meta-analysis using a random-effects model. An error-in-variables linear regression model was used to compare observed and predicted values. The minimum treatment effect on DFS necessary to predict a non-zero treatment effect on OS was estimated by calculating the surrogate threshold effect. **Results:** OS-time correlated strongly with DFS-time. HRs for OS and DFS were highly similar for all single trials. The meta-analysis yielded almost identical overall HRs for treatment effects on OS and DFS. The determination coefficient for the association between HRs for OS and DFS was 0.912 (95% confidence interval 0.75-1.0), indicating a strong trial-level surrogacy between OS and DFS. The surrogate threshold effect was calculated at 0.79, indicating that a future trial yielding a hazard ratio for the treatment effect on DFS $<$ 0.79 could be expected with a 95% probability to yield a hazard ratio for the treatment effect on OS $<$ 1. **Conclusions:** DFS and OS strongly correlate both after neoadjuvant therapy followed by surgery and after surgery alone for gastroesophageal adenocarcinoma. Likewise, the treatment effects on the two endpoints are very similar. Consequently, DFS can be regarded an appropriate surrogate endpoint for OS in trials on neoadjuvant therapy for gastroesophageal adenocarcinoma. Research Sponsor: None.

4534 **Poster Session (Board #142), Fri, 8:00 AM-11:00 AM**

First-in-human phase I study of BVAC-B cell therapy in HER2-positive advanced gastric cancer.

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Background: BVAC-B is an autologous B cell- and monocyte-based immunotherapeutic vaccine transfected with recombinant HER2/neu gene and loaded with alpha-galactosyl ceramide, a natural killer T cell ligand. It may have activity against HER2/neu positive cancer. Preclinical data in mouse models have shown promising anti-tumor activity by eliciting broad spectrum of immune responses against HER2/neu positive tumor cells. We report here the results of phase 1 study of BVAC-B in HER2 positive advanced gastric cancer. **Methods:** Metastatic gastric cancer with IHC $>$ 1+ of HER2/neu were eligible for enrollment. Two weeks before treatment, subjects were admitted to hospital for collection of PBMC and plasma by lymphapheresis. The PBMC were sent to Cellid for vaccine manufacturing which took a day. BVAC-B was given intravenously at 0, 4, 8, and 12 weeks. Subjects received low (2.5X 10^7 cells/dose), medium (5.0X 10^7 cells/dose) or high dose (1.0X 10^8 cells/dose). Endpoints included safety, tolerability and MTD for phase 2 trial. Exploratory outcomes included immune responses after BVAC-B administration. **Results:** As of January 29, 2020, 8 subjects were treated with BVAC-B at doses of 2.5X 10^7 cells/dose (n=1), 5.0X 10^7 cells/dose (n=1) and 1.0X 10^8 cells/dose (n=6). Median line of therapy at which BVAC-B was administered was 4 (range, 2-9). Mean duration treatment was 1.8 (range 1-4) cycles. The most common treatment related adverse events were fever (n=4, 50%). One subject enrolled in medium dose experienced cytokine release syndrome (G2) with high fever (39.3℃) and hypotension 8 hours after first administration, but was manageable with hydration and supportive management. Other adverse events included increase of AST and ALT (G1, n=1 and G2, n=2), and hypotension (G1, n=1). There were no adverse events which led to treatment discontinuation. Immunologic response analysis showed that BVAC-B induced activation of natural killer T cells, natural killer cells, HER2/neu specific T cells, and release of HER2/neu specific antibody upon vaccinations in few patients who were evaluated. **Conclusions:** BVAC B is feasible and has acceptable toxicity profile. We considered all dose evaluated in this study available for phase 2 study, given that the maximum tolerated dose is expected to exceed the maximum dose administered in this study. For clinically relevant effect, further studies are warranted, including earlier line of exposure to BVAC-B as well as combination treatments. Clinical trial information: NCT03425773. Research Sponsor: Ministry of Trade, Industry & Energy (MOTIE), Korea Institute for Advancement of Technology (KIAT) through the Research and Business Development Program (No. N056300021).

4535 **Poster Session (Board #143), Fri, 8:00 AM-11:00 AM**

Personalized neoantigen/cancer testis antigen nanovaccine (PVAC) mobilize specific therapeutic immunity for high-risk resected gastric cancer.

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Background: 35% of stage IIIB/C Gastric cancer patients will recurrent after D2 gastrectomy within one year. Mutation-derived epitopes (neoantigens) has been demonstrated to induce tumor cell specific immune responses controlling the tumor growth. Nanovaccine can increase antigen presentation efficiency and elicit potent antitumor T cell responses with robust therapeutic efficacy. We hypothesized that vaccination with neoantigens/cancer testis (CT) antigens could expand pre-existing and induce antigen-specific T-cells populations, favouring of tumor control enhancement. Here, we report the first-in-human application of this concept in gastric cancer. **Methods:** Patient-specific mutation-containing neoantigens were selected on the basis of tumour-specific mutations whole-exome sequencing (WES) and RNA sequencing. Cancer testis antigens were obtained according to immunohistochemical staining and HLA-binding affinity prediction. PVAC is an amphiphiles nanovaccine loaded with multiple personalized neoantigens/cancer testis antigens designed to induce antigen specific T cells and associated antitumor responses. PVAC will be administrated to stage IIIB/IIIC gastric carcinoma after six cycles of adjuvant chemotherapy (S-1/Oxaliplatin or S-1/docetaxel). Each patient received PVAC by subcutaneous injection on Days 1, 4, 8, 15, 22, 43, 64, 85, 169, administrated with the adjuvant montanide ISA 51 VG. Safety, immunogenicity and clinical efficacy will be evaluated. **Results:** 25 stage IIIB or IIIC gastric cancer patients were enrolled in this study. Mean age was 54.3 years old (range: 34-70), and ECOG performance scores were 0 or 1. Repeated dosing has been well tolerated with mild local discomfort and no DLTs. Three patients were observed grade 2 local skin reactions in the injection sites. No SAEs related to PVAC have been observed. Among median follow up time of 12.6 months (range: 8.5-25.0 months), only two patients had local recurrence at 24.0 months and 10.5 months after surgery, respectivelt. The rest 23 patients remain disease free on study. Neoantigen specific T cell responses have been detected by IFN-γ Elispot from PBMCs. **Conclusions:** PVAC is a multiple neoantigen/CT antigens nanovaccine that personalizes tumor specific antigens and the individual patient's capacity to respond. Addition of PVAC may prolong progression-free survival (PFS) after the standard of care chemotherapy. Clinical trial information: ChiCTR1800017319. Research Sponsor: the National Natural Science Foundation of China.

4536 **Poster Session (Board #144), Fri, 8:00 AM-11:00 AM**

Camrelizumab combined with FOLFOX as neoadjuvant therapy for resectable locally advanced gastric and gastroesophageal junction adenocarcinoma.

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Background: Neoadjuvant chemotherapy has been demonstrated to improve the pathological complete response(pCR) and 5-year survival rate of patients with locally advanced gastric and gastroesophageal junction adenocarcinoma (GC/GEJC). Immunotherapy has become a new promising treatment for advanced GC/GEJC. Therefore, we intended to evaluate the safety and efficacy of Camrelizumab (anti-PD-1 antibody) combined with FOLFOX as the neoadjuvant therapy for patients with locally advanced GC/GEJC. **Methods:** Eligiblepatients were locally advanced GC/GEJC with clinical stage≥T2 and/or positive lymphoglandula confirmed by endoscopic ultrasonography (EUS) and imaging. They received 4 cycles neoadjuvant therapy which including Camrelizumab(200mg ivgtt D1), FOLFOX(Oxaliplatin 85mg/m^2 ivgtt D1, 5-Fu 400mg/m^2 iv D1, LV 200mg/m^2 ivgtt D1, 5-Fu 2.4mg/m^2 CIV 46 hours) every 14 days. Imaging evaluation was performed in 2-4 weeks after neoadjuvant therapy. Patients without progression disease (PD) received D2 radical gastrectomy. The primary endpoint was pCR, the secondary endpoints were R0 resection rate and safety. **Results:** From July 24 2019 to January 31 2020, 16 patients were eligible. The median age was 57 years (29-72 years). A total of 11(69%) males and 5(31%) females, ECOG PS 0 (n=9, 56%), ECOG PS 1 (n=7, 44%). All the patients completed 4 cycles treatment and none of them was confirmed PD by image. One of the patients refused gastrectomy and withdraw from the study. The other 15 patients underwent operation. Unfortunately, intraperitoneal metastases were confirmed in 2 patients during operation. 13 patients received D2 radical gastrectomy and all of them experienced R0 resection. Among the 13 evaluable patients, 1 patient (8%) was observed pCR, 3 patients (23%) experienced TRG1, 10 patients (77%) achieved stage reduction. Notably, 8 patients (62%) had lymphonodus pCR. The grade 3-4 treatment-related AEs were neutropenia (n=3, 19%), leukopenia (n=2, 13%) and anorexia (n=1, 6%). No serious AEs resulted in termination of treatment. Either severe immune-related AEs or treatment-related death was not observed. **Conclusions:** Camrelizumab combined with FOLFOX as neoadjuvant regimen in patients with locally advanced GC/GEJC showed promising pCR with good tolerance. Clinical trial information: NCT03939962. Research Sponsor: Jiangsu Hengrui Medicine Co., Ltd.

Patient characteristics.

Characteristics	N	%
Clinical stage (T≥3)	16	100
Clinical stage (N≥1)	16	100
HER-2 postive	0	0
MMR deficient	0	0
EBV postive	2	13
PD-L1 CPS<1	7	44
PD-L1 5<CPS≥1	4	25
PD-L1 CPS≥5	5	31

4537 **Poster Session (Board #145), Fri, 8:00 AM-11:00 AM**

The association of tissue tumor mutational burden (tTMB) using the Foundation Medicine genomic platform with efficacy of pembrolizumab versus paclitaxel in patients (pts) with gastric cancer (GC) from KEYNOTE-061.

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Background: KEYNOTE-061 (NCT02370498) was a randomized, open-label, phase 3 study of pembrolizumab vs paclitaxel in pts with advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma with tumor progression after first-line therapy (N = 592). In this analysis, we evaluated tTMB using FoundationOne CDx (F1CDx; Foundation Medicine) in pts with gastric or GEJ cancer in KEYNOTE-061. **Methods:** In pts with evaluable F1CDx tTMB data (n = 204), we analyzed the association of tTMB with confirmed objective response rate (ORR), progression-free survival (PFS), and overall survival (OS) within each treatment arm using one-sided (pembrolizumab) and two-sided (paclitaxel) Wald test nominal *P* for logistic regression (ORR) and Cox proportional hazards regression (PFS; OS) adjusted for ECOG performance status; significance was prespecified at 0.05. The clinical utility of tTMB was assessed using the prespecified cutoff of 10 mut/Mb for F1CDx. Clinical data cutoff: Oct 26, 2017. **Results:** tTMB was positively associated with ORR ($P < 0.001$; AUROC, 0.68), PFS ($P < 0.001$), and OS ($P = 0.003$) with pembrolizumab but not paclitaxel (ORR, $P = 0.047$; AUROC, 0.30; PFS, $P = 0.605$; OS, $P = 0.084$). Pt outcomes by tTMB cutoff are reported in the Table; prevalence of TMB ≥10 mut/Mb was 17%. In pts with microsatellite stable disease-only, HRs (95% CI) by treatment arm for OS by F1CDx cutoff were 0.40 (0.14-1.17) for tTMB ≥10 mut/Mb (n = 21) vs 0.97 (0.70-1.34) for tTMB <10 mut/Mb (n = 168). **Conclusions:** In this exploratory analysis from KEYNOTE-061, tTMB as determined by F1CDx demonstrated a positive association with clinical outcomes with pembrolizumab, but not paclitaxel, in pts with GC; these findings are consistent with those reported with whole exome sequencing. Pembrolizumab demonstrated an OS benefit vs paclitaxel in the subgroup with tTMB ≥10 mut/Mb, which remained when pts with microsatellite instability-high disease were excluded. Clinical trial information: NCT02370498. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

	tTMB <10 mut/Mb, pembrolizumab (n = 88)	tTMB <10 mut/Mb, paclitaxel (n = 81)	tTMB ≥10 mut/Mb, pembrolizumab (n = 20)	tTMB ≥10 mut/Mb, paclitaxel (n = 15)
ORR, % (95% CI)	10.2 (4.8-18.5)	14.8 (7.9-24.4)	40.0 (19.1-63.9)	13.3 (1.7-40.5)
PFS, mo, median (95% CI)	1.5 (1.5-2.1)	3.4 (2.8-4.2)	5.7 (1.5-NR)	6.5 (4.1-NR)
Pembrolizumab vs paclitaxel, HR (95% CI)	1.45 (1.06-1.98)	—	0.69 (0.31-1.52)	—
OS, mo, median (95% CI)	5.1 (3.6-8.6)	7.8 (5.8-9.4)	NR (9.1-NR)	8.1 (6.5-14.4)
Pembrolizumab vs paclitaxel, HR (95% CI)	0.97 (0.70-1.34)	—	0.34 (0.14-0.83)	—

4538 **Poster Session (Board #146), Fri, 8:00 AM-11:00 AM**

PILGRIM: Phase III clinical trial in evaluating the role of hyperthermic intraperitoneal chemotherapy for locally advanced gastric cancer patients after radical gastrectomy with D2 lymphadenectomy(HIPEC-01).

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Background: Gastric cancer remains the 3rd leading cancer related death worldwide due to early disease recurrence. We hypothesize that hyperthermic intraperitoneal chemotherapy (HIPEC) may effectively prevent local regional recurrence for locally advanced gastric cancer patients who received curative intent surgery. **Methods:** Pathology proven gastric cancer patients with clinical T3/T4NxM0 disease are eligible for the study and will be randomized to either control group, who will receive standard radical gastrectomy and D2 lymph node dissection or HIPEC group, who will receive the same surgery and HIPEC with paclitaxel x 2 within the first week after surgery. All patients will receive either XELOX or SOX adjuvant chemotherapy. The primary end point is overall survival. **Results:** 648 patients from 16 high volume gastric medical centers were enrolled between May, 2015 and March, 2019. 331 and 317 patients were randomized to control and HIPEC groups respectively. The median follow-up time is 12.1 months. The common grade 3/4 toxicities ($>$ 5%) in control and HIPEC groups are anemia 6% vs. 4.1%, intraabdominal infection 5.4% vs. 3.8%, pneumonia 9.7% vs. 9.8%, fever 10.6% vs. 11.4% and hypoalbunemia 15.1% vs. 16.7% respectively. All three perioperative death (within 30 days after surgery) occurred in control group. One patient died from duodenum stump leak which led to multiple organ failure. One patient died from anastomotic led to intraabdominal infection and shock. The 3rd death was suicide caused by severe depression. At the time of this report, the number of event has not reached for final efficacy analysis. **Conclusions:** It is safe to administer HIPEC to patients received radical gastrectomy with D2 lymph node dissection within one week of surgery. The primary analysis will be expected in one year. Clinical trial information: NCT02356276. Research Sponsor: The Clinical Research Promotion Project of Guangzhou Medical University for Building High Level University; The Guangzhou High-Level Clinical Key Specialty Construction.

4539 **Poster Session (Board #147), Fri, 8:00 AM-11:00 AM**

Translational analysis of esophageal adenocarcinoma (EAC) patients treated with oxaliplatin and capecitabine (Xelox) +/- the dual ErbB inhibitor AZD8931 in the DEBIOC study.

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Background: The Dual Erb B Inhibition in Oesophago-gastric Cancer (DEBIOC) trial reported an acceptable safety profile for neoadjuvant Xelox +/- AZD8931 but limited efficacy. We utilized EAC patient samples from DEBIOC to evaluate the impact of neoadjuvant Xelox +/-AZD8931 on biological pathways using a unique software driven solution. **Methods:** 24 pre-treatment FFPE EAC biopsies and 17 matched surgical resection specimens were transcriptionally profiled using the Almac Diagnostics XceI Array. Gene expression data was analyzed using the Almac clara^{T} total mRNA report V3.0.0, reporting on 92 gene expression signatures and 7337 single genes associated with 10 key biologies. Paired Wilcoxon tests (5% significance level) were used to evaluate changes in clara^{T} scores pre- and post-treatment. EGFR and Her2 expression were assessed by IHC and FISH. **Results:** 15 patients received Xelox+AZD8931 and 9 Xelox alone. Hierarchical clustering of biopsies identified 4 major clusters: Inflammation active, Genomic Instability active, EGFR & MAPK active, and EMT & Angiogenesis active. Comparison of signature scores pre- and post- neoadjuvant treatment demonstrated a significant reduction in scores relating to DNA damage repair (DDR) deficiency (Almac DNA Damage assay, $p< 0.0001$; BRCAness Profile, $p= 0.0025$; HRD Gene Signature, $p< 0.0001$; BRCA1ness Signature, $p= 0.0004$) and a significant increase in angiogenesis signatures (Almac Angiogenesis Assay, $p= 0.0002$; Angio Predictive G model, $p= 0.0228$; Angiogenesis Signature A, $p= 0.0034$) and EMT signatures (EMT Signature, $p= 0.0031$, EMT Enrichment Score, $p= 0.0013$, Pan-Can EMT Signature B, $p= 0.0001$). Comparing pre- and post-treatment signature scores in patients treated with Xelox +/-AZD8931 revealed a significant reduction in EGFR Sensitivity Signature ($p= 0.0088$), ERBB2-specific Gene Expression Signature ($p= 0.0127$) and Hallmark PI3K-AKT-MTOR Signaling ($p= 0.0195$) in those treated with Xelox + AZD8931 in keeping with the mechanism of action of AZD8931. Downregulation of AKT signaling was confirmed in AZD8931 treated and resistant cell lines. **Conclusions:** We report the use of a novel software tool to apply 92 gene expression signatures to EAC biopsy and resection specimens from the DEBIOC trial to provide insight into mechanisms of action. Neoadjuvant treatment was associated with a reduction in DDR deficiency and an increase in angiogenesis and EMT signatures whilst a reduction in EGFR, Her2 and AKT pathways was noted with AZD8931 treatment. Research Sponsor: AstraZeneca, Other Government Agency, Cancer Research UK, OGcancerNI, Wellcome Trust.

4540 **Poster Session (Board #148), Fri, 8:00 AM-11:00 AM**

Phase Ib/II open-label, randomized evaluation of 2L atezolizumab (atezo) + PEGPH20 versus control in MORPHEUS-pancreatic ductal adenocarcinoma (M-PDAC) and MORPHEUS-gastric cancer (M-GC).

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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 cancers. Within MORPHEUS, atezo (anti–PD-L1) was tested with PEGylated recombinant human hyaluronidase (PEGPH20), an anti–stromal and extracellular matrix modulator, in patients (pts) with metastatic (m) PDAC or advanced/mGC. **Methods:** In 2 separate randomized trials, eligible pts with 2L mPDAC or mGC received atezo (1200 mg IV q3w) + PEGPH20 (3 μg/kg IV on D1, 8, 15). Control tx for M-PDAC (NCT03193190) was mFOLFOX6 or gemcitabine + *nab*-paclitaxel. In M-GC (NCT03281369), control tx was ramucirumab + paclitaxel. Primary endpoints were ORR (investigator-assessed RECIST 1.1) and safety. **Results:** Pts were followed up for ≥ 18 wk in M-PDAC (data cutoff: Aug 5, 2019) and ≥ 24 wk in M-GC (data cutoff, Jul 11, 2019). In M-PDAC, 66 pts received atezo + PEGPH20 and 42 received control in both preliminary and expansion phases. Confirmed ORRs were 6.1% (95% CI: 1.7, 14.8) and 2.4% (95% CI: 0.06, 12.6), respectively. Duration of response ranged from 5.3 to 11.3 mo in tx arm and was 3.9 mo in control. Median PFS was 1.5 mo (95% CI: 1.4, 2.6) and 2.3 mo (95% CI: 1.6, 4.0), respectively. Median OS was 7.1 mo (95% CI: 4.6, 9.5) and 6.8 mo (95% CI: 5.6, 8.3). Updated survival data will be presented. Respectively, 62.2% and 59.5% of pts had Gr 3-4 AEs; Gr 5 AEs were seen in 4.5% and 2.4% of pts; serious AEs (SAEs) occurred in 45.5% and 45.2% of pts; 16.7% and 4.8% of pts had tx-related AEs leading to tx withdrawal. The most common tx-related AEs were myalgia (65.2%) and peripheral edema (28.8%) in the combination arm. In M-GC, 13 pts received atezo + PEGPH20 and 12 received control. Confirmed ORRs were 0% (95% CI: 0, 24.7) and 16.7% (95% CI: 2.1, 48.4), respectively. Gr 3-4 AEs were seen in 30.8% and 75.0% of pts, respectively. No Gr 5 AEs occurred in either arm. SAEs occurred in 7.7% and 50.0% of pts, respectively. Only 1 pt in the control arm had a tx-related AE leading to tx withdrawal. While tumor hyaluronan (HA) appears to be associated with poor prognosis in the M-PDAC control, there was no clear association between HA levels and response to atezo + PEGPH20. PK data will also be presented. **Conclusions:** Limited efficacy was seen with the chemotherapy-free combination of atezo + PEGPH20 in PDAC. No efficacy was seen in GC. The safety of atezo + PEGPH20 was consistent with each agent's known safety profile; no new safety signals were identified. Clinical trial information: NCT03193190. Research Sponsor: F. Hoffmann La-Roche Ltd.

4541 **Poster Session (Board #149), Fri, 8:00 AM-11:00 AM**

Enhanced efficacy of anti-VEGFR2/taxane therapy after progression on immune checkpoint inhibition (ICI) in patients (pts) with metastatic gastroesophageal adenocarcinoma (mGEA).

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Background: Anti-VEGFR2 therapy (ramucirumab/paclitaxel [RAM/TAX]) and ICI are approved as 2nd- and 3rd-line therapy (Tx), respectively, for pts with mGEA. We unexpectedly saw durable responses in 2 pts on RAM/TAX after progression on an ICI trial (KN-059; PMID 29674442). We performed a pilot to examine the clinical activity of ICI followed by RAM/TAX. Then we retrospectively compared the outcomes of pts who received this serial Tx to pts who received RAM/TAX without prior ICI. **Methods:** All pts with mGEA at Mayo Clinic who received RAM/TAX (2014-19) were included (N = 87). Outcomes were best objective response rate (ORR: complete [CR] or partial response) per RECIST1.1, progression-free survival (PFS), duration of response (DOR), and overall survival (OS). Chi square and multivariate (MV) logistic and Cox regression were used. **Results:** 15 consecutive pts with measurable mGEA received ICI immediately followed by RAM/TAX after irRECIST progression. Most pts (95%) did not respond to ICI. Yet on RAM/TAX, 100% (15/15) had tumor reduction (range -8% to -100%) with an ORR of 73% (11/15), including 3 CRs. In these pts (who received ICI followed by RAMTAX), PFS on RAMTAX was longer than on last chemotherapy before ICI (12.3 vs 3.0 m, $P < .001$). Outcomes on RAM/TAX in these pts were significantly better than in pts who received RAM/TAX alone (see Table). Associations were strengthened after adjusting for total lines of Tx, line of Tx of RAM/TAX, age, and ECOG PS. Exploratory analysis of paired tumor biopsies collected pre-ICI and on RAM/TAX in a small subset revealed that the frequency of intratumoral immunosuppressive FOXP3^{+} Tregs decreased on RAM/TAX, whereas the frequency of antitumor CD8^{+} T cells was preserved. **Conclusions:** RAM/TAX immediately preceded by ICI was associated with significantly higher OS, ORR, and DOR than RAM/TAX alone, suggesting ICI may enhance efficacy of subsequent anti-VEGFR/taxane therapy. This novel sequence of therapy will be tested prospectively in a new randomized phase 2 trial (NCT04069273).
Research Sponsor: None.

	RAM/TAX ...		
	With preceding ICI *n = 19* [a]	Without preceding ICI *n = 68*	p
ORR	58%	18%	< .001
DOR	10.5 m	4.3 m	.021
OS	15.0 m	7.6 m	.003

[a]Includes 4 pts with non-measurable disease

4543 **Poster Session (Board #151), Fri, 8:00 AM-11:00 AM**

Impact of frontline doublet versus triplet therapy on clinical outcomes: Exploratory analysis from the RAINBOW study.

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Background: Treatment (tx) of advanced gastric cancer (GC/GEJ) is highly heterogeneous, with substantial variability in tx patterns. Frontline tx choice may affect outcomes of subsequent tx, thereby influencing choice/efficacy of second-line (2L) tx. In RAINBOW, 2L ramucirumab(R) plus paclitaxel(P) significantly improved overall survival (OS) of patients (pts) with GC/GEJ. Here we explore efficacy, safety and quality of life (QoL) based on prior tx. **Methods:** Pts were grouped into doublet (DB) or triplet (TP) regimens based on prior cytotoxic tx received. OS and PFS were estimated using Kaplan-Meier method and tx effects on OS and PFS were evaluated by Cox PH model; safety and QoL were assessed descriptively for DB vs TP. **Results:** Use of DB and TP was similar between arms, with 23% in R+P and 26% in placebo (PB)+P arm receiving TP. Baseline characteristics were generally balanced between tx arms within DB and TP subgroups, with majority of TP administered in western regions (91%). Pts ≥65 years of age was 40% for DB and 28% for TP. DB pts (n = 498; 75%) received S1+cis (n = 97, 15%) and cape+ox (n = 71; 11%) as most common prior tx, while TP pts (n = 163; 25%) received epi+cape+ox (n = 74, 11%) and epi+cis+5FU (n = 53, 8%). Similar to ITT population, R+P improved OS and PFS in both DB and TP subgroups (Table). Patterns of overall and Grade ≥3 TEAEs between arms were similar regardless of prior tx. Higher rates of serious TEAEs were reported in TP pts (57%, 49%) than DB pts (44%, 40%) in R+P and PBO+P arms, respectively. Similar trend was observed for TEAEs leading to discontinuation for TP (40%, 30%) vs DB (29%, 22%) in respective tx arms. Baseline QoL scores were similar between tx arms within subgroups, but mean scores were > 5 points worse (range 0-100) for prior TP for role functioning, fatigue, pain, and appetite loss. Changes in mean scores were generally similar between arms and within subgroups. **Conclusions:** This exploratory analysis of RAINBOW suggests that although safety-related outcomes were less favorable in pts with prior TP, regardless of tx arm, similar improvements in efficacy were noted for R+P irrespective of prior DB or TP. Clinical trial information: NCT01170663. Research Sponsor: Eli Lilly and Company.

	Received prior DB		Received prior TP		ITT	
	R+P (N = 253)	PB+P (N = 246)	R+P (N = 76)	PB+P (N = 87)	R+P (N = 330)	PB+P (N = 335)
mOS, mo	9.8	7.8	8.1	5.5	9.6	7.4
(95%CI)	(9.0, 11.2)	(6.9, 9.0)	(6.0, 11.0)	(4.2, 7.5)	(8.5, 10.8)	(6.3, 8.4)
HR (95%CI)	0.86 (0.70, 1.05)		0.69 (0.49, 0.98)		0.81 (0.68, 0.96)	
mPFS, mo	4.4	2.9	4.6	2.9	4.4	2.9
(95%CI)	(4.2, 5.4)	(2.8, 3.6)	(3.8, 5.6)	(2.3, 3.5)	(4.2, 5.3)	(2.8, 3.0)
HR (95%CI)	0.65 (0.54, 0.79)		0.59 (0.41, 0.85)		0.64 (0.54, 0.75)	

4544 **Poster Session (Board #152), Fri, 8:00 AM-11:00 AM**

Impact of body measurements (BM) on overall survival (OS) and quality of life (QoL) in real-world patients (pts) with metastatic esophageal cancer.

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Background: Body fat and muscle influence prognosis in many cancer types. However, this association is unclear for real-world MEC pts, who are often in worse performance status than their previous baseline. In addition, the relationship of BM at presentation and QoL is unknown. We used real-world MEC pts to assess the importance of BM in OS and QoL. **Methods:** BM were done at baseline computed tomography in MEC pts, treated from 2006-2014 at the Princess Margaret Cancer Centre. Two radiologists (correlation 0.9-1.0) assessed L3 level using SliceOMatic to determine Skeletal Muscle Index (SMI - muscle area at L3 normalized by height), Visceral Adiposity Tissue (VAT), and Subcutaneous Adiposity Tissue (SAT). We used previously published cut-offs for sarcopenia based on sex and BMI, and the highest tertile as the cut-off for adiposity. We used prospectively collected QoL surveys including EuroQol 5D-5L (EQ5D) and the Functional Assessment of Cancer Therapy – Esophageal (FACT-E). **Results:** Of 200 pts, 164 (82%) were male, 180 (92%) were non-Asian; mean age was 62 y; ECOG: 0-1 = 142 (71%), 2 = 58 (29%); 69% had adenocarcinoma; 5% were underweight, 44% normal weight, 30% overweight, and 21% obese. 40 (20%) pts completed QoL measures. We found that 104 (52%) were sarcopenic at baseline, 66 (33%) had high VAT, and 67 (34%) had high SAT. A multivariable Cox model showed that sarcopenia and VAT were independent prognostic variables for three-year OS: sarcopenia increased the risk of death by 50% (adjusted hazard ratio, aHR 1.50, p 0.02), whereas every 100-cm^2 increase in VAT improved OS by 24% (aHR 0.76, p 0.03). Finally, sarcopenic pts had significantly worse physical well-being (p 0.01) on FACT-E after adjusting for sex and age. Numerically, the EQ5D also showed lower scores in sarcopenic pts but this was not statistically significant (p 0.18). **Conclusions:** In MEC pts, sarcopenia and low visceral adiposity result in worse OS; sarcopenia is also significantly associated with poor QoL. Future work will need to focus on potential rehabilitation strategies such as nutritional support and exercise training to offset the poor prognosis associated with sarcopenia and reduced adiposity. Research Sponsor: None.

	aHR (95% CI)	P-value
Sarcopenic (ref: non-sarcopenic)	1.50 (1.0-2.1)	0.02
VAT (per 100cm2)	0.97 (0.9-0.9)	0.03
SAT (per 100cm2)	1.01 (0.9-1.0)	0.39
BMI < 18.5 (ref: 18.5-24.9)	1.36 (0.6-2.8)	0.41
BMI 25-29.9 (ref: 18.5-24.9)	0.81 (0.5-1.2)	0.35
BMI 30+ (ref: 18.5-24.9)	1.28 (0.7-2.2)	0.39

Cox model, OS adjusted for age, sex, ECOG, number of metastatic sites.

4545 **Poster Session (Board #153), Fri, 8:00 AM-11:00 AM**

Final analysis of single-arm confirmatory study of definitive chemoradiotherapy including salvage treatment in patients with clinical stage II/III esophageal carcinoma: JCOG0909.

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Background: Definitive chemoradiotherapy (dCRT) consisting of 5-fluorouracil (5-FU) and cisplatin (CDDP) with 60 Gy radiotherapy (RT) for clinical (c) Stage II/III esophageal carcinoma (EC) is a standard treatment for patients (pts) refusing surgery (S) in Japan based on the previous trial (JCOG9906). However, poor survival, high incidence of late toxicities, and severe complications of salvage S are problems. We conducted a single-arm confirmatory study of CRT modifications including salvage treatment (ST) to reduce CRT toxicities and facilitate ST to improve survival. We reported the 3-year survival at 2018 ASCO Annual Meeting. We report the final data after 5-year follow-up. **Methods:** EC pts with cStage II/III (UICC 6th, non-T4), PS 0-1, and age 20-75 years were eligible. Chemotherapy (CT) was CDDP (75 mg/m^2 on days 1, 29) and 5-FU (1000 mg/m^2/d on days 1-4, 29-32). RT was administered to a total dose of 50.4 Gy with elective nodal irradiation of 41.4 Gy. Good responders after dCRT received additional 1-2 cycles of CT. For residual or recurrent disease, salvage endoscopic resection (ER) or S was performed based on the prespecified criteria. Planned sample size was 95, with one-sided alpha of 5% and power of 80%, expected and threshold 3-year overall survival (OS) as 55% and 42%. Key secondary endpoint was ST related toxicity. Final analysis was planned after 5-year follow-up for all pts. **Results:** From 4/2010 to 8/2014, 96 pts were enrolled, two were ineligible and 94 were included in efficacy analysis (cStage IIA/IIB/III, 22/38/34). Complete response was achieved in 55 pts (59%). Salvage ER and S were performed in 5 (5%) and 27 pts (29%). R0 resection of salvage S was achieved in 23 (85%). With a median follow-up of 5.95 years, 3- and 5-year OS was 74.2% (90% CI 65.9-80.8%) and 64.5% (95% CI 53.9-73.3%). 5-year progression-free survival and esophagectomy-free survival were 48.3% (95% CI 37.9-58.0%) and 54.9% (95% CI 44.3-64.4%). 5-year OS after salvage S was 31.0% and hazard ratio of R1-2 to R0 was 5.635 (95% CI: 1.818-17.467). No complications occurred after salvage ER. Five pts (19%) showed $\geq$ grade 3 operative complications and 1 treatment related death due to bronchus-pulmonary artery fistula occurred after salvage S. Only 9 pts (9.6%) showed grade 3 late toxicities. And no late operative complications more than grade 3 were observed. **Conclusions:** This combined modality treatment of dCRT with ST showed acceptable toxicities, favorable 5-year survival, and promising esophageal preservation. Clinical trial information: jRCTs031180110. Research Sponsor: National Cancer Center Research and Development Funds.

4546 **Poster Session (Board #154), Fri, 8:00 AM-11:00 AM**

Evaluation of spatiotemporal heterogeneity of tumor mutational burden (TMB) in gastroesophageal adenocarcinoma (GEA) at baseline diagnosis and after chemotherapy.

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Background: Tumor mutational burden (TMB) may be a predictive marker for response to anti-PD1/PDL1 agents (IO). Molecular heterogeneity of various biomarkers for GEA has been established. To characterize heterogeneity of TMB and its clinical relevance, we compared TMB in primary (1^O) & metastatic (met) tumors at baseline newly diagnosed stage IV advanced GEA (aGEA), and before & after chemotherapy treatment (tx) for stage II–IV GEA. We assessed the prognostic relevance of TMB in aGEA. **Methods:** We retrospectively reviewed a cohort of 127 patients (pts) diagnosed with GEA in 2012–2019, for a total of 280 tumor samples with TMB data. TMB level was defined as low ($\leq$5/Mb), intermediate (int) ($>$ 5/Mb, $\leq$15/Mb), or high (hi) ($\geq$15/Mb), determined by Foundation One. Analysis was performed by Fisher's exact test for PDL1/TMB, McNemar's test for paired TMB, and univariate Cox proportional-hazards model for overall survival (OS). **Results:** Of 280 tumors, 50% (140/280) had low TMB, 45% (125/280) int TMB, & 5% (15/280) hi TMB. TMB ranged 0–58.6/Mb (median 5.3/Mb). Of tumors with hi TMB, 53% (8/15) were MSI-Hi, while of MSI-Hi tumors, 100% (8/8) were TMB hi. TMB level did not correlate with PDL1 status (p= 0.83). Concordance between TMB levels of paired baseline 1^O and baseline met tumors was 66% (29/44) (Table). TMB level was lower in the met than in the 1^O in 23% (10/44) of cases, and higher in the met in 11% (5/44). Of 4 TMB hi baseline 1^O tumors, 2 were not TMB hi in the met; of 40 TMB low/int baseline 1^O tumors, 0 were TMB hi in the met (p= 0.16). Post-tx tumors exhibited 71% (42/59) concordance of TMB levels compared to pre-tx 1^O tumors. Of 2 TMB hi baseline tumors, 1 was not TMB hi in the post-tx tumor; of 57 TMB low/int baseline tumors, 0 were TMB hi in the post-tx tumor (p= 0.32). In pts with aGEA at diagnosis, OS did not significantly differ depending on baseline 1^O tumor TMB level (median OS of 21.4 [95% CI 15.4–27.9] months for TMB low, 14.6 [10.9–23.5] months for TMB int, and 9.6 [3.9–NA] for TMB hi; p= 0.3), nor depending on baseline met TMB level. **Conclusions:** Notable baseline spatial discordance of TMB was observed, particularly TMB hi 1^O to low/int met. Discordance was also observed before & after tx, without significant increase towards TMB hi temporally. Spatiotemporal heterogeneity may impact the role of TMB as a predictive biomarker & warrants further study. Research Sponsor: U.S. National Institutes of Health, Other Foundation.

	Baseline met TMB low	Baseline met TMB int	Baseline met TMB hi	Post-tx TMB low	Post-tx TMB int	Post-tx TMB hi
Baseline 1^O TMB low	16	5	0	21	7	0
Baseline 1^O TMB int	8	11	0	9	20	0
Baseline 1^O TMB hi	1	1	2	0	1	1

4547 **Poster Session (Board #155), Fri, 8:00 AM-11:00 AM**

Morphologic and molecular analysis of early-onset gastroesophageal adenocarcinomas.

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Background: The incidence of early-onset gastroesophageal adenocarcinomas (EO-GEA) is increasing, and these tumors now constitute $>$ 30% of all gastroesophageal cancers. Besides hereditary gastric cancer syndromes, which form ~3% of EO-GEA, the morphologic and molecular spectrum of these tumors is not well-studied. **Methods:** Next-generation sequencing (NGS) data obtained from routine clinical care from patients with EO-GEA, defined as age $\leq$50 years, from 3 tertiary care centers was evaluated and compared with tumor profiles of 2,081 patients with GEA from cBioPortal for Cancer Genomics. Available histologic slides were reviewed, and the tumors were classified into Lauren and WHO subtypes. Tumor-detected pathogenic variants of potential germline origin were identified from the NGS data. **Results:** The study cohort was formed by 79 patients with gastroesophageal (42%) and gastric (58%) adenocarcinoma. The most commonly mutated genes included *TP53* (28.5%), *CDH1* (10%), *ARID1A* (5%), *KRAS* (3.9%) and *PIK3CA* (3.9%). EO-GEA were less likely to harbor *TP53* (28.5% vs. 57.5%, p 0.003) and *ARID1A* (5% vs. 20.6%, p 0.002) mutations when compared with cBioPortal data. Based on the Lauren scheme, the tumors were classified into intestinal (40%), diffuse (24%), mixed (12%), and indeterminate (15%) subtypes. Driver mutations in *CDH1*, *TP53*, *FBXW7*, *BAP1* genes were seen in diffuse/mixed subtype, and *TP53*, *ARID1A*, *KRAS*, *PIK3CA*, *APC*, *ATM*, *NBN*, *MUTYH* genes in intestinal subtype. The indeterminate subtype showed *TP53* mutations and additional alterations, including *SMARCB1*/*SMARCA4* loss leading to rhabdoid/undifferentiated morphology. *ERBB2* amplification was more likely to be present in intestinal and indeterminate subtypes (p = 0.003).*CD274* amplification/PD-L1 expression was more likely to be present in indeterminate subtype ($p < 0.0001$). Potential germline variants included mutations in gastric cancer susceptibility genes such as *CDH1* (2.5%) and *APC* (1%), and other cancer susceptibility genes such as *ATM* (4%), *NBN* (1%), *MUTYH* (1%) and *POLD1* (1%). **Conclusions:** The molecular profile of EO-GEA is distinct from traditional gastric cancers. Histologic subtypes of EO-GEA correlate with distinct genomic alterations. Our findings also support multigene germline panel testing in parallel for patients with EO-GEA. Research Sponsor: None.

Perioperative FLOT in elderly patients with resectable gastric cancer: Subgroup analysis from the observational RealFLOT study.

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Background: The treatment strategy for patients with resectable gastric cancer changed in the last few years with perioperative treatments. FLOT regimen (fluorouracil, oxaliplatin, docetaxel) turned out to be feasible and effective, offering significant improvement in survival outcomes. However, the safety profile of triplet therapies for elderly patients deserves a special attention and, consequently, the best treatment strategy for these patients is still debated. **Methods:** Focusing on the elderly patient population (age ≥65 years), real-world data from patients with resectable gastric or gastro-oesophageal junction (GEJ) adenocarcinoma (T≥2 and/or N+) enrolled in the observational RealFLOT study were collected. **Results:** A total of 206 patients with resectable gastric or GEJ adenocarcinoma received perioperative FLOT at 15 Italian centers in routine clinical practice, between September 2016 and September 2019. The median age was 63 years (range 36-77) and 43% of patients enrolled (n = 89) were ≥65 years. Among elderly patients, 46 (52%) received FLOT for at least 4 full-dose cycles in the preoperative phase, 82 (92%) underwent surgery, and 56 (62%) started the postoperative phase. The primary end point of the study, pathological complete response (pCR) rate, was similar among patients aged ≥65 and < 65 (6.7% vs 7.7%, respectively). The distribution of pathological stages did not differ according to age (p = 0.473), and disease-free survival (DFS) is unrelated to the age of patients (log-rank 0.57; p = 0.89). The incidence of grade (G) 3-4 adverse events (AEs) was similar in the two age groups (Table) and the 30-day mortality rates after surgery did not differ according to age. **Conclusions:** FLOT regimen demonstrated to be feasible and safe in elderly patients since no differences were observed in terms of pCR, DFS and safety profile according to age. Research Sponsor: None.

Preoperative and postoperative G3-4 AEs registered.

Preoperative	Patients ≥65 (n = 89)	Patients < 65 (n = 117)
- Hematological	17%	22%
- Gastrointestinal	10%	4%
Postoperative	**Patients ≥65 (n = 56)**	**Patients < 65 (n = 86)**
- Hematological	14%	19%
- Gastrointestinal	9%	10%

4549 **Poster Session (Board #157), Fri, 8:00 AM-11:00 AM**

Interim safety analysis of the DANTE trial: Perioperative atezolizumab in combination with FLOT versus FLOT alone in patients with resectable esophagogastric adenocarcinoma—A randomized, open-label phase II trial of the German Gastric Group at the AIO and SAKK.

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Background: The DANTE study evaluates atezolizumab in the perioperative treatment of locally advanced, potentially resectable gastric or GEJ adenocarcinoma in combination with perioperative FLOT. Here, we report the protocol-defined interim safety analysis. **Methods:** DANTE is a multinational, prospective, multicenter, randomized, investigator-initiated, open label phase II trial. Patients (pts) with locally advanced, potentially resectable adenocarcinoma of the stomach and GEJ (≥cT2 and/or N-positive) without distant metastases are enrolled. Pts are randomized 1:1 to 4 pre-operative 2-week cycles of FLOT followed by surgery and 4 additional cycles of FLOT plus atezolizumab at 840 mg every 2 weeks, followed by a total of 8 additional cycles of atezolizumab at 1200 mg every 3 weeks as monotherapy (arm A) or FLOT alone (arm B). Primary endpoint is time to disease progression or relapse after surgery (PFS/DFS). **Results:** Recruitment started in Sep 2018; by Feb 2020, a total of 175 pts have been randomized. This analysis is based on the first 40 pts (20 pts in each arm). The pts had a median age of 62 y and 75% of pts had an ECOG PS of 0 in both arms. The cohort was well balanced in terms of tumor location and clinical stage. 5% of the 40 patients (overall 7.4% of 175 pts enrolled) showed microsatellite instability. 90% of pts enrolled completed all pre-operative cycles in each arm. Total number of adverse events with relation to study treatment was 154 in arm A and 148 in arm B. Total number of serious adverse events (SAE; related or not) was 16 in Arm A and 14 in arm B. 20% of pts in each arm had an SAE due to perioperative morbidity. No surgical mortality was observed. 18 and 19 pts proceeded to operation in arms A and B, respectively. Premature treatment discontinuation occurred in 2 pts in each arm: disease progression (1) and deterioration of general health condition (1) in arm A; and pts' wish (1) and death (1) in arm B. Median hospitalization time was 15 days in arm A and 16 days in arm B. **Conclusions:** Perioperative atezolizumab plus FLOT is feasible and safe. The study continues recruitment. Clinical trial information: NCT03421288. Research Sponsor: Roche.

4550 **Poster Session (Board #158), Fri, 8:00 AM-11:00 AM**

A population-based study on gender differences in tumor and treatment characteristics and survival of curable gastroesophageal cancer.

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Background: Although curative treatment options for gastroesophageal cancer are identical for men and women, outcomes may vary. This study examined differences in tumor and treatment characteristics and survival between men and women with potentially curable gastroesophageal cancer. **Methods:** Nationwide data was acquired from the Netherlands Cancer Registry. Patients with a potentially curable gastroesophageal carcinoma (cT1-T4a or cTx, any cN, cM0 or cMx) diagnosed between 2006 and 2017 were selected. Patient stratification was performed for tumor location and histology. The primary endpoint, relative survival, was compared between men and women with esophageal adenocarcinoma (EAC), esophageal squamous cell carcinoma (ESCC) and gastric adenocarcinoma (GAC), adjusted for the normal life expectancy for men and women separately. **Results:** In total, 13,391 patients with an EAC (79.1% men), 5,103 patients with an ESCC (54.7% men), and 8,149 patients with a GAC (60.1% men) were included. Women with gastroesophageal cancer were older than men. Lower cT-stages were observed in women with EAC and ESCC (both $p < 0.001$) and lower cN-stages were observed in women in all groups, although clinical T- and N-stage were more frequently graded as cTx and cNx in women. In women, EAC tumors were less frequently located in the distal esophagus (70.4% vs. 58.6%, $p < 0.001$), ESCC tumors had a more proximal tumor location ($p < 0.001$), and GAC tumors were more frequently located at the antrum (32.3% vs. 37.2%, $p < 0.001$). For EAC and GAC, but not for ESCC, men were more frequently allocated to a potentially curative treatment; endoscopic resection, surgical resection or definitive chemoradiotherapy (EAC: 74.6% vs. 60.1%, $p < 0.001$; GAC: 69.0% vs. 65.4%, p 0.001; ESCC: p 0.117). An inferior 5-year relative survival was observed in women with EAC (34.3% vs. 30.1%, $p < 0.001$) and GAC (36.1% vs. 33.2%, p 0.016). In women with ESCC a superior 5-year relative survival was observed (24.4% vs 28.5%, p 0.001). **Conclusions:** Remarkable differences in 5-year relative survival were observed between men and women with gastroesophageal cancer, in addition to important differences in tumor stage, tumor location and treatment. Strikingly, men with esophageal and gastric adenocarcinoma were more frequently allocated to a potentially curative treatment compared to women. These findings illustrate the need for further exploration and consideration of gender differences in gastroesophageal cancer treatment. Research Sponsor: None.

4551 **Poster Session (Board #159), Fri, 8:00 AM-11:00 AM**

Diagnostic accuracy of CT-staging of advanced gastric cancer following neoadjuvant chemotherapy.

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Background: Neoadjuvant or perioperative chemotherapy has been accepted as a standard treatment globally in patients (pts) with locally advanced gastric cancer (LAGC). In PRODIGY phase III study (n = 530), we have demonstrated that neoadjuvant chemotherapy with DOS regimen (docetaxel, oxaliplatin, S-1) led to significant tumor downstaging and improved PFS in Korean LAGC pts (Kang, et al. ESMO 2019). Although CT has been performed to re-stage the tumor after neoadjuvant chemotherapy, there has been a relative paucity of diagnostic accuracy data. This study is to evaluate the diagnostic performance of restaging of LAGC after neoadjuvant chemotherapy using CT in PRODIGY study population. **Methods:** Of 266 pts, who had been diagnosed LAGC of T2-4 or N+ stage as assessed with CT and randomized to neoadjuvant chemotherapy arm (CSC) in PRODIGY study, 214 pts underwent gastrectomy were included in this analysis. The post-chemotherapy T- and N- stage was determined based on CT scan taken just prior to surgery and compared with the pathologic stage (AJCC 7th edition). Two experienced radiologists independently evaluated depth of primary tumor and reached consensus if any discrepancy between two readers. Diameter of short axis of the largest regional lymph node was measured to predict metastatic lymph node. Result of histopathologic T- and N-staging using surgical specimen was used as reference standard. **Results:** The study cohort consisted of pathologic T0 (n = 22), T1(n = 39), T2(n = 31), T3(n = 79), and T4(n = 43). The overall diagnostic accuracy of CT was 45%. For each T-stage, accuracy of T0,T1,T2,T3, and T4 was 0%, 26%, 29%, 55% and 79%, respectively. Rate of over- and under- staging was 47% and 8%, respectively. Accuracy for prediction of downstaging to early gastric cancer (T0-T1) was 83%. Interobserver agreement of T-staging was moderate (k = 0.41). There were 98 patients of N+ and 116 patients of N- at histopathology. Area under the curve of receiver operating characteristics to differentiate lymph node metastasis was 0.63. Sensitivity and specificity of size criteria of the largest lymph node (cut off value: $>$ 6mm, $>$ 7mm, and $>$ 8mm) to predict pathologic N+ were 90% and 17%, 78% and 34%, and 68% and 51%, respectively. **Conclusions:** Re-staging using CT after neoadjuvant chemotherapy showed suboptimal accuracy and over-staged residual tumor. However, it predicted downstaging of gastric cancer with high accuracy. Research Sponsor: None.

4553 **Poster Session (Board #161), Fri, 8:00 AM-11:00 AM**

Prediction of esophageal fistula from esophageal cancer CT images using multi-view multi-scale attentional convolutional neural network (MM-Atten-CNN).

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Background: We aimed to propose a risk model based on MM-Atten-CNN for predicting esophageal fistula in patients with esophageal cancer (EC) from computerized tomography (CT) -based radiomics. **Methods:** EC patients who didn't received esophageal surgery between July 2014 and August 2019 were collected. Of these, 186 patients (cases) who developed esophageal fistula were enrolled and compared with 372 controls (1:2 matched with the diagnosis time of EC, sex, marriage, and race). All 558 patients were divided into training set (n = 390) and validation set (n = 168) randomly. The MM-Atten-CNN risk model was trained over 2D slices from nine views of planes, where there were three patches of contextual CT, segmented tumor and neighbouring information in each view. In the training set (130 cases and 260 controls), data augmentation was performed including pixel shifting [-10, -5, +5, +10] and rotation [-10, +10]. In total, there were (130+260) *16*2 = 12480 subjects used for training. Finally, the risk model was validated in the validation set (56 cases and 112 controls) and measured by accuracy (acc), sensitivity (sen), and specificity (spe). **Results:** The developed risk model achieved (acc, sen, spe) of (0.839, 0.807, 0.926), which were more predictive for the occurrence of esophageal fistula when compared to CNN models using single coronal view (acc 0.763, sen 0.581, spe 0.837), multi-view 2D contextual CT slices (acc 0.779, sen 0.656, spe 0.896), and 3D CNN using contextual CT volumes (acc 0.781, sen 0.689, spe 0.852). **Conclusions:** MM-Atten-CNN CT-based model improved the performance of esophageal fistula risk prediction, which has the potential to assist individualized stratification and treatment planning in EC patients. Research Sponsor: None.

PET-directed chemoradiation (CRT) with induction FOLFOX compared to induction carboplatin/paclitaxel (CP) in patients with locally advanced esophageal adenocarcinoma (EA).

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Background: Induction chemotherapy with PET-directed CRT and surgery is the standard treatment for locally advanced EA at our institution. Following results of the CALGB 80803 trial, FOLFOX has recently replaced CP as the preferred induction regimen. **Methods:** We retrospectively evaluated patients with locally advanced EA treated with induction CP vs FOLFOX, followed by trimodality therapy between January 2010 and June 2019. Patients treated with CP with RT followed by surgery without induction chemo were also included. We compared pathological complete response (pCR) and near pCR (ypN0 with ≥90% response) rates in the induction FOLFOX group to the induction CP and no-induction groups. Univariable and multivariable analyses were used to adjust for confounding factors. Disease-free survival (DFS) was estimated by the Kaplan-Meier method and compared between groups using max-combo weighted log rank test. **Results:** 445 patients were included. Patients in the induction FOLFOX group had significantly higher pCR and near pCR rates vs induction CP patients. Notably, pCR rate was 38% among FOLFOX PET responders vs 19% in non-responders. In multivariable analysis, compared to induction CP, induction FOLFOX administration was an independent predictor of near pCR (OR: 2.22, 95%CI: 1.20-4.20, p = 0.012). Compared to 24% pCR rate among no-induction patients, induction FOLFOX pCR rate was slightly higher at 32%. DFS by 2-years was higher in induction FOLFOX compared to no-induction-treated patients (62% vs. 42%, p = 0.05). Postoperative complication rates were similar among the three groups. **Conclusions:** PET-directed CRT with FOLFOX instead of CP improves pCR and near pCR rates. Improved DFS was observed in the FOLFOX vs no-induction patients. Longer follow-up is needed to confirm any survival benefits. Research Sponsor: None.

Treatment Group	Induction FOLFOX	Induction CP	p-value (Induction FOLFOX vs Induction CP)	No-induction	p-value (Induction FOLFOX vs no-induction)
Total Number	71	237		137	
Number of PET Responders	50	140		N/A	
pCR: n (%)	23 (32.4%)	38 (16.0%)	0.004	33 (24%)	0.2
pCR in PET Responders	19/50 (38%)	29/140 (21%)	0.022		
pCR in PET Non-Responders	4/21 (19%)	9/97 (9.3%)	0.2		
Near pCR: n (%)	40 (56.3%)	81 (34.2%)	0.001	60 (44%)	0.11
Near pCR in PET Responders	29/50 (58%)	56/140 (40%)	0.032		
Near pCR in PET Non-Responders	11/21 (52%)	25/97 (26%)	0.034		
Median Follow-Up among survivors in Months (range)	12.3 (5.3-78.6)	41.1 (0.7-108.5)		18.7 (0.7-82.7)	
2-year DFS (95% CI)	62% (48-78%)	51% (45-58%)	0.23	42% (34-53%)	0.05

4556 **Poster Session (Board #164), Fri, 8:00 AM-11:00 AM**

Intestinal and tumor microbiome analysis combined with metabolomics of the anti-PD-L1 phase II PERFECT trial for resectable esophageal adenocarcinoma.

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Background: Both human and rodent studies provide evidence for a role of the microbiome in patients who respond to checkpoint inhibition (CI). So far, no study has unraveled the physiological link between intestinal and tumor microbiome composition in relation to response to CI. The PERFECT trial was a single-arm phase II feasibility study investigating the addition of atezolizumab (PD-L1 inhibitor) to neoadjuvant chemoradiotherapy (nCRT) for resectable esophageal adenocarcinoma (NCT03087864). An exploratory objective of this trial was to evaluate intestinal and tumor microbiome composition including plasma metabolomics as potential biomarkers for immunological and pathological response. **Methods:** Using 16S rRNA gene sequencing, we analyzed fecal, duodenal and tumor samples at baseline (V0), 3 weeks after start of atezolizumab (V1), and 1 week before surgery (V2). We compared microbiome composition and metabolomics from patients with pathological complete response (pCR; ypT0N0) to patients with a pathological incomplete response. Differences in alpha diversity metrics were tested using mixed linear models. Beta-diversity associations were assessed using permutational MANOVA (adonis) and multilevel PCA (mixOmics). Biomarkers were identified using a machine learning model (XGboost) feature selection. Plasma metabolomics (Metabolon) were determined with liquid chromatography mass spectrometry (LC-MS). **Results:** Microbiome profiles were significantly altered after start of treatment in all sample types. None of the sample types showed a relation between alpha or beta diversity and pCR. On taxonomical level, we found that the tumor and duodenal baseline samples were weak predictors for response (AUC 0.60 and 0.62, respectively), but better compared to fecal microbiome composition (AUC = 0.49). We identified the top 20 microbes that predicted pCR best in tumor and fecal samples and found significant correlations with metabolites involved in bile acid metabolism. **Conclusions:** Both tumor and duodenal baseline biopsies were better predictors of pathological response compared to fecal microbiome. Microbes predictive of pCR showed significant correlations with metabolites involved in bile acid metabolism, which is known to indirectly influence immunosurveillance in cancer. Data on immune response in relation to the microbiome and metabolomics are expected Spring 2020. Clinical trial information: NCT03087864. Research Sponsor: Roche.

4557 **Poster Session (Board #165), Fri, 8:00 AM-11:00 AM**

Prognostic significance of nutritional markers in metastatic gastric and esophageal adenocarcinoma.

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Background: Malnutrition and sarcopenia (defined as low skeletal muscle mass) are recognized as poor prognostic factors in many cancers. Studies to date in gastroesophageal cancer have largely focused on patients (pts) undergoing curative intent surgery. This study aims to evaluate the prognostic utility of nutritional markers and sarcopenia in pts with de novo metastatic gastric and esophageal adenocarcinoma (GEA). **Methods:** Pts with de novo metastatic GEA seen at the Princess Margaret Cancer Centre from 2010-2016 with available pre-treatment abdominal computed tomography imaging were identified from an institutional database. Nutritional index (NRI) was calculated using weight and albumin, with moderate/severe malnutrition defined as NRI < 97.5. Skeletal muscle index (SMI) normalized by height was calculated at the L3 level using Slice-O-Matic software. Sarcopenia was defined as SMI $<$ $34.4 cm^2/m^2$ in women and $< 45.4 cm^2/m^2$ in men based on previously established consensus. **Results:** Of 175 consecutive pts, median age was 61, 69% were male, 79% had ECOG performance status 0-1, and 71% received chemotherapy. Median BMI was 24.2 (range 15.7-39.8), 70% of pts had $> 5\%$ weight loss in the preceding 3 months, and 29% had moderate/severe malnutrition. 68 pts (39%) were sarcopenic, of whom 46% were malnourished. Median overall survival (OS) was 9.3 months (95% CI 7.3-11.4) for all pts. OS was significantly worse in malnourished pts (5.5 vs 10.9 months, $p = 0.000475$) and displayed a non-significant trend in sarcopenic pts (7.8 vs 10.6 months, $p = 0.186$). On univariable Cox proportional hazards (PH) analysis, ECOG ($p < 0.001$), number of metastatic sites ($p = 0.029$) and NRI ($p < 0.001$) were significant prognostic factors, while BMI ($p = 0.57$) and sarcopenia ($p = 0.19$) were not. On multivariable Cox PH analysis, ECOG ($p < 0.001$) and NRI ($p = 0.025$) remained significant as poor prognostic factors for OS. **Conclusions:** This study demonstrates in a large cohort of de novo metastatic GEA pts that ECOG and NRI were significantly associated with poor OS. NRI was superior to BMI alone. Early identification of malnourished pts using NRI may allow for supportive interventions to optimize nutritional status. Further study is needed to determine whether these factors can be modified to improve prognosis in these pts. Research Sponsor: None.

4558 **Poster Session (Board #166), Fri, 8:00 AM-11:00 AM**

Molecular correlates of PD-L1 expression in patients (pts) with gastroesophageal (GE) cancers.

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Background: The increased PD-L1 expression evaluated by combined positive score (CPS) is associated with improved efficacy of immunotherapy in GE cancers. The impact of tumor molecular alterations on PD-L1 expression is still not well-studied. We aimed to characterize specific molecular features of tumors with different CPS levels in GE cancers. **Methods:** 2,707 GE tumors [1,662 gastric/GE junction adenocarcinoma (GA), 856 esophageal adenocarcinoma (EA), 75 esophageal squamous (ES) and 114 GE unspecified] collected between 2000.8 and 2019.7 were analyzed using NextGen DNA sequencing (NGS), immunohistochemistry (IHC) and fragment analysis (FA) (Caris Life Sciences, Phoenix, AZ). Tumor mutation burden (TMB) was calculated based on somatic nonsynonymous missense mutations. dMMR/MSI status was evaluated by a combination of IHC, FA and NGS. PD-L1 expression measured by IHC (22c3) was evaluated by CPS scores. Molecular alterations were compared in three groups (CPS $\geq$ 10, H; CPS = 1~9, M; CPS = 0, L) using Fisher-Exact or Chi-square and adjusted for multiple comparison by Benjamini-Hochberg. Significance was determined by adjusted (adj) $p < .05$. **Results:** Overall, CPS-H, M, and L were seen in 18% (n = 494), 28% (n = 765) and 53% (n = 1,448) of GE tumors respectively. CPS-H was the most prevalent in ES (43%) followed by GA (19%) and lowest in EA (14%). Overall, TMB was similar between CPS-L and M, but was significantly increased in H (average TMB = 8.4 vs. 8.6 vs. 11 mt/MB, adj $p < .0001$); the effect was seen in EA and GA, but not in ES. An overall significant association between MSI/dMMR status and PD-L1 expression levels was seen (2%, 3.2% and 12% in CPS-L, M and H, adj $p < .05$) in GE tumors; the significance was seen in GA, but not in EA or ES. Amplifications of *PD-L1* (H: 1.5%, M: 0.1% and L: 0) and *PD-L2* (H: 1.1%, M: 0.1%, L: 0) were the highest in CPS-H, while *ASPSCR1* (H: 0, M: 0, L: 1%) and *TNFRSF14* (H: 0, M: 0.4, L: 2%) were the lowest (adj $p < .01$). Genes involved in epigenetic modification (top 5: *ARID1A*, *ASXL1*, *BCL9*, *BCOR*, *CREBBP*), MAPK (*KRAS*, *MAP2K1*) and mismatch repair (*MLH1*, *MSH6*) had the highest mutation rates in CPS-H, compared to M and L ($p < .0001$). In contrast, *CDH1* had higher mutation rates in CPS-L (12%), compared to M and H (5% and 5%) ($p < .0001$). **Conclusions:** This is the largest study to investigate the distinct molecular landscape of pts with different PD-L1 expression levels in GE cancers. Our data may provide novel insights for pt selection (e.g. pts with gene mutations involved in epigenetic modification) and the development of rational combination immunotherapy (e.g. drugs targeting MAPK pathway). Research Sponsor: National Cancer Institute (grant number P30CA014089), The Gloria Borges WunderGlo Foundation-The Wunder Project, Dhont Family Foundation, San Pedro Peninsula Cancer Guild, Daniel Butler Research Fund and Call to Cure Fund.

4559 **Poster Session (Board #167), Fri, 8:00 AM-11:00 AM**

Pembrolizumab with trastuzumab and chemotherapy (PTC) in HER2-positive metastatic esophagogastric cancer (mEG): Plasma and tumor-based biomarker analysis.

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Background: Pembrolizumab can be safely combined with trastuzumab and chemotherapy and has promising activity with median OS 27 months and 91% objective response rate in HER2-positive mEG cancer irrespective of PD-L1 status (NCT02954536; Janjigian ESMO 2019). Tumor biopsies and blood samples were collected in this phase II trial to identify molecular and immune predictors of response and resistance to PTC. **Methods:** Pre-treatment and post-progression biopsies were analyzed using WES and IHC (HER2, PD-L1). Peripheral blood was collected pre-treatment, every 9 weeks on-treatment and at progression for plasma ctDNA (Guardant 360, Guardant Health, Redwood, CA). Tumor-matched DNA alterations were identified by correlating ctDNA and solid tumor WES results. Landmark PFS analysis was used to compare ctDNA clearance status at 9 weeks post-treatment. **Results:** Baseline ctDNA was analysed from 31 of 37 patients of whom 84% (26/31) had tumor-matched ctDNA detected at baseline. Patients who cleared ctDNA at 9 weeks (n = 17/23) achieved a longer median PFS than those who did not - mPFS 12.3 months (95% CI 7.44-NA vs 3.9 months (95% CI 2.01-NA) (log-rank p = 0.02). On serial blood monitoring of 16 patients with eventual radiographic progression, ctDNA re-appearance preceded CT detection in 8 (50%) patients. WES was completed in 31 patients with pre-treatment, and 12 patients post-progression, including matched samples from 10 patients. Loss of HER2 over-expression/amplification was noted in 44% (7/16) of post-progression samples by IHC/FISH (2 IHC 0/1, 5 FISH-). In paired post-progression samples on WES, we observed loss of *ERBB2* in 2 patients, and new amplifications of *CCND1/3*, *FGF3/4/19*, *CDK6/12*, *KRAS*, *MYC*, and *MET*, as well as mutations in *KRAS, PIK3CD and PIK3RA*. Plasma analysis at progression demonstrated copy number increases and/or new amplifications in *MET*, *CKD6*, *PIK3CA*, *KRAS*, *FGFR2*, *EGFR* and *CCDN1* as well as *KRAS*, *RB1*, *PTEN*, *NF1, NOTCH1*, *BRAF*, and *FGFR1* mutations. **Conclusions:** The majority of patients with previously untreated HER2 positive mEG have detectable plasma ctDNA at baseline. The re-appearance of ctDNA during therapy may serve as an early predictor of progression and help identify genetic drivers of acquired resistance. Loss of *ERBB2* over-expression/amplification and activating MAPK alterations occur at PTC progression. Evaluation of tumor immune environment by multiplex IHC and additional ctDNA analysis is underway. Research Sponsor: U.S. National Institutes of Health, Conquer Cancer Foundation of the American Society of Clinical Oncology, Other Foundation, Other Government Agency.

4560 **Poster Session (Board #168), Fri, 8:00 AM-11:00 AM**

A phase II study of efficacy and safety of RC48-ADC in patients with locally advanced or metastatic HER2-overexpressing gastric or gastroesophageal junction cancers.

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Background: RC48-ADC is an antibody-drug conjugate (ADC) drug comprised of a novel humanized anti-HER2 IgG1, a linker, and a microtubule inhibitor, MMAE. The MoA included inhibition of HER2 signal pathway and cytotoxicity of MMAE. RC48-ADC has demonstrated promising anti-tumor activity in pre-clinical and early clinical studies. The current study is designed to evaluate the efficacy and safety of RC48-ADC in heavily treated patients with HER2-overexpressing (IHC 2+ or 3+) gastric or gastro-esophageal junction cancers. **Methods:** This is an open-label, multicenter, single-arm, phase II study. Eligibility criteria include: histologically confirmed gastric or gastro-esophageal junction cancers, HER2-overexpression (IHC 2+ or 3+), ECOG PS 0-1, post-to ≥2 prior systemic treatment. The patients received RC48-ADC, 2.5 mg/kg, q2w until disease progression, unacceptable toxicity, withdrawal, or study termination. The primary endpoint was ORR. PFS, OS, and safety were also evaluated. **Results:** Patient enrollment started in July 2017, and completed in November 2019. By the data cut-off date on 17-Dec-2019, 127 patients were enrolled. The median age was 58 years. At baseline, 59 patients (46.5%) had received ≥ 3 lines prior treatment. For the overall 127 patients, the investigator-assessed confirmed ORR was 18.1% (95% CI: 11.8%, 25.9%). Sub-group ORR was 19.4% and 16.9% for the patients post to 2 lines and ≥ 3 lines, respectively. For the 111 patients who were monitored for ≥ 2 cycles of efficacy assessments (i.e. 12 weeks), the ORR was 20.7% (95% CI: 13.6%, 29.5%). For the 127 patients, the mPFS was 3.8 months (95% CI: 2.7, 4.0, 89 events [70.1%]) and the mOS was 7.6 months (95% CI: 6.6, 9.2, 52 events [40.9%]). The most commonly reported treatment-related AEs were leukopenia (52.0%), alopecia (51.2%), neutropenia (48.0%), and fatigue (42.5%). **Conclusions:** RC48-ADC demonstrated a clinically meaningful response and survival benefit in the heavily treated patients with HER2-overexpressing gastric or gastro-esophageal junction cancers. The safety profile was in line with the previously reported data of RC48-ADC. RC48-ADC showed positive benefit/risk ratio for the target population. Clinical trial information: NCT03556345. Research Sponsor: RemGen, Ltd.

4561 **Poster Session (Board #169), Fri, 8:00 AM-11:00 AM**

Personalized antibodies for gastroesophageal adenocarcinoma (PANGEA): Secondary and final primary efficacy analyses.

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Background: Targeted therapies (tx) have had limited benefit in advanced (aGEA) due to baseline spatial (primary vs metastatic tumor PT/MT) & temporal molecular heterogeneity (BMH/TMH). We previously reported PANGEA methods & results: 35% BMH rate & 1^0 OS results achieving 1yr OS of 66% & mOS of 16.4 months (m) using the personalized tx strategy (Catenacci *et al.* GI ASCO 2020 Abstr356). Here we will report the TMH rates at progressive disease points (PD1 & PD2), ORR/PFS/DCR in each of 3 tx lines, time to strategy failure (TTF), & updated OS/safety. **Methods:** PANGEA enrolled newly diagnosed aGEA pts who then received up to 3 cytotoxic (cx) tx lines (L). Baseline tissue biomarker profiling (BP) was mandated on PT/MT & PD1/PD2, & ctDNA analysis throughout. After initiating 1L cx & upon learning MT BP results, antibody (AN) was added by a predefined prioritized tx algorithm incorporating tissue & blood BP (Table). At PD1, pts went to 2L cx + initial AN. Upon results of PD1 BP, pts changed AN only if BP evolved per tx algorithm. The same was done at PD2. The 1^0 endpoint was 1yr OS; enrolling 68 pts provided 80% power to detect a 63% 1yr OS compared to historical 50% 1yr OS (HR 0.67), using a 1-sided test (0.10 alpha). **Results:** 80 pts were enrolled, & 68 tx'd per protocol. At data cut-off 2/1/20, 15 pts were still on trial with only 2 of these pts on tx $<$12m (8 pts in 1L, 5 in 2L, 2 in 3L). All 68 pts had at least 1 dose of 1L tx, 87% 2L tx, & 36% 3L tx. AN assigned by the tx algorithm at 1L, OS, TTF, & $ORR_1/PFS_1/DCR_1$ of 1L tx are shown in Table; 2L & 3L ORR/DCR outcomes will be shown. The 3yr & 4yr OS rates were 12% & 8%. TMH leading to molecular subgroup change by tx algorithm was 51% after 1L & 36% after 2L; details & results by subgroup will be provided. Any grade $>$3 non-heme tox thru all 3 tx lines was seen in 25% of pts. **Conclusions:** PANGEA showed superior 1^0 & 2^0 endpoint efficacy, even when excluding HER2- pts, compared to historical outcomes. Clinical trial information: NCT02213289. Research Sponsor: U.S. National Institutes of Health.

		Total N=80		ORR_1			$mPFS_1$	
PTA[1]	1L AN	N (%)	1Yr OS[5]	%	DCR_1	mOS	m	mTTF
IO[2]	nivolumab	5 (6)	67	100	100	21.2	7.9	19.9
MSI-H		1 (1)	100					
PDL1>10		4 (5)	50					
TMB-H >15		0						
EBV+		0						
HER2 amp[3]	trastuzumab	16 (20)	73	93	100	26.1	15.1	24.6
EGFR amp[3]	ABT-806	8 (10)	75	67	100	14.9	6.4	12.9
FGFR2 amp[3]	none[4]	4 (5)	33	33	67	5.5	4.4	4.4
	FPA-144	3 (4)	100					
		1 (1)						
MET amp[3]	none[4]	9 (11)	33	43	78	10.7	7.3	9.4
RAS-like	ramucirumab	20 (25)	62	63	95	15.1	9.4	13.7
EGFR expressed	ABT-806	9 (11)	44	43	100	6.7	4.9	5.6
All-negative	ramucirumab	9 (11)	70	75	100	14	8.1	12.8
Per Protocol (ITT)	**ALL**	**68 (85)**	**66**	**72**	**99**	**15.7**	**8.2**	**13.8**
IIT excluding HER2	ALL but Tras	42 (53)	64	64	98	14.9	7.8	12.9

1 MT priority over PT 2 priority over HER2 only 2L+ 3 priority to highest gene copy 4 not in ITT

4562 **Poster Session (Board #170), Fri, 8:00 AM-11:00 AM**

Health-related quality-of-life assessment in accordance with reconstruction procedures for distal gastrectomy for stage I gastric cancer using data from JCOG0912.

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Background: There are three major reconstruction methods after gastrectomy for distal gastric cancer; Billroth-I (B-I), Roux-en-Y (RY) and pylorus-preserving gastrectomy (PPG). These procedures can affect postoperative health-related quality-of-life (HRQoL), but the method is often selected due to physician's preference or each institutional policy without solid evidence. We aimed to explore differences in HRQoL after each reconstruction procedure selected in JCOG0912, a phase III noninferiority trial comparing open and laparoscopic distal gastrectomies for stage I gastric cancer. **Methods:** Among 33 institutions participated in JCOG0912, 4 major cancer centers were selected for HRQoL assessment. HRQoL was assessed using the EORTC QLQ-C30 and STO22 before (baseline) and at 1, 3, 12, and 36 months after surgery as preplanned exploratory analysis. **Results:** Excluding 2 patients who didn't answer the questionnaire, 590 patients were analyzed in this study. For reconstruction, B-I was performed for 222 patients (37.7%), RY for 178 (30.2%) and PPG for 189 (32.1%). Proportion of the opted reconstruction procedures was not different in open and laparoscopic gastrectomies. Global health status (GHS) scores of QLQ-C30 were not different among 3 groups at any time point. In comparison of B-I and RY, B-I was better than RY in constipation, while RY was better than B-I in diarrhea and reflux symptoms. In comparison of B-I and PPG, B-I was better than PPG in constipation and reflux symptoms, while PPG was better than B-I in diarrhea. When comparing RY and PPG, RY was better than PPG in constipation and reflux symptoms, while PPG was better than RY in taste (table). **Conclusions:** GHS scores were similar regardless of the reconstruction procedure, however postoperative symptoms including reflux, constipation, and diarrhea were various according to reconstruction methods. Research Sponsor: Japan National Cancer Center, Ministry of Health, Labour and Welfare of Japan, Japan Agency for Medical Research and Development.

		Months after surgery	HRQoL score	*p*
B-I (reference: RY)	Constipation	1	-7.3	0.016
	Diarrhea	1/3/12/36	7.2/7.2/8.1/8.0	0.003/0.003/0.001/ < 0.001
	Reflux	36	3.5	0.043
B-I (reference: PPG)	Constipation	1/3/12/36	-10.1/-11.2/-8.2/-7.6	0.002/ < 0.001/0.005/0.008
	Diarrhea	1/3/12	5.5/11.3/9.7	0.031/ < 0.001/ < 0.001
	Reflux	1/3/12	-6.7/-4.7/-6.0	0.001/ < 0.001/ < 0.001/ < 0.001
RY (reference: PPG)	Constipation	3/12/36	-7.9/-6.5/-6.5	0.005/0.022/0.021
	Reflux	1/3/12/36	-6.6/-5.7/-8.9/-6.9	0.001/ < 0.001/ < 0.001/ < 0.001
	Taste	3/12/36	5.3/3.9/3.1	0.014/0.044/0.040

4563 **Poster Session (Board #171), Fri, 8:00 AM-11:00 AM**

Cabozantinib (cabo) combined with durvalumab (durva) in gastroesophageal (GE) cancer and other gastrointestinal (GI) malignancies: Preliminary phase Ib CAMILLA study results.

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Background: Cabo targets multiple tyrosine kinases, including VEGFR, MET, and AXL, and has been reported to show immunomodulatory properties that may counteract tumor-induced immunosuppression, providing a rationale for combining it with PD-L1 inhibitors like durva. We conducted a phase Ib GI basket trial to evaluate the safety & efficacy of this regimen in advanced GE adenocarcinoma (GEA), colorectal cancer (CRC), & hepatocellular carcinoma (HCC). **Methods:** Patients received cabo and durva in 3+3 dose escalation then expansion to determine the dose limiting toxicity (DLT), Recommended Phase 2 Dose (RP2D), ORR, PFS & OS. Cabo was dosed at 20mg QD, 40mg QD, and 60mg QD in the first, second, and third cohorts respectively. Durva was dosed at 1500mg IV Q4W in all cohorts. DLT window was 28 days. Scans were obtained every 8 wks. Treatment beyond progression was allowed. **Results:** 23 Pts (16 M, 7 F), median age 60 yrs (range 33-79) were currently enrolled. 12 in the dose escalation cohort with cabo 20mg (6 pts), or 40mg (3 pts), or 60mg (3 pts). 11 pts enrolled in the dose expansion cohort with cabo 60mg. 8 pts had GEA, 13 pts had CRC, and 2 pts had HCC. Median number of prior chemotherapies was 3 (range 1-3). 3 pts were not evaluable for DLT due to missing $\geq$30% of DLT window doses, not related to DLT. No DLTs were observed. Drug-related Grade (G) 1&2 AEs included fatigue (83%), abnormal LFTs (39%), anorexia (26%), diarrhea (26%), nausea (13%), & hand foot syndrome (13%). One pt each developed drug related G3 hypertension, hyperthyroidism, thrombocytopenia, & thromboembolic event, all occurring outside the DLT window. 19 pts were evaluable for response: 4 PR (2 GEA & 2 CRC), 12 SD, 3 PD; ORR 21%; clinical benefit rate 84%; median time to PD 16 wks (range 8-40+). **Conclusions:** RP2D was determined to be Cabo 60mg QD and Durva 1500mg Q4W. Enrollment to phase I dose expansion is ongoing. RP2D may be adjusted based on additional experience & long-term tolerability. Early efficacy data was encouraging. This is an investigator-initiated trial funded by Exelixis & Astrazeneca. Clinical trial information: NCT03539822. Research Sponsor: AstraZeneca and Exelixis.

4564 **Poster Session (Board #172), Fri, 8:00 AM-11:00 AM**

Final results of a phase III randomized trial of comparison of three paclitaxel-based regimens concurrent with radiotherapy for patients with local advanced esophageal squamous cell carcinoma.

Dashan Ai, Jinjun Ye, Yun Chen, Qi Liu, Xiangpeng Zheng, Yunhai Li, Shihong Wei, Jiancheng Li, Qin Lin, Hui Luo, Jianzhong Cao, Jialiang Zhou, Guang Huang, Min Fan, Kailiang Wu, Huanjun Yang, Zhengfei Zhu, Weixin Zhao, Ling Li, Kuaile Zhao; Fudan University Shanghai Cancer Center, Shanghai, China; Jiangsu Cancer Hospital, Nanjing, China; Huadong Hospital Affiliated to Fudan University, Shanghai, China; Fudan University Shanghai Cancer Center Minhang Branch, Shanghai, China; Department of Radiation Oncology, Gansu Province Cancer Hospital, Lanzhou, China; Fujian Cancer Hospital, Fuzhou, China; The First Affiliated Hospital of Xiamen University, Xiamen, China; Department of Radiation Oncology, Jiangxi Province Cancer Hospital, Nanchang, China; Shanxi Provincial Cancer Hospital, Shanxi, China; Affiliated Hospital of Jiangnan University, Wuxi, China; Department of Radiation Oncology, People's Hospital of Hainan Province, Haikou, China; Department of Radiation Oncology, Fudan University Shanghai Cancer Center, Shanghai, China

Background: Paclitaxel (PTX) is effective in concurrent chemoradiation (CCR) against esophageal squamous cell carcinoma (ESCC). Which regimen, among cisplatin (DDP) (TP), carboplatin (CBP) (TC) or 5-Fu (TF) in combination with PTX concurrent with radiotherapy, provides best prognosis with minimum adverse events (AEs) is still unknown. **Methods:** The study compared two pairs of regimens: TF vs. TP and TF vs. TC concurrent with radiotherapy. Patients with histologically confirmed ESCC (clinical stage II, III or IVa) 20 were randomized into the three groups. Patients in TP group were treated with 2 cycles of CCR followed by 2 cycles of consolidation chemotherapy with TP (DDP 25 mg/m2/d, d1-3, PTX 175 mg/m2, d1, q28d). Patients in TF group were treated with 6 cycles of TF (5-Fu 300 mg/m2, civ 96h, PTX 50 mg/m2, d1, qw) in CCR followed by 2 cycles of TF (5-FU 1800 mg/m2, civ 72h, PTX 175 mg/m2, d1, q28d) in consolidation chemotherapy. Patients in TC group were treated with 6 cycles of TC (CBP AUC = 2, d1, PTX 50 mg/m2, d1, qw) in CCR followed by 2 cycles of TC (CBP AUC = 5, d1, PTX 175 mg/m2 d1, q28d) in consolidation chemotherapy. The radiotherapy dose in all groups was 61.2 Gy delivered in 34 fractions. The primary endpoint was overall survival (OS) and the secondary endpoints were progression-free survival (PFS) and adverse events. **Results:** Between July 2015 and January 2018, 321 ESCC patients in 11 centers were enrolled. Median follow-up of patients who survived was 36.3 months (IQR 27.9–45.2). The 3-yr OS was 58.2% in TF group and 59.5% in both TP and TC group. (TF vs. TP, HR 0.935, 95% CI 0.627-1.417; TF vs. TC, HR 0.881, 95% CI 0.578-1.342; P = 0.839). No significant differences were found in 3-yr PFS between TF, TP and TC groups [48.3% vs. 45.5%(TP) or 48.3% (TC). P = 0.820]. TP group had a significant higher incidence of acute Grade 3/4 neutropenia [60.7% vs. 16.8%(TF) or 32.7%(TC)], thrombocytopenia [13.1% vs. 2.8%(TF) or 4.7%(TC)], anemia [5.6% vs. 1.9%(TF) or 3.7% (TC)], fatigue [10.3% vs. 1.9%(TF) or 0.9%(TC)] and vomiting [5.6% vs. 0%(TF) or 0.9%(TC))]than other two groups (P< 0.05). TF group had a significant higher incidence of Grade 3/4/5 esophagitis [11.2% vs. 0.9%(TP) or 4.7%(TC))]and pneumonitis [4.6% vs. 0%(TP) or 1.9% (TC)]than other two groups (P< 0.05). **Conclusions:** No statistical differences were found in OS and PFS among TF, TP and TC groups. TC might be an option used in CCR in ESCC patients with mild of side effects compared with other two groups, although it did not significantly prolong OS. Clinical trial information: NCT02459457. Research Sponsor: 2015 Prospective Clinical Research Fund of Fudan University Shanghai Cancer Center.

4565 **Poster Session (Board #173), Fri, 8:00 AM-11:00 AM**

Second primary malignancies in patients with clinical T1bN0 esophageal squamous cell carcinoma after definitive therapies: Supplementary analysis of the JCOG trial, JCOG0502.

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Background: Esophageal squamous cell carcinoma (ESCC) is associated with synchronous or metachronous cancer at other primary sites. Previous studies have suggested that patients (pts) with ESCC are still at a high risk of second primary malignancies after definitive therapies. In particular, early-stage ESCCs result in good prognosis, which is associated with a higher risk of second primary malignancies. **Methods:** The JCOG0502 was a phase III trial, which included a randomized and a non-randomized part and compared esophagectomy with definitive chemoradiotherapy in clinical T1bN0 ESCC. We additionally reviewed data of all pts enrolled in the JCOG0502 for second primary malignancies. Lugol-voiding lesions (LVLs) were assessed in the noncancerous esophageal mucosa before the treatments. **Results:** Among 379 enrolled pts, 213 pts received esophagectomy and the remaining received chemoradiotherapy. Patient characteristics of overall cohort were as follows: male, 85%; median age, 63 (range, 41–75) years; upper- /middle- /lower thoracic esophagus, 11/63/27%; alcohol consumption history, 79%; smoking history, 66%; prevalence of no LVLs/several LVLs/many LVLs/unknown, 45/36/8/11%. With a median follow-up of 7.1 years, a total of 118 second malignancies were observed in 99 pts (26%). Cumulative incidences of second malignancies after 3, 5, 10 years were 9, 15, 36%, respectively. Most common primary tumor sites were head and neck (35%), followed by stomach (20%) and lung (14%). In multivariable analyses, several LVLs [hazard ratio (HR): 2.24, 95% confidential interval (CI): 1.32–3.81, vs. no LVLs] and many LVLs (HR: 2.88, 95% CI: 1.27–6.52, vs. no LVLs) were significantly associated with the development of second malignancies. Regarding the three most common types of cancers, 62 out of the 77 cancers (81%) were diagnosed in clinical stage 0–I. Seventeen pts died due to second primary malignancies. There were 4 and 3 deaths from head and neck and lung cancer, respectively. Whereas, mortality caused by stomach cancer was not observed. **Conclusions:** In the JCOG0502, the incidence of second malignancies was high, indicating that careful follow-up is required for ESCC pts even after treatment completion. The presence of LVLs in esophagus was identified as an independent predictive factor for second primary malignancies, which may be useful for surveillance strategies. Clinical trial information: UMIN000000551. Research Sponsor: Japanese Ministry of Health, Labour and Welfare.

4566 **Poster Session (Board #174), Fri, 8:00 AM-11:00 AM**

Prognostic role of mismatch repair deficiency (MMR-D) in patients receiving first-line fluoropyrimidine and platinum (FP) doublet chemotherapy for metastatic and locally advanced unresectable gastric cancers (GCs).

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Background: Although chemotherapy has been suggested to have the potential to cause a detrimental effect on treatment outcomes of localized GC with MMR-D, it remains unclear whether chemotherapy for metastatic/recurrent/unresectable GC with MMR-D would also adversely affect the survival outcomes. Anti PD-1 antibody (Ab) showed remarkable efficacy in patients with MMR-D and is being actively investigated in combination with cytotoxic chemotherapy. Hence, we aim to evaluate the impact of MMR status on treatment outcomes of advanced GC. **Methods:** We reviewed our database to identify all patients with HER2 negative, metastatic, recurrent, and locally advanced unresectable GC who received FP doublet chemotherapy from January 2015 to August 2018. For those who had an available tumor tissue, MMR protein expression was assessed by immunohistochemistry (IHC) and correlated with clinical characteristics and treatment outcomes. **Results:** Out of 895 patients identified from the database, 543 underwent IHC testing for MMR. The median age was 58 years (range, 24 – 86) with male comprising 64.0%. Most patients had initially metastatic disease (n = 382, 70.3%) followed by recurrent (n = 127, 23.3%) and locally advanced unresectable disease (n = 34, 6.3%). MMR-D was found in 4.4% (n = 24) and associated with age $\geq$ 65 years (50% vs. 29.9%; P = 0.04) and signet ring cell histology (0% vs. 17.7%, P = 0.01). According to our prognostic model (Koo DH et al, 2011), only 4.2% of patients with MMR-D were classified as Poor-risk group (vs. 16.8% of patients with MMR-P, p= 0.10). In the Good-risk group, patients with MMR-D (n = 10) had significantly shorter median progression-free survival (PFS, 6.0 vs. 9.0 months, P = 0.05) and overall survival (OS, 10.1 vs 20.9 months, P = 0.047) compared to those with MMR-P (n = 188), while there was no significant difference in survival outcomes depending on MMR status in the Moderate and Poor-risk groups. In multivariate analysis for OS, MMR status was a significant prognostic factor for OS in Good-risk group GC patients. **Conclusions:** GC patients with MMR-D had poorer median PFS and OS than those with MMR-P on standard cytotoxic chemotherapy in the Good-risk group. Thus, for Good-risk GC patients with MMR-D, anti PD-1 Ab alone might be considered rather than combining cytotoxic chemotherapy. Further investigation with next-generation sequencing is in process to determine underlying molecular mechanisms and will be presented in ASCO 2020. Research Sponsor: None.

4567 **Poster Session (Board #175), Fri, 8:00 AM-11:00 AM**

HER2 heterogeneity in adenocarcinoma of the distal esophagus and stomach.

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Background: Patients with HER2 positive adenocarcinoma of the esophagus or stomach are eligible for HER2 targeted therapy, which can improve survival in selected patients. Previous research shows that HER2 gene amplification and HER2 overexpression is frequently heterogeneous within these tumors. Biopsies taken from heterogeneous tumors for predictive testing may therefore result in false-negative outcomes. The objective of this study was to assess HER2 amplification and expression in biopsies and paired resection specimens with adenocarcinoma of the esophagus or stomach, from patients who did not receive neoadjuvant systemic therapy. **Methods:** Paired biopsies and resection specimens of patients with adenocarcinomas of the esophagus or stomach were retrospectively selected. Immunostaining was performed on all samples using antibody 4B5 (Ventana Medical Systems) and *Silver-In-Situ-Hybridization* was performed in selected cases. Scoring for HER2 was performed according to the method described by Hofmann et al. (2008). **Results:** We included 378 cases for analysis. In both biopsies and resection specimens 14% of the cases were HER2 positive. Intratumor heterogeneity in HER2 positive tumors was present in 45% (*n*= 24/53) in biopsies and 75% (*n*= 39/52) in resection specimens. In HER2 positive resection specimens, 65% (*n*= 34/52) of paired biopsies were also positive. In the 18 remaining discordant tumors (resection HER2 positive, biopsy negative), intratumor heterogeneity was present in 16/18 cases. For HER2 negative resection specimens all paired biopsies were also HER2 negative. SISH was performed in 110 tumors. Agreement of HER2 gene amplification between biopsy and resection specimens was observed in 86% (n = 95/110). Five HER2 negative biopsies were positive in the resection specimen. **Conclusions:** The results of this study indicate that predictive HER2 assessment in adenocarcinoma of the esophagus or stomach can lead to false negative results based on biopsies. As a result, patients with HER2 positive tumors can unintentionally be denied neoadjuvant HER2 targeted therapy. The set of patients investigated in this present study is unique because of the absence of any systemic and/or radiation therapy between the biopsy and the resection of the tumor. Hopefully these results can help in developing methods for improved patient selection for HER2 targeted therapy. Research Sponsor: F. Hoffmann-La Roche AG.

4568 **Poster Session (Board #176), Fri, 8:00 AM-11:00 AM**

PD-L1 positive esophagogastric (EG) cancer is associated with distinct bacteria.

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Background: Pembrolizumab is approved for chemotherapy-refractory PD-L1 CPS >1 mEG cancer. In clinical trials, pts with MSI-H, EBV+ and PD-L1 CPS >10 EG cancers derive the greatest benefit with immune checkpoint blockade (ICB). Pre-clinical data suggest that the gut microbiome modulates response to ICB; however, the EG cancer microbiome has not been characterized in EG cancer with respect to PD-L1 and MSI-H status. Therefore, we evaluated the EG tumor microbiome in the context of PD-L1 expression in order to define biologically unique EG tumor phenotypes for future therapeutic development. **Methods:** Clinical and pathologic characteristics, including age, stage at diagnosis, tumor PD-L1 CPS, HER2 IHC, EBV ISH, genomic analysis, treatment history and survival status were reviewed. CPS was stratified *a priori* using cutoffs of >1/>10/>20 due to biologic differences. MSK-IMPACT, a capture-based next-generation sequencing platform that detects mutations, copy-number alterations, and select fusions was used to detect non-human bacterial reads identified in the NCBI NT database. Bacterial species found in >2 pts were analyzed and stratified by highest PD-L1 CPS score for each individual patient (Vanderbilt, AMP 2018) and Bonferroni correction was used for odds ratio (OR) confidence intervals where each unique species was considered an independent hypothesis. **Results:** Molecular data from 311 pts was clinically annotated. PD-L1 results (Table) correlated with bacterial species identified on tumor sequencing. PD-L1 CPS >1 was associated with *Selenomonas sputigena* (OR: 8.2, 95% CI:1.2-53.6), and PD-L1 CPS >20 was associated with presence of *Bifidobacterium dentium* (OR: 7.4, 95% CI:1.1-48.5) and *Prevotella denticola* (OR: 4.2, 95% CI: 1.1-16.6) after multiple comparison correction for the 166 bacterial species identified in the cohort. No differences were seen between PD-L1 < 10 vs >10. Four patients were also found to have EBV+ tumors using this approach, including the 1/54 patients identified by EBER ISH. **Conclusions:** PD-L1 > 20 EG cancer represents a biologically unique subset, enriched for *Bifidobacterium dentium* and *Prevotella denticola*. Correlation between PD-L1 expression, microbial and immune environment, and survival on ICB is underway. Research Sponsor: U.S. National Institutes of Health, Conquer Cancer Foundation of the American Society of Clinical Oncology.

PD-L1	All Pts (%) n = 313	MSI-H (%) n = 16	EBV+ (%) n = 4
CPS < 1	152 (49)	2 (12.5)	0
CPS 1-9	92 (29)	2 (12.5)	1 (25)
CPS 10-19	28 (9)	4 (25)	1 (25)
CPS >20	41 (13)	8 (50)	2 (50)

4569 **Poster Session (Board #177), Fri, 8:00 AM-11:00 AM**

Radiotherapy after esophageal cancer stenting (ROCS): A pragmatic randomized controlled trial evaluating the role of palliative radiotherapy in maintaining swallow.

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Background: Most patients with oesophageal cancer (OC) present with incurable disease; 80% of new cases, and deaths, occur in low and middle income nations. Median survival for advanced disease is 3-5 months, a majority requiring intervention for dysphagia. Insertion of self expanding metal stents is the commonest way of palliating, but dysphagia may recur within three months owing to tumour progression. Evidence reviews have called for trials of combination treatment for OC dysphagia. The ROCS study (funding - UK NIHR programme) examined effectiveness of palliative radiotherapy, following stent, in maintaining swallow. It also examined impact on quality of life, bleeding events, and survival. **Methods:** A multicentre RCT with follow up monthly for a year. Patients referred for stent insertion as primary management of dysphagia related to incurable OC were recruited in secondary care, with all planned follow up at home. Patients were randomised 1:1 to stent insertion alone or stent insertion plus palliative radiotherapy at a dose of 20Gy in five fractions or 30Gy in ten fractions. Primary outcome was difference in proportions of participants with recurrent dysphagia at 12 weeks, defined as deterioration of 11 points or more in the dysphagia scale of the EORTC QLQ-OG25 questionnaire. Secondary outcomes included quality of life, bleeding risk, survival. **Results:** 220 patients were randomised Dec 2013-Aug 2018 at 23 UK sites. Addition of radiotherapy did not reduce the proportion of primary events at 12 weeks: 49% in control arm vs 45% in the intervention, adjusted OR 0.82 (95%CI 0.40-1.68; p = 0.587) and it was less cost effective. Sensitivity analyses did not alter the results. Dysphagia deterioration-free survival was similar in both arms: adjusted HR 0.92 (95%CI 0.68-1.26; p = 0.618). Median survival was 19.7 weeks in control arm and 18.9 weeks in the intervention. Those in the radiotherapy arm had significantly fewer bleeding events (18.6% compared to 10.3%), giving a number needed to treat of 12. **Conclusions:** Palliative external beam radiotherapy is widely accessible to patients with advanced cancer. ROCS is the largest trial assessing its role in combination with stenting for OC dysphagia, and is the first to prospectively assess impact on bleeding risk. It demonstrates no reduction in risk of dysphagia recurrence at 12 weeks, nor impact on survival. Reductions in bleeding events should be considered in the context of patient described trade offs of fatigue and burdens of attending hospital. Clinical trial information: NCT01915693. Research Sponsor: UK National Institute for Health Research Health Technology Assessment (HTA) Programme.

4570 **Poster Session (Board #178), Fri, 8:00 AM-11:00 AM**

Identification of SLX4 as the most frequently mutated gene in homologous recombination deficiency in Asian gastric cancer.

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Background: Gastric cancer is the third most common malignancy worldwide. Homologous recombination (HR) is a type of genetic recombination, and homologous recombination deficiency (HRD) is highly involved in multiple types of cancers and can predict response to anticancer therapies. However, homologous recombination deficiency is not well characterized in patients with Asian gastric cancer. **Methods:** 196 Asian patients with gastric cancer were analyzed in this study. A list of 102 genes related to HRD was compiled based on previous literature. Haplox 605-gene panel was used to capture the sequencing library. Mutations related to HRD were analyzed following next-generation sequencing. In addition, tumor mutational burden (TMB) was calculated by dividing the total number of mutations by the size of the coding region. The correlation analysis between HRD and TMB was also conducted. **Results:** In total, 43 (21.94%) of 196 Asian patients with gastric cancer harbored at least one HRD gene. The top 10 mutant HRD genes included *SLX4* (3.57%), *ATR* (2.04%), *RECQL* (1.53%), *NBN* (1.53%), *ERCC4* (1.53%), *BAP1* (1.53%), *ATM* (1.53%), *RAD54L* (1.02%), *BRCA1* (1.02%) and *PARP1* (1.02%). In addition, the occurrence of HRD mutations was significantly correlated with a higher TMB. The median TMB of HRD group (8.28 muts/Mb) was significantly higher than that of the Non-HRD group (3.07 muts/Mb) ($p < 0.01$). The overall upper quantile value (4.80 muts/Mb) was used to screen patients with high TMB (TMB-H). The TMB-H in HRD group was significantly higher than the Non-HRD group (44.19% VS 17.92%, $p < 0.01$). **Conclusions:** Our study described that *SLX4* was the most frequently mutated HR-related gene in Asian gastric cancer. Moreover, the positive correlation with homologous recombination deficiency (HRD) and tumor mutational burden (TMB) was observed in these patients. Research Sponsor: None.

4571 **Poster Session (Board #179), Fri, 8:00 AM-11:00 AM**

A novel gene signature for predicting response to chemoradiotherapy in locally advanced esophageal adenocarcinoma.

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Background: While neoadjuvant chemoradiotherapy (CRT) has emerged as an important treatment modality in patients with locally advanced esophageal adenocarcinoma (EAC), ~60%-70% of patients do not respond to such treatments; but are exposed to their toxicity nonetheless. This highlights the clinical need for the development of biomarkers that can robustly predict response to CRT and spare others from the toxicity and expense associated with these treatments. Herein, we systematically and comprehensively identified a biomarker signature that predicts response to neoadjuvant therapy in EAC patients. **Methods:** A cohort of 31 EAC patients treated with chemotherapy or chemoradiotherapy was assembled, with a majority of patients receiving carboplatin, paclitaxel and concurrent radiotherapy. Specifically, we performed a capture based targeted sequencing in *paired* biopsy specimens obtained at baseline and 3-6 weeks post-treatment. In addition, we also analyzed the predictive potential of a panel of immune-related genes (TIM3, LAG3, IDO1 and CXCL9) in these matched pre- and post-treatment tissues. **Results:** In our cohort, based upon pathologic response to neoadjuvant CRT, 8 EAC patients were categorized as non-responders, while 23 were deemed as responders to CRT. Among responders, the most frequently mutated genes were MKI67, SYNE1, PCLO, RECQL4, MSH3, NOTCH2, ILR7, CIITA, LRRK2 and EML4, and the overall tumor mutation burden (TMB) was significantly reduced for these genes in post-treatment samples (P=5.73E-03). Similarly, in non-responders NLRP1, MAP3K1, ASMTL, and ALK harbored frequent mutations, and the TMB was significantly reduced for these genes in post-treatment samples (P=5.57E-03). We compared responders and non-responders from the pre-treatment samples and identified differentially mutated genes including EPHA5, ZNF217, RELN, PALB2 and MYO18A. Similarly, responders had all four immune-related genes significantly up-regulated in post-treatment samples than pre-treatment samples. We constructed a risk-stratification model that comprised of mutational score from 5 differentially mutated genes, together with 4 immune-related genes, which achieved an AUC of 0.96 in predicting response to CRT in EAC patients (P=1.03E-04). **Conclusions:** Using a systematic biomarker discovery approach, we have developed a novel biomarker signature that robustly predicts response to CRT in EAC patients and has a significant potential for personalized management of locally advanced EAC patients.
Research Sponsor: None.

4572 **Poster Session (Board #180), Fri, 8:00 AM-11:00 AM**

Durvalumab following multimodality therapy for locally advanced esophageal and GEJ adenocarcinoma: Updated survival and early translational results from Big Ten Cancer Research Consortium Study.

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Background: Concurrent chemoradiation(CRT) followed by esophagectomy is a standard of care for locally advanced esophageal(LA-EAC) and GEJ adenocarcinoma. Approximately 50% of patients(pts) experience disease relapse within the 1st yr after treatment(tx) completion. Immune checkpoint inhibitors have activity in metastatic PD-L1 positive EAC. Preclinical studies have shown radiation +/- chemotherapy upregulates PD-1/PD-L1 pathway. **Methods:** We conducted a phase II trial evaluating safety and efficacy of PD-L1 inhibitor durvalumab(durva) in pts with LA-EAC and GEJ adenocarcinoma who had residual disease in surgical specimen after neoadjuvant CRT and R0 resection. Pts received durva 1500mg IV every 4 weeks for up to 1yr. **Results:** Initially 24 pts were enrolled, study was expanded to enroll additional 13 pts. Median age: 61yrs (range, 43-73). 31 received carbo/paclitaxel and 6 received cis/5-FU concurrently with RT. 24(64.9%) pts had positive lymph nodes(LN) at the time of surgery following CRT: N3(n = 3,8.1%), N2(n = 10, 27%), N1(n = 11,29.7%).17 pts relapsed: 11 on tx, 6 had late relapses. 3/5 late relapses were locoregional and were re-treated with chemo-RT. Remaining relapses were systemic with lung and LN being the most common sites. 2 of 3 pts who developed grade 3 irAEs are alive and disease free at 17 and 23 mo. RFS/OS:1 yr- 79.2%/95.5%, 2yr-55.5%/67.4%. 20/37 pts have HER-2 status available: 5/6 HER2 positive pts had disease relapse, 1 is undergoing tx. Molecular profiling is available on 8 relapsed pts: all were microsatellite stable with low TMB and PD-L1 $<$ 10% CPS. Mutations in DNA repair genes (*ARID1A, ATM, ATR, CHEK2*), and *PIK3CA* E542K were more prevalent among late relapsing pts. Circulating tumor cells (CTCs) analysis is available for 10/37 pts. 4/5 pts where CTCs increased from C1 to C4 had disease relapse. Molecular profiling of the remaining pts and correlation of PD-L1 expression, TMB, specific genes mutations, CTCs, and Immunoscore with outcomes with durva is being evaluated will be presented at the meeting. **Conclusions:** Adjuvant durva following trimodality therapy for LA-EAC and GEJ adenocarcinoma improved 1-yr RFS to 79.2% compared to historical rate of 50%.2-yr RFS and OS data are encouraging in this high risk pt population. HER-2 positivity may be associated with lack of benefit from durva. Mutations in DNA repair genes are prevalent in pts with delayed relapse. Rise in CTCs during durva tx may be an early marker of disease relapse. Clinical trial information: NCT02639065. Research Sponsor: AstraZeneca/MedImmune.

4574 **Poster Session (Board #182), Fri, 8:00 AM-11:00 AM**

Hepatic arterial infusion of oxaliplatin plus raltitrexed in patients with unresectable hepatocellular carcinoma (HAIROX): A phase II, single-arm, prospective study.

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Background: Chemoembolisation and oral sorafenib are the recommended treatment for unresectable hepatocellular carcinoma (HCC); however, some patients respond poorly to these. Hepatic arterial infusion (HAI) chemotherapy may have potential benefit in these patients. We aimed to investigate the efficacy and safety of HAI of oxaliplatin plus raltitrexed in patients with unresectable HCC. **Methods:** In this phase II, single-arm clinical trial, we enrolled patients aged 18–70 years with unresectable HCC at the Fujian Cancer Hospital (China). We performed HAI with oxaliplatin (100 mg/m^2 for 4 hours) and raltitrexed (3 mg/m^2 for 1 hour). Treatment was repeated every 3 weeks and was discontinued either because of disease progression, unacceptable toxicity levels, or refusal of further treatment. We used Simon's two-stage design. The primary endpoint was the objective response rate according to the Response Evaluation Criteria in Solid Tumors version 1.1. **Results:** Fifty-one patients were screened between January 5, 2018 and August 7, 2019. Of these, 39 patients (34 men and 5 women; median age, 53 years) were enrolled and included in the intention-to-treat population. Objective response was achieved in 18 (51.4%) of 35 patients in the per-protocol population and in 18 (46.2%) of 39 patients in the intention-to-treat population. Treatment-related grade 4 adverse events or deaths were not reported, and the observed grade 3 adverse events were elevated aspartate aminotransferase levels (5 [12.8%]), elevated alanine aminotransferase levels (1 [2.6%]), leukopenia (1 [2.6%]), thrombocytopenia (1 [2.6%]), and abdominal infection (1 [2.6%]). **Conclusions:** HAI of oxaliplatin plus raltitrexed showed promising efficacy and acceptable toxicity levels in patients unresectable HCC, and further evaluation is warranted. Clinical trial information: ChiCTR-OOC-17014182. Research Sponsor: None.

Treatment responses of HAI of oxaliplatin plus raltitrexed in unresectable HCC.

	Intention-to-treat population (n=39)	Per-protocol population (n=35)
Complete response	1(2.6%)	1(2.9%)
Partial response	17(43.6%)	17(48.6%)
Stable disease	13(33.3%)	13(37.1)
Overall response	18(46.2%)	18(51.4%)
Disease control	31(79.5%)	31(88.6%)

4575 **Poster Session (Board #183), Fri, 8:00 AM-11:00 AM**

Peripheral blood immune correlates associated with TGF-β inhibition (galunisertib) and stereotactic body radiotherapy (SBRT) in patients with advanced hepatocellular carcinoma (HCC).

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Background: TGF-β is a pleiotropic cytokine with immunosuppressive activity. In mouse models, blockade of TGF-β signaling enhances the activity of radiation and invokes T cell dependent anti-tumor immunity. We previously reported preliminary safety and efficacy results from a pilot study combining galunisertib (LY2157299), an oral TGF-β inhibitor, with SBRT for the treatment of patients with advanced HCC. Here, we investigate immunological mechanisms and potential biomarkers associated with therapeutic activity. **Methods:** Patients with advanced HCC who had progressed on or refused sorafenib were treated with galunisertib (150 mg PO BID) on days 1-14 of each 28-day cycle. SBRT (18 Gy) was delivered in a single dose between days 15-28 of cycle 1. Blood was collected at baseline, following two weeks of galunisertib and following SBRT for high-dimensional analysis using a 37-marker CyTOF panel. Patients were dichotomized based on best response as either progressor (PD) or non-progressor (PR+SD). The frequency of immune subsets was compared between groups. **Results:** Fifteen patients were enrolled and treated. One patient was not evaluable. The most common adverse event was grade 1 or 2 fatigue in 53% of patients. The only possibly-related grade 3 event was achalasia in one patient which coincided with disease progression. Two patients achieved a PR and six patients had SD (DCR 57%) with a median progression-free survival of 3.7 months and a median overall survival of 9.0 months. For most patients, regardless of outcome, galunisertib treatment was associated with a decrease in activated Ki67+ Treg cells. However, pre-treatment immune composition within the blood of progressors and non-progressors was distinct. At baseline, progressors had an increased frequency of naive-like CD8+ T cells, whereas non-progressors had an increased frequency of non-classical monocytes. After combination therapy, only non-progressors showed a significant increase in CD8+PD1+TIGIT+ T cells. **Conclusions:** Galunisertib combined with SBRT was well-tolerated with modest efficacy. Immune profiling of the blood revealed distinct pre- and post-treatment signatures that differentiated patients with progression versus non-progression. These findings show that the combination of anti-TGF-β therapy with radiation can mediate disease control and identify potential correlates of efficacy. Clinical trial information: NCT02906397. Research Sponsor: Lilly Oncology, Conquer Cancer Foundation of the American Society of Clinical Oncology, U.S. National Institutes of Health.

4576 **Poster Session (Board #184), Fri, 8:00 AM-11:00 AM**

IDH1 mutation detection in plasma circulating tumor DNA (ctDNA) and association with clinical response in patients with advanced intrahepatic cholangiocarcinoma (IHC) from the phase III ClarIDHy study.

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Background: Mutations in isocitrate dehydrogenase 1 (*IDH1*) are detected in ~13% of IHCs. Ivosidenib (IVO) is a first-in-class, oral inhibitor of the mutant IDH1 (mIDH1) protein. In ClarIDHy, a global, phase 3, double-blind study in previously treated patients with advanced m*IDH1* IHC (N = 186), IVO demonstrated an improvement in progression-free survival (PFS) vs placebo (hazard ratio 0.37, $p < 0.001$) (Abou-Alfa et al., Ann Oncol 2019; NCT02989857). Feasibility of m*IDH1* detection in plasma ctDNA from patients with IHC was demonstrated and was highly concordant with mutation status in tumor tissue (Aguado-Fraile et al., Cancer Res 2019). This analysis was extended to the larger patient cohort from ClarIDHy, and longitudinal m*IDH1* detection from ctDNA was assessed and correlated with clinical response. **Methods:** Baseline plasma and tumor tissue samples were obtained before randomization; longitudinal plasma samples were collected on day 1 of each treatment cycle. m*IDH1* status in tissue was prospectively and centrally confirmed using Oncomine Focus Assay. A BEAMing digital PCR test was used for quantification of m*IDH1* in plasma. *IDH1* mutation clearance (*IDH1*-MC) was achieved when plasma m*IDH1* variant allele frequency was below the assay's sensitivity (0.02% for R132C/L/S/G; 0.04% for R132H). **Results:** m*IDH1* detection in plasma ctDNA and tissue was concordant in 92% (193/210) of samples screened. As of 31 Jan 2019, median PFS was 2.7 months for IVO vs 1.4 months for placebo. Longitudinal analysis with biomarker data available as of Jan 2020 demonstrated *IDH1*-MC in plasma from 10 IVO-treated patients with PFS $\geq$2.7 months (n = 36) vs 0 patients with PFS $<$ 2.7 months (n = 40). No *IDH1*-MC was observed in patients treated with placebo, irrespective of response (n = 49). **Conclusions:** These results reinforce the feasibility of *IDH1*-R132 detection in plasma from patients with IHC, with a 92% concordance with detection in tumor tissue, supporting m*IDH1* detection in liquid biopsy as a viable patient selection strategy where tissue exhaustion can limit conventional methods. Plasma *IDH1*-MC was also observed in a subset of IVO-treated patients who achieved disease control. Clinical trial information: NCT02989857. Research Sponsor: Agios Pharmaceuticals, Inc.

4577 **Poster Session (Board #185), Fri, 8:00 AM-11:00 AM**

Algorithm for blood-based panel of methylated DNA and protein markers to detect early-stage hepatocellular carcinoma with high specificity.

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Background: Hepatocellular carcinoma (HCC) is a leading cause of cancer-related deaths worldwide. Though biannual ultrasound surveillance with or without alpha-fetoprotein (AFP) testing is recommended for at-risk patients, its sensitivity for early-stage HCC detection is suboptimal. We therefore evaluated performance of a biomarker panel incorporating methylated DNA markers (MDMs) and proteins for early HCC detection in at-risk patients with chronic liver disease. **Methods:** In an international, multicenter, case-control study, blood specimens were collected from patients with HCC per AASLD criteria and controls matched for age and liver disease etiology. All patients had underlying cirrhosis or chronic HBV infection. Whole blood was collected in cell-free DNA stabilizing and serum-separation tubes and shipped to a central laboratory for processing. The levels of 5 MDMs, AFP, and AFP-L3 were assessed along with age and sex. We used 537 samples in a 5-fold validation for developing a LASSO regression algorithm to classify samples as HCC positive or negative. Model robustness was tested by perturbing the data *in silico* and analyzing results with the predictive algorithm. Algorithm performance was compared to AFP alone and the GALAD score (Gender, Age, AFP-L3, AFP, and DCP). **Results:** The study included 136 HCC cases (81 early-stage—BCLC stage 0/A) and 401 controls. With specificity set at 89%, we developed a model using sex, AFP, and 3 MDMs (HOXA1, TSPYL5, B3GALT6) with higher sensitivity (70%) for early-stage HCC compared to GALAD (54%) or AFP (31% at 20 ng/mL or 52% at ≥7.7 ng/mL) (Table). The AUC for the HCC marker panel was 0.91 (95% CI 0.89 – 0.94) compared to GALAD (0.88; 95% CI 0.85 – 0.91) or AFP (0.84; 95% CI 0.81 – 0.87). The panel performed similarly in viral (AUC = 0.94) and non-viral (AUC = 0.89) etiologies. **Conclusions:** The robust algorithm based on novel blood-based biomarkers presented here provides higher sensitivity for early-stage HCC compared to other available blood-based biomarkers and, therefore, could significantly impact HCC clinical management and patient outcomes. Further clinical studies to validate the algorithm are ongoing. Clinical trial information: NCT03628651. Research Sponsor: Exact Sciences.

Performance of HCC marker panel.

	Sensitivity % (95% CI)		Specificity % (95% CI)	All-Stage AUC (95% CI)
	Early-Stage	All-Stage		
Current HCC marker panel	70 (60 – 80)	81 (74 – 87)	89 (86 – 92)	0.91 (0.89 – 0.94)
GALAD	54 (43 – 65)	68 (59 – 75)	89 (86 – 92)	0.88 (0.85 – 0.91)
AFP (≥7.7 ng/mL)	52 (41 – 63)	64 (56 – 72)	89 (86 – 92)	0.84 (0.81 – 0.87)
AFP (20 ng/mL)	31 (21 – 42)	46 (38 – 55)	98 (96 – 99)	

4578 **Poster Session (Board #186), Fri, 8:00 AM-11:00 AM**

Associating liver partition and portal vein ligation for staged hepatectomy versus portal vein embolization in staged hepatectomy for hepatocellular carcinoma: A randomized comparative study.

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Background: Both Portal Vein Embolization (PVE) and Associating Liver Partition and Portal vein ligation for Staged hepatectomy (ALPPS) have been used in patients with unresectable hepatocellular carcinoma (HCC) due to insufficient volumes in future liver remnant (FLR). But it remains unclear for which thetapy has better long-term overall survival. **Methods:** This study was a single-center, prospective randomized comparative study. Patients were randomly assigned in a 1:1 ratio to the 2 groups. The primary endpoints was three-year overall survival rates. **Results:** Between November 2014 to June 2016, 76 patients with unresectable HCC due to inadequate volume of FLR were randomly assigned to ALPPS groups (n = 38) and PVE groups (n = 38). Thirty-seven patients (97.4%) in the ALPPS Group compared with 25 patients (65.8%) in the PVE Group were able to undergo staged hepatectomy (risk ratio 1.48, 95% CI 1.17-1.87, $p < 0.001$). The three-year overall survival (OS) rate of the ALPPS group (65.8%) (95% CI 50.7-80.9) was significantly better than the PVE Group (42.1%) (95% CI 26.4-57.8), (HR 0.50, 95% CI 0.26-0.98, two-sided p = 0.036). Major postoperative complications rates after the stage-2 hepatectomy were 54.1% in the ALPPS group and 20.0% in the PVE group ((risk ratio 2.70, 95% CI 1.17-6.25, p = 0.007). **Conclusions:** ALPPS resulted in significantly better long-term overall survival outcomes, at the expenses of a significantly higher perioperative morbidity rate compared with PVE in patients who had initially unresectable HCC. Clinical trial information: ChiCTR-IOC-14005646. Research Sponsor: Science Fund for Creative Research Groups, NSFC, China, (81521091).

4579 **Poster Session (Board #187), Fri, 8:00 AM-11:00 AM**

Primary tumor (p-bx) versus metastatic tumor (m-bx) tissue versus liquid biopsy (lb) in intrahepatic cholangiocarcinoma (IHCC): A comparative comprehensive genomic profiling (CGP) study.

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Background: Genomic alterations (GA) characteristic of IHCC are well known. We queried whether GA from Pbx would differ from Mbx and Lbx in IHCC. **Methods:** Hybrid-capture based CGP was performed on 1,268 tissue samples of advanced stage IHCC using Pbx in 1,048 cases and Mbx from 220 cases and 364 Lbx cases (solid tissue: 318-327 genes, Lbx: 72 genes). Tumor mutational burden (TMB) was determined on 0.8-1.1 Mbp of sequenced DNA. PD-L1 expression in tumor cells (Dako 22C3) was measured by IHC. **Results:** Mbx sites included: lymph nodes (63), soft tissues (47), peritoneum (34), lung/pleura (27), omentum (15), bone (10), abdomen (7), GYN tract (5), liver (4), brain (2), Upper GI (2), colon (2), bladder (1), and adrenal (1). The GA/sample and biomarkers of immuno-oncology (IO) drug response were similarThe *KRAS* mutation frequency including G12C alterations was doubled in Mbx compared to Pbx and Lbx ($p < 0.001$). Frequencies of untargetable GA were similar overall. *IDH1* ($p < 0.001$) and *FGFR2* GA known to be enriched in IHCC were less frequent in Mbx than Pbx. Both *IDH1* and *FGFR2* were identified in Lbx. GA in *STK11* ($p < 0.001$) and *SMAD4* ($p = 0.0016$) were more frequently identified in Mbx. **Conclusions:** GA found in Pbx vs Mbx and Lbx in IHCC are significantly different; the Mbx cohort features greater *KRAS* and lower *IDH1* and *FGFR2* GA. Lbx detected more IDH1 GA than Mbx. This suggests that the Mbx group may contain non-IHCC cases whose metastatic lesions were actually derived from other primary sites and incorrectly assigned the diagnosis of IHCC. Research Sponsor: Foundation Medicine Inc.

	Pbx	Mbx	Lbx
Cases	1,048	220	364
Males/Females	49%/51%	56%/44%	52%/48%
Median age (range)	65 (23-89+)	64 (29-89+)	66 (29-88)
GA/tumor	4.2	4.3	-
Top Currently Untargetable GA	*TP53* 32%	*TP53* 35%	*TP53* 40%
	CDKN2A 31%	*CDKN2A* 32%	*CDKN2A* (SV only) 4%
	CDKN2B 23%	*CDKN2B* 24%	*CDKN2B* (SV only) 1%
	ARID1A 19%	*ARID1A* 16%	*ARID1A* -
			KRAS 13%
	KRAS 16%	*KRAS* 34%	*MTAP* -
	MTAP 16%	*MTAP* 16%	*BAP1* -
	BAP1 15%	*BAP1* 11%	*TERT* 6%
	TERT 8%	*TERT* 4%	*SMAD4* -
	SMAD4 5%	*SMAD4* 11%	*MYC* 1%
	MYC 5%	*MYC* 5%	
Top Potentially Targetable GA	*IDH1* 16%	*IDH1* 6%	*IDH1* 9%
	FGFR2 11%	*FGFR2* 8%	*FGFR2* 4%
	ERBB2 8%	*ERBB2* 6%	*ERBB2* 4%
	PIK3CA 7%	*PIK3CA* 8%	*PIK3CA* 7%
	BRAF 6%	*BRAF* 4%	*BRAF* 4%
	IDH2 4%	*IDH2* 5%	*IDH2* 3%
	KRAS G12C < 1%	*KRAS* G12C 2%	*IDH2* 3%
			KRAS G12C 1%
IO Resistance GA	*PBRM1* 12%	*PBRM1* 14%	*PBRM1* -
	STK11 2%	*STK11* 8%	*STK11* 3%
	MDM2 4%	*MDM2* 7%	*MDM2* 2%
	KEAP1 1%	*KEAP1* < 1%	*KEAP1* -
MSI-High	< 1%	1%	0% (n = 224)
Median TMB	2.5	2.5	-
TMB > 10 mut/Mb	4%	4%	-
TMB > 20 mut/Mb	1%	1%	-
PD-L1 IHC Low Positive	15% (n = 345)	18% (n = 66)	-
PD-L1 IHC High Positive	5% (n = 345)	4% (n = 66)	-

4580 **Poster Session (Board #188), Fri, 8:00 AM-11:00 AM**

Adjuvant lenvatinib in combination with TACE for hepatocellular carcinoma patients with high risk of postoperative relapse (LANCE): Interim results from a muticenter prospective cohort study.

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Background: Surgical resection was the main treatment for hepatocellular carcinoma (HCC) in China. Multiple clinical studies had demonstrated that the overall survival (OS) of the surgical resection group was significantly better than the transcatheter arterial chemoembolization (TACE) or radiotherapy group even for HCC patients with BCLC stage B or C. There was no standard adjuvant therapy for HCC patients to decrease the post-operative tumor relapse. For HCC patients with high recurrence risk, TACE significantly reduced tumor recurrence, prolonged the disease free survival (DFS) and OS, and was recommended as the adjuvant therapy. However, its effect is not very satisfactory. The purpose of this study was to assess the efficacy and safety of lenvatinib in combination with TACE versus TACE alone as adjuvant therapy in HCC patients with high recurrence risk after resection. **Methods:** This is a muticenter prospective cohort study. The criteria of HCC patients with high postoperative recurrence risk included: accompanied with gross vascular or bile duct invasion (tumor thrombi in portal vein, hepatic vein or bile duct); or tumor rupture or invasion of adjacent organs; or grade 2 of microvascular invasion (MVI) (M2) along with the tumor number more than 3 or the maximum diameter of tumor larger than 8cm or tumor showed invasive growth with unclear boundaries and imcomplete capsules. The patients were divided into two groups, the lenvatinb (8mg qd for weights $<$ 60kg and 12mg qd for weights$\geq$60kg) in combination with TACE (Len+TACE) group and the TACE group. **Results:** A total of 90 patients were enrolled into the study, while 45 patients in the Len+TACE group and 45 in TACE group. The media age was 52 years (range from 23 to 73 years). Most patients were males (82.2%) and 66 patients had HBV background (73.3%). There were no significant differences between the two groups in the baseline clinicopathological characteristics including gender, age, HBV background, liver cirrhosis, liver function, tumor characteristic and AFP level. The media DFS was 12.0 months (95% CI 8.0-NA) in the Len+ TACE group, which was longer than that of TACE group (8.0 months, 95% CI 6.0-12.0, P = 0.0359; HR 0.5, 95% CI 0.3-1.0). The most common grade 3 or 4 adverse events were hypertension (11.1%) and diarrhea (7.7%) in the Len+TACE group. **Conclusions:** Lenvatinib in combination with TACE was effective and safe as adjuvant therapy, which can prolong the DFS of HCC patients with high recurrence risk after resection. Clinical trial information: NCT03838796. Research Sponsor: China National Key Projects for Infectious Disease (No.2017ZX10203207).

4581 **Poster Session (Board #189), Fri, 8:00 AM-11:00 AM**

A multicenter nonrandomized controlled trial to evaluate the efficacy of surgery versus radiofrequency ablation for small hepatocellular carcinoma (SURF cohort trial).

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Background: In parallel with a multicenter randomized controlled trial that reported an equal recurrence-free survival (RFS) of early-stage hepatocellular carcinoma (HCC) patients who underwent either surgery (SUR) or radiofrequency ablation (RFA), we also enrolled HCC patients who fulfilled the enrollment criteria but did not give consent to participate in the RCT. **Methods:** All patients gave informed consent to participate in this study. Inclusion criteria were as follows: primary HCC with less than or equal to 3 tumors, each measuring 3 cm or smaller; without vascular invasion or extrahepatic metastasis; Child-Pugh score of 7 or less; and ages between 20 and 79 years. The feasibility for both treatments was confirmed by a joint chart review by surgeons and hepatologists. The primary endpoint was RFS and overall survival. A pre-specified interim analysis was performed to compare RFS. **Results:** Between April 2009 and August 2015, 740 patients (371 in SUR, 369 in RFA) were enrolled from 49 participating hospitals in Japan. The SUR group had significantly fewer patients with chronic hepatitis C (56.6% vs. 69.4%), higher median value of platelet count (145 vs. 120×10^9/L), and more patients with $>$ 2 cm tumors (49.9% vs. 27.9%); most patients had a single tumor (91.1% vs. 88.3%). During the median follow-up period of 5 years, tumor recurrence was observed in 192 of SUR and 218 of RFA with 3-year RFS being 66.0% and 61.7%, respectively ($P = 0.091$). In subgroup analysis, RFS was significantly better in SUR in patients with $\leq$ 2 cm tumors (62.9% vs. 51.7% in 3 years; hazard ratio [HR] 0.72, 95% confidence interval [CI] 0.56-0.93; $P = 0.014$), whereas the difference was not significant in those with $>$ 2 cm tumors (52.7% vs. 46.4%; HR 0.85, 95% CI 0.63-1.18; $P = 0.34$). The adjusted HR for RFS using inversed probability of treatment weighting was 0.89 (95% CI, 0.72-1.10; $P = 0.287$). **Conclusions:** The imbalance in patient characteristics reflected a real-world practice. Factors related to background liver disease rather than tumor characteristics might have a larger impact on the recurrence in early HCC. Clinical trial information: C000001796. Research Sponsor: Health Labour Sciences Research Grant from The Ministry of Health Labour and Welfare of Japan.

4582 **Poster Session (Board #190), Fri, 8:00 AM-11:00 AM**

A multicenter randomized phase II study of nivolumab in combination with gemcitabine/cisplatin or ipilimumab as first-line therapy for patients with advanced unresectable biliary tract cancer (BilT-01).

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Background: Patients (pts) with advanced biliary tract cancers (BTC) have poor prognosis with a median overall survival (OS) less than 12 months (mos). This randomized phase 2, multi-institutional, study was designed to investigate the role of combinational immunotherapy, using nivolumab (nivo) with gemcitabine (gem)/cisplatin (cis), or nivo with ipilimumab (ipi) in pts with untreated advanced BTC. **Methods:** Key eligibility criteria include histologically confirmed unresectable or metastatic BTC without prior systemic therapy, measurable disease per RECISTv1.1, ECOG PS 0-1, and absence of autoimmune disease or chronic steroid use. Arm A included gem 1000 mg/m^2 and cis 25 mg/m^2 d1, 8 Q3w + nivo 360 mg d1 Q3w for 6 mos followed by nivo 240 mg Q2w monotherapy for a total duration of 2 yrs; Arm B included nivo 240 mg Q2w and ipi 1 mg/kg Q6w for 2 yrs, in absence of disease progression. Primary endpoint is progression-free survival (PFS) rate at 6 mos with an alternative hypothesis of 80% (null hypothesis of 59%, one-sided alpha 0.05, power 80%) for each non-comparative arm. Secondary endpoints include overall response rate (ORR) per immune related (ir) RECIST, median PFS and OS and safety. Exploratory objectives include biomarker analysis using include sequential whole exome/transcriptome and immune cell subsets in tissue and blood. **Results:** 71 eligible pts (49% male, 83% Caucasian) with 35 in Arm and 36 in Arm B with a median age of 62 (range 20-80) yrs, and majority with metastatic disease (90%) were enrolled across 6 US sites. PFS rate at 6 mos was 70% in Arm A and 18.6% in Arm B. The median PFS was 8.8 mos (95% CI, 6.1 to 11.3) in Arm A and 4.1 mos (95% CI, 2.4-5.2) in Arm B. Ten patients on Arm A and 2 on Arm B remain on active treatment; additional 7 are in follow-up for OS. ORR, safety data and median OS evaluation are underway and will be presented at the meeting. Exploratory analyses are pending. **Conclusions:** The observed PFS rates at 6 mos in either arm are insufficient to reject the null hypothesis of 59% PFS at 6 months. While Arm B is inferior, Arm A appears to be as effective as standard of care although OS estimates are pending maturity. Clinical trial information: NCT03101566. Research Sponsor: Bristol-Myer's Squibb, University of Michigan Rogel Cancer Center.

4583 **Poster Session (Board #191), Fri, 8:00 AM-11:00 AM**

Adjuvant concurrent chemoradiotherapy in extrahepatic cholangiocarcinoma.

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Background: Resected cholangiocarcinomas are rare and have high relapse rates. Adjuvant chemotherapy is the standard of care (BiLCAP Trial). Adjuvant radiation therapy benefit is not well defined. This study aims to evaluate survival outcomes of the effect of adjuvant chemoradiotherapy compared to chemotherapy in extrahepatic cholangiocarcinoma (EHC) using the National Cancer Database (NCDB). **Methods:** Patients with resected EHC between 2004 and 2013 were identified from the NCDB using ICD-O-3 histology and topography codes: 8140, 8160, 8161, 8162 and C24.0. Patients with neoadjuvant therapy were excluded from this analysis. Univariate and multivariable analyses were conducted, and Kaplan-Meier Curves were used to compare overall survival (OS) based on treatment received. **Results:** A total of 236 EHC patients were identified. Males comprised 60.6% and 88.1% were Caucasian. Median age was 64 (range, 31-84) years. The majority were distal (72.0%, N = 157) followed by perihilar (20.6%, N = 45), hilar (6.4%, N = 14) and cystic (0.9%, N = 2). Distribution across stages I-III was 28.8% (N = 68), 56.8% (N = 134), and 14.4% (N = 34), consecutively. Adjuvant chemotherapy was given in 37.7% (N = 89) and adjuvant chemoradiotherapy in 62.3% (N = 147). The median dose of radiation was 50.4 Gy. Adjuvant chemoradiotherapy was mostly given in regional node positive disease (p = 0.016) and negative surgical margin (p = 0.002) compared to regional node negative disease and positive surgical margin, respectively. The use of adjuvant chemoradiotherapy was associated with improved OS compared to chemotherapy alone in univariate (HR 0.64; 95% CI 0.44-0.93; p = 0.019) and multivariable analysis (HR 0.65; 95% CI 0.44-0.96; p = 0.030). Median survival and 1 year-OS for patients that received chemoradiotherapy was 33.8 months (95% CI 28, NA) and 87.7% (80.9%, 92.1%) compared to chemotherapy alone which was 23.8 months (95% CI 18.9, 35.4) and 75.5% (64.9%, 83.3%). **Conclusions:** Adjuvant chemoradiotherapy was associated with improved survival in patients with resected EHC compared to chemotherapy alone. This conclusion warrants further prospective studies to confirm these results. Research Sponsor: None.

4584 **Poster Session (Board #192), Fri, 8:00 AM-11:00 AM**

Different organ-specific response to nivolumab to determine the survival outcome of patients with advanced hepatocellular carcinoma (aHCC).

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Background: Previously, two phase III clinical trials of immune checkpoint inhibitors (ICI) failed to meet their primary endpoints, leading to doubts regarding the clinical activity of ICI monotherapy in patients with aHCC. Here, we comprehensively examined clinicopathological factors and estimated their association with survival outcomes in aHCC patients treated with nivolumab. **Methods:** A total of 261 eligible patients from 5 high-volume centers who were treated with nivolumab between June 9, 2012 and March 14, 2018 and had measurable diseases were reviewed. We reviewed more than 80 clinicopathological factors and categorized them into 6 areas: 1) demographics (n = 16); 2) baseline laboratory values (n = 19); 3) tumor burden (n = 12); 4) previous treatment (n = 12); 5) treatment response (n = 5); 6) toxicity profiles (n = 18). Their association with survival outcomes were evaluated, and organ-specific response evaluation, adapted from RECIST 1.1, was conducted. **Results:** Of the 261 patients, 218 (84%) had extrahepatic spread. The median follow-up time was 4.5 months. The median progression-free survival (PFS) and overall survival (OS) were 2.3 months (95% CI, 1.8-2.8) and 6.3 months (95% CI, 5.0-8.2). Objective response rate was 15%. Subgroup analyses revealed that compensated liver function (Child-Pugh score A5/6), surrogate markers for low tumor burden (low AFP, low PIVKA, and low LDH level), inflammatory markers (low C-reactive protein [CRP], low erythrocyte sedimentation rate [ESR], low neutrophil-to-lymphocyte ratio [NLR], high lymphocyte-to-monocyte ratio [LMR]), and low intrahepatic tumor burden were significantly associated with longer OS. A total of 456 individual lesions (liver, n = 249; lung, n = 124; lymph node, n = 35; others such as boner soft tissues, n = 48) were examined. Organ-specific response rates (hepatic tumor, 9%; lung, 25%; lymph node, 37%; others metastasis, 15%) were different, of which intrahepatic tumor was the least responsive organ to ICI treatment in aHCC. **Conclusions:** Underlying liver function, the tumor extent and burden, and the degree of plasma lymphocytes are crucial for determining tumor response to ICI in aHCC. Antitumor immune response to ICI differs in an organ-specific manner. The hepatic tumors of HCC may be less responsive to nivolumab than extrahepatic lesions. Research Sponsor: None.

4585 **Poster Session (Board #193), Fri, 8:00 AM-11:00 AM**

Clinical value of atezolizumab + bevacizumab for first-line unresectable hepatocellular carcinoma (HCC): A network meta-analysis.

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Background: The IMbrave150 pivotal study in unresectable HCC showed superiority of atezolizumab + bevacizumab (atezo + bev) vs sorafenib for OS and PFS. Based on these data supporting first-line atezo + bev for HCC, we conducted a network meta-analysis (NMA) to compare the efficacy of atezo + bev with other systemic and local therapies approved for HCC. **Methods:** A systematic literature review identified randomized controlled trials in adults with locally advanced or metastatic HCC and no prior systemic therapy for HCC. Studies of therapies now approved for any line of HCC treatment with data reported for first-line treatment since sorafenib approval in 2007 were eligible. Screening of 8783 records yielded 55 trials for inclusion; 9 studies were eligible for the evidence network. Reported hazard ratios (HRs) for OS and PFS were extracted from published studies. The IMbrave150, REFLECT and CheckMate-459 study populations were considered sufficiently similar to compare. A generalized linear model with random effects was used to estimate indirect treatment effects. Informative priors for the heterogeneity of treatment effects across trials were adopted given the limited number of trials to inform each pairwise comparison. HRs with 95% credible intervals (CrIs) and Bayesian posterior probability of atezo + bev being superior to other treatments were calculated for each treatment comparison. The base case NMA compared the relative efficacy of atezo + bev vs sorafenib observed in the IMbrave150 study with the relative effect of other therapies. Sensitivity analyses were performed to compare subgroup results as appropriate based on disease etiology, extrahepatic spread and geography. **Results:** NMA results suggested improved OS with atezo + bev vs lenvatinib (HR, 0.63; 95% CrI: 0.32, 1.25; probability of atezo + bev being superior to lenvatinib: 93.7%) or nivolumab (HR, 0.68; 95% CrI: 0.35, 1.38; probability of atezo + bev being superior to nivolumab: 90.3%) and improved PFS with atezo + bev vs lenvatinib (HR, 0.91; 95% CrI: 0.23, 3.65; probability of atezo + bev being superior to lenvatinib: 61.5%) or nivolumab (HR, 0.63; 95% CrI: 0.16, 2.59; probability of atezo + bev being superior to nivolumab: 85.5%). **Conclusions:** This NMA suggested greater OS and PFS benefits with first-line atezo + bev treatment vs other therapies approved for treatment of unresectable HCC. Research Sponsor: F. Hoffmann-La Roche, Ltd.

4586 **Poster Session (Board #194), Fri, 8:00 AM-11:00 AM**

A randomized phase II feasibility study of individualized stereotactic body radiation therapy (SBRT) versus transarterial chemoembolization (TACE) with DEBDOX beads as a bridge to transplant in hepatocellular carcinoma (HCC).

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Background: For HCC pts undergoing LT, loco-regional treatment as a "bridge" is standard. The best bridging modality is unclear. SBRT is safe and effective when used in pts with advanced HCC. We prospectively compared SBRT to TACE as a bridge for HCC pts undergoing LT. **Methods:** From 9/2014-10/2019, 60 pts within Milan Criteria with CTP Class A/B8 cirrhosis were consented. 54 pts were randomized to TACE vs. SBRT. TACE pts (n =30) were scheduled to receive 2 treatments one month apart utilizing DEBDOX beads. TACE pts were hospitalized after each TACE. Pts receiving SBRT (n =24) received a median total dose of 45Gy delivered over 5 fractions using fiducials. Mean liver dose, Veff, and NTCP determined prescription dose. Pts were assessed by using mRECIST criteria at 2 months and every 3 months thereafter until LT or death. Toxicity and QOL were assessed before treatment, during treatment, two weeks post-treatment, and then every three months using the PIQ-6 Pain Impact Questionnaire and the SF-36v2 Health Survey. The 1° endpoint was time to recurrent or residual dz. Secondary endpoints were toxicity, pathologic response, radiologic response, number of subsequent treatments, cost, and QOL. 50 pts are evaluable for review. **Results:** See table. **Conclusions:** For early stage HCC patients with CTP Class A/B liver cirrhosis, SBRT appears as effective as TACE at controlling HCC prior to LT, may engender less toxicity, and eliminates the need for hospitalization. A larger multi-center trial is ongoing. Clinical trial information: NCT02182687. Research Sponsor: Wise Grant, Pharmaceutical/Biotech Company.

Demographics	SBRT (n=21)	TACE (n=29)
Med. CTP score	6.0	6.0
Stage I HCC	81.0%	86.2%
Med. Time to 1° endpoint (mos)	10.4 (95%CI: 4.2 to 12.0)	9.2 (95%CI: 5.3 to 11.0)
QOL	SBRT (n=14)	TACE (n=26)
ΔPain sum score	0.7+/-4.5	3.9+/-7.4
ΔWML score	0.4+/-5.8	4.1+/-8.2
SF36v2:		
ΔPCS	-3.7+/-5.2	-2.0=/-4.8
ΔMCS	3.3+/-5.7	-1.5+/-4.9

4587 **Poster Session (Board #195), Fri, 8:00 AM-11:00 AM**

Effect of pembrolizumab (pembro) on hepatitis B viral (HBV) load and aminotransferase (ALT) levels in patients (pts) with advanced hepatocellular carcinoma (aHCC) in KEYNOTE-224 and KEYNOTE-240.

Stephen Lam Chan, Andrew X. Zhu, Richard S. Finn, Julien Edeline, Sadahisa Ogasawara, Jennifer J. Knox, Bruno Daniele, Baek-Yeol Ryoo, Philippe Merle, Mohamed Bouattour, Ho-Yeong Lim, Yee Chao, Thomas Yau, Barbara Anne Haber, Usha Malhotra, Chih-Chin Liu, Masatoshi Kudo, Ann-Lii Cheng; The Chinese University of Hong Kong, Hong Kong, China; Massachusetts General Hospital, Harvard Medical School, Boston, MA; David Geffen School of Medicine at UCLA, Los Angeles, CA; Centre Eugéne Marquis, Rennes, France; Graduate School of Medicine, Chiba University, Chiba, Japan; Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada; Ospedale del Mare, Naples, Italy; Asan Medical Center, Seoul, South Korea; Hôpital de la Croix-Rousse, Hospices Civils de Lyon, Lyon, France; Hôpital Beaujon, Assistance Publique Hôpitaux de Paris, Clichy, France; Samsung Medical Center, Sungkyunkwan University, Seoul, South Korea; Department of Oncology, Taipei Veterans General Hospital, Taipei City, Taiwan; The University of Hong Kong, Queen Mary Hospital, Hong Kong, China; Merck & Co., Inc., Kenilworth, NJ; School of Medicine, Kindai University, Osaka, Japan; National Taiwan University Hospital Cancer Center, Taipei City, Taiwan

Background: The effect of PD-1 inhibition on HBV infection is unclear, and pts with HBV are often excluded from trials. This analysis evaluated HBV viral load and liver function (ALT levels) in pts with HBV infection in 2 trials of pembro: KEYNOTE-224 and KEYNOTE-240. **Methods:** Eligible pts with aHCC post first-line sorafenib and controlled HBV received pembro 200 mg IV Q3W until progression. Pts with active HBV (HBsAg positive and/or HBV DNA detectable) and inactive HBV (anti-HBc positive, HBsAg negative, and HBV DNA not detectable) at baseline (BL) were included. **Results:** Of 104 pts in KEYNOTE-224 and 413 pts in KEYNOTE-240, 8 (7.7%) and 101 (24.5%) had active HBV and 13 (12.5%) and 102 (24.7%) had inactive HBV, respectively. All pts with HBV received nucleos(t)ide analogs. In KEYNOTE-240, 2 (2.8%) pts with active HBV in the pembro arm and 1 (3.4%) in placebo (pbo) had a $>$ 1 log increase (incr) of HBV DNA and 1000 IU/mL over BL; none in the pembro arm were associated with ALT elevation. No pts with inactive HBV in KEYNOTE-240 and no pts in KEYNOTE-224 had a $>$ 1 log incr and 1000 IU/mL over BL. No pts in KEYNOTE-224 and 28 (38.9%) with active HBV and 1 (1.4%) with inactive HBV in the pembro arm, and 8 (27.6%) with active HBV and 0 with inactive HBV in the pbo arm in KEYNOTE-240 had a $>$ 1 log decrease (decr) in HBV DNA. **Conclusions:** Few pts with aHCC and HBV had viral load incr with pembro. In KEYNOTE-240 no clinically meaningful differences between pembro and pbo were observed. ALT elevation was not associated with viral load incr with pembro. These data suggest that pembro is unlikely to significantly affect underlying HBV infection in pts with aHCC receiving HBV antiviral therapy. Clinical trial information: KEYNOTE-224, NCT02702414; KEYNOTE-240, NCT02702401. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Pts with HBV, n (%)	Active HBV KEYNOTE-224 Cohort 1 Pembro (n = 8)	Active HBV KEYNOTE-240 Pembro (n = 72)	Active HBV KEYNOTE-240 Pbo (n = 29)	Inactive HBV KEYNOTE-224 Cohort 1 Pembro (n = 13)	Inactive HBV KEYNOTE-240 Pembro (n = 73)	Inactive HBV KEYNOTE-240 Pbo (n = 29)
> 1 log decr	0	28 (38.9)	8 (27.6)	0	1 (1.4)	0
> 1 log incr + 1000 IU/mL	0	2 (2.8)	1 (3.4)	0	0	0
> 2 log incr	0	3 (4.2)	1 (3.4)	0	1 (1.4)	0
> 3 log incr	0	0	1 (3.4)	0	0	0
ALT ≥3×BL + > 100 U/L post-BL	1 (12.5)	6 (8.3)	3 (10.3)	1 (7.7)	15 (20.6)	2 (6.9)
ALT and AST to > 5×ULN and/or > 3×BL	1 (12.5)	6 (8.3)	3 (10.3)	0	12 (16.4)	5 (17.2)
> 1 log incr + 1000 IU/mL + ALT elevation[a]	0	0	1 (3.4)	0	0	0
2 log incr + ALT ≥3×BL + > 100 U/L post-BL	0	0	1 (3.4)	0	0	0

[a]ALT elevation: met 1 of 3 criteria ± 7 days of time of viral flare:
1) BL ALT < 2×ULN and post-BL ALT ≥5×ULN
2) BL ALT ≥2×ULN and post-BL ALT > 3×BL level
3) ALT > 500 U/L regardless of BL level

4588 **Poster Session (Board #196), Fri, 8:00 AM-11:00 AM**

Combination immunotherapy with ipilimumab and nivolumab in patients with advanced biliary tract cancers.

Oliver Klein, Damien Kee, Adnan Nagrial, Ben Markman, Craig Underhill, Michael Michael, Caroline Lum, Andreas Behren, Jodie Palmer, Niall C. Tebbutt, Matteo S. Carlino, Jonathan S. Cebon; Medical Oncology Unit, Austin Health, Heidelberg, Australia; Peter MacCallum Cancer Centre, Melbourne, Australia; Blacktown Hospital, Sydney, NSW, Australia; Monash Health and Monash University, Melbourne, Australia; Albury-Wodonga Regional Cancer Centre, Albury-Wodonga, Australia; Division of Cancer Medicine, Peter MacCallum Cancer Centre, Melbourne, Australia; St Vincent's Hospital Melbourne, Melbourne, Australia; Olivia Newton-John Cancer Research Institute, Melbourne, Australia; Olivia Newton-John Cancer Research Institute, Heidelberg, Australia; Olivia Newton-John Cancer and Wellness Centre, Victoria, Australia; Westmead Hospital, Sydney, NSW, Australia; Ludwig Institute for Cancer Research, Heidelberg, Australia

Background: Patients (pts) with advanced biliary tract cancers (BTC) have a poor prognosis with first and second line chemotherapy resulting in modest survival benefits. Immunotherapy using single agent anti-PD-1 therapy has also shown low activity with an objective response rate (ORR) of less than 10%. Combined CTLA-4/PD-1 blockade using ipilimumab (ipi) and nivolumab (nivo) has demonstrated superior efficacy compared to single agent anti-PD-1 therapy in pts with advanced melanoma and renal cell carcinoma. To date, no trials in BTC pts with ipi/nivo therapy have been reported. **Methods:** 39 pts with metastatic BTCs were enrolled into the CA 209-538 clinical trial for rare cancers. Patients received nivo 3mg/kg and ipi 1mg/kg q 3 weekly for 4 doses, followed by nivo 3mg/kg q 2 weekly. Treatment continued for up to 96 weeks, or until disease progression or the development of unacceptable toxicity. Response (RECIST 1.1) was assessed every 12 weeks. The primary endpoint was clinical benefit rate (CBR = CR +PR + SD). Exploratory endpoints include correlation of efficacy with biomarkers including PD-L1 expression and tumour mutation burden. **Results:** 39 pts with BTC were enrolled and 33 pts (85%) had received at least one prior line of systemic treatment (0-2 lines). The ORR was 24% and the CBR 45% with the median duration of response not been reached (range 2-26+months). Responses were observed in 3/14 intrahepatic, 1/10 extrahepatic, 0/2 unspecified cholangiocarcinoma and 5/13 gallbladder ca pts. None of the responding pts had a microsatellite instable tumour. 2 pts with durable partial responses were subsequently rendered surgically free of disease. Median OS and PFS were 6.1 and 3.1 months respectively. 22 (56%) pts experienced an immune –related adverse event (irAE) with grade3/4 irAEs being observed in 8 (20%) pts. **Conclusions:** Combination immunotherapy with ipi/nivo demonstrates significant clinical activity in a subset of patients with advanced microsatellite stable BTC. The response rate compares favourably to clinical trials investigating single agent anti-PD-1 therapy. Clinical trial information: NCT02923934. Research Sponsor: Australian Federal Department of Health.

4589 **Poster Session (Board #197), Fri, 8:00 AM-11:00 AM**

Genomics and translational precision oncology for 803 patients with biliary tract cancer.

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Background: Both incidence and mortality of biliary tract cancer (BTC) are increasing, and BTCs are characterized by poor prognosis and limited antitumoral treatments. There is no well-received regimen as the non-first-line treatment in patients with advanced BTCs, leading to the urgency of umbrella-setting personalized therapies according to genomic alterations. **Methods:** We performed genomic sequencing in a total of 803 BTCs, including 160 patients with whole-exome sequencing and 643 patients with hybrid capture–based comprehensive genomic profiling. Our molecular tumor board developed precise targeted therapies for patients with actionable targets. **Results:** Overall, the median tumor mutation burden was 3.0 (IQR: 0.8-6.1) Mut/Mb, with 10.5% patients of hypermutated BTCs. The most frequently mutated genes included *TP53* (51%), *KRAS* (23%), *ARID1A* (16%) and *SMAD4* (11%). The most common genes with significantly amplified oncogenes were *CCND1* (6.97%), *MET* (6.72%) and *MDM2* (6.6%), while the frequently deleted tumor-suppressor genes are *CDKN2A* (5.73%) and *CDKN2B* (5.35%). The mutational map of BTCs highlighted pathways of receptor-tyrosine kinase (RTK)/RAS and *p53* signaling were frequently altered. Somatic truncating mutations of mismatch repair genes were identified in 6.1% (49/803) of patients, and germline pathogenic mutations in DNA damage response genes occurred in 8% (64/803) of BTCs. In addition, we demonstrate the amplified chromosomal focal at 7q31.2 was an oncogenic factor and it independently predicts both disease-free survival and overall survival of BTC patients. When molecular screening was linked to targeted therapies, 25.4% (204/803) of patients could match biomarker-assigned drug treatment (BADT). The frequent actionable biomarkers included amplifications of *ERBB2* and *MET*, *FGFR2/3* fusions and *IDH1* mutations. For 46 patients with refractory BTCs received BADT, the objective response rate was 26.1%, with a median progression-free survival (mPFS) of 5.0 (95%CI: 3.5-6.5) months, and 56.8% patients achieved a $\geq$1.3 ratio of PFS2/PFS1. 4 of 6 (67%) patients with high microsatellite instability (MSI-H) BTCs had a responsive status after immunotherapy of PD1 inhibitor, confirming that MSI-H status was a robust biomarker of anti-PD1 treatments. **Conclusions:** Our study established the largest cohort in Chinese BTC patients to investigate the tumor mutational profiling and its translational clinical applications. Clinical trial information: NCT02715089. Research Sponsor: International Science and Technology Cooperation Projects.

4590 **Poster Session (Board #198), Fri, 8:00 AM-11:00 AM**

A phase II open-label, single-center, nonrandomized trial of Y90-radioembolization in combination with nivolumab in Asian patients with advanced hepatocellular carcinoma: CA 209-678.

Wai Meng David Tai, Kelvin Siu Hoong Loke, Apoorva Gogna, Sze Huey Tan, David Chee Eng Ng, Tiffany Priyanthi Hennedige, Farah Irani, Joycelyn Jie Xin Lee, Chow Wei Too, Matthew C.H. Ng, Chee Kian Tham, Justina Yick Ching Lam, Si-Lin Koo, Alexander Chung, Han Chong Toh, Choon Hua Thng, Kiat Hon Lim, Joe Poh Sheng Yeong, Chung Yip Chan, Su Pin Choo; National Cancer Center Singapore, Singapore, Singapore; Singapore General Hospital, Singapore, Singapore; Division of Clinical Trials and Epidemiological Sciences, National Cancer Centre, Singapore, Singapore; Department of Medical Oncology, National Cancer Centre Singapore, Singapore, Singapore; National Cancer Centre Singapore, Singapore, Singapore; National Cancer Centre, Singapore, Singapore; Tessa Therapeutics Pte Ltd, Singapore, Singapore; National Cancer Center Singapore, Curie Oncology, Singapore, Singapore

Background: Nivolumab (N) and Y90-radioembolization (RE) are both therapeutic options in advanced hepatocellular carcinoma (aHCC). Increasing evidence suggests that radiotherapy synergizes with immune checkpoint inhibitors to augment anti-tumour effects. **Methods:** Eligible Child-Pugh A aHCC patients (pts) were treated with Y90-RE followed by N 240mg, 21 days after Y90-RE and every 2 weeks thereafter. Pre- and on-treatment tumor biopsies together with circulating biomarkers were obtained. Primary end-point was overall response rate (ORR) (per RECIST v 1.1). Overall response was defined as the composite overall response observed for the lesions within Y90-RE field and outside Y90-RE field. Key secondary end points included disease control rate (DCR), progression free survival (PFS), overall survival (OS), and safety. 36 evaluable pts were needed to assess whether the addition of N improved the ORR of Y90-RE from 21% to 41% as determined by Simon two-stage optimal design with 80% power and one sided significance level of 0.05. **Results:** Forty pts were enrolled of which 36 were evaluable. At baseline: 63.9% were HepB in aetiology; 63.9% BCLC stage C; 47.2% had AFP $>$ 400ng/mL; number of liver lesions – median 5 (range 1- 20); size of largest liver lesion – median 80mm (range 14-177mm); 27.8% had prior TACE; and 13.9% had prior systemic therapy. ORR was 31% (95% CI 16.4 - 48.1%). Eight out of 11 responders had not progressed at study cut-off. DCR was 58.3%. 81% of target lesions within Y90-RE field regressed. With a median follow up of 16.4 months, median PFS and OS were 4.6 months (95% CI 2.3m - 8.4m) and 15.1 months (95% CI 7.8m - NE) respectively. Six- and 12-month PFS rates were 44.2% (95% CI 27.3% - 59.9%) and 26.1% (95% CI 11.2% - 43.8%) respectively. Overall, N+ Y90-RE was well tolerated and safe; only 11% had grade 3/4 treatment related adverse events (AEs). Responders demonstrated significant alterations of LIF, MIG and Eotaxin3 levels in the pre-treatment cytokine analyses. **Conclusions:** Combination N+Y90-RE resulted in an encouraging ORR of 31% (95% CI 16.4 - 48.1%) in aHCC. 81% of target lesions within Y90-RE field regressed suggesting synergy in combining Y90-RE with nivolumab. This combination is safe and tolerable with low G3/4 treatment related AEs of 11%. Further biomarker analyses will be presented at the meeting. Clinical trial information: NCT03033446. Research Sponsor: National Medical Research Council Singapore, BMS, SIRTEX.

4591 **Poster Session (Board #199), Fri, 8:00 AM-11:00 AM**

A retrospective analysis of post second-line chemotherapy treatment outcomes for patients with advanced or metastatic cholangiocarcinoma and FGFR2 fusions.

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Background: Cholangiocarcinoma (CCA) is the most common biliary tract malignancy with an estimated incidence of 8,000–10,000 patients/year in the US. Chemotherapy is the most common second-line treatment with reported outcomes in patients with CCA. Response rates of $<$ 10% and median progression-free survival (PFS) times of ~3–4 months have been reported with second-line chemotherapy regimens, including FOLFOX in the ABC-06 trial. Fibroblast growth factor receptor 2 (*FGFR2*) fusions occur in 13–17% of CCA and multiple targeted agents are in development for patients with *FGFR2* fusions. To date, the outcome of patients with CCA and *FGFR2* fusions receiving standard second-line chemotherapy is unknown. **Methods:** Patients with advanced CCA and *FGFR2* fusions after prior treatment with gemcitabine-based chemotherapy were enrolled in a single-arm phase 2 study (NCT02150967) and received the FGFR1–3 selective TKI infigratinib (previously BGJ398) 125 mg orally qd on d1–21, cycles repeated q28 days until unacceptable toxicity, disease progression, investigator discretion, or withdrawal of consent. A retrospective analysis of a subset of patients who received infigratinib as third- or later-line treatment was performed. Investigator-assessed PFS and best overall response (BOR, per RECIST 1.1) following second-line chemotherapy (pre-infigratinib) and third-line or later-line infigratinib were calculated. **Results:** Of the 71 patients (44 women; median age 53 years) with *FGFR2* fusions enrolled at the time of analysis (datacut 8 August 2018), 37 (52%) were included in this retrospective analysis. Median PFS with standard second-line chemotherapy was 4.63 months (95% CI 2.69–7.16) compared with 6.77 months (95% CI 3.94–7.79) for third- and later-line infigratinib. BOR for second-line chemotherapy was 5.4% (95% CI 0.7–18.2) compared with 21.6% for third- and later-line infigratinib (95% CI 9.8–38.2). **Conclusions:** Outcomes from second-line chemotherapy in patients with CCA and *FGFR2* fusions were similar to those reported in the literature for all patients with CCA regardless of genomic status and remain dismal. Infigratinib administered as third- and later-line treatment resulted in a meaningful PFS and ORR benefit in patients with CCA and *FGFR2* fusions. Clinical trial information: NCT02150967. Research Sponsor: QED Therapeutics.

4592 **Poster Session (Board #200), Fri, 8:00 AM-11:00 AM**

Clinical activity and safety of penpulimab (Anti-PD-1) with anlotinib as first-line therapy for advanced hepatocellular carcinoma (HCC).

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Background: Advanced HCC is a deadly disease with few systemic therapeutic options. VEGF blockade potentiates the effect of PD-1 inhibition by opposing the immunosuppressive effects of VEGF-A (increased DC maturation, enhanced T-cell infiltration, reduced MDSCs and Tregs in tumors). A sBLA has been submitted for an anti-PD-L1 + anti-VEGF combination as 1L treatment for advanced HCC. Penpulimab is a novel humanized anti-PD-1 IgG1 antibody with complete removal of Fc receptor mediated effect, and featuring slow antigen binding off-rate and high receptor occupancy. 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, treatment-naive pts with advanced HCC received penpulimab 200mg Q3W in combination with anlotinib 8mg QD (2 weeks on 1 week off) until loss of clinical benefit or unacceptable toxicity. The primary objectives were to assess antitumor activity by ORR (RECIST v1.1). The secondary objectives were to assess antitumor activity by DCR, DoR, TTP, and to assess the safety and tolerability of the combination. **Results:** As of Jan 14, 2020, 31 pts (median age 56 years [23-74], male 81%, ECOG 0/1 [64%/36%], BCLC B/C [23%/77%], HBV/HCV [61%/7%]) received combined therapy (a median of 6 [1-15] doses). Treatment-related adverse events (TRAEs) occurred in 93.5% of pts (G3 in 9.7% [3/31], no G4, and leading to treatment discontinuation in 6.5% [2/31]). Most frequent TRAEs were increased AST (35.5%), increased ALT (29%), asthenia (22.6%), decreased platelet count (19.4%), increased blood bilirubin (19.4%), increased bilirubin conjugated (19.4%), and rash (16.1%). Of 25 evaluable pts (with the opportunity to be followed-up for $\geq$2 scans, 12 weeks), confirmed ORR was 24% (6/25) and DCR was 84% (21/25). Five responders remained in response with DoR ranging 1.4+ to 6.9+ months. Median TTP was not reached and 6m-TTP rate was 63% (95% CI: 38%, 81%). **Conclusions:** Penpulimab in combination with anlotinib had a manageable safety profile and encouraging antitumor activities in patients with advanced HCC. No unexpected AEs were identified beyond the established safety profile for each agent. Evaluation of penpulimab + anlotinib (10 mg QD) in a phase 3 study for 1L HCC is currently underway. Clinical trial information: NCT04172571. Research Sponsor: Akeso Biopharma, Inc., Zhongshan, China.

4593 **Poster Session (Board #201), Fri, 8:00 AM-11:00 AM**

Perioperative circulating tumor DNA analysis to predict patient prognosis in liver cancer.

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Background: Resection is a major method for early-stage liver cancer patients. Unfortunately, there still a few patients with post-operation recurrences. Circulating tumor DNA (ctDNA) had been reported as a biomarker in reflecting tumor load and treatment efficacy in some cancer species. Here, we report an application of ctDNA in the perioperative period of liver cancer using targeted sequencing with a 1021-gene panel. **Methods:** 97 patients diagnosed with liver cancer were enrolled in this study. Postoperative peripheral blood samples were collected within 7 days after surgery and analyzed using hybridization capture based NGS ERSeq method from all patients. Whether a mutant gene was detected in the peripheral blood was defined as ctDNA(+) and ctDNA(-), respectively. **Results:** Multivariate Cox analysis showed that the post-operation ctDNA was an independent poor prognostic predictor (AFP, RR: 1.0002, 95% CI: 1.0001-1.0002; ctDNA, RR: 3.738, CI: 1.872-7.691). 21 patients were ctDNA(+), and all of them had recurrenced (21/21, 100%), while 76 patients were ctDNA(-), and only 12 (12/76, 15.8%) patients had recurrenced. The median disease-free survival time was 5.0 months in ctDNA(+) group and the ctDNA(-) group had not reach the median time (Log-rank test, $P < 0.0001$). ctDNA combined with AFP would effectively predict the prognosis of patients after surgery. AFP(H) (> = 400 ng/mL) and ctDNA(+) patients have the worst prognosis and all of the patients had relapsed, while AFP(L) (< 400 ng/mL) and ctDNA(-) patients had the best prognosis, with less than 20% of patients had relapsed (Log-rank test, $P < 0.0001$). The median disease-free survival time was 2.0, 6.0 and 7.0 months in ctDNA(+)-AFP(H) (n = 8), ctDNA(-)-AFP(H) (n = 30) and ctDNA(+)-AFP(L) (n = 13) groups, respectively, while ctDNA(-)-AFP(L) group (n = 46) had not reach the median time statistically (Log-rank test, $P = 0.0364$). **Conclusions:** In summary, Perioperative ctDNA detection has great potential value clinically, and it also suggests that patients with positive ctDNA after surgery should receive some adjuvant treatments as soon as possible to improve the survival time. Research Sponsor: National Nature Science Foundation of China.

4594 **Poster Session (Board #202), Fri, 8:00 AM-11:00 AM**

Predictive value of changes in plasma vascular endothelial growth factor at eight weeks after lenvatinib administration in patients with unresectable hepatocellular carcinoma.

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Background: Lenvatinib (LEN) has been used in patients with unresectable hepatocellular carcinoma (u-HCC) and there is no established predictive biomarker. Previously it was reported that a plasma vascular endothelial growth factor (VEGF) concentration decrease at 8 weeks after starting sorafenib might predict favorable overall survival (OS) in patients with u-HCC (Tsuchiya, et al. Cancer, 2013). We aimed to investigate the value of changes in plasma VEGF at 8 weeks after LEN administration in patients with u-HCC. **Methods:** Forty-six patients with u-HCC who received LEN between April 2018 and August 2019 at our institution were enrolled. Plasma concentrations of VEGF and serum α-fetoprotein (AFP) levels were measured at baseline, 4 and 8 weeks after administration of LEN. A VEGF decrease was defined as $>$ 5% decrease during 8 weeks after the beginning of LEN therapy. AFP response was defined as $>$ 20% decrease during 8 weeks according to the previous reports. **Results:** Median overall survival (OS) was not reached and progression-free survival (PFS) was 5.9 months. Median observation period and treatment duration were 10.1 and 6.3 months. The objective response rate and disease control rate by mRECIST criteria were 43.5% and 82.6%. Median PFS in patients who had a VEGF decrease at week 8 (n = 29) was significantly longer than those who did not have a VEGF decrease (n = 17; 7.1 months vs 5.0 months; p = 0.014). AFP response was not associated with PFS. There were no significant differences in baseline VEGF, AFP, ALBI score, and extrahepatic metastasis between the patients with and without a VEGF decrease. A VEGF decrease was significantly associated with radiological objective response (p = 0.001) and 18 of 20 patients who achieved CR (n = 3) or PR (n = 17) had a VEGF response in LEN therapy. **Conclusions:** A decrease of plasma VEGF level at 8 weeks in patients with u-HCC on LEN was significantly associated with PFS. Changes in plasma VEGF could become a new biomarker for molecular targeted therapies including VEGF inhibitors in patients with unresectable HCC. Research Sponsor: Japan Agency for Medical Research and Development.

4595 **Poster Session (Board #203), Fri, 8:00 AM-11:00 AM**

Comparison of response using mRECIST versus RECIST 1.1 Criteria in advanced hepatocellular carcinoma: A retrospective analysis of multicenter clinical trials.

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Background: mRECIST 2010 criteria for Hepatocellular Carcinoma (HCC) response assessment were focused on a concept of measuring viable tumor tissue showing enhancement in arterial phase of contrast enhanced CT/MRI, whereas RECIST 1.1 focuses mainly on the morphological measurements quantifying the tumor size irrespective of viability of the tumor and associated response to therapy. RECIST 1.1 does not address measures of antitumor activity other than tumor shrinkage, underestimating responses in HCC. **Methods:** We retrospectively analyzed multiple, phase III, multi-center clinical trials using both mRECIST and RECIST 1.1 criteria, read separately. The intent was to compare the overall responses at post-baseline assessments read independently by the two criteria. A total of 1682 subjects with 6159 post-baseline imaging timepoints were included in the analysis. The Overall response rate (ORR) as measured by sum of complete response (CR) and partial response(PR) and the Complete response rate (CRR) were evaluated. In addition, we also assessed the number of not evaluable (NE) time points by each criteria separately. We tested the following hypotheses 1. mRECIST may have better ORR and CRR compared to RECIST 1.1. 2. RECIST 1.1 may have more timepoints with Stable disease (SD) compared to mRECIST. 3. mRECIST may have more Not evaluable (NE) timepoints due to stringent imaging specifications. **Results:** The results are tabulated in the table below: **Conclusions:** The results above suggest that mRECIST shows more than double the CRR than RECIST 1.1, and the ORR is 62% higher using mRECIST than RECIST 1.1. Stable disease as expected was more commonly observed in RECIST 1.1 analysis. A NE response was 60% more common in mRECIST criteria evaluation. Our analysis confirms that reduction in viable tumor/enhancing area using contrast-enhanced radiologic imaging is the more optimal method to assess treatment response in HCC, and using RECIST 1.1 tumor measurement of a longest diameter as the sole measure of response, may not be adequate in response assessment for HCC. Our analysis validates and supports more widespread adoption of mRECIST in HCC tumor response assessment. Our results also indicate the need for uniform image acquisition and rigorous image quality control for a valid response in mRECIST criteria.
Research Sponsor: None.

mRECIST versus RECIST 1.1 Overall Response.

	mRECIST	RECIST 1.1
CR	111	46
PR	1497	966
SD/NN (Stable Disease/Non-CR Non-PD)	1994	2661
PD (Progressive Disease)	2509	2457
NE	48	29
ORR	26.10%	16.41%
CRR	1.8%	0.7%

4596 **Poster Session (Board #204), Fri, 8:00 AM-11:00 AM**

Complete responses (CR) in patients receiving atezolizumab (atezo) + bevacizumab (bev) versus sorafenib (sor) in IMbrave150: A phase III clinical trial for unresectable hepatocellular carcinoma (HCC).

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Background: In the Phase III IMbrave150 trial, statistically significant and clinically meaningful improvements in OS and PFS were seen with atezo + bev vs sor in pts with unresectable HCC who had not received prior systemic therapy (Cheng, ESMO Asia, 2019). Historically, CR rates have been low in HCC clinical trials. Here we report the baseline characteristics for IMbrave150 pts with a CR. **Methods:** IMbrave150 enrolled systemic treatment-naive pts with unresectable HCC. 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. Co-primary endpoints were OS and PFS by independent review facility (IRF)–assessed RECIST 1.1. The key secondary endpoints IRF ORR per RECIST 1.1 and IRF ORR per HCC mRECIST were also part of the study statistical testing hierarchy. **Results:** The ITT population included 336 pts randomized to atezo + bev and 165 pts randomized to sor. With a median follow-up of 8.6 mo (data cutoff, Aug 29, 2019), OS HR was 0.58 (95% CI: 0.42, 0.79; $P = 0.0006$) and PFS HR was 0.59 (95% CI: 0.47, 0.76; $P < 0.0001$) with atezo + bev vs sor. ORR was 27% vs 12% ($P < 0.0001$) per IRF RECIST 1.1 and 33% vs 13% ($P < 0.0001$) per IRF HCC mRECIST with atezo + bev vs sor, respectively. For responders (per IRF RECIST 1.1), median time to response was 2.8 mo (range, 1.2-11.3) with atezo + bev and 3.3 mo (range, 1.2-7.2) with sor. CR per IRF-assessed RECIST 1.1 was achieved by 18 pts in the atezo + bev arm and 0 pts in the sor arm. The baseline characteristics for atezo + bev CR pts are shown in the table. Additional characteristics will be shown. **Conclusions:** IMbrave150 demonstrated statistically significant and clinically meaningful improvement in both OS and PFS with atezo + bev vs sor in pts with unresectable HCC who have not received prior systemic therapy. Pts achieved CRs regardless of poor prognostic factors or etiology. Atezo + bev may be a practice-changing treatment for pts with unresectable HCC. Clinical trial information: NCT03434379. Research Sponsor: F. Hoffmann-La Roche, Ltd.

n (%)	CR pts; atezo + bev (n = 18)	All pts; atezo + bev (n = 336)
≥ 65 y	7 (39)	161 (48)
Asia excluding Japan | Rest of world	8 (44) | 10 (56)	133 (40) | 203 (60)
ECOG PS 1	5 (28)	127 (38)
Etiology, HBV | HCV | non-viral	9 (50) | 5 (28) | 4 (22)	164 (49) | 72 (21) | 100 (30)
Child-Pugh class, A5 | A6	12 (67) | 6 (33)	239 (72) | 94 (28) (n = 334)
BCLC stage, A | B | C	1 (6) | 4 (22) | 13 (72)	8 (2) | 52 (16) | 276 (82)
MVI | EHS | MVI and/or EHS	6 (33) | 10 (56) | 12 (67)	129 (38) | 212 (63) | 258 (77)
AFP ≥ 400 ng/mL	3 (17)	126 (38)
Prior local therapy	12 (67)	161 (48)

4597 **Poster Session (Board #205), Fri, 8:00 AM-11:00 AM**

Results from TreeTopp: A randomized phase II study of the efficacy and safety of varlitinib plus capecitabine versus placebo in second-line (2L) advanced or metastatic biliary tract cancer (BTC).

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Background: Patients with advanced or metastatic BTC who progress on first-line (1L) gemcitabine-based doublet chemotherapy have few 2L treatment options. Varlitinib is a reversible small molecule pan human epidermal growth factor receptor (HER) inhibitor with low nanomolar potency against HER1 (EGFR), HER2 and HER4 with promising early results in advanced BTC. **Methods:** TreeTopp (NCT03093870) was a global, multicenter, double blind phase 2 study in which patients with advanced BTC who progressed after 1L therapy that included ≥6 doses of gemcitabine, with radiographically measurable disease based on RECIST v1.1, ECOG PS 0 or 1 and albumin ≥3 g/dL were randomized (1:1) to varlitinib (300 mg BID) plus capecitabine (1000 mg/m^2 BID 14 days on/ 7 off)(V+C) or placebo plus capecitabine (P+C). The dual primary endpoints were Objective Response Rate (ORR) and Progression Free Survival (PFS) defined as the time from randomization to radiological progression assessed by Independent Central Review. Secondary end points included Overall Survival (OS). **Results:** Overall, 127 patients were randomized (V+C, n = 64; P+C, n = 63) from May−Dec 2018 and demographics/baseline characteristics were generally well balanced, although the V+C arm had a lower proportion of females vs. P+C (31% vs. 48%). The odds ratio for ORR was numerically higher with V+C vs. P+C was 2.278 (9.4% vs. 4.8%, p = 0.42), the HR for PFS for V+C vs. P+C was 0.90 (median PFS, 2.8 vs. 2.8 months; p = 0.63), and the HR for OS for P+C vs. V+C was 1.11 (median OS, 7.8 vs. 7.5 months; p = 0.66). Although not powered to evaluate sub-group interactions, in sub-group analysis, V+C showed PFS benefit versus P+C in two sub-groups; gallbladder cancer (GBC, HR = 0.55, 95% CI: 0.25, 1.22; median PFS, 2.9 vs. 1.6 months) and females (HR = 0.59, 95% CI: 0.28, 1.23; median PFS, 4.1 vs. 2.8 months). There was no PFS benefit for V+C vs. P+C among males and non-GBC. Toxicities were generally balanced between arms apart from a slightly higher incidence of hyperbilirubinemia, diarrhea and fatigue in the V+C vs. P+C arm. Grade 3/4 toxicities were reported in 66% and 59% of patients in the V+C and P+C arms, respectively. **Conclusions:** V+C is well tolerated but did not improve ORR, PFS or OS vs. P+C in 2L advanced BTC. Exploratory analyses suggested that patients with GBC and female patients achieved comparatively higher median PFS with V+C vs. P+C. Clinical trial information: NCT03093870. Research Sponsor: ASLAN Pharmaceuticals.

4598 **Poster Session (Board #206), Fri, 8:00 AM-11:00 AM**

Comprehensive gene expression analysis of IDH1/2 mutant biliary cancers (BC).

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Background: Isocitrate dehydrogenases (IDH) mutations (mut) identify a distinct subtype of BC that has yet to be fully characterized. We recently showed that *IDH1/2* mutant (mIDH) BC harbor specific gene alterations involving chromatin remodeling and DNA repair, and a differential immune markers profile compared to other mIDH GI tumors. Here we aim to further dissect the molecular profile of mIDH BC through a comprehensive gene expression profiling analysis. **Methods:** 524 BC samples (303 intrahepatic cholangiocarcinoma, IHCC, 67 extrahepatic cholangiocarcinoma, EHCC, 141 gallbladder, 13 unspecified) collected between February to December of 2019 were included. Samples were analyzed using NextGen DNA sequencing (NextSeq, 592 gene panel), whole transcriptome RNA sequencing (NovaSeq) and immunohistochemistry (Caris Life Sciences, Phoenix, AZ). EBseq was used to identify differentially expressed genes in mIDH vs wild type (WT) tumors with control for FDR ($Q < 0.2$). Pathway and functional enrichment analysis was performed using g:Profiler and Enrichr. **Results:** mIDH frequency in our cohort was 11.4% (60/524), with higher prevalence of *IDH1* mut (8.8%). IHCC showed the highest mut prevalence: *IDH1* 13.5%, *IDH2* 4.6%. mIDH was more common in females ($P = 0.0036$). A total of 774 genes were significantly differentially expressed between mIDH and WT: 582 underexpressed (Fold change, FC: 0.025~0.699); 192 overexpressed (FC: 1.43~3.3). Pathway enrichment showed a significant decrease of gene expression in cytokine-cytokine receptor interaction ($Q = 0.002$) and inflammatory response genes ($Q = 0.005$) in mIDH. Interferon-γ- and PD1 signaling-related genes expression was significantly lower in mIDH vs WT ($Q = 0.02$) including *IFNG* (FC 0.32), *NKG7* (FC 0.36), *CD8B* (FC 0.37), *BATF* (FC 0.40), *PD1* (FC 0.53), *SLAMF6* (FC 0.55) and *PD-L2* (FC 0.60). Wnt and cadherin signaling were also enriched for altered expression in several genes in mIDH BC ($Q = 3.86e\text{-}7$ and < 0.00001, respectively). **Conclusions:** To our knowledge, this is the largest and most extensive gene expression profiling study focused on mIDH BC. Our data show for the first time a distinct gene expression profile characterizing mIDH tumors which display significant downregulation of inflammatory response pathways and immune-related genes. These findings contribute to further the understanding of mIDH BC and may inform the future development of rational combination therapies. Research Sponsor: NCI P30CA014089, the Gloria Borges WunderGlo Foundation-The Wunder Project, the Dhont Family Foundation, the San Pedro Peninsula Cancer Guild, the Daniel Butler Research Fund, the Call to Cure Research Fund and the Fong Research Project.

4599 **Poster Session (Board #207), Fri, 8:00 AM-11:00 AM**

Final results of a randomized, open label, perioperative phase II study evaluating nivolumab alone or nivolumab plus ipilimumab in patients with resectable HCC.

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Background: In resectable hepatocellular carcinoma (HCC) surgical resection is associated with high recurrence rates. However, there is no approved neoadjuvant or adjuvant therapies yet. Neoadjuvant immunotherapy effect has never been reported in this setting in HCC. **Methods:** This is a randomized phase II trial of nivolumab (Arm A) or nivolumab + ipilimumab (Arm B) as peri-operative treatment for patients (pts) with HCC who are eligible for surgical resection. Pts in Arm A are given nivolumab 240 mg iv, every 2 weeks (wks) for a total of 3 doses followed by surgery on week 6. Pts in Arm B are treated with nivolumab per same schedule as arm A plus concurrent ipilimumab 1 mg/kg on day 1. Adjuvant part of study starts 4 weeks after surgery, with Nivolumab at 480 mg iv every 4 weeks for 2 years in arm A. Pts in Arm B are treated with nivolumab per same schedule as arm A plus concurrent ipilimumab 1 mg/kg every 6 weeks times 4 doses after resection. The primary objective was the safety/tolerability of nivolumab +/- ipilimumab. Secondary objectives include overall response rate, pathologic complete response (pCR) rate and time to progression. Exploratory objectives include evaluating the pre- and post-treatment immunological changes in tumor tissues and peripheral blood. **Results:** 30 patients were enrolled, 2 patients withdrew consent, one patient was not eligible at time of therapy, and 27 randomized (13 to Arm A and 14 to Arm B). 21 patients proceeded with resection as planned and surgery was aborted for 6 patients; 1 for frozen abdomen due to old surgery, 2 for small residual volume, and 3 for progressive disease. Pts age ranged between 32-83 yo, 75 % were males, 7 pts had HCV, 7 had HBV and 7 had no hepatitis. Pathologic complete response (pCR) was observed in 5/21 pts (24% pCR rate) – 2 in Arm A and 3 Arm B, and 3/21 pts (16%) – 1 in Arm A, 2 in Arm B, achieved major pathologic response (necrosis effect of 50-99%). 5 patients in Arm B and 1 in Arm A experienced grade 3 or higher toxicity prior to surgery. No grade 4 or higher toxicity were observed and surgery was not delayed or cancelled due to oxicity. **Conclusions:** Our study reached its primary endpoint of safety. Importantly, we report a 40% pathologic response rate = pCR rate of 24%, and major necrosis rate of 16% for resectable HCC after preoperative immunotherapy in a randomized phase II pilot trial. After future validation, these promising results may contribute to a paradigm shift in the perioperative treatment of resectable HCC. Clinical trial information: NCT03222076. Research Sponsor: M.D. Anderson Cancer Center.

4600 **Poster Session (Board #208), Fri, 8:00 AM-11:00 AM**

Genome-wide plasma cell-free DNA methylation profiling to identify high-performing biomarkers for early detection of hepatocellular carcinoma.

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Background: Hepatocellular carcinoma (HCC) represents the second most common cause of cancer deaths worldwide. □-fetoprotein (AFP) is the most common serological test used for screening and diagnosis of HCC. However, it is widely recognized that AFP has lower sensitivity with sub-optimal specificity. Tumor-originated circulating cell-free DNA (cfDNA) provides new opportunity for non-invasive detection of liver cancer. **Methods:** HCC-specific differentially methylated regions (DMRs) were identified by whole genome bisulfite sequencing (WGBS) in 44 pairs of HCC tissues and adjacent tissues. We then performed methylome profiling on cfDNA from HCC patients and healthy individuals by targeted bisulfite sequencing covering genome-wide CpG islands, shelves, and shores. We employed machine learning approaches to build diagnostic models based on cfDNA regional methylation level to classify the plasma of HCC (n = 140) from that of healthy individuals (n = 84). Further analyses were performed in the validation cohort, including 155 HCC patients, and a control group with 96 healthy individuals, 21 chronic hepatitis B infection (CHB)/liver cirrhosis (LC) patients and 34 patients with benign hepatic lesions (BHL). Area under the receiver operating characteristic curve (AUC-ROC) was used to evaluate diagnostic performance. **Results:** A random forest classifier achieved an AUC of 0.97 (sensitivity: 92.9%; specificity: 89.4%) with 10-fold cross-validation using a panel of 39 DMR markers. The AUC of the diagnostic panel was 0.93 (sensitivity: 81.3%; specificity: 90.7%) in validation cohort, and it performed equally well in detecting BCLC stage 0+A (AUC = 0.90; sensitivity: 74.7%) and AFP negative (AUC = 0.92; sensitivity: 79.4%) HCC, as well as differentiating HCC from CHB/LC and BHL. Based on these results, we have further developed a small targeted bisulfite sequencing panel covering 127 CpG sites for non-invasive diagnosis of HCC. The panel had similar performance in training and validation cohorts, an AUC of 0.96 (sensitivity: 90.7%, specificity: 88.2%) in the training set, and 0.91 (sensitivity: 80.0%, specificity: 88.7%) in the validation set. **Conclusions:** Our diagnostic panel with 39 DMR markers showed high sensitivity and specificity in HCC diagnosis as well as surveillance in high-risk populations for developing HCC. More importantly, simple diagnostic model show similar diagnostic performance for early HCC diagnosis, which was easily to transfer to clinical application in the future. Research Sponsor: BGI Genomics.

4601 **Poster Session (Board #209), Fri, 8:00 AM-11:00 AM**

Phase Ib dose escalation and cohort expansion study of the novel myeloid differentiating agent MTL-CEBPA in combination with sorafenib in patients with advanced hepatocellular carcinoma (HCC).

Debashis Sarker, Mikael Sodergren, Elizabeth Ruth Plummer, Bristi Basu, Tim Meyer, Kai-Wen Huang, T.R. Jeffry Evans, Duncan Spalding, Yuk Ting Ma, Daniel H. Palmer, Cheng Ean Chee, David James Pinato, Vikash Reebye, Daniel McVeigh, Nina Raulf, Jenni Vasara, Pinelopi Andrikakou, Robert Habib, David Blakey, Nagy A. Habib; Guy's Hospital, King's College London, London, United Kingdom; Imperial College London, London, United Kingdom; Northern Centre for Cancer Care, Newcastle-upon-Tyne, United Kingdom; Addenbrooke's Hospital, Cambridge, United Kingdom; University College London Cancer Institute, London, United Kingdom; National Taiwan University Hospital, Taipei, Taiwan; University of Glasgow, Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom; Department of Hepatobiliary Oncology, New Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom; University of Liverpool, Liverpool, United Kingdom; National University Cancer Institute, Singapore, Singapore; Department of Surgery and Cancer, Imperial College, London, London, United Kingdom; MINA Therapeutics, London, United Kingdom; Imperial College, London, United Kingdom; MiNA Therapeutics, London, United Kingdom

Background: MTL-CEBPA is the first small activating RNA to enter clinical trials and upregulates C/EBPα, a master regulator of myeloid cell differentiation. We previously reported a favourable safety profile of MTL-CEBPA as a single agent in HCC (Sarker D et al, ASCO 2018). After discontinuation of MTL-CEBPA, 3 out of 5 patients (pts) treated with sorafenib off study had a complete response (CR) of 7-18 months duration; 2 pts of which demonstrated resolution of lung metastases for $>$ 1 year. Here we provide new data on pts prospectively treated with MTL-CEBPA + sorafenib. **Methods:** Primary objective was to assess safety and tolerability of MTL-CEBPA 90-130mg/m^2 QW or BIW in combination with sorafenib 400mg BD administered to HCC patients either concomitantly or sequentially, in cohorts either tyrosine kinase inhibitor (TKI) naive or resistant. Secondary objectives included preliminary assessment of activity by response rate (RECIST v1.1) and immune landscape analysis. **Results:** As at the cut off date of 1 Feb 2020, 12 pts have been treated with MTL-CEBPA co-administered with sorafenib and 14 pts with MTL-CEBPA followed by sorafenib (23M/3F, median age 65.5years, range 44-83, ECOG PS 0/1: 18/8). The most common treatment-related AEs (all grades/grade 3-4) in these groups include facial flushing (4/0), raised AST (4/2) raised ALT (2/1), fatigue (5/0), raised ALP (2/0), and anaemia (2/2), diarrhoea (3/0), rash (2/0) and anorexia (1/0). Of 14 evaluable pts in the TKI naive cohorts, 2 pts had CR, 3 pts had partial response and 7 had stable disease. 9/10 pts in the TKI resistant cohorts evaluable for efficacy had stable disease. Flow cytometry demonstrated statistically significant decreases in frequency of immature CD66$^+$CD10$^-$ neutrophils and myeloid derived suppressor cells. IHC demonstrated significant reduction in M2 macrophages in tumour biopsies. **Conclusions:** MTL-CEBPA + sorafenib is well tolerated with an acceptable safety profile. This study has confirmed signals of objective response to the combination treatment in TKI naïve HCC patients with viral aetiology, warranting expanded development in these patients. Updated efficacy and safety data will be presented. Clinical trial information: NCT02716012. Research Sponsor: MiNA Therapeutics.

	TKI naïve		TKI resistant	
Best objective response (n)	**Viral**	**Non-viral**	**Viral**	**Non-viral**
Complete Response	2	0	0	0
Partial Response	2	1	0	0
Stable Disease	3	4	5	4
Progressive Disease	1	1	0	1
Total Evaluable	8	6	5	5
Non-Evaluable (withdrawn)	3	5	0	0
Non-Evaluable (ongoing)	1	1	1	0

4602 **Poster Session (Board #210), Fri, 8:00 AM-11:00 AM**

Immediate post-thermal ablation biopsy of colorectal liver metastases to predict oncologic outcomes.

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Background: Thermal ablation (TA) is used as a local cure for selected colorectal liver metastases (CLM) with minimal risk. A critical limitation of TA has been early local tumor progression (LTP). The goal of this study is to establish the role of ablation zone (AZ) biopsy in predicting LTP. **Methods:** This institutional review board-approved prospective study included patients with CLM of 5cm or less in maximum diameter, with confined liver disease or stable, limited extrahepatic disease. Both radiofrequency(RF) and microwave(MW) ablation modalities were used. A biopsy of the center and margin of the AZ was performed immediately after ablation. The applicators were also examined for the presence of viable tumor cells. All samples containing morphologically identified tumor cells were further interrogated with immunohistochemistry to determine the proliferative and viability potential of the detected tumor cells. Ablation margin size was evaluated on the first CT scan performed 4–8 weeks after ablation and was confirmed by 3D assessment with Ablation Confirmation Software (Neuwave™). Variables were evaluated as predictors of time to LTP with the competing-risks model (uni- and multivariate analyses). **Results:** Between November 2009 and February 2019, 102 patients with 182 CLMs were enrolled. Mean tumor size was 2.0 cm (range, 0.6–4.8 cm). MW was used in 95/182 (52%) tumors and RF in 87/182 (48%). Median follow-up was 19 months. Technical effectiveness was evident in 178/182 (97%) ablated tumors on the first contrast material–enhanced CT at 4–8-weeks post-ablation. The cumulative incidence of LTP at 12 months was 19% (95% confidence interval [CI]: 14, 27). Samples from 64 (35%) of the 178 technically successful cases contained viable tumor. At univariate analysis, tumor size, minimal margin size, and biopsy results were significant in predicting LTP. In a multivariate model, margin size of less than 5 mm ($P < .001$; hazard ratio [HR], 4.3), and positive biopsy results ($P = .02$; HR, 1.8) remained significant. LTP within 12 months after TA was noted in 3% (95% CI: 1, 6) of tumor-negative biopsy CLMs with margins of at least 5 mm. **Conclusions:** Biopsy and pathologic examination of the AZ predicts LTP regardless of TA modality used. This can optimize ablation as a potential local cure for patients with limited CLM. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

4603 **Poster Session (Board #211), Fri, 8:00 AM-11:00 AM**

A randomized phase II study of oxaliplatin/5-FU (mFOLFOX) versus irinotecan/5-FU (mFOLFIRI) chemotherapy in locally advanced or metastatic biliary tract cancer refractory to first-line gemcitabine/cisplatin chemotherapy.

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Background: In locally advanced or metastatic biliary tract cancer (BTC), second-line chemotherapy is challenging after progression from first-line gemcitabine/cisplatin, although mFOLFOX has been proven to be superior to active symptom control in ABC-06 trial. Irinotecan is an active drug in other gastrointestinal cancers. This study evaluated whether mFOLFIRI was superior to mFOLFOX in second-line treatment of BTC. **Methods:** Patients diagnosed with BTC with disease progression after prior gemcitabine/cisplatin were randomized (1:1) to either mFOLFOX (oxaliplatin 100mg/m2 over 2 hours, leucovorin 100mg/m2 over 2 hours, 5-fluorouracil 2400mg/m2 over 46 hours, every 2 weeks) or mFOLFIRI (irinotecan 150mg/m2 over 2 hours, leucovorin 100mg/m2 over 2 hours, 5-fluorouracil 2400mg/m2 over 46 hours). Randomization was stratified by tumor location (intrahepatic vs extrahepatic vs gallbladder vs ampulla of vater) and ECOG performance status (0, 1 vs 2). Primary end-point was overall survival (OS) rate at 6 months. **Results:** In total, 120 patients were enrolled and 114 patients were treated (mFOLFOX:57, mFOLFIRI:57). Median age was 63 years old. Most patients had ECOG 0/1 (89.5%). Tumor location was intrahepatic in 47 patients (41.2%), extrahepatic in 27 (23.7%), gallbladder in 35 (30.7%) and ampulla of vater in 5 (4.4%). At the median follow-up duration of 10.7 months (95% CI, 8.2-13.2), 6-month OS rate was 58.1% in mFOLFOX and 46.0% in mFOLFIRI. Of 102 evaluable patients (mFOLFOX:51, mFOFIRI:51), objective response rate and disease control rate were 5.9% (95% CI, 0-12.4) and 64.7% (95% CI, 51.6-77.8) in mFOLFOX and 3.9% (95% CI, 0-9.2) and 58.8% (95% CI, 45.3-72.3) in mFOLFIRI. Median progression-free survival was 2.8 months (95% CI, 2.3-3.3) in mFOLFOX and 2.1 months (95% CI, 1.3-2.9) in mFOLFIRI ($p = 0.682$). Median OS was 6.6 months (95% CI, 5.6-7.6) in mFOLFOX and 5.9 months (95% CI, 4.3-7.5) in mFOLFIRI ($p = 0.887$). The most common grade 3/4 adverse events were neutropenia (26.3%) and AST/ALT elevation (15.8%) in mFOLFOX and neutropenia (24.6%) and anemia (17.5%) in mFOLFIRI. Peripheral neuropathy (36.8%) and thrombocytopenia (35.1%) in mFOLFOX and vomiting (19.3%) and cholangitis (10.5%) in mFOLFIRI occurred more frequently. No chemotherapy-related deaths were reported. **Conclusions:** In second-line treatment of BTC, mFOLFIRI was tolerable But, mFOLFIRI was not superior to mFOLFOX. Adverse events were different between two groups. Clinical trial information: NCT03464968. Research Sponsor: CJ health care, Jeil pharmaceutical company.

4604 **Poster Session (Board #212), Fri, 8:00 AM-11:00 AM**

Safety of ^{177}Lu-DOTATATE in patients with advanced neuroendocrine tumors: Data from a U.S. expanded access program.

Martin S. Auerbach, Edward M. Wolin, Val Nassiri, Per Broberg, Ghassan El-Haddad; Department of Molecular and Medical Pharmacology, University of California, Los Angeles, CA; Center for Carcinoid and Neuroendocrine Tumors at the Tish Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY; Advanced Accelerator Applications, Millburn, NJ; Advanced Accelerator Applications, Geneva, Switzerland; Radionuclide Therapy Program at H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL

Background: The NETTER-1 clinical trial showed that peptide receptor radionuclide therapy (PRRT) with ^{177}Lu-DOTATATE increased progression-free survival in patients with somatostatin-receptor-positive advanced midgut neuroendocrine tumors (NETs) compared with high-dose octreotide long-acting repeatable, and was associated with few serious adverse events (AEs). To assess the safety profile of ^{177}Lu-DOTATATE in a real-world population, we analyzed safety data from a US expanded access program (NCT02705313). **Methods:** Patients had inoperable, histologically proven, somatostatin-receptor-positive, locally advanced or metastatic midgut NETs (Ki-67 index $\leq$ 20%) that progressed after somatostatin analog therapy. Exclusion criteria were: surgery, radiotherapy or chemotherapy in the last 12 weeks; treatment with an interferon, mTOR inhibitor, or other systemic therapy in the last 4 weeks; or ongoing octreotide therapy that could not be interrupted for PRRT. Patients with impaired renal function (serum creatinine $>$ 1.7 mg/dL or creatinine clearance $<$ 50 mL/min) or serious coexisting conditions were excluded. The analysis included patients who received $\geq$ 1 cycle of ^{177}Lu-DOTATATE between July 5, 2016 and December 21, 2018. Data were collected from the first cycle to the latest data collection point (up to October 7, 2019). **Results:** 299 patients received a mean ^{177}Lu-DOTATATE cumulative dose of 552 mCi (20.4 GBq) (standard deviation [SD]: 220 mCi [8.1 GBq]) over a mean of 2.8 cycles (SD: 1.1). Mean age was 60.8 years (SD: 11.7); 38.5% of patients were men. Over a mean follow-up of 131 days (SD: 87), 48.8% of patients reported treatment-related AEs (TRAEs), with a maximum severity of grade 1, 2 and 3 for 26.8% (n = 80), 18.1% (n = 54) and 4.0% (n = 12) of patients, respectively; there were no grade 4–5 TRAEs. The most common TRAEs of any grade ($\geq$ 5.0% of patients) were nausea (31.1%), vomiting (13.7%), fatigue (9.4%) and thrombocytopenia (6.0%). The most prevalent grade 3 TRAEs were lymphocyte count decrease (1.0%) and thrombocytopenia (0.7%). Serious TRAEs occurred in 1.0% of patients (carcinoid crisis, dehydration, syncope and vomiting). AEs led to dose modification in 1.7% of patients, dose delay in 6.4% (most commonly due to nausea [2.0%] or thrombocytopenia [2.0%]) and discontinuation in 1.3% (due to thrombocytopenia [1.0%] and extravasation [0.3%]). **Conclusions:** In a real-world population of US patients with advanced midgut NETs, ^{177}Lu-DOTATATE treatment was well tolerated with few TRAEs, consistent with the safety profile in the NETTER-1 trial. Clinical trial information: NCT02705313. Research Sponsor: Advanced Accelerator Applications, a Novartis company.

4605 **Poster Session (Board #213), Fri, 8:00 AM-11:00 AM**

Risk of cancer-specific death for patients diagnosed with neuroendocrine tumors: A population-based analysis.

Julie Hallet, Calvin Law, Simron Singh, Alyson Mahar, Sten Myrehaug, Victoria Zuk, Haoyu Zhao, Angela Assal, Natalie Coburn; Odette Cancer Centre, Toronto, ON, Canada; Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada; Sunnybrook Odette Cancer Center, University of Toronto, Toronto, ON, Canada; University of Manitoba, Winnipeg, MB, Canada; Sunnybrook Health Sciences Centre, Toronto, ON, Canada; Sunnybrook Research Institute, Toronto, ON, Canada; ICES, Toronto, ON, Canada; Odette Cancer Centre, Sunnybrook Hospital, Toronto, ON, Canada

Background: While patients with neuroendocrine tumours (NETs) are known to experience prolonged overall survival, the contribution of cancer-specific and non-cancer deaths is undefined. We examined cancer-specific and non-cancer death after NET diagnosis. **Methods:** We conducted a population-based retrospective cohort study of adult patients with NETs from 2001-2015 by linking administrative healthcare datasets. Using competing-risks methods, we estimated the cumulative incidence of cancer-specific and non-cancer death and stratified by primary NET site and metastatic status. Sub-distribution hazard models examined prognostic factors. **Results:** Among 8,607 included patients, median follow-up was 42 months (interquartile range: 17-82). The risk of cancer-specific was higher than that of non-cancer death, with 27.3% (95%CI: 26.3-28.4%) and 5.6% (95%CI: 5.1-6.1%) at 5 years. Cancer-specific deaths largely exceeded non-cancer deaths in synchronous and metachronous metastatic NETs. Patterns varied by primary tumour site, with highest risks of cancer-specific death in broncho-pulmonary and pancreatic NETs. For non-metastatic gastric, small intestine, colonic, and rectal NETs, the risk of non-cancer death exceeded that of cancer-specific deaths. Advancing age, higher material deprivation, and metastases were independently associated with higher hazards, and female sex and high comorbidity burden with lower hazards of cancer-specific death. **Conclusions:** Among all NETs, the risk of dying from cancer is higher than that of dying from other causes. Heterogeneity exists by primary NET site. Some patients with non-metastatic NETs are more likely to die from non-cancer than from cancer causes. This information is important for counselling, decision-making, and design of future trials. Cancer-specific mortality should be included in outcomes when assessing treatment strategies. Research Sponsor: CIHR.

4606 **Poster Session (Board #214), Fri, 8:00 AM-11:00 AM**

Outcome analyses in patients with metastatic gastroenteropancreatic neuroendocrine tumors receiving peptide receptor radionuclide therapy with ^{177}Lu-DOTATATE – Impact of treatment order and combination on mortality.

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Background: Neuroendocrine tumors of the gastroenteropancreatic tract present heterogeneous with several systemic treatment options in the advanced setting. PRRT with ^{177}Lu-DOTATATE targeting the SSTR-2 receptor of these tumors showed effective responses in the NETTER-1 trial in the short as well as long term follow-up of patients. The aim of our study was to determine the HRQoL and outcome of GEP-NET patients. **Methods:** 41 GEP-NET patients who received ^{177}Lu-DOTATATE (mean: 3 cycles) between 2012 and 2017 at University Hospital Zurich (USZ) were included in this retrospective analysis. HRQoL parameters (fatigue, insomnia, loss of appetite, abdominal pain, nausea, emesis, diarrhea, weight loss) were assessed before and after treatment. At least 3 weeks after the last PRRT cycle, data on blood parameters, HRQoL, and overall survival data were extracted from patient records. To determine factors influencing the success of PRRT therapy and survival, we recorded pre- and post-PRRT treatments (e.g. selective internal radiation therapy/SIRT, somatostatin analogue therapy/SSA, TKI or chemotherapy) and the time-point of PRRT in the therapeutic sequence was analyzed. **Results:** Baseline rates of HRQoL and ECOG performance status were assessed (baseline mean: ECOG 0). PRRT was well tolerated, with most patients reporting no significant deterioration in HRQoL after treatment. Blood parameters (hemoglobin, leucocyte and platelet counts, creatinine) and glomerular filtration rate were not significantly affected by PRRT therapy. The number of previous treatments did not influence survival after PRRT; neither did the length of the time period between first diagnosis and PRRT. Patients with a SIRT treatment prior to PRRT had an elevated mortality odds ratio of 4.083. If SIRT was applied to patients with a pancreatic tumor, the mortality odds ratio was 1.33 compared to patients without a pancreatic tumor. Post-PRRT SSA increased the odds for survival, with a mortality odds ratio of 2.33 for patients without SSA after PRRT. **Conclusions:** Patients with advanced GEP-NETs may benefit from PRRT with ^{177}Lu-DOTATATE, as this treatment appears to be well tolerated and does not significantly impair the HRQoL or symptom load. SIRT before PRRT seems to lower the chances of response and reduces survival instead using this sequence vice versa. This trend was also seen if SSA was not used after PRRT. But these trends have to be proven in prospective trials. Research Sponsor: None.

4607 **Poster Session (Board #215), Fri, 8:00 AM-11:00 AM**

Multicenter analysis of treatment outcomes for well differentiated grade 3 neuroendocrine tumors (NET G3).

Leonidas Apostolidis, Arianna Dal Buono, Elettra Merola, Henning Jann, Dirk Jaeger, Bertram Wiedenmann, Eva Caroline Winkler, Marianne Pavel; Department of Medical Oncology, National Center for Tumor Diseases, Heidelberg University Hospital, Heidelberg, Germany; Department of Gastroenterology and Hepatology, Charité University Medicine, Berlin, Germany; Department of Endocrinology, Friedrich Alexander University Erlangen-Nürnberg, Erlangen, Germany

Background: Well differentiated grade 3 neuroendocrine tumors (NET G3) have been distinguished from poorly differentiated neuroendocrine carcinomas (NEC) in the most current WHO classifications from 2017 and 2019. Retrospective data suggest that commonly applied first-line chemotherapy protocols with cisplatin or carboplatin in combination with etoposide (PE) are less effective in NET G3 than NEC. Therefore, current treatment guidelines suggest alternative first-line treatment protocols like temozolomide-based (TEM), streptozotocin-based (STZ) and FOLFOX which have only been studied in second-line so far. The aim of this multicenter analysis was to evaluate treatment outcomes for NET G3 with a focus on the efficacy of different first-line regimens. **Methods:** We performed retrospective analysis of all patients with NET G3 in the NEN databases of 3 German cancer centers. All histopathological findings were reviewed by the investigators in order to comply with the most current WHO classification. **Results:** A total of 131 patients could be identified. Median Ki67 was 30 %, primary tumors were located in the pancreas in 71 % of cases, 20 patients had a history of prior NET G1/G2 diagnosis. Median overall survival (OS) was 138.1 months with a median follow-up of 20.4 months. 125 patients received palliative first-line therapy: PE n = 34, FOLFOX n = 36, TEM (mostly temozolomide+capecitabine) n = 21, STZ n = 19, other (including targeted agents, somatostatin analogues, PRRT and multimodal combination approaches) n = 15. Overall response (ORR) and disease control rate was 35.3 % and 67.6 % for PE, 52.8 % and 80.6 % for FOLFOX, 28.6 % and 66.7 % for TEM, 47.4 % and 68.4 % for STZ, 20.0 % and 73.3 % for other respectively. Median progression-free survival for PE was 5.2 months. Compared to PE, PFS in the other treatment groups was 6.0 months for FOLFOX (p = 0.164), 12.0 months for TEM (p = 0.059), 5.7 months for STZ (p = 0.519), 14.1 months for other (p = 0.003). All non-PE patients combined showed a significantly prolonged PFS vs. PE (9.0 vs. 5.2 months; p = 0.011). 89 patients received second-line systemic therapy with a median PFS of 5.3 months. **Conclusions:** In this first multicenter analysis of different treatment strategies for NET G3, patients receiving upfront treatment with non-PE regimens had a significantly prolonged PFS. Of the single defined protocols, FOLFOX showed the highest ORR, and TEM the longest PFS. Further prospective evaluation of the optimal therapeutic strategy for this newly defined tumor entity is needed. Research Sponsor: None.

4608 **Poster Session (Board #216), Fri, 8:00 AM-11:00 AM**

Australasian Gastrointestinal Trials Group (AGITG) CONTROL NET Study: Phase II study evaluating the activity of ^{177}Lu-Octreotate peptide receptor radionuclide therapy (LuTate PRRT) and capecitabine, temozolomide CAPTEM)—First results for pancreas and updated midgut neuroendocrine tumors (pNETS, mNETS).

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Background: CAPTEM is an accepted regimen for patients (pts) with advanced pNETs. Single agent ^{177}Lu-Octreotate PRRT is now a standard of care for progressive WHO Grade (G) 1/2 mNETs. High activity was seen with LuTate/CAPTEM in a single arm Phase I/II trial. This study was undertaken to determine the relative activity of adding CAPTEM to LuTate PRRT in pts with mNETs and pNETs. **Methods:** Non-comparative randomised open label parallel group phase II trial with 2:1 randomisation to PRRT/CAPTEM (experimental arm) vs. PRRT (mNETs control) and CAPTEM (pNETS control). PRRT/CAPTEM: 7.8GBq LuTate day(D) 10, 8 weekly (wkly) x 4, with b.i.d. oral CAP 750mg/m^2 D1-14 & TEM 75mg/m^{2}D10-14, 8 wkly x 4; PRRT: 8 wkly x 4; CAPTEM 8 wkly x 4. Primary endpoint: Progression free survival (PFS). mNETS- at 15 months (mo) assuming 15mo PFS 66.4% in control arm, aiming for PFS ^{3} 80%; pNETS- at 12mo assuming 12mo PFS 60% in control arm, aiming for PFS ^{3} 75%. Secondary endpoints: Objective tumour response rate (complete or partial) (OTRR), clinical benefit rate (OTRR, stable disease) (CBR), toxicity, quality of life. **Results:** 75 pts enrolled (Dec 2015 – Nov 2018): mNETs 33 PRRT/CAPTEM and 14 PRRT; pNETS 19 PRRT/CAPTEM and 9 CAPTEM. mNETS: Median follow-up 35mo; 15mo PFS was 90% (95% CI: 73-97%) v 92% (95% CI: 57-99%); OTRR 31% vs 15%; and CBR 97% vs 92% for PRRT/CAPTEM v PRRT respectively. Treatment related adverse events (AEs): 24/32 PRRT/CAPTEM pts had at least one G3 event (75%) vs 5/13 (38%, PRRT); and 4/32 pts at least one G4 event (13%) v 1/13 (8%) respectively, mostly haematologic (haem). Only one patient failed to complete therapy (PRRT/CAPTEM). pNETS: Median follow-up 34mo; 12mo PFS was 76% (95% CI: 48-90%) v 67% (95% CI: 28-88%); OTRR 68% vs 33%; and CBR 100% vs 100% for PRRT/CAPTEM v CAPTEM respectively. Treatment related AEs: 5/18 PRRT/CAPTEM pts had at least one G3 event (28%) vs 3/9 (33%) CAPTEM; 3/18 pts at least one G4 event (17%) v 1/9 (11%) respectively. **Conclusions:** CAPTEM/PRRT is active, meeting its target landmark PFS for CAPTEM/PRRT (12mo pNETs; 15mo mNETs) with numerically greater OTRR in both pNETs and mNETs, but with more haem toxicity in mNETs. As activity was high in both control arms longer follow up is required to determine if the relative activity of PRRT/CAPTEM is sufficient to warrant Phase III evaluation. Clinical trial information: ACTRN12615000909527. Research Sponsor: Unicorn Foundation, Tour de Cure Australia.

4609 **Poster Session (Board #217), Fri, 8:00 AM-11:00 AM**

Pretherapeutic ^{68}Ga-DOTATATE PET SUV predictors of survival of radionuclide therapy for metastatic neuroendocrine tumors.

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Background: Peptide receptor radionuclide therapy (PRRT) is an effective treatment option in patients with advanced neuroendocrine tumours (NETs). Patients are pre-selected based on ^{68}Gallium-DOTA-(0-Tyr3)-octreotate Positron Emission Tomography (^{68}Ga-DOTATATE PET) uptake. The level of uptake in tumour on the baseline ^{68}Ga-DOTATATE PET scan has been explored as a predictor of response in NETs with inconclusive evidence. The aim of this study is to determine the correlation between ^{68}Ga-DOTATATE PET SUV parameters to survival outcomes. **Methods:** We retrospectively analysed 142 lesions (up to five lesions per patient) in 73 patients with NET undergoing PRRT with ^{177}Lutetium octreotate (8.0-8.3GBq) and pretherapeutic ^{68}Ga-DOTATATE PET/CT in a single institution. Standardised uptake values (SUVs) max and mean were correlated with progression-free survival (PFS) and overall survival (OS). **Results:** A total of 73 patients were included in the analysis. The median age was 63 (28-89) years. NET origin was gastroenteric (49%), pancreatic [pNET] (38%), bronchial (10%) and other (3%). Ki-67 proliferation index ($<$ 3%: 36%, 3-20%: 36%, $>$ 20%- $<$ 50%: 8%, unknown: 21%) was seen. Pretherapeutic SUV max but not SUV mean was higher in pNETs (P = 0.04). No difference was seen with Ki-67 index. The median PFS was 32 (95%CI: 26-38) months. Median PFS was reduced with increasing ECOG performance status [PS] (P= 0.029), increasing tumour grade (P = 0.003), increasing Ki-67 proliferation index (P = 0.013), reduced SUV max (P= 0.003), reduced SUV mean (P= 0.001). Multivariate analysis confirmed SUV mean (HR =-1.71 [95%CI: -2.66- -0.80]; P$<$0.01) and Ki-67 index (HR = 1.11 [1.06-1.17]; P $<$ 0.01) as maintaining significance when incorporating ECOG PS (HR = 1.96 [0.68-5.47]; P = 0.22). The mean OS was 40 [37-44] months. A higher SUV max (SUV max $<$ 30: 34 [30-40] months vs SUV max $>$ 30: 48 [44-51]; P$<$0.01) and higher SUV mean (SUV mean $<$ 20: 33 [28-39] months vs SUV mean $>$ 20: 47 [43-51]; P$<$0.01) were associated with improved mean OS. Mean OS was not affected by ECOG performance status (P = 0.896), primary site of origin (P = 0.567) and Ki-67 index (P = 0.110). **Conclusions:** ^{68}Ga-DOTATATE PET SUV measures correlated with an improved PFS on multivariate analysis as well as improved OS in this select group of patients suitable for PRRT. Those patients with lower SUV mean may benefit from escalation of therapy such as increasing administered therapeutic activity. Research Sponsor: None.

4610 **Poster Session (Board #218), Fri, 8:00 AM-11:00 AM**

Efficacy and safety of surufatinib in United States (US) patients (pts) with neuroendocrine tumors (NETs).

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Background: Surufatinib (S) is a targeted inhibitor of tyrosine kinases VEGFR1, 2, & 3, FGFR1, and CSF-1R. Safety and efficacy of S has previously been studied in China in early phase development, and in 2 randomized phase 3 placebo controlled trials (NCT02588170 & NCT02589821). These trials enrolled pts with NETs of extrapancreatic (epNET) and pancreatic (panNET) origin, respectively. Both trials are completed, stopping at their pre-planned interim analysis after meeting the primary endpoint of improved PFS. S demonstrated significant efficacy in pts with advanced epNETs, achieving a median Progression Free Survival [mPFS] of 9.2 v 3.8 months when compared to placebo. The mPFS achieved in pts with advanced panNETs is currently pending future disclosure at an upcoming scientific conference. **Methods:** A dose escalation (ESC)/expansion (EXP) study was conducted to evaluate and confirm the effects of S in US pts. Dose ESC was completed and the maximum tolerated dose and recommend phase 2 dose was determined to be 300mg QD; the same as previous trials. The primary objective of EXP was to evaluate anticancer activity in pts with select indications including panNETs and epNETs. **Results:** As of 21-Jan-20, 32 pts with heavily pre-treated progressive NETs (median prior lines of treatment [Tx]: 3; range 1-8) were enrolled. The 32 pts included 16 pts with panNET and 16 with epNET. All previously received everolimus and/or sunitinib. The median duration of Tx at the time of the data cut-off was 19 wks for all pts; 30.9 wks for panNET and 11 for epNET. 19 pts remain on active Tx (13 epNET and 6 panNET pts), 9 pts discontinued due to progression of disease, 2 withdrew consent and 2 discontinued due to adverse event (AE) (grade 3 tricuspid valve insufficiency, and grade 3 GI bleed). An objective response rate of 9.4% was observed. 3 panNET pts achieved a confirmed partial response (PR) and 1 had an unconfirmed PR per RECIST 1.1; no epNET pts achieved a PR. The safety profile of S remains consistent with previously completed trials. 27 pts (84.4%) had reported at least one adverse event (AE), and 16 pts (50%) reported $\geq$ grade 3 AE's. The most common AE's reported were: hypertension, fatigue, diarrhea, proteinuria and nausea. Pharmacokinetics (PK) analyses has shown similar exposure in panNET and epNET pts as was observed in ESC, and pts from the collective pool of pts. **Conclusions:** S has demonstrated promising antitumor activity in US pts with progressive NETs with a manageable safety profile. Additionally, PK and dose exposure data is consistent with trial results from large randomized phase 3 trials. Clinical trial information: NCT02549937. Research Sponsor: Hutchison MediPharma International Inc.

4611 **Poster Session (Board #219), Fri, 8:00 AM-11:00 AM**

Correlation of DLL3 expression in gastroenteropancreatic neuroendocrine neoplasms with loss of RB1 and prognostic significance.

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Background: Neuroendocrine neoplasms (NENs) are a rare subgroup of tumors with challenging management due to their unpredictable and heterogeneous behaviour. The identification of clinically useful biomarkers is a top priority need in this disease. The negative notch regulator DLL3 has gained increasing attention in small cell lung carcinoma, large cell neuroendocrine carcinoma and neuroendocrine prostate cancer, confirming the tumor suppressor function of Notch-1 signaling in neuroendocrine cells. **Methods:** A retrospective immunohistochemical analysis of DLL3, PD-L1 and RB1 was performed on FFPE samples from 43 patients with gastroenteropancreatic (GEP)-NENs and correlated with clinical characteristics. **Results:** DLL3 was expressed in high-grade (G3) GEP-NENs. The presence of DLL3 was significantly associated with poorly differentiated NEC (77.8% positive tumors), while none of the patients with well-differentiated NET expressed this marker. Expression of DLL3 was correlated with loss of RB1 and negative ^{68}Ga-PET/CT scan. The 85.7% of DLL3- positive tumors showed loss of RB1 expression, while only 1 out of 35 DLL3- negative tumors had RB1 loss. DLL3 was expressed in 75% of patients with negative ^{68}Ga-PET/CT, while only in 25% of patients with positive ^{68}Ga-PET/CT scan. The presence of DLL3 was negatively associated with PFS and OS. Median PFS was 41.9 months in DLL3-negative patients versus 7.9 months in DLL3-positive patients; median OS was 72.9 months in DLL3-negative patients versus 11.7 months in DLL3-positive patients. No correlation was found with DLL3 and PD-L1 expression. The presence of PD-L1 was not associated with any clinical characteristics. **Conclusions:** DLL3 is expressed in high grade GEP-NENs and is associated with loss of RB1, negative ^{68}Ga-PET/CT scan and unfavourable clinical outcome. The presence of DLL3 discriminates poorly differentiated NEC from well-differentiated NET. DLL3 could represent the ideal prognostic factor to stratify patients with GEP-NENs and a candidate therapeutic target in NEC patients. Research Sponsor: None.

4612 **Poster Session (Board #220), Fri, 8:00 AM-11:00 AM**

Inefficacy of chromogranin a assays as neuroendocrine tumor diagnostic tools compared to the NETest.

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Background: Chromogranin A (CgA) remains a commonly used diagnostic and monitoring tool for neuroendocrine tumor disease despite NCCN guidelines identifying it as a category 3 (major concerns about utility) biomarker. Several commercial assays have been developed to measure this protein (or its fragments) and are available both at CLIA-certified laboratories (USA) as well as in NET Centres of Excellence (CoEs - Europe). CgA is typically reimbursed by insurance companies and appears in several guidelines (e.g., ENETS). We sought to directly evaluate the accuracy of detecting NET disease using two different CgA assays, one in the USA (NEOLISA, EuroDiagnostica, IBL-America, CLIA-certified laboratory) and one in an ENETS CoE (CgA ELISA, Demeditec Diagnostics, Germany). We compared the results to the NETest, a circulating mRNA assay, recently validated as an *IVD* for NETs. **Methods:** Patients: NETs (n=258) including lung: n=43; duodenum n=9; gastric: n=44; pancreas: n=67; small bowel: n=40; appendix: n=10; rectum: n=45. No image-evidence of disease (n=122) (IND) and image-positive disease (IPD) (n=136). CgA assays (plasma): NEOLISA, ULN >108ng/ml, DD: ULN>99ng/ml. Data mean±SEM. NETest (whole blood): qRT-PCR - multianalyte algorithmic analyses, CLIA-laboratory. All samples de-identified and assessed blinded. Statistics: Mann-Whitney U-test, Pearson correlation & McNemar-test. **Results:** In the entire group (n=258), NEOLISA assay CgA levels were significantly (p<0.0001) higher (216±91ng/ml) vs. the DD-assay (76±8ng/ml). The assays exhibited a high concordance in output (Pearson r=0.81, p<0.0001), but there were 10.9% (n=31) discordant results. This reflected the NEOLISA assay detecting more CgA-positive samples. IPD group: CgA-positives were detected in 48/136 (35%, NEOLISA) vs. 28 (21%, DD-assay). McNemar's Chi^2=15.04, p<0.001 OR: 11.0, indicating the NEOLISA was significantly better than the DD-assay. The NETest, in contrast, was positive in 135/136 (99%; OR: 87-106, p<0.0001). IND group: CgA-positives were detected in 12/122 (10%, NEOLISA) vs. 9 (7%, DD-assay; p=NS). The majority (75%) of positives were associated with gastric NETs. The NETest was positive in 7 (6%); 4 were gastric NETs and 3 exhibited elevated CgA. **Conclusions:** Two standard CgA assays used for NET management (one accepted by Medicare in the USA, the second used at a CoE in Europe) only detect NET disease in 21-35% of cases. In contrast, a circulating mRNA fingerprint, the NETest, is ~99% accurate for detecting NET disease. Research Sponsor: None.

4613 **Poster Session (Board #221), Fri, 8:00 AM-11:00 AM**

Health-related quality-of-life results from SANET-ep: A phase III study of surufatinib versus placebo for advanced extrapancreatic neuroendocrine tumors.

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Background: In the phase 3 study (SANET-ep, NCT02588170), surufatinib significantly prolonged progression free survival compared with placebo in patients with progressive, well-differentiated advanced extrapancreatic neuroendocrine tumors (epNETs) (ESMO 2019 Abs. LBA76). Here, we report the results of health-related quality-of-life (HRQoL) from this study. **Methods:** Eligible patients were randomized in a 2:1 ratio to receive surufatinib or placebo, 300 mg, orally, once daily, until disease progression or intolerable adverse events. Patient-reported outcome questionnaires, including the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and the QLQ-G.I.NET-21, were collected at baseline, Day 15 of the first cycle (28 Days/cycle), and Day 1 of every cycle thereafter and at discontinuation. Time until definitive deterioration (TUDD) was defined as time from randomization to deterioration of 10 points in domain score compared with baseline score (without subsequent observations of deterioration of less than 10 point or any improvement as compared to baseline score), or death due to any cause. TUDD and mean change from baseline based on a longitudinal repeated measures analysis of each domain were analyzed retrospectively. Significance testing was at two-sided 0.05 without adjustment for multiplicity. **Results:** Of 198 pts randomized (surufatinib n = 129; placebo n = 69), 197 (99.5%) patients completed HRQoL questionnaires at baseline. The questionnaire compliance rate was >90% for most on-treatment assessments. The TUDD was significantly longer in the surufatinib arm versus the placebo arm in the dyspnea domain (hazard ratio [HR] 0.52, p = 0.0103) and social function scale (HR 0.58, p = 0.0222), while the TUDD of diarrhea was significantly shorter in the surufatinib arm compared to placebo (HR 2.68, p = 0.0074). There was no significant difference of TUDD in the remaining domains of QLQ-C30 and G.I.NET-21. There was also no significant difference of the mean change of scores from baseline by repeated measures in the domains between the two arms except diarrhea (increase of 14.0 points [95% CI 9.6, 18.4] in the surufatinib arm versus 2.1 points [95% CI -4.1, 8.4] in the placebo arm, p = 0.0007). **Conclusions:** Treatment with surufatinib resulted in superior efficacy, acceptable toxicity, while generally maintaining HRQoL, which support surufatinib as a treatment option in this patient population that was previously treated with available therapies for epNETs. Clinical trial information: NCT02588170. Research Sponsor: Hutchison MediPharma Limited.

4614 **Poster Session (Board #222), Fri, 8:00 AM-11:00 AM**

Toxicity analysis of capecitabine/temozolomide in NETs.

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Background: The capecitabine/temozolomide regimen has significant activity in advanced NETs. Concerns exist regarding risk of opportunistic infections and long-term myelotoxicity. Analysis of large patient cohorts is needed for evaluation of rare toxicities and for assessment of risk factors. **Methods:** Retrospective study of all patients with advanced neuroendocrine neoplasms seen at the Moffitt Cancer Center between 1/2008 and 6/2019 who received treatment with CAPTEM. Patients who initiated treatment at outside institutions were included if they were prescribed treatment at appropriate doses and if complete records were available. **Results:** 462 patients met eligibility criteria for evaluation: 210 (45%) females and 252 (55%) males with a median age of 59. Median starting doses of CAP and TEM were 658mg/m^2 and 180mg/m^2 respectively. Median duration on treatment was 8 months. 25% of patients required a dose reduction and 16% discontinued due to toxicity of any grade. Incidence of grade 4 thrombocytopenia was 7%: 10% in females and 5% in males ($p = 0.02$). 4 cases were complicated by bleeding (0.8%). Incidence of grade 4 neutropenia was 3%: 5% in females and 1% in males ($p = 0.004$). Incidence of grade 4 lymphopenia was 2%. Only one case (0.2%) of suspected PCP was observed in a patient taking corticosteroids. There were 5 cases of herpes zoster and no other opportunistic infections. 3 patients developed myelodysplastic or myeloproliferative disease, all of whom had also received prior PRRT with Lutetium-Dotatate. There were no acute treatment related deaths, although one patient died 2 months after a thrombocytopenic bleed. **Conclusions:** Severe myelotoxicity is rare, but risks of grade 4 thrombocytopenia and neutropenia are significantly increased in females compared to males. Gender-based dosing should be considered. While alkylating agents are often associated with MDS, there were no cases except among patients who also had received PRRT, a known risk factor. PCP is not a significant risk with this regimen in patients not concurrently on corticosteroids. Research Sponsor: None.

4615 **Poster Session (Board #223), Fri, 8:00 AM-11:00 AM**

Phase II clinical trial of nab-paclitaxel plus gemcitabine in elderly patients with previously untreated locally advanced or metastatic pancreatic adenocarcinoma: BIBABRAX study.

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Background: FOLFIRINOX and nab-paclitaxel plus gemcitabine (nab-P+G) are the standard of care in the first-line treatment of mPC patients (pt) with good performance status. However, no standards of care exist for elderly ($>$ 70 years) pt as they are usually excluded in clinical trials. This study aimed to evaluate whether the clinical benefit of nab-P+G could be extended to elderly pt with mPC. **Methods:** This was an open-label, single-arm, multicenter, phase II trial, to assess the efficacy and safety of Nab-P+G in elderly pt ($\geq$ 70 years) with ECOG PS 0–1 and untreated unresectable locally advanced or metastatic PC. Pt received four-week cycles of intravenous (i.v.) nab-paclitaxel 125 mg/m2, followed by i.v. gemcitabine 1,000 mg/m2, on days 1, 8 and 15, until disease progression. Efficacy was evaluated according RECIST v 1.1 criteria and safety according NCI-CTCAE v 4.0 criteria. **Results:** Eighty pt were enrolled in the study. Median age was 74.6 years (range 70-87.9), 57.5% were men, 71% had ECOG PS 1 and 86% metastatic disease. 16.3% of patients had a history of prior tumor surgical resection, 12.5% received chemotherapy and 3.8% radiotherapy. Primary tumor was located in head (32.5%), tail (25.0%) and body (22.5%). Nab-P and G was reduced in 49% and 41% of pt respectively. 15 pt definitely interrupt study treatment due to toxicity: neurotoxicity (7), asthenia (5), neutropenia (1), leukocytosis (1) and hepatotoxicity (1). Time until definite deterioration (reduction $\geq$10 points as compared to baseline in EORTC-QLQ C30) was 1.6 months and deterioration-free rate at 3 months was 54.3%. Overall response rate was 13.8%, clinical benefit rate 67.5%, median PFS 7.2 months and median OS 9.2 months. The most common treatment-related adverse events were asthenia (60.0%), diarrhea (40.0%), neutropenia (33.8%), hair loss (28.8%), thrombocytopenia (26.3%), and nausea (23.8%). Only asthenia and neutropenia presented a relatively high incidence of grade 3 and 4 toxicities (21.3%). At least 1 SAE was reported in 55% of pt. **Conclusions:** BIBABRAX study confirms the clinical benefit of nab-P+G in an elderly population with mPC, in terms of survival, clinical response and tolerance, therefore it could be considered a treatment option for elderly patients. However, it was unable to demonstrate the preplanned benefit on the quality of life. Further research is needed on treatment strategies that could reduce deterioration of the quality of life in these pt. Clinical trial information: NCT02391662. Research Sponsor: Celgene.

4617 **Poster Session (Board #225), Fri, 8:00 AM-11:00 AM**

Circulating tumor DNA is prognostic and potentially predictive of eryaspase efficacy in patients with advanced pancreatic adenocarcinoma.

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Background: Eryaspase is composed of L-asparaginase encapsulated in erythrocytes. It has demonstrated significant efficacy in combination with chemotherapy in a randomized phase 2 trial in second-line in patients with advanced pancreatic adenocarcinoma. We assessed, in this study, the prognostic and predictive value of circulating tumor DNA (ctDNA) in plasma samples of patients included in the eryaspase phase 2 trial. **Methods:** Samples prospectively collected pre-treatment at each 28-day cycle were centrally analyzed by next-generation sequencing (BPER method). Prognostic values of baseline ctDNA and ctDNA early changes between day 0 and 28 were assessed in both arms combined on objective response rate (ORR), progression free survival (PFS) and overall survival (OS). We conducted interaction test between ctDNA positivity and treatment arm, and the predictive value of ctDNA for eryaspase efficacy was investigated. **Results:** Patients with at least one available plasma sample have been included (n = 122/141). The presence of ctDNA at baseline was identified in 68% (77/113) of patients and was an independent negative prognostic factor for OS (4.6 vs 8.8 months; p = 0.0025) and PFS (1.6 vs 3.3 months; p = 0.00043). Early change in ctDNA levels was assessed by separating patients into three categories (one without detectable ctDNA, and two according to radio median value between day 0 and day 28) that were significantly correlated with ORR, PFS and OS. A significant interaction was observed between the presence of ctDNA and eryaspase efficacy. In patients with ctDNA detectable at baseline, eryaspase was associated with better PFS (HR = 0.53; 95% CI: 0.3-0.94) and OS (HR = 0.52; 95% CI: 0.29-0.91). **Conclusions:** We confirm from a prospective randomized trial that 1/ the presence of ctDNA at baseline is a major prognostic factor, 2/ the early change of ctDNA correlates with treatment outcome and 3/ the ctDNA could be a predictive biomarker of eryaspase efficacy. Clinical trial information: NCT02195180. Research Sponsor: Erytech.

4618 **Poster Session (Board #226), Fri, 8:00 AM-11:00 AM**

Concordance between independent and investigator assessment of disease-free survival (DFS) in the APACT trial.

Michele Reni, Hanno Riess, Eileen Mary O'Reilly, James Andrew Reeves, Elena Chiorean, Thomas J. George, Werner Scheithauer, Artru Pascal, Markus Lerch, Warren S. Brenner, Yoo-Joung Ko, Josep Tabernero, Eric Van Cutsem, Philip Agop Philip, David Goldstein, Jordan Berlin, Andrew Biankin, Margaret A. Tempero; IRCCS Ospedale, San Raffaele Scientific Institute, Milan, Italy; Charité Universitätsmedizin, Berlin, Germany; Memorial Sloan Kettering Cancer Center, New York, NY; Florida Cancer Specialists South/Sarah Cannon Research Institute, Ft. Myers, FL; University of Washington and Fred Hutchinson Cancer Research Center, Seattle, WA; University of Florida Health Cancer Center, Gainesville, FL; Medical University of Vienna, Vienna, Austria; Clinique Saint Jean, Lyon, France; Department of Medicine A, University Medicine Greifswald, Greifswald, Germany; Boca Raton Regional Hospital, Boca Raton, FL; Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, ON, Canada; Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; University Hospitals Gasthuisberg Leuven, KU Leuven, Leuven, Belgium; Karmanos Cancer Institute, Detroit, MI; Nelune Cancer Centre, Prince of Wales Hospital and University of New South Wales, Randwick, NSW, Australia; Vanderbilt University, Nashville, TN; University of Glasgow, Glasgow, United Kingdom; School of Medicine, University of California, San Francisco, CA

Background: APACT was a phase III trial of adjuvant *nab*-paclitaxel + gemcitabine (*nab*-P + Gem) vs Gem alone in patients with resected pancreatic cancer (PC) and the first adjuvant PC trial to use independently assessed DFS as the primary endpoint (DFS by investigator review was a prespecified sensitivity analysis). We examined concordance between independent and investigator DFS review. **Methods:** For the independent assessment, reviewers determined recurrence by computed tomography or magnetic resonance imaging but were blinded to treatment and clinical data. Investigator-assessed DFS was based on all available data. Concordance was summarized by κ statistics. Patients who did not have recurrence or were alive were censored at the last tumor assessment date with disease-free status or the randomization date if the last tumor assessment with disease-free status was missing. Patients who received new anticancer therapy or cancer-related surgery prior to recurrence or death were censored at the date of last tumor assessment with disease-free status prior to the start of new anticancer therapy or cancer-related surgery or the randomization date if the last tumor assessment date with disease-free status prior to the start of subsequent new anticancer therapy or cancer-related surgery was missing. All censoring rules were the same for analysis of DFS by independent and investigator review. **Results:** Median DFS by independent review was 19.4 (*nab*-P + Gem) vs 18.8 (Gem) months (hazard ratio [HR] 0.88; 95% CI, 0.73 - 1.06; $P = 0.18$); median investigator-assessed DFS was 16.6 (*nab*-P + Gem) vs 13.7 (Gem) months (HR 0.82; 95% CI, 0.69 - 0.97; nominal $P = 0.017$). Moderate concordance was found between independent- and investigator-assessed DFS (Table); similar results were observed in the *nab*-P + Gem (concordance, 78%; κ coefficient, 0.56) and Gem alone (concordance, 76%; κ coefficient, 0.53) arms. **Conclusions:** The results reflect the complexities of defining the recurrence timepoint accurately and suggest that radiological review in the absence of clinical context is suboptimal for recurrence detection in resected PC. These findings may inform future clinical trial design. Registration: EudraCT (2013-003398-91); ClinicalTrials.gov (NCT01964430). Clinical trial information: NCT01964430. Research Sponsor: Bristol-Myers Squibb.

Concordance of DFS (Total; N = 814).

		Investigator	
	Independent	**No (n = 293)**	**Yes (n = 521)**
Concordance, n (%)	No (n = 427)	266 (33)	161 (20)
	Yes (n = 387)	27 (3)	360 (44)
κ coefficient (95% CI)		0.54 (0.49 - 0.60)	

4619 **Poster Session (Board #227), Fri, 8:00 AM-11:00 AM**

PANasta Trial: Cattell Warren versus Blumgart techniques of pancreatico-jejunostomy following pancreato-duodenectomy—A double-blinded multi-centered trial, trial results.

Christopher Halloran, John P. Neoptolemos, Kellie Platt, Richard Jackson, Srikanth Reddy, Derek Oreilly, Andreas Prachalias, Daniel H. Palmer, Krishna Menon, Brian Davidson, Dhanny Gomez, Paula Ghaneh; University of Liverpool, Liverpool, United Kingdom; Liverpool Clinical Trials Centre, Liverpool, United Kingdom; Oxford University Hospitals NHS Trust, Oxford, United Kingdom; North Manchester General Hospital, Manchester, United Kingdom; Liver Care Group, London, United Kingdom; LIver Care Group, London, United Kingdom; Royal Free Hospital and University College of London, London, United Kingdom; Department of Hepatobiliary and Pancreatic Surgery, Nottingham, United Kingdom

Background: Pancreatic anastomosis failure following pancreatic head excision, for suspected pancreatic cancer, leads to longer recovery and failure to start or complete adjuvant chemotherapy. The aim of this study is to evaluate whether a Blumgart anastomosis (BA) reduces the post operative pancreatic fistula (POPF) rate compared to a more traditional Cattell-Warren anastomosis (CWA). **Methods:** Patients with suspected pancreatic cancer, undergoing elective pancreato-duodenectomy were randomized intra-operatively to either a BA or a CWA. Anastomoses were constructed according to prior agreed techniques and an operative manual describing key surgical steps. Quality control of these key steps and adherence to the arm of randomization was ensured by operative photographs. Surgical drain amylase was measured post-operatively to establish the primary end point of POPF. These were graded A (biochemical) or B and C (clinically relevant, CR-POPF). Secondary endpoints included: Entry in adjuvant therapy, hospital stay, mortality and survival. Overall survival was estimated using the method of Kaplan Meier and defined as the time from randomisation until death by any cause with alive patients censored at the end of study date. **Results:** Between May 5 2015 and August 7 2017, 238 patients were randomized, 2 patients withdrew, leaving 236 patients for analysis (112 BA, 124 CWA). Median age was 70 years, 63% were men. Median time from diagnosis to randomization (surgery) was 33 days for both arms. In the BA arm there were 28 POPF's (15-A, 10-B and 3-C) and 32 in the CWA arm (18-A, 12-B and 2-C), p = 0.887. In total 27 patients (11.4%) developed a CR-POPF, BA 13 (5.5%), CWA 14 (5.9%), p = 0.857. 75% of eligible patients entered chemotherapy, with a median (IQR) time to the start treatment of 2.55 (2.27, 3.15) months for the BA group and 2.87 (2.56, 3.75) for the CWA group. Median hospital stay (IQR) in days was 13 (10-24) for BA and 14.5 (10-22) for CWA, p = 0.232. The overall surgical related mortally at 90 days was 1.7%. 44 study deaths were observed, 35 were due to disease progression (BA 19, CWA 16). A hazard ratio (95% CI) of 0.72 (0.4, 1.311) shows better, but not statistically significant survival for the CWA group. **Conclusions:** This is the largest surgical trial ever conducted comparing these techniques and there was no significant difference in the POPF rate between the BA and CWA anastomoses. In a UK population the clinically relevant POPF rate is 11% and 75% of eligible patients enter chemotherapy. Clinical trial information: ISRCTN52263879. Research Sponsor: Cancer Research UK.

4620 **Poster Session (Board #228), Fri, 8:00 AM-11:00 AM**

Landscape of DNA-damage-repair/homologous recombination deficiency (DDR/HRD) in hepatopancreaticobiliary (HPB) cancers.

Wungki Park, Ethan Sokol, Jiapeng Chen, Kenneth H. Yu, Danny Khalil, James J. Harding, Imane H. El Dika, Nadeem Riaz, Ghassan K. Abou-Alfa, David Paul Kelsen, Christine A Iacobuzio-Donahue, Eileen Mary O'Reilly; Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY; Foundation Medicine, Inc., Cambridge, MA; Sloan Kettering Institute, Memorial Sloan Kettering Cancer Center, New York, NY; Memorial Sloan Kettering Cancer Center/Weill Cornell Medical College, New York, NY; Memorial Sloan Kettering Cancer Center, New York, NY

Background: Biallelic HR-gene mutations (HRm) confer HRD and sensitivity to DDR-targeted therapies including platinum and PARPi in pancreatic cancer (PDAC). The landscape of DDR/HRD phenotypes in HPB cancers and their clinical implication is yet to be evaluated, the subject of this effort. **Methods:** Hybrid capture-based comprehensive genomic profiling was performed in a CLIA-certified, CAP-accredited lab (Foundation Medicine, Inc.) on up to 395 genes, including the HR-genes (*BRCA1/2, PALB2, RAD50/51B/C/D, MRE11, ATRX, ATR, ATM, BAP1, BRIP1, CHEK2, NBN,* and *FANCA*). Putative DDR/HRD phenotype was assessed using percent genome under LOH (gLOH) (PMID: 28916367). Variant zygosity was assessed as previously described (PMID: 29415044). From an independent PDAC subgroup among HPB cancers, we evaluated their outcomes on first-line platinum. **Results:** From a total of 11,174 tumors, pathogenic DDR/HRm were identified in 18% (1980/11174) of HPB cancers, 15% (863/5941) of PDAC, 25% (744/2998) of cholangiocarcinoma, 15% (141/958) of hepatocellular carcinoma, and 17% (152/873) of gallbladder carcinoma. We observed a majority (63%) of DDR/HRm with LOH. Rigorous filtering for tumor purity and copy number quality metrics yielded 34% (4051/11774) cases evaluable. The median gLOH of any biallelic DDR/HRm was 12.9% compared to 8.8% in no DDR/HRm (p=5.7E-33). Strength of the association varied by gene, with the strongest association in *BRCA1* (22.3, p=1.5E-10), *BRCA2* (20.1, p=1.7E-35), *RAD51C* (16.7, p=7.8E-4), *PALB2* (16.4, p=1.4E-5), *BRIP1* (14.3, p=0.02), *RAD51B* (13.7, p=0.02), and *ATM* (13.6, p=7.7E-12) (Table). Most other DDR/HR-genes and monoallelic DDR/HRm had weak gLOH. PDAC accounted for 60% of this HPB dataset. In an independent dataset of PDAC at MSK (n=262), biallelic DDR/HRm patients (n=29, 11%) had mostly germline mutations and had significantly improved median PFS on first-line platinum vs. non-platinum (13.3 [95%CI: 9.57-NR] vs 3.8 [95%CI: 2.79-NR] months, $p<0.0001$). **Conclusions:** Biallelic DDR/HRm is a distinct population of HPB cancers beyond PDAC and may confer better phenotype in DDR-targeted treatment. Further independent validation is underway. Research Sponsor: U.S. National Institutes of Health, Parker Institute for Cancer Immunotherapy MSKCC Pilot Award.

gLOH in biallelic HRm. (Total n=4051).

Gene	Biallelic Total (n=438, 10.8%)	Median gLOH biallelic	gLOH >16% biallelic (n, %)	p-value (biallelic vs. no_HRD)
no_HRD (Reference)	(3241, 80)	8.76	(469, 14.5)	
BRCA1	(23, 0.57)	22.3	(16, 69.6)	1.45E-10
BRCA2	(83, 2.0)	20.1	(66, 79.5)	1.66E-35
RAD51C	(8, 0.20)	16.7	(5, 62.5)	0.00078
RAD51B	(7, 0.17)	13.7	(3, 42.9)	0.016

4621 **Poster Session (Board #229), Fri, 8:00 AM-11:00 AM**

Olaparib sensitivity observed in metastatic pancreatic cancer (mPaC) with a wide spectrum of germline *BRCA1* and *BRCA2* mutations (gBRCAm).

Talia Golan, Hedy L. Kindler, Philipp Schatz, Teodora Goranova, Gershon Y. Locker, Karen Cui, Katia Schlienger, David McGuinness, J. Andrew Williams, Maria Orr, Thorsten Gutjahr, Yu-Zhen Liu; The Oncology Institute Sheba Medical Center, Tel-Hashomer, Israel; University of Chicago, Chicago, IL; AstraZeneca, Gothenburg, Sweden; AstraZeneca, Cambridge, United Kingdom; AstraZeneca, Gaithersburg, MD; Merck & Co., Inc., Kenilworth, NJ

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

4622 **Poster Session (Board #230), Fri, 8:00 AM-11:00 AM**

A phase I trial targeting advanced or metastatic pancreatic cancer using a combination of standard chemotherapy and adoptively transferred nonengineered, multiantigen specific T cells in the first-line setting (TACTOPS).

Brandon George Smaglo, Benjamin Leon Musher, Spyridoula Vasileiou, Manik Kuvalekar, Ayumi Watanabe, Catherine Robertson, Tao Wang, Monica Francois, Carlos Almeida Ramos, LaQuisa Hill, George Van Buren, William Fisher, Tannaz Armaghany, Yvonne Sada, Juan Fernando Vera Valdes, Bambi Grilley, Adrian P Gee, Helen E. Heslop, Premal D. Lulla, Ann M. Leen; Baylor College of Medicine, Houston, TX; Texas Children's Hospital, Houston, TX; Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, TX; Westchase Oncology Center, Houston, TX; Center for Cell and Gene Therapy, Baylor College of Medicine, Houston Methodist Hospital and Texas Children's Hospital, Houston, TX

Background: Immunotherapy is emerging as a potent therapy for a range of hematologic malignancies and solid tumors. To target pancreatic carcinoma we have developed an autologous, non-engineered T cell therapy using T cell lines that simultaneously target the tumor-associated antigens (TAAs) PRAME, SSX2, MAGEA4, NY-ESO-1 and Survivin. These multiTAA-specific T-cell lines could be consistently prepared by culturing PBMCs in the presence of a Th1-polarizing/pro-proliferative cytokine cocktail, and adding autologous pepmix-loaded DCs as APCs. **Methods:** Patients with locally advanced or metastatic pancreatic adenocarcinoma who achieved cancer control with three months of standard chemotherapy were eligible to receive up to 6 infusions of multiTAA T-cells (fixed dose - $1x10^7$ cells/m^2). While also continuing the same chemotherapy, T-cells were given at monthly intervals from month four, onwards. The primary study endpoints were safety and feasibility of completing all 6 planned infusions, with secondary and tertiary endpoints including anti-tumor effects, patient survival, in vivo expansion and T cell persistence of the infused cells as well as recruitment of the endogenous immune system. **Results:** Between June 2018 and December 2019, we treated 13 patients with multiTAA T-cells. For 12/13 patients, we generated sufficient cells for all 6 planned doses; 2 doses were available for the remaining patient. Of the 13 patients, 8 maintained cancer control for a longer than expected duration, compared to historical controls. With administration of T-cells, 3 of these 8 patients had partial responses and 1 patient had a radiographic complete response (per RECIST). These responses were seen in patients with metastatic cancer. Notably, no patient had infusion-related systemic- or neuro-toxicity. Thus, infusion of autologous multiTAA-targeted T cells directed to PRAME, SSX2, MAGEA4, NY-ESO-1 and Survivin has been safe and provided durable clinical benefit to patients with pancreatic adenocarcinoma. **Conclusions:** Autologous, TAA cytotoxic T-cells can reliably be generated and safely administered to patients in conjunction with standard of care chemotherapy. In some patients, addition of T-cells may extend duration of first line therapy cancer control and induce additional tumor responses, and activation of the endogenous immune system has been documented in all patients. Exploration in a higher phase study is warranted. Clinical trial information: NCT03192462. Research Sponsor: V-Foundation and PanCan.

4623 **Poster Session (Board #231), Fri, 8:00 AM-11:00 AM**

Survival outcomes of patients with resectable pancreatic cancer treated with upfront surgery versus neoadjuvant chemotherapy: A retrospective tertiary care center experience.

Fang Liu, Matthew Mirsky, Sulin Wu, Pingfu Fu, Shufen Cao, John Shanahan, Ravi Kumar Kyasaram, Prantesh Jain, Jeffrey Hardacre, John Brian Ammori, Jordan Michael Winter, David Lawrence Bajor; University Hospital, Cleveland, OH; University Hospitals of Cleveland, Cleveland, OH; Department of Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, OH; Department of Biostats and Epidemiology, Case Western Reserve University, Cleveland, OH; University Hospitals Seidman Cancer Center, Cleveland, OH; University Hospitals-Seidman Cancer Center, Case Western Reserve University, Cleveland, OH; Memorial Sloan Kettering Cancer Center, New York, NY; University Hospitals Seidman Cancer Center, Case Comprehensive Cancer Center, Case Western Reserve University, Cleveland, OH

Background: The role of neoadjuvant chemotherapy (NAC) for resectable pancreatic cancer (RPC) remains controversial. We sought to compare the outcomes of NAC with upfront surgery (UFS). **Methods:** The study retrospectively enrolled patients with RPC who had UFS or received neoadjuvant FOLFIRINOX (FFX) or gemcitabine plus albumin-bound paclitaxel (GA). Between-group differences were assessed with T-test for continuous variables, and Chi-square / Fisher's exact test for categorical variables. The overall survival (OS) and recurrence-free survival (RFS) were determined by the Kaplan-Meier method with Wilcoxon test for the difference between groups. The effects of NAC vs. UFS on OS and RFS were further estimated using Cox regression controlling the effects of age and CA 19-9. **Results:** Between 2011 and 2019, 131 patients with RPC underwent UFS followed by adjuvant chemotherapy (gemcitabine, n = 65; gemcitabine/capecitabine, n = 18; FFX, n = 9). Up to 32 patients (24.4%) could not receive adjuvant chemotherapy due to surgical complications or poor recovery. Total 50 patients with RPC received NAC (FFX, n = 32; GA, n = 18). Median of 5.5 cycles of FFX or 3 cycles of GA were given prior to surgery. Resection rate was 72% (FFX 62.5%; GA 88.9%). The rest (28%) were no longer surgical candidates due to disease progression rather than toxicities from NAC. On surgical pathological review, complete resection (R0) was achieved in 83.3% of resected cases after NAC (FFX 90%; GA 75%) and 79.4% with UFS. The tumor size distribution was: pT1 11.1%, pT2 41.7%, pT3 44.4% with NAC; pT1 5.4%, pT2 18.3%, pT3 76.3% with UFS. The nodal status distribution was: pN0 27.8%, pN1 55.5%, pN2 16.7% with NAC; pN0 23.7%, pN1 71.0%, pN2 5.3% with UFS. Median pre-treatment CA 19-9 was 321.95 unit/mL in the NAC group and 79.99 unit/mL in the UFS group ($p = 0.009$). Median age was 70.5 in the NAC group and 72 in the UFS group ($p = 0.374$). There was no significant difference in the performance status between the two groups. In Kaplan-Meier analysis, there was a significant difference of OS between UFS and NAC with median OS of 648 days under UFS versus 884 days under NAC ($p = 0.029$); the median of RFS was 390 days under UFS versus 392 days under NAC ($p = 0.953$). The hazard ratio (NAC vs UFS) adjusted for CA19-9 and age was 0.7 ($p = 0.176$) for OS and 0.98 ($p = 0.918$) for RFS. **Conclusions:** We observed a signal of tumor downstaging, higher R0 rate, and improved OS with NAC compared with UFS. Further prospective trials are needed to validate these results. Research Sponsor: None.

4624 **Poster Session (Board #232), Fri, 8:00 AM-11:00 AM**

Liposomal irinotecan plus fluorouracil/leucovorin versus FOLFIRINOX as the second-line chemotherapy for patients with metastatic pancreatic cancer: Multicenter study of the Korean Cancer Study Group (KCSG).

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Background: There is no clear consensus on the second-line treatment for patients with metastatic pancreatic cancer (mPC). The aim of this study was to compare the efficacy and tolerability between liposomal irinotecan (nal-IRI) plus fluorouralcil/leucovorin (FL) and FOLFIRINOX (oxaliplatin/irinotecan/leucovorin/fluorouracil) in patients who failed to first-line gemcitabine-based therapy. **Methods:** In this retrospective study, 378 mPC patients who received nal-IRI/FL (n = 104) or FOLFIRINOX (n = 274) as the second-line treatment across 11 institutions from January 2015 to August 2019 were analyzed. The primary end point was progression free survival (PFS), and secondary end points were overall survival (OS), overall response rate, and tolerability. **Results:** There were no significant differences between the two groups in terms of baseline characteristics, except first-line regimen (previous gemcitabine/nab-paclitaxel, nal-IRI/FL, 85.6% vs. FOLFIRINOX, 51.5%; previous gemcitabine monotherapy, 5.8% vs. 24.5%). The median follow-up time was 6.0 months. The median PFS (nal-IRI/FL, 3.7 months vs. FOLFIRINOX, 5.0 months) and OS (nal-IRI/FL, 7.7 months vs. FOLFRINOX, 9.7 months) were comparable between two groups (P = 0.40 and 0.13, respectively). The overall response rate was not significantly different between two groups (nal-IRI/FL, 14% vs. FOLFRINOX, 16%; P = 0.644). In multivariate analysis, poor ECOG status, presence of liver metastasis, high NLR, and high CA19-9 were independent prognostic factors for PFS and OS, but chemotherapy regimen (nal-IRI/FL vs. FOLFRINOX) was not. In a subgroup analysis of patients with liver metastasis, FOLFIRINOX exerted significant PFS (median: 2.1 months vs. 4.1 months for nal-IRI/FL vs. FOLFIRINOX, respectively; P = 0.02) and OS (median: 6.7 months vs. 8.4 months for nal-IRI/FL vs. FOLFIRINOX, respectively; P = 0.04) benefit compared with nal-IRI/FL. Grade 3 neutropenia or higher were more frequently observed in FOLFIRINOX (47.2%) than nal-IRI/FL (35%) (P = 0.033). Grade 3 peripheral neuropathy was also common in FOLFIRIONX (5.9%) group compared with nal-IRI/FL (1.0%) (P = 0.049). **Conclusions:** In second-line setting for mPC after progression on gemcitabine-based therapy, both nal-IRI/FL and FOLFIRINOX regimen showed comparable efficacy and acceptable safety outcomes. FOLFIRINOX regimen might be preferentially considered in patients with liver metastasis. Research Sponsor: None.

4625 **Poster Session (Board #233), Fri, 8:00 AM-11:00 AM**

Real-life results from the prospective QoliXane trial of the platform for outcome, quality of life, and translational research on pancreatic cancer (PARAGON) registry.

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Background: Gemcitabine and nab-paclitaxel (NPG) is standard first-line therapy for metastatic pancreatic cancer (mPC), but the pivotal study did not include quality of life (QoL) analyses. **Methods:** The QOLIXANE-PARAGON study started as a prospective, non-interventional, multicenter study conducted in Germany and transitioned into a permanent registry for pancreatic cancer patients (pts) considering all types of treatments. This report focuses on the pts enrolled into the QOLIXANE portion of the study. Pts were recruited from 95 German centers. QoL was prospectively measured via EORTC-C30 questionnaires (prior to and every month thereafter): therapy and efficacy parameters were prospectively collected. QoL and efficacy endpoints were analyzed in the intention-to-treat population (ITT). The primary endpoint was the rate of pts without deterioration of QoL/Global Health Score (QoL/GHS) at 3 months. **Results:** 600 pts were enrolled. Mean GHS/QoL score at baseline was low and was 46.2 (SD 22.8). Median progression-free survival was 5.85 months (95% CI, 5.23 to 6.25). Median overall survival (OS) was 8.91 months (95% CI, 7.89 to 10.19). The KM-analysis showed that 61% and 41% of pts had maintained QoL/GHS after 3 and 6 months, respectively. Median time to deterioration of QoL/GHS was 4.68 months (95% CI, 4.04 to 5.59). Mean QoL/GHS improved from 46.1 (SD 22.7) at baseline to 52.8 (SD 21.3) after 6 months. In the QoL response analysis, 34.6%, 37.4% and 28% of evaluable pts had improved, stable and worse QoL/GHS after 3 months, respectively. In the Cox regression analysis, GHS/QoL scores strongly predicted survival with a HR of 0.86 ($p < 0.0001$). **Conclusions:** QoliXane the largest study on QoL of mPC. It shows that time to deterioration of QoL is short but that a relevant group of mPC in first line have improved or maintained QoL after 3 and 6 months and that QoL is a predictor of pts outcome. Clinical trial information: NCT02691052. Research Sponsor: Celgene.

4626 **Poster Session (Board #234), Fri, 8:00 AM-11:00 AM**

POLO: Quality-adjusted (QA) progression-free survival (PFS) and patient (pt)-centered outcomes with maintenance olaparib in pts with metastatic pancreatic cancer (mPaC).

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Background: In the Phase III POLO trial (NCT02184195), maintenance olaparib significantly prolonged PFS vs placebo in pts with a germline *BRCA1* and/or *BRCA2* mutation (gBRCAm) and mPaC (median 7.4 vs. 3.8 months). The aim of maintenance treatment is to extend PFS and survival without compromising health-related quality of life due to adverse events. The duration of time spent without symptoms or toxicities (TWiST) and the QA-PFS were assessed in a post hoc analysis of the POLO trial. **Methods:** Patients were randomized 3:2 to receive maintenance olaparib (tablets; 300 mg bid) or placebo. Restricted mean (RM)-PFS was calculated by estimating the area under the Kaplan–Meier PFS curve between randomization and 29.8 months after randomization (maximum follow-up for the placebo arm in POLO). Patient-centered outcomes were assessed by QA-PFS (derived from the product of the EQ-5D-5L single-index utility score from randomization to disease progression and RM-PFS) and TWiST (RM-PFS minus time with toxicity after randomization). **Results:** RM-PFS was significantly longer with olaparib, with a between-treatment difference of 4.8 months (P=0.009; Table). Over this period, no significant or meaningful differences in mean EQ-5D-5L index were observed between treatment groups. The corresponding mean QA-PFS was significantly longer with olaparib vs placebo. TWiST analysis demonstrated a benefit with olaparib over placebo (Table): between-arm difference, 3.8 months (P=0.039) for the primary analysis (criteria 1: grade ≥2 nausea, vomiting or fatigue). Sensitivity analysis (criteria 1 plus abdominal pain, diarrhea, decreased appetite or constipation) also revealed a trend toward benefit with olaparib (difference: 3.4 months, P=0.062). **Conclusions:** Consistent with the primary PFS analysis of the POLO trial, RM-PFS and QA-PFS were significantly longer with maintenance olaparib than with placebo. As demonstrated by the findings of the TWiST analyses, the PFS benefit observed with olaparib in pts with a gBRCAm and mPaC persists even when symptoms of toxicity are considered. Clinical trial information: NCT02184195. Research Sponsor: AstraZeneca and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, US.

Endpoints (months)	Placebo N=62	Olaparib N=92	Difference (*P*)
RM-PFS	7.01	11.78	4.77 (0.009)
Mean EQ-5D-5L*	0.81	0.78	−0.03 (0.28)
Mean QA-PFS	5.65	9.18	3.53 (0.016)
Mean TWiST (primary analysis)	6.89	10.69	3.81 (0.039)
Mean TWiST (sensitivity analysis)	6.80	10.18	3.39 (0.062)

*Higher scores indicate better health status.

4628 **Poster Session (Board #236), Fri, 8:00 AM-11:00 AM**

Safety and efficacy of biweekly gemcitabine in combination with capecitabine (GemCap) in elderly and frail patients (pts) with resected pancreatic cancer (PC).

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Background: ESPAC-4 study showed that GemCap conferred a survival benefit over gemcitabine monotherapy in resected PC patients. ESPAC-4 included patients with median age of 65 years (37-81) and ECOG performance status (PS) of 0 (43%), 1 (54%) and 2 (2%) who received a median cumulative dose of gemcitabine of 15,000 mg/m2, capecitabine. Here we present our experience with an adopted biweekly regimen of GemCap in patients who were ≥ 75 years and those who were deemed not suitable for ESPAC-4 regimen. **Methods:** Patients ≥ 75 years with resected PC, ECOG PS of 0-2 and no prior treatments were included. Patients were treated with a modified regimen of gemcitabine (1000-2000 mg/m2) every 2 weeks and capecitabine (800-1000 mg/m2) day 1-7 every 2 weeks. Patients were evaluated for progression-free survival (PFS), overall survival (OS) and sites of recurrence. Toxicities were graded according to NCI CTCAE v5.0. **Results:** Thirty-five (22M, 13F) patients, ≥ 75 (median age 79) treated with biweekly Gem-Cap adjuvant treatment. 7 (28%) patients had ECOG PS of 1 and 28 (72%) had ECOG PS of 2. There were 5, 7 and 16 patients with stage I, II and III disease. Nine patients (25%) had R1 and 26 (75%) had R0 resection. The median PFS and OS were 8.0 months and 22.0 months. Nine (25%) had local recurrence, 21 (60%) had metastatic disease and 3 (8.6%) had NED. Two patients were lost to follow-up. The most frequent toxicities were grades 1-2 anemia (20%), thrombocytopenia (8%) and hand-foot syndrome (HFS) (10%). Grade ≥3 included diarrhea (4%) and HFS (1%) with no treatment-related discontinuations. Treatment compliance was 100%. Delays were necessary in 7% of cases and dose reduction was required in 4% of cases. There was no treatment related death. **Conclusions:** This schedule of biweekly GemCap regimen suggests an acceptable option in for elderly, frail patients with PC and warrants further exploration in patients not suitable for FOLFIRINOX, full dose GemCap or a clinical trial. This regimen required fewer dose reduction, omission or delays and allowed to administer pegylated-filgrastim. Previous studies have also shown decreased toxicity and equal efficacy of 7/7 schedule of capecitabine. Moreover, fewer visits to oncology and related expense do favor towards benefit. Additionally, this tolerable regimen is ideal to be combined with immunotherapy in clinical trials for this patient population. Research Sponsor: None.

4629 **Poster Session (Board #237), Fri, 8:00 AM-11:00 AM**

Enrichment of alterations in targetable molecular pathways in KRAS wild-type (WT) pancreatic cancer (PC).

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Background: Genomic profiling has identified KRAS mutations in 88-90% of PC. KRAS WT tumors represent a molecularly heterogeneous group that may harbor targetable alterations (TA). We studied KRAS WT PC using NextGen sequencing (NGS) and whole transcriptome sequencing (WTS) to characterize the molecular landscape of this unique group and to assess the prevalence of TA. **Methods:** A total of 1164 PC tumors were tested at Caris Life Sciences by NGS (592 genes), WTS (NovaSeq), IHC and fragment analysis. Comparison of KRAS WT vs. mutant (MT) was done by Fisher-Exact or Chi2 and was corrected for multiple tests. **Results:** The KRAS WT cohort included 144 tumors (12.4%). No differences were seen in gender (female: 46% in both WT & MT) and age (median: 66 & 67) compared to KRAS MT. In KRAS WT tumors, targetable fusions tested by WTS and pathogenic mutations by NGS were seen in 22% (32 of 144) and 52% (75 of 144) respectively; potentially targetable amplifications (amp) were seen in 5 additional tumors. No TA were seen in 22% of WT tumors. Key alterations are in Table. Alterations inducing MAPK activation, including BRAF, RAF1, NF1 and GNAS changes were seen in 38 (26%) tumors. Frequent alterations were seen in FGFR genes (11 tumors), MET (4, including 1 exon 14 skip), and ERBB receptor and ligands (10). Fusions in ALK, ROS1, RET and NOTCH1 were seen (8), largely exclusive of other drivers. Wnt, PI3K, chromatin remodeling (CR) and DDR changes were common and sometimes seen concurrent with other alterations. Compared to KRAS MT, no difference of PD-L1 or TMB-H was seen. BRAF, APC, PBRM1, CTNNB1 mutations, MDM2 amp, gene fusions and MSI-H/dMMR were all more frequent in KRAS WT tumors (corrected $p < 0.05$). **Conclusions:** KRAS WT PC is enriched with TA (e.g., BRAF, ALK, ROS1, NRG1, MSI-H). The use of WTS in combination with NGS identifies activated molecular pathways in the majority of KRAS WT tumors. Based on our findings, comprehensive profiling of PC at the DNA and RNA level is recommended to provide patients with therapeutic opportunities beyond standard treatments. Research Sponsor: None.

KRAS WT PC (mutation = M; amp = A; fusion = F).

	Alterations	N
MAPK: 38	BRAF total	27
	BRAF-F	10
	M-class I	6
	M-class II inframe-del I other	4|5
	M- class III	2
	RAF1 F	2
	NF1 M	5
	GNAS M	5
	KRAS A	2
Met: 4	Met A	3
	Met F I exon14 skip	1|1
FGFRs: 11	FGFR2 F I A I M	6|1|1
	FGFR3 F I A	1|1
	FGFR4 A	1
ERBB & ligands: 10	ERBB2 M I A I F	3|2|1
	EGFR A I F	1|1
	NRG1 F	2
Wnt: 19	APC M	8
	CTNNB1 M	5
	RNF43 M	5
	RSPO3 F	1
DDR: 19	BRCA2 I 1 M	9|1
	ATM M	6
	CHEK2 M	1
	PALB2 M	2
PI3K: 9	PIK3CA M	4
	PTEN M	2
	AKT2 I 3 A	2|1
Additional F: 8	ALK F	3
	ROS1 F	1
	RET F	3
	NOTCH1 F	1
CR: 30	PBRM1 M	8
	BAP1 M	3
	ARID1A M	18
	ARID2 M	4

4630 **Poster Session (Board #238), Fri, 8:00 AM-11:00 AM**

Outcomes and Immunogenicity of pancreatic cancer stratified by the HRDetect score.

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Background: The HRDetect score uses whole genome sequencing (WGS) to incorporate patterns of substitution base signatures and structural variation to identify tumours deficient in homologous recombination repair (HRD). HRD-tumours, with a higher mutational burden, may be more immunogenic. **Methods:** We applied HRDetect to 182 resected pancreatic cancers (PDA) and 233 advanced PDA enrolled on the COMPASS trial; both cohorts underwent WGS after tumour enrichment. Patients were classified as high(^{hi}) or low(^{lo}) according to the published score threshold of 0.7; clinical characteristics and survival outcomes were determined. Immunogenicity of the cohorts was explored by analyzing cytolytic activity (CYT) as measured by RNA expression of perforin and granzyme A. **Results:** 14% of resected (25/182) and 14% of advanced cases (32/233) were considered HRDetect^{hi}. The median age at PDA diagnosis was younger in HRDetect^{hi} vs HRDetect^{lo} (61 vs 66 years, p = 0.005), with no difference in sex between groups. Of the 57 cases identified, 37 (65%) were considered true HRD-PDA with inactivation of *BRCA1, BRCA2, PALB2, RAD51C* and *XRCC2*. The remaining 20 cases, were considered false positives for HRD; of these 7 had evidence of a tandem duplicator phenotype with duplications ranging from 10Kbp to 1Mbp in size and 13 had no defining genomic characteristics of the HRD-subtype. In resected PDA, the HRDetect score after adjusting for stage, was not prognostic. In contrast in a multivariable analysis of advanced cases, both HRDetect (HR 0.51, 95% CI 0.30-0.87, p = 0.01) and the Moffitt RNA classifier were highly prognostic (HR 1.99, 95% CI 1.32-3.00, p = 0.0001) with improved survival in HRDetect^{hi} and classical PDA. Of patients receiving platinum in advanced disease (n = 128) HRDetect^{hi} PDA had longer survival compared to the HRDetect^{lo} (15.6 vs. 9.9 months, p = 0.02) although the interaction term between chemotherapy regimen (gemcitabine vs. platinum) and HRDetect score was not significant in this cohort. HRDetect^{hi} tumours had increased cytolytic activity than HRDetect^{lo} PDA; furthermore, within the cohort of HRDetect^{hi} PDA, higher CYT scores were evident in primary lesions compared to metastatic sites sequenced. **Conclusions:** A high HRDetect score is prognostic in advanced PDA where patients treated with platinum have longest survival. HRDetect^{hi} tumours have increased cytolytic activity with differences observed between primary and metastatic lesions. Research Sponsor: Ontario Institute of Cancer Research, Pancreas Cancer Canada.

4631 **Poster Session (Board #239), Fri, 8:00 AM-11:00 AM**

Paclitaxel protein bound (A) plus gemcitabine (G) plus cisplatin (C), and paricalcitol (P) neoadjuvant therapy for localized pancreatic ductal adenocarcinoma (PDAC).

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Background: Localized PDAC management has recently evolved. Due to concerns over micro metastases at diagnosis the use of neoadjuvant chemotherapy for PDAC has become more common. Typical therapies involve the use of multiagent systemic chemotherapies with or without radiation therapy. In retrospective studies, Cancer Antigen 19-9 (CA 19-9) normalization in borderline resectable (BR) and locally advanced (LA) PDAC has been associated with greater OS. The addition of cisplatin (C) to gemcitabine (G) and paclitaxel protein bound (A), has shown promising clinical data in a previously reported study in advanced PDAC [JAMA Oncol. 2020;6(1):125-132]. We conducted a prospective, phase 2 clinical trial of patients with resectable (R), BR, and LA PDAC utilizing a regimen combining A + G + C + paricalcitol (P) with the primary endpoint of CA 19-9 normalization (NCT03138720). **Methods:** Eligibility criteria include patients with histologically confirmed R, BR, or LA PDAC, elevated CA 19-9, and a KPS $\geq$ 70% with normal end organ function. Doses are A 125 mg/m2, G 1000 mg/m2, C 25 mg/ m2, P at a fixed dose of 25 μg on days 1, 8 of a 21-day cycle (all treatment IV). Primary objective is to evaluate CA 19-9 normalization with the neoadjuvant chemotherapy. Secondary objectives are to assess R0 rate, pathologic complete response (pCR), safety and tolerability, radiologic response rate, and 2 year overall survival (OS) from date of study entry. Exploratory objectives include evaluating imaging biomarkers and vascular involvement by tumor in relation to therapy. **Results:** To date 24 of the planned 24 patients have been enrolled. 13 male, 11 female; age range 49 to 84 yo. Patient classifications is 8 R; 7 BR; 9 LAPC. Median baseline CA 19-9 156 (range 45-3674). Most common drug related grade (gr) 3-4 adverse events (AEs) are: thrombocytopenia gr 3 29%, gr 4 25%, anemia gr 3 45.8%, gr 4 4.2%, and hypophosphatemia gr 3 8.3%. CA 19-9 normalization occurred in 50% (12/24) who have completed at least 1 cycle of treatment. To date, 14 individuals went to surgery, with 13/14 achieving R0, (1 pCR). Overall response rate in measurable patients is 38% (1 CR, 8 PR). Median OS and 2-year survival data are not yet matured. **Conclusions:** In patients with non-metastatic PDAC, the use of A+G+C+P resulted in a CA 19-9 normalization rate in 50% of individuals. The study is ongoing and OS data is maturing. Clinical trial information: NCT03138720. Research Sponsor: HonorHealth Foundatio, Marley Foundation, Stand Up to Cancer, Seena Magowitz Foundation.

4632 **Poster Session (Board #240), Fri, 8:00 AM-11:00 AM**

Interim data: Phase I/IIa study of EGFR-targeted EDV nanocells carrying cytotoxic drug PNU-159682 (E-EDV-D682) with immunomodulatory adjuvant EDVs carrying α-galactosyl ceramide (EDV-GC) in patients with recurrent, metastatic pancreatic cancer.

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Background: Targeted EDV nanocells loaded with doxorubicin and microRNA16a have shown excellent safety profiles in Phase I trials in recurrent glioma and mesothelioma. This planned safety analysis of an ongoing first-in-human, open label Phase I/IIa study in patients with treatment-refractory metastatic pancreatic cancer, assesses safety, biologic and clinical activity of EGFR-targeted EDV nanocells carrying cytotoxic drug PNU-159682, designed to overcome drug resistance, combined with EDV nanocells carrying immunomodulatory adjuvant α-galactosyl ceramide, designed to stimulate anti-tumour immune response. **Methods:** 9 patients with advanced pancreatic cancer enrolled in the dose escalation phase to evaluate safety of the EDV combination. Doses gradually escalated from 2 x 10^9 EDVs/dose to a maximum of 7 x 10^9 EDVs/dose in Week 7, with subsequent dosing at the maximum dose achieved in Cycle 1. iRECIST criteria was used to assess tumour response after each cycle, and blood was collected each cycle for cytokine and PBMC analysis. **Results:** Combination EDVs were well tolerated with no DLTs, and no drug related SAEs. A minority of patients experienced G1 infusion reactions, which responded promptly to supportive treatment. PR or SD was achieved at 8 weeks in 8/9 patients (CBR 89%), with responses confirmed at 4 months in 4/5 evaluable patients (80%), with 2 durable responses seen beyond 6 months. Exploratory analyses have revealed elevation of IFN-α and IFN-γ in almost all evaluable patients (6/8). In addition, we observed elevated CD8+ T cells (2/8), iNKT, dendritic and NK cells (3/8), and a reduction in exhausted CD8+ T cells (3/8), suggesting activation of both innate and adaptive immune responses. **Conclusions:** EDVs carrying the cytotoxic drug and immune adjuvant are safe and well tolerated. Early signals point to durable responses, possibly related to the development of an innate and adaptive immune response along with cytotoxic effects on drug resistant tumour cells. The Phase IIa study plans to enrol an additional 35 patients to further evaluate safety and anti-tumour efficacy. Clinical trial information: ACTRN12619000385145. Research Sponsor: EnGeneIC Pty Ltd.

4633 **Poster Session (Board #241), Fri, 8:00 AM-11:00 AM**

Single-nucleus RNA-seq of frozen archival primary pancreatic ductal adenocarcinoma uncovers multi-compartment intratumoral heterogeneity associated with neoadjuvant treatment.

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Background: Pancreatic ductal adenocarcinoma (PDAC) remains a treatment-refractory disease and existing molecular subtypes do not inform clinical decisions. Previously identified bulk transcriptomic subtypes of PDAC were often unintentionally driven by "contaminating" stroma. RNA extraction from pancreatic tissue is difficult and prior single-cell RNA-seq efforts have been limited by suboptimal dissociation/RNA quality and poor performance in the setting of neoadjuvant treatment. We developed a robust single-nucleus RNA-seq (sNuc-seq) technique compatible with frozen archival PDAC specimens. **Methods:** Single nuclei suspensions were extracted from frozen primary PDAC specimens (n = 27) derived from patients with (borderline)-resectable PDAC who underwent surgical resection with or without neoadjuvant chemoradiotherapy (CRT). Approximately 170,000 nuclei were processed with the 10x Genomics Single Cell 3' v3 pipeline and gene expression libraries were sequenced (Illumina HiSeq X). **Results:** Distinct nuclei clusters with gene expression profiles/inferred copy number variation analysis consistent with neoplastic, acinar, ductal, fibroblast, endothelial, endocrine, lymphocyte, and myeloid populations were identified with proportions similar to corresponding multiplexed ion beam imaging. Non-negative matrix factorization revealed intra-tumoral heterogeneity shared across patients. Neoplastic cells featured eight distinct transcriptional topics characterized by developmental (epithelial, mesenchymal, endoderm progenitor, neural progenitor) and environmental (anabolic, catabolic, cycling, hypoxic) programs. CAFs exhibited four different transcriptional topics (activated/desmoplastic, myofibroblast, neurogenic, osteochondral). Differential gene expression and gene set enrichment analyses demonstrated that CRT was associated with an enrichment in myogenic programs in CAFs, activation pathways in immune cells, and type I/II interferons in malignant cells. CRT was also associated with a depletion in developmental programs within malignant cells. **Conclusions:** We uncovered significant intratumoral heterogeneity and treatment-associated differences in the malignant, fibroblast, and immune compartments of PDAC using sNuc-seq. Deconvolution of clinically-annotated bulk RNA-seq cohorts and characterization of intercellular interactions with receptor-ligand analysis and spatial transcriptomics are ongoing. Research Sponsor: Lustgarten Foundation, Conquer Cancer Foundation of the American Society of Clinical Oncology, U.S. National Institutes of Health.

4634 **Poster Session (Board #242), Fri, 8:00 AM-11:00 AM**

A phase I study of nanoliposomal irinotecan and 5-fluorouracil/folinic acid in combination with interleukin-1-alpha antagonist for advanced pancreatic cancer patients with cachexia (OnFX).

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Background: Interleukin-1-alpha (IL-1α) promotes tumor inflammation by shaping the tumor microenvironment, including tumor infiltrating myeloid cell recruitment, angiogenesis, and skewing and suppression of anti-tumor immunity. IL-1a inhibition in cancer subjects increased lean body mass and decreased fatigue, pain, and appetite loss. We report results of a single site phase 1 trial for an IL-1α antagonist (bermekimab) in combination with nanoliposomal irinotecan (Nal-Iri) and 5-fluorouracil (5FU)/folinic acid (FA) in patients with advanced pancreatic adenocarcinoma and cachexia who have failed gemcitabine-based chemotherapy. **Methods:** A Bayesian adaptive design based on escalation with overdose control was used. Data are presented as frequency (percentage, %) for categorical variables and mean ($\pm$ standard deviation) for continuous variables. Lean body mass (LBM) and fat mass were assessed at cycle 1 and 3, and T-test was used to assess changes. **Results:** Of 21 pts enrolled, 18 were evaluable. Median age was 68. Bermekimab in combination with nanoliposomal irinotecan (70 mg/m2) and 5-fluorouracil (2400mg/m2) was well tolerated at the highest dose level (12mg/kg). 10 pts experienced grade 3/4 toxicities including sepsis, anemia, hypokalemia, neutropenia, or leukopenia. There were no instances of grade 3/4 diarrhea. Ten pts (56%) had weight stability ($<$ 0.1 kg/BMI). Efficacy results include PR (n = 4, 22%), SD (n = 13, 72%), and PD (n = 1, 6%). PFS 7.7 m (95% CI: 4.34-12.73) and OS 10.5 m (95% CI: 5.79-17.70) were reported. LBM and fat mass change was -1.6 kg ($\pm$ 2.0; p-value = 0.003) and -1.4 kg ($\pm$ 1.7; p-value = 0.004). CRP was 20.4 ($\pm$ 35.6) at cycle 1 and decreased significantly (p-value = 0.005). Serum VEGF decreased from C1 to C3 (p-value = 0.007). QLQ-PAN26 domains improved, particularly hepatic function (p = 0.04). FAACT scores improved for functional well-being (p = 0.02). Average daily step counts increased by 589 steps/day (p = 0.29) and resting heart rate decreased by 2.5 beats per minute (p = 0.005), as assessed by actigraphy. **Conclusions:** Bermekimab, nano-liposomal irinotecan and 5-fluorouracil in refractory pancreatic cancer patients with cachexia was well-tolerated with promising efficacy and improvements in patient performance. Clinical trial information: NCT03207724. Research Sponsor: Ipsen.

4635 **Poster Session (Board #243), Fri, 8:00 AM-11:00 AM**

A single-arm, open-label, phase I study of CPI-613 (Devimistat) in combination with gemcitabine and nab-paclitaxel for patients with locally advanced or metastatic pancreatic adenocarcinoma.

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Background: Glycolic and mitochondrial metabolism are aberrant in pancreatic cancer and translate into chemoresistance. Inhibition of glutamine metabolism can potentially synergize with therapies that increase intracellular reactive oxygen species, such as nab-paclitaxel. CPI- 613 is a novel antimitochondrial agent developed by Rafael Pharmaceuticals that showed promising clinical activity in combination with modified FOLFIRINOX in patients with stage IV pancreatic cancer. Preclinical data suggested possible synergy of CPI-613 with nab-paclitaxel. **Methods:** Single arm, open-label, phase I study of CPI-613 with gemcitabine and nab-paclitaxel in patients with locally advanced or metastatic pancreatic cancer to determine MTD, safety, and preliminary efficacy of CPI-613 in combination with chemotherapy. Key eligibility criteria included: histologically documented and measurable locally-advanced or metastatic, PDAC. ECOG performance status 0-2; and first line systemic treatment. CPI-613 was infused intravenously with a starting dose of 500 mg/m^2 followed by modified dose nab-paclitaxel (100mg/m2) and gemcitabine (800 mg/m2) on Days 1, 8, and 15 of a 28-day cycle. The the primary endpoint, the MTD of CPI-613 was determined by a two-stage, dose-escalation schema, with 6-month treatment duration for patients exhibiting treatment response. Secondary endpoints were treatment-related adverse events, complete response (CR) and partial response (PR). **Results:** From February 2018 to 2020, 26 patients were screened, (23 metastatic and 3 locally advanced), 22 patients enrolled and 18 patients underwent a restaging scan. As of the time of submission 3 patients are still on active treatment. Patient demographics were: median age of 65, ECOG was 0-1, The MTD of CPI- 613 was determined to be 1500 mg/m^2. The dose limiting toxicities were not achieved. Overall the treatment was well tolerated with toxicities mainly related to chemotherapy; most common grade 3 and 4 toxicities were hematologic toxicity and neuropathy. 1 patient achieved CR, 9 PR, 8 stable disease and 1 progressive disease for an objective response rate of 50% with a CR rate of 5.5%. **Conclusions:** The results demonstrate that CPI 613 can be safely administered with gemcitabine and nab-paclitaxel at doses up to 1,500 m/g2. Efficacy data suggest synergy with chemotherapy. Further clinical studies of CPI-613 efficacy in pancreatic cancer are in progress. Clinical trial information: NCT03435289. Research Sponsor: Rafael Pharmaceuticals, 1 Duncan Drive, Cranbury, NJ, Atlantic Health System.

4636 **Poster Session (Board #244), Fri, 8:00 AM-11:00 AM**

Pharmacokinetically-guided 5-FU dose optimization within the preoperative FOLFOXIRI regimen in resectable pancreatic cancer patients.

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Background: Neoadjuvant therapy is an increasingly used approach in patients with resectable pancreatic cancer (PC). A positive link between chemotherapy dose intensity and patients' outcome has been suggested in PC. The aim of this study was to rule out whether 5-FU pharmacokinetic (PK) parameters correlate with outcome in resectable PC patients treated with preoperative FOLFOXIRI. **Methods:** Patients with resectable and borderline resectable PC treated with Oxaliplatin (85mg/m^2), Leucovorin (400mg/m^2), Irinotecan (150 mg/m^2) and 5-FU (initial dose of 3200 mg/m^2 in 46h infusion and subsequent doses based on PK-guided dose adjustements targeting an AUC of 25-30 mcg*h/ml) were included. 5-FU PK analysis was performed taking two plasma samples during 5-FU infusion in at least two cycles. Drug concentrations were analysed by High-Perfomanced Liquid Chromatography. After induction polychemotherapy (IPCT), patients with no progressive disease received chemoradiation (CRT) (50.4 Gy with concurrent Capecitabine and Oxaliplatin) followed by surgical resection 4 to 6 weeks after the completion of CRT. Subsequent follow-up until disease progression was remained. An exploratory analysis with Log-Rank test was performed to assess progression free survival (PFS) based on 5-FU AUC values. **Results:** From November 2012 to October 2018, 29 patients were retrospectively assessed: median age 63 (46-75); M/F rate 20/9; R0 resection rate of 90% in the intention-to-treat analysis. The pathological response according to CAP classification was 0, 1, 2 and 3 in 14, 58, 19.5 and 8.5%, respectively; and median number of resected lymph nodes was 11 (2-22), with lymph node infiltration (ypN1) in 14% of patients. Grade 3-4 IPCT related toxicities and grade 3 CRT related toxicities were reported in 40 and 30% of patients, respectively. Median PFS was 723 days (24 months) and median 5-FU AUC 28.5 mcg*h/ml (23-53). Median PFS for patients with 5-FU AUC $\geq$27 mcg*h/ml was 29 months versus 15 months in patients with 5-FU AUC $<$ 27 mcg*h/ml (adjusted hazard ratio for disease progression 0.223; 95% CI = 0.059-0.848; p = 0.028; in a model controlled by age, sex and irinotecan dose intensity). **Conclusions:** 5-FU pharmacokinetic parameters achieving a target of AUC $\geq$ 27 mcg*h/ml seem to correlate with longer PFS in this subset of patients. Research Sponsor: None.

4637 **Poster Session (Board #245), Fri, 8:00 AM-11:00 AM**

Olaparib (O) in patients (pts) with pancreatic cancer with BRCA1/2 inactivating mutations: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) study.

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Background: TAPUR is a phase II basket study evaluating anti-tumor activity of commercially available targeted agents in pts with advanced cancers with genomic alterations. Results in a cohort of pancreatic cancer pts with germline or somatic BRCA1/2 inactivating mutations treated with O are reported. **Methods:** Eligible pts had advanced pancreatic cancer, no standard treatment (tx) options available, measurable disease, ECOG Performance Status (PS) 0-2, and adequate organ function. Genomic testing was performed in CLIA-certified, CAP-accredited site selected labs. Pts received O tablets or capsules dosed at 300 mg (n=27) or 400 mg (n=3), respectively, orally twice daily until disease progression. Simon 2-stage design tested the null disease control (DC) (objective response (OR) or stable disease at 16+ weeks (wks) (SD16+) according to RECIST) rate of 15% vs. 35% (power = 0.85; α = 0.10). If $\geq$2 of 10 pts in stage 1 have DC, 18 more pts are enrolled. If $\geq$7 of 28 pts have DC, the tx is worthy of further study. Secondary endpoints are progression-free survival (PFS), overall survival (OS), and safety. **Results:** Thirty pts with *BRCA1/2* inactivating mutations were enrolled from Nov 2016 to Aug 2019; 20 were previously treated with platinum based therapy. Two were not evaluable and excluded from efficacy analyses. Demographics and outcomes are summarized in Table. One partial response (PR) and 7 SD16+ were observed for DC and OR rates of 31% (90% CI: 18% - 40%) and 4% (95% CI: 0% - 18%), respectively. Seven pts had at least one grade 3 AE or SAE at least possibly related to O including anemia, diarrhea, fever, elevated liver enzymes, enterocolitis, increased bilirubin, and oral mucositis. **Conclusions:** Monotherapy O showed anti-tumor activity in heavily pre-treated pts with pancreatic cancer with germline (5/12 pts with OR or SD16+) or somatic (3/16 pts with OR or SD16+) *BRCA1/2* inactivating mutations extending findings of recent studies of O in pts with advanced pancreatic cancer. Clinical trial information: NCT02693535. Research Sponsor: AstraZeneca, Pharmaceutical/Biotech Company.

Demographics and Efficacy Outcomes (N=30).	
Median age, yrs (range)	**60 (44, 78)**
Male, %	63
ECOG PS, %	
0	30
1	57
2	13
Prior systemic regimens, %	
1-2	47
≥3	53
DC rate, % (OR or SD16+) (90% CI)[1]	31 (18, 40)
OR rate, % (95% CI)[1]	4 (0, 18)
Median PFS, wks (95% CI)[1]	8.1 (7.9, 15.1)
Median OS, wks (95% CI)[1]	43.0 (28.1, NA)
1 year OS rate, % (95% CI)[1]	47.2 (19.7, 70.7)

[1]N=28

4638 **Poster Session (Board #246), Fri, 8:00 AM-11:00 AM**

A phase II trial of preoperative FOLFIRINOX followed by gemcitabine-based chemo-radiotherapy in patients with borderline resectable pancreatic ductal adenocarcinoma (BR PDAC).

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Background: Preoperative (preop) therapy is widely accepted as the standard of care for patients (pt) with BR PDAC with limited evidence for a specific regimen. This study aimed to assess the efficacy of FOLFIRINOX (FOL) chemotherapy followed by gemcitabine-based chemo-radiotherapy (RT) as preop therapy in pt with BR-PDAC. **Methods:** This single arm Simon two stage phase II trial in pt with BR PDAC was conducted in two phases. The first phase included 4 cycles of FOL, and the second included weekly gemcitabine (1000 mg/m2) for 6 cycles with concomitant intensity-modulated RT (50.4 Gy in 28 fractions)(Gem/RT).The primary aim was to compare R0 resection rate (H_0: $\leq$40% vs $H_a \geq$60%) using one-sample one-sided Z test. Secondary outcomes, including overall survival (OS) and progression-free survival (PFS) were assessed using Kaplan-Meier method. **Results:** Of 22 enrolled pt, 18 (81.8%) completed preoperative treatment. Median age at diagnosis was 63.4 years and 12 (54.5%) were female. There were 10 (45.5%) Hispanics, 4 (18.2%) non-Hispanic black, and 8 (36.4%) non-Hispanic white. Tumor location was predominantly head/neck (21, 95.5%), 15 (68.1%) had T2/3, and 9 (40.9%) had N2 (clinical) disease. Fourteen (64.6%) pt, had venous involvement, 5 (22.7%) had arterial, and 3 (13.6%), both. In the first phase, 20 (90.9%) completed 4 cycles of FOL, 6 (27.3%) required dose-reduction and dose was delayed in 12 (54.5%). Stable disease (SD) was achieved in 10 (52.6%), partial response (PR) in 8 (42.1%) and disease progression (PD) in 1 (5.3%) pt. Of 21 pt that entered the second phase, 18 (85.7%) completed 6 cycles of Gem/RT, 5 (26.3%) required dose-reduction and dose was delayed in 6 (31.6%). SD was achieved in 10 (55.6%), PR in 3 (16.7%) and PD in 5 (27.8%). All pt experienced at least one grade 1 adverse event (AE) and 12 (54.5%) at least one grade 3/4 AE, of which neutropenia was the most common-11 (50%). Of the 15 (68.1%) pt who underwent surgical resection, 12 (80%) achieved R0 margins and 5 (33.3%) required vascular reconstruction. The R0 rate among pt that received $>$1 cycle of FOLFIRINOX was 54.5%. Adjuvant chemotherapy was offered to 6/15 pt (40%). The PFS and OS will be reported. **Conclusions:** An R0 resection rate of 54.5% with this limited sample size is significant at the 10% level. Neoadjuvant FOLFIRINOX followed by concomitant Gem/RT was well-tolerated. The study will be amended to include adjuvant FOL in line with the PRODIGE intergroup adjuvant study results. Clinical trial information: NCT01897454. Research Sponsor: None.

4639 **Poster Session (Board #247), Fri, 8:00 AM-11:00 AM**

FOLFIRINOX de-escalation in advanced pancreatic cancer (aPC): A multicenter real-life study.

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Background: FOLFIRINOX (5FU, irinotecan, and oxaliplatin) is a reference first line (L1) of chemotherapy (CT) in fit patients (Pts) with advanced pancreatic cancer (aPC). Limiting toxicities (in particular, neuropathy) are frequent and maintaining quality of life without a lack of efficacy is a crucial need. Modalities and efficacy of maintenance strategy in aPC remain scarcely studied. Our study describes the French practices of a FOLFIRINOX de-escalation and maintenance in a real-life multicentric cohort. **Methods:** We performed a retrospective multicentric study in 5 French centers. Pts receiving FOLFIRINOX L1 for aPC were recruited between January 2011 and December 2018. FOLFIRINOX de-escalation was defined as stopping oxaliplatin and/or irinotecan in patients without tumor progression, after at least 4 cycles of FOLFIRINOX. Maintenance schedules were oral capecitabine or intravenous (IV) 5FU, FOLFOX or FOLFIRI. Primary endpoint was overall survival (OS). Secondary endpoints were first progression-free survival (PFS1) and, in case of reintroduction of FOLFIRINOX, second progression free survival (PFS2). OS and PFS were estimated using the Kaplan-Meier method and compared using the log-rank test. **Results:** Among the 321 patients included, 147 (46%) received a maintenance therapy. Median age was 60.0 (53–66), 35 (24%) had locally advanced PC and 91 (62%) had metastatic PC. The median total number of cycles was 14.0 (11.0–19.0), including 4.5 (2.0–9.0) of maintenance CT. Median OS was 16.1 months (95%CI = 13.7-20.3). Median PFS1 was 8.8 months (95%CI = 8.3-9.7). The preferred maintenance regimen was fluoropyrimidine (FP) in 66 (45%), vs FOLFIRI in 52 (35%) and FOLFOX in 25 (17%). Eighty-two percent of Pts received a second-line chemotherapy. Among 118 Pts who received a maintenance CT with FOLFIRI or FP, there was no difference in PFS1 (median: 9.0 vs 9.3, respectively, p = 0.31) or OS (median: 16.6 versus 18.7, p = 0.60) between the 2 maintenance regimens. After progression under maintenance CT with FOLFIRI or FP, reintroduction of FOLFIRINOX was performed in 16.1% of Pts, with a median PFS2 of 3.4 months (95%CI = 2.5-23.2). As previously reported in the PANOPTIMOX trial, the rates of G3-4 toxicity were significantly higher during FP maintenance CT than with FOLFIRI (41% vs 9%, p = 0.03), especially neuropathy (41% vs 9%). **Conclusions:** FOLFIRINOX de-escalation in aPC is largely used in France. Fluoropyrimidine maintenance chemotherapy appears to be as effective as FOLFIRI. Research Sponsor: None.

4640 **Poster Session (Board #248), Fri, 8:00 AM-11:00 AM**

A phase Ib study of sEphB4-HSA combined with first-line chemotherapy in patients (pts) with advanced pancreatic (PC) and biliary cancers (BC).

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Background: EphB4, a receptor kinase expressed in most epithelial tumors, binds EphrinB2 to affect cancer cell growth, apoptosis and angiogenesis. EphB4 overexpression is associated with advanced stage and shorter survival in multiple cancers. sEphB4-HSA, the albumin-bound extracellular fragment of EphB4, is a first-in-class inhibitor which blocks EphB4-EphrinB2 bidirectional signaling and results in downstream suppression of KRAS, PI3K, and promotes recruitment of CD3 and CD8 T cells into the tumor. The RP2D of sEphB4-HSA is 10 mg/Kg IV q week. Here, we report on sEphB4-HSA in combination with standard first-line chemotherapy. **Methods:** Pts with advanced PC or BC and no prior therapy for metastatic disease were eligible and enrolled into separate cohorts. Pts with PC received gemcitabine 1,000 mg/m2 + nab-paclitaxel 125 mg/m2 on Days 1, 8, 15 of a 28-day cycle. Pts with BC received gemcitabine 1,000 mg/m2 + cisplatin 25 mg/m2 on Days 1, 8 of a 21-day cycle. sEphB4-HSA 10 mg/kg IV was given weekly starting in Cycle 2. Response was assessed every 2 cycles. Primary endpoint was safety and tolerability; secondary endpoints were objective response rate (ORR) by RECIST 1.1, PFS, OS. Expression of EphrinB2 and EphB4 in tumor was examined by IHC and classified as 1+ (weak staining); 2+ (moderate staining); 3+ (strong, uniform staining). **Results:** A total of 44 pts with advanced PC (n = 21) and BC (n = 23; 70% gallbladder cancer) were enrolled. Median age 66 yrs; ECOG 1 (70%), 52% male. Median number of cycles received were 5 (PC) and 7 (BC). Median PFS was 5.6 mo in PC and 5.8 mo in BC (95% CI: 3.1-8.1 [PC]; 2.7-7.0 [BC]). Median OS was 7.9 mo in PC and 9.1 mo in BC (95% CI: 6.5-15.0 [PC]; 5.4-15.0 [BC]). In response evaluable pts (20 PC, 22 BC), ORR was 40% in PC (95% CI: 21%, 63%) and 23% in BC (95% CI: 9%, 45%). Stable disease was noted in 48% of PC and 61% of BC pts. The most common grade 3 or 4 treatment-related AEs in $\geq$10% of pts in both cohorts combined were hypertension (n = 16; 36%), neutropenia (n = 15; 34%), anemia (n = 14; 32%), thrombocytopenia (n = 7, 16%), fatigue (n = 7, 16%). In the PC cohort, there was an association between EphB4 expression and objective response (p = 0.009). **Conclusions:** sEphB4-HSA has a manageable safety profile in combination with chemotherapy in pts with PC and BC. Clinical activity is manifested by a high disease control rate in both cohorts and a promising RR in PC. Additional biomarker analyses will be presented. Future studies combining chemoimmunotherapy with sEphB4-HSA in pancreatic cancer are planned. Clinical trial information: NCT02495896. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.

4641 **Poster Session (Board #249), Fri, 8:00 AM-11:00 AM**

Comprehensive analysis of KRAS variants in patients (pts) with pancreatic cancer (PDAC): Clinical/molecular correlations and real-world outcomes across standard therapies.

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Background: Approximately 90% of PDAC tumors are driven by activating KRAS mutations. The biological and clinical impact of common KRAS variants (e.g. G12D, G12V, G12R) and less common variants (e.g. G12C, Q61H, Q61R) remains largely unknown despite the emergence of variant-specific treatment strategies. **Methods:** We retrospectively analyzed real-world outcomes from 1475 PDAC pts who underwent molecular profiling via the Know Your Tumor program. Overall survival (OS) and progression-free survival (PFS) were analyzed by choice of 1st line standard therapies. Outcomes in pts with specific KRAS mutations were compared against the KRAS G12D cohort using Cox regression. Based on our prior data, tumor profiles with actionable molecular findings (DDR mutations or other drivers) were evaluated separately. **Results:** The prognostic/predictive value of specific KRAS variants revealed differences in real-world outcomes (Table). OS was greater in pts with KRAS G12V and G12R variants, as was PFS on 5FU-Based Therapy (e.g. FOLFIRINOX) but not for Gemcitabine/nab-Paclitaxel. Opposing trends were noted for KRAS Q61. Pts with KRAS wild type tumors as well as both actionable subgroups also had an improved OS. **Conclusions:** In this large national dataset, we demonstrate that KRAS mutation status and specific variants appear to be prognostic as well as predictive in pancreatic cancer. Research Sponsor: Pancreatic Cancer Action Network (patient advocacy organization), Perthera (private healthcare company).

Real-world outcomes by KRAS mutation in PDAC.

KRAS Variant (% Prevalence)	OS Since Diagnosis of Advanced Disease (Years)		1st Line Gemcitabine / nab-Pactlitaxel (Months)		1st Line 5FU-Based Regimens (Months)	
	mOS (n)	p-val (HR)	mPFS (n)	p-val (HR)	mPFS (n)	p-val (HR)
G12D (36.9%)	1.24y (324)	**0.011 (1.29)**	7.9m (118)	0.47 (0.88)	8.4m (109)	**0.021 (1.58)**
G12V (27.0%)	1.47 (226)	**0.022 (0.76)**	6.1 (78)	0.12 (1.41)	11.2m (67)	**0.025 (0.59)**
G12R (15.5%)	1.45 (106)	**0.034 (0.73)**	9.9 (32)	0.59 (0.87)	10.1 (39)	**0.021 (0.51)**
G12C (1.2%)	0.62 (8)	0.8 (0.88)	5.4 (1)	0.29 (2.96)	N/R (2)	-
Q61 (5.8%)	1.26 (47)	0.81 (0.95)	9.1 (22)	0.9 (0.96)	4.3 (11)	0.95 (1.03)
Other (1.3%)	1.3 (11)	0.81 (0.88)	2.8 (3)	**0.0071 (5.22)**	2.0 (3)	0.27 (3.16)
Wild Type (12.4%)	2.2 (66)	**0.0018 (0.54)**	8.77 (28)	0.36 (0.75)	N/R (19)	0.18 (0.53)
Actionable (DDR Mutation)	1.96 (165)	**4.3e-07 (0.5)**	8.13 58)	0.25 (1.28)	16.17 (40)	**0.00025 (0.29)**
Actionable (Other Driver)	1.56 (98)	**0.0086 (0.67)**	6.53 (35)	0.099 (1.56)	7.47 (39)	0.71 (1.11)

4642 **Poster Session (Board #250), Fri, 8:00 AM-11:00 AM**

Cobimetinib plus gemcitabine is an active combination in KRAS G12R-mutated in previously chemotherapy-treated and failed pancreatic patients.

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Background: he KRAS proto-oncogene is involved in the RAS/MAPK pathway. Various G12X mutations have been examined with the most common mutations being G12D (40%), G12V (30%), and G12R (15-20%) in pancreatic cancer patients. Throughout the course of studying the G12X mutations, we have observed that not all KRAS mutations are equal. Preclinical data shows G12R is impaired in pI3Kα signaling, as compared to KRAS G12V/D. This mechanism is important in PDAC as it allows tumor growth to be sustained. In preclinical studies, PDX derived tumors were transplanted in mice and were treated with a MEK inhibitor plus chemotherapy, which demonstrated a greater tumor regression than either agent alone. Therefore, we have decided to treat patients with Gemcitabine alongside a 2^{nd} generation MEK inhibitor (Cobimetinib). **Methods:** In our single arm study, 13 KRAS mutated pancreatic patients (KRAS G12D, G12V, and G12R) received the combination of Cobimetinib 20mg BID weekly for three weeks alongside Gemcitabine at 1000mg/m^2 weekly, followed by one week of rest. The above constitutes one cycle. **Results:** Patients were divided into two groups; *Group 1* consists of seven patients that were KRAS G12D/G12V mutated, and *Group 2* included six KRAS G12R mutated patients. In Group 1, seven patients on treatment progressed and died within two months on the study. In Group 2, one achieved PR and others stable disease. Median progression-free survival was 6.0 months (95% CI 3-9.3 months) and median OS has not been reached. All patients are alive at 8 months. Common adverse reactions include rash, fatigue, nausea, and vomiting. Cancer antigen 19-9 decreased in $\geq$ 50 of all patients in the latter group. We would like to report our positive study to the society. Moreover, we intend to confirm the study in a larger patient cohort. **Conclusions:** Pancreatic cancer patients that demonstrate KRAS G12R mutations are treatable with a new active combination chemotherapy. Research Sponsor: None.

4643 **Poster Session (Board #251), Fri, 8:00 AM-11:00 AM**

A pilot study to determine the feasibility of a customized low glycemic load diet in patients with stage I-III colorectal cancer.

Michelle Elizabeth Treasure, Alicia Thomas, Stephen Ganocy, Augustine Hong, Smitha S. Krishnamurthi, David Lawrence Bajor, Nathan A. Berger, Neal J. Meropol; Cleveland Clinic Foundation, Cleveland, OH; Case Western Reserve University, Cleveland, OH; University Hospitals Seidman Cancer Center, Cleveland, OH; Cleveland Clinic Cancer Center, Case Comprehensive Cancer Center, Case Western Reserve University, Cleveland, OH; University Hospitals Seidman Cancer Center, Case Comprehensive Cancer Center, Case Western Reserve University, Cleveland, OH; Case Western Reserve Univ, Cleveland, OH; Flatiron Health, New York, NY and Case Comprehensive Cancer Center, Cleveland, OH

Background: Observational evidence associates energy balance factors, particularly diet, with survival in patients with colorectal cancer (CRC). Consumption of a diet with high glycemic indices has been associated with inferior cancer-specific outcomes, but there is limited prospective evidence that alterations in dietary habits improve cancer outcomes. This was a pilot study to determine the feasibility and acceptability of following a low glycemic load (GL) diet in patients with stage I-III CRC and to assess the nutritional resources necessary to follow the diet. **Methods:** 18 patients with stage I-III CRC, who completed definitive cancer therapy and consumed an avg daily GL $>$ 150 participated in a 12 week, tailored, in-person dietary intervention with a target GL of $\leq$102. Compliance was assessed using 24 hour telephone recalls. Acceptability of the diet was assessed using a food acceptability questionnaire, and exploratory correlative laboratories were assessed monthly. **Results:** 67% of patients were compliant with a low GL diet $\geq$ 75% of the time, over a 12 week time period. Majority of participants experienced a decrease in BMI and waist circumference, 28% experienced meaningful weight loss defined as $\geq$ 5%. The nutritionist spent an avg of 6.97 hours (SD 2.18) in-person and 1.58 hours (SD 0.68) by phone with each participant. In the overall group, significant decreases were seen in total cholesterol (7.2% decrease; t = -2.33, p = 0.03), VLDL (26.8% decrease; t = -2.33, p = 0.03) and triglycerides (26.6% decrease; t = -2.29; p = 0.04). All participants were satisfied with the diet; 43% were extremely satisfied. 75% of participants liked the foods they were able to eat "very much" or "extremely". All participants felt the in-person meetings were helpful. 77% did not feel an online video could replace the in-person meetings. 62% of participants did not feel a virtual meeting (e.g skype, etc.) could replace the in- person meeting while 38% felt it could. **Conclusions:** Patients with stage I-III CRC are able to follow a low GL diet with an in-person dietary intervention. Significant decreases in laboratory measures confirm the efficacy of the diet in altering metabolic indices. All participants who completed the study were satisfied with the diet, the majority of whom enjoyed the foods and planned to continue to follow the diet after study completion. The majority felt in-person contact with the nutritionist was essential to their success. This study was an essential step in designing a larger scale trial to evaluate the impact of low GL diet on cancer outcomes. Clinical trial information: NCT02129218. Research Sponsor: Clinical and Translational Science Collaborative of Cleveland 4UL1TR002548-01 from the National Center for advancing Translational Sciences (NCATS) component of the National Institutes of Health and NIH Roadmap for medial research, Other Foundation.

Ramucirumab in patients with advanced HCC and elevated alpha-fetoprotein (AFP): Outcomes by treatment-emergent ascites.

Andrew X. Zhu, Masafumi Ikeda, Peter R. Galle, Tatsuya Yamashita, Josep Llovet, Kun Liang, Chunxiao Wang, Sachi Sakaguchi, Paolo Abada, Ryan C Widau, Masatoshi Kudo; Harvard Medical School, Massachusetts General Hospital, Boston, MA; National Cancer Center Hospital East, Kashiwa, Japan; University Medical Center, Mainz, Germany; Department of Gastroenterology, Kanazawa University Hospital, Kanazawa, Japan; Mount Sinai School of Medicine, New York, NY; Eli Lilly and Company, Indianapolis, IN; Lilly, Indianapolis, IN; Department of Gastroenterology and Hepatology, Kindai University Faculty of Medicine, Osaka, Japan

Background: REACH and REACH-2 investigated ramucirumab (RAM) vs placebo (PL) in patients (pts) with advanced HCC following sorafenib, with REACH-2 enrolling only pts with baseline AFP ≥400 ng/mL. Ascites is common in HCC and associated with poorer outcomes. An exploratory analysis of outcomes by treatment-emergent (TE)-ascites was done. **Methods:** Pts with HCC, Child-Pugh A, ECOG PS ≤1, prior sorafenib, and no clinically meaningful ascites were randomized (REACH 1:1; REACH-2 2:1) to RAM 8 mg/kg or PL Q2W. A pooled meta-analysis of independent pt data (stratified by study) from REACH-2 and REACH (AFP ≥400 mg/mL) was done. OS and PFS were evaluated by Kaplan-Meier estimator and Cox models. Prognosis of TE-ascites in OS was evaluated by multivariate Cox models (adjusted for baseline ECOG PS, AFP, macrovascular invasion (MVI), and treatment [trt]). **Results:** Baseline characteristics were generally balanced between TE-ascites and non-ascites pts; however, more pts with ascites had MVI at baseline. Any-grade ascites was reported at a higher rate in RAM than PL (66 [21%] vs 33 [15%] pts, respectively), with most being low grade. Rate of Gr ≥3 ascites was similar between arms (15 [5%] vs 9 [4%] pts). Median time to onset (43 vs 47 days) and median duration of ascites (13 vs 18 days) were similar in RAM vs PL, with furosemide (22%) and spironolactone (19%) as most common trt and paracentesis (18%) as most common procedure for ascites in both arms. Ascites trended as a prognostic factor for OS after adjustment (with vs without; HR=1.3, 95% CI: 0.99, 1.62). Ascites was more commonly linked with hypoalbuminemia (odds ratio 4.9, 95% CI: 2.5, 9.3), but was not associated with proteinuria or hypertension. TEAEs occurred more frequently in pts with ascites in both arms. The most frequent Gr ≥3 TEAE in pts with ascites was hypertension. One RAM pt discontinued trt due to ascites. RAM trt was beneficial irrespective of presence of ascites (Table), and pts with ascites received more post-discontinuation therapy on RAM than PL (18% vs 6%). **Conclusions:** Acknowledging limitations of sample size, RAM provided a survival benefit in pts who did or did not experience TE-ascites. RAM was well tolerated and no new safety findings were observed. Clinical trial information: NCT011400347; NCT02435433. Research Sponsor: Eli Lilly and Company.

Efficacy.

	With Ascites		Without Ascites		Total Pooled Population	
	RAM N=66	PL N=33	RAM N=250	PL N=193	RAM N=316	PL N=226
OS, Median (mos)	6.7	3.4	8.3	5.9	8.1	5.0
HR (95% CI)	0.30 (0.18, 0.49)		0.77 (0.62, 0.95)		0.69 (0.57, 0.84)	
PFS, Median (mos)	4.2	2.0	2.7	1.5	2.8	1.5
HR (95% CI)	0.46 (0.29, 0.74)		0.62 (0.50, 0.77)		0.57 (0.47, 0.69)	

4645 **Poster Session (Board #253), Fri, 8:00 AM-11:00 AM**

Adjuvant chemoradiotherapy impact on the overall survival of completely resected ampullary and periampullary carcinoma: An updated meta-analysis.

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Background: Ampullary and Periampullary carcinomas (APAC) are uncommon gastrointestinal cancers that are often amenable to surgical resection. The benefit of postoperative adjuvant chemoradiotherapy (ACRT) in patients with completely resected localized AC has been controversial. A meta-analysis which was conducted in 2017 found no associated survival benefit for adjuvant therapies in APAC. However, this meta-analysis was methodologically flawed and combined studies that used adjuvant chemotherapy alone with those that used ACRT. The purpose of this meta-analysis is to evaluate the impact of ACRT on the overall survival (OS) of patients with completely resected APAC incorporating more recent studies. **Methods:** A review of the medical literature was conducted using online databases. Inclusion criteria consisted of resected Ampullary and Periampullary carcinoma, English language, publications from 1999 to the present, comparative studies reporting OS with hazard ratios (HR) or Kaplan-Meier curves of patients that underwent ACRT versus those that did not, and studies that reported the aggregate OS data of adjuvant therapies where the preponderance of the cohort received ACRT. Adjuvant chemotherapy studies and those that reported aggregate OS for a cohort with preponderance of adjuvant chemotherapy were excluded. A meta-analysis was conducted using an inverse variance method with a random-effects model. **Results:** Sixteen retrospective series with a total of 1122 patients were included and analyzed. The majority of APAC patients that received ACRT tended to have high risk features. Four of these studies analyzed their OS data for the high risk APAC patients in addition to the cohort as a whole. Intra-arterial chemotherapy and concomitant radiotherapy was used in one study. ACRT was found to be significantly associated with better OS in patients with completely resected APAC (HR 0.76, 95%CI: 0.65-0.88, $p < 0.001$). **Conclusions:** This is the first meta-analysis to show that adjuvant chemoradiotherapy is associated with a survival benefit in patients with completely resected high risk Ampullary and Periampullary carcinoma. In the absence of randomized clinical trials, this meta-analysis represents the most compelling data supporting the use of ACRT in this patient population. Research Sponsor: None.

TPS4646 **Poster Session (Board #254), Fri, 8:00 AM-11:00 AM**

Randomized phase III trial to evaluate omentum preserving gastrectomy for patients with resectable advanced gastric cancer: JCOG1711 (ROAD-GC).

Takanobu Yamada, Takaki Yoshikawa, Yuya Sato, Ryunosuke Machida, Junki Mizusawa, Hiroshi Katayama, Masanori Tokunaga, Yasunori Nishida, Jun Hihara, Masaya Watanabe, Yasuhiro Choda, Souya Nunobe, Junya Fujita, Masahide Kaji, Norimasa Fukushima, Seiji Ito, Narikazu Boku, Masanori Terashima; Kanagawa Cancer Center, Yokohama, Japan; National Cancer Center Hospital, Tokyo, Japan; Tokyo Medical and Dental University Hospital, Tokyo, Japan; Japan Clinical Oncology Group Data Center/Operations Office, National Cancer Center Hospital, Tokyo, Japan; National Cancer Center Hospital East, Kashiwa, Japan; Keiyukai Sapporo Hospital, Sapporo, Japan; Department of Surgery, Hiroshima City Asa Citizens Hospital, Hiroshima, Japan; Shizuoka General Hospital, Shizuoka, Japan; Hiroshima City Hospital, Hiroshima, Japan; Cancer Institute Hospital, Tokyo, Japan; Department of Surgery, Sakai City Medical Center, Sakai, Japan; Toyama Prefectural Central Hospital, Toyama, Japan; Yamagata Prefectural Central Hospital, Yamagata, Japan; Aichi Cancer Center Hospital, Aichi, Japan; Department of Gastrointestinal Medical Oncology, National Cancer Center Hospital, Tokyo, Japan; Division of Gastric Surgery, Shizuoka Cancer Center, Shizuoka, Japan

Background: Standard surgery for resectable advanced gastric cancer is D2 (standardized extended lymph node dissection) gastrectomy with omentectomy. The reason why omentectomy has been performed is as follows; (1) principal surgery for gastrointestinal cancers is en-block resection of mesothelium including regional lymph nodes. Omentum is a part of the mesothelium of the stomach. (2) Cancer cells implanted into the peritoneal cavity aggregated in the milky-spot of the omentum and formed peritoneal dissemination in an animal model. (3) By special staining, micrometastasis detected in the omentum. There is some arguments for this theory. (1) no prospective study showed survival benefit of omentectomy as compared with omentum preservation. (2) anatomically, milky-spot is found not only in the omentum but also in other mesothelium or Douglas pouch. (3) JCOG1001 phase III study showed no survival benefit of bursectomy against non-bursectomy although bursa is a part of mesothelium of the stomach. (4) Anti-immunity is accelerated by antigen presentation by macrophage in the milky-spot of the omentum. Preservation of the omentum may have several benefits; (1) decrease in blood loss and operation time, (2) preservation of physical function by omentum such as reaction to peritonitis and prevention of adhesion, and (3) overcoming difficulties in laparoscopic omentectomy and avoidance of organ injury during surgery. **Methods:** The study is multicenter randomized phase III trial designed to confirm non-inferiority of omentum preservation to omentectomy for resectable advanced gastric cancer. Patients aged 20-79 years, histologically proven gastric adenocarcinoma, clinical subserosal/serosal invasion, and expected R0 (curative) resection are randomly assigned (1:1) during surgery to either omentum preservation or omentectomy. Total or distal gastrectomy with D2 dissection is performed in both arms. Laparoscopic gastrectomy is not allowed. Intraoperative photographs of the dissected field are centrally reviewed for all patients for quality control. The primary endpoint is relapse-free survival (RFS) and the secondary endpoints are overall survival, blood loss, operation time, and adverse events. Sample size was set at 1050 considering expected 3-year RFS of 77% in both arms with non-inferiority margin of 5%, one-sided alpha of 5%, and power of 80%. Planned accrual and follow up period are 6.5 years and 3 years respectively. The trial was activated in March 2019, and 177 patients are enrolled as of January 2020. Clinical trial information: UMIN000036253. Research Sponsor: None.

TPS4647 **Poster Session (Board #255), Fri, 8:00 AM-11:00 AM**

POF (paclitaxel/oxaliplatin/5-FU/leucovorin) versus SOX/CAPOX/FOLFOX as a postoperative adjuvant chemotherapy for curatively resected stage III gastric cancer: Study protocol for a randomized controlled trial, FNF-014 trial.

Liyu Su, Chunxiang Li, Feng Huang, Lu chuan Chen, Lisheng Cai, Jiayi Li, Shen Zhao, Rongbo Lin, FNF Independent Investigations Group; Gastrointestinal Medical Oncology, Fujian Cancer Hospital & Fujian Medical University Cancer Hospital, Fuzhou, China; The Second Affiliated Hospital of Fujian Medical Univiersity, Quanzhou, China; Fujian Cancer Hospital & Fujian Medical University Cancer Hospital, Fuzhou, China; Fujian Provincial Cancer Hospital, Fuzhou, China; Department of General Surgery, Zhangzhou Affiliated Hospital of Fujian Medical University, Zhangzhou, China; Department of Medical oncology,Xiamen Key Laboratory of Antitumor Drug Transformation Research, The First Affiliated Hospital of Xiamen University, Teaching Hospital of Fujian Medical University, Xiamen, China; Gastrointestinal Medical Oncology, Fujian Cancer Hospital, Fuzhou, China

Background: Postoperative chemotherapy (S-1, CAPOX, or Docetaxel/S-1) is a standard treatment for stage II/III gastric cancer in Asia. With regard to single agent or doublet, the need for improvement has consistently been pointed out because of the relatively poor outcome for patients with stage III gastric cancer. Triplet (FLOT) has shown significant survival benefits in perioperative setting. POF, our regiment similar to FLOT, demonstrated priority to doublet (FOLFOX) in advanced setting (2019 ASCO-GI). We conducted a randomized, multicenter, phase III study to compare triplet to doublet regimens for patients with stage III gastric cancer. **Methods:** This is currently enrolling patients (n = 544) with pathologic stage III gastric cancer after D2 lymph node dissection. Patients are randomized 1:1 and stratified by tumor stage (IIIA, IIIB, or IIIC, AJCC 8th) into POF or SOX/CAPOX/FOLFOX (chosen by the clinicians). SOX: oxaliplatin 130 mg/m2 on day 1, oral S-1 80mg/m2 divided by two on days 1 to 14 every 21 days for 8 cycles. CAPOX: oxaliplatin 130 mg/m2 on day 1, oral capecitabine 1000 mg/m2 twice daily on days 1 to 14 every 21 days for 8 cycles. FOLFOX: oxaliplatin 85 mg/m2, levo-leucovorin 200 mg/m2, and 5-FU 400 mg/m2 bolus on day 1, then 5-FU 2400 mg/m2 continuous infusion over 46 hours, every 14 days for 12 cycles. Three doublets were chosen by the clinicians. POF: paclitaxel 135 mg/m2, followed by FOLFOX omitted 5-FU bolus, every 14 days for 12 cycles. Eligibility criteria: patients aged 18-70 years, primary histologically proven gastric adenocarcinoma (including adenocarcinoma of the gastroesophageal junction) of stage III with no evidence of metastatic disease, R0 resection with D2 lymph node dissection, good performance status (ECOG PS $\leq$1). Subjects must be able to take orally, and without other concomitant medical conditions that required treatment, initially treated with curative surgery followed by chemotherapy within 42 days. Life expectancy estimated more than 6 months. Adequate organ function. All patients provided written informed consent prior to treatment. Key exclusion criteria: patients with other primary malignancies, gastrointestinal bleeding. The primary end point is 3-year disease-free survival. Secondary end points are 3-year overall survival, 5-year overall survival, 5-year disease-free survival, and adverse events. Clinical trial information: NCT03788226. Research Sponsor: None.

TPS4648 **Poster Session (Board #256), Fri, 8:00 AM-11:00 AM**

Phase III study of first-line zolbetuximab + CAPOX versus placebo + CAPOX in Claudin 18.2$^+$/HER2$^-$advanced or metastatic gastric or gastroesophageal junction adenocarcinoma: GLOW.

Manish A. Shah, Jaffer A. Ajani, Salah-Eddin Al-Batran, Yung-Jue Bang, Daniel Catenacci, Peter C. Enzinger, David H. Ilson, Sunnie Kim, Florian Lordick, Kohei Shitara, Eric Van Cutsem, Ahsan Arozullah, Jung Wook Park, Rui-hua Xu; Weill Cornell Medical College, New York, NY; The University of Texas - MD Anderson Cancer Center, Houston, TX; Institut für Klinisch-Onkologische Forschung, Frankfurt, Germany; Seoul National University College of Medicine, Seoul, South Korea; Gastrointestinal Oncology Program, The University of Chicago, Chicago, IL; Dana-Farber Cancer Institute, Boston, MA; Memorial Sloan Kettering Cancer Center, New York, NY; University of Colorado Comprehensive Cancer Center, Aurora, CO; University Cancer Center Leipzig, Leipzig, Germany; National Cancer Center Hospital East, Kashiwa, Japan; University Hospitals Gasthuisberg Leuven, KU Leuven, Leuven, Belgium; Astellas Pharma Global Development, Inc., Northbrook, IL; Sun Yat-sen University Cancer Centre, Guangzhou, China

Background: Gastric cancer is the fourth leading cause of cancer death worldwide. Capecitabine + oxaliplatin (CAPOX) is a standard first-line treatment for advanced gastric cancer. Claudin (CLDN)18.2 has emerged as a promising targetable biomarker. In healthy tissue, CLDN18.2, a tight junction protein, is confined to gastric mucosa (ie, cells in the pit and base regions of gastric glands). Upon malignant transformation, structural loss in gastric or gastroesophageal junction (G/GEJ) adenocarcinoma cells may allow antibodies more access to previously unavailable CLDN18.2. Zolbetuximab is a chimeric IgG1 monoclonal antibody that specifically binds to CLDN18.2 and mediates cell death through antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity. Results of a phase 2 study (NCT01630083) showed prolonged survival of patients with CLDN18.2-positive (CLDN18.2$^+$) advanced G/GEJ adenocarcinoma treated with zolbetuximab + epirubicin, oxaliplatin, and capecitabine (EOX) vs EOX alone. **Methods:** This phase 3, double-blind, placebo-controlled study (NCT03653507) will enroll ~500 adult patients from global sites. Patients are required to have CLDN18.2$^+$/HER2$^-$ locally advanced unresectable or metastatic G or GEJ adenocarcinoma that is radiographically evaluable per RECIST v1.1. Patients are not permitted to have received prior treatment with chemotherapy for advanced or metastatic G or GEJ adenocarcinoma. Patients will be randomly assigned 1:1 to receive either zolbetuximab plus CAPOX or placebo plus CAPOX. Randomization will be stratified by region (Asia vs non-Asia), number of metastatic sites (0 to 2 vs $\geq$3), and prior gastrectomy (yes vs no). Zolbetuximab will be administered at a loading dose of 800 mg/m^2 IV on Cycle 1 Day 1 followed by 600 mg/m^2 IV every 3 weeks. Central testing of tumor tissue will determine CLDN18.2 and HER2 status (if unknown); patients will be considered CLDN18.2$^+$ if $\geq$75% of tumor cells demonstrate moderate-to-strong membranous immunohistochemical staining. The primary objective is to compare progression-free survival between treatment arms. Secondary endpoints are overall survival; objective response rate; duration of response; and the safety/tolerability, pharmacokinetics, and immunogenicity of zolbetuximab. As of January 31, 2020, 127 sites were active and open to enrollment. Clinical trial information: NCT03653507. Research Sponsor: Astellas Pharma, Inc.

TPS4649 **Poster Session (Board #257), Fri, 8:00 AM-11:00 AM**

Trial in progress: A phase I study of AMG 199, a half-life extended bispecific T-cell engager (HLE BiTE) immune therapy, targeting MUC17 in patients with gastric and gastroesophageal junction (G/GEJ) cancer.

Joseph Chao, Elvira Buxó, Andrés Cervantes, Farshid Dayyani, Caio Max Sao Pedro Rocha Lima, Richard Greil, Hanneke W.M. Van Laarhoven, Sylvie Lorenzen, Volker Heinemann, Roman Kischel, Kohei Shitara, Florian Lordick; City of Hope Comprehensive Cancer Center, Duarte, CA; Vall d'Hebron University Hospital, Barcelona, Spain; University of Valencia, Valencia, Spain; University of California Irvine, Irvine, CA; NRG Oncology, and Wake Forest University Baptist Medical Center, Winston-Salem, NC; Department of Internal Medicine III with Hematology, Medical Oncology, Hemostaseology, Infectious Diseases, Rheumatology, Oncologic Center, Paracelsus Medical University, Salzburg, Austria; University of Amsterdam, Amsterdam, Netherlands; Technische Universität München, Muenchen, Germany; University Hospital Munich, LMU Munich, Munich, Germany; Amgen Research (Munich) GmbH, München, Germany; National Cancer Center Hospital East, Chiba, Japan; University Cancer Center Leipzig, Leipzig, Germany

Background: Prognosis for advanced G/GEJ cancer is poor and new treatment modalities are urgently needed. MUC17 is a transmembrane protein overexpressed and differentially localized on the cell membrane of G/GEJ cancer cells; expression and localization in normal cells is much more limited. AMG 199 is an HLE BiTE immune therapy designed to engage CD3-positive T cells to MUC17-positive G/GEJ cancer cells, mediate redirected tumor cell lysis, and induce T cell activation and proliferation. A clinical trial is being conducted for this novel and targeted immune therapy agent in patients with MUC17-positive G/GEJ cancer. **Methods:** This is a first-in-human phase 1, open-label, dose escalating study (NCT04117958) evaluating AMG 199 in patients with MUC17-positive G/GEJ cancer. Key eligibility criteria include metastatic or locally advanced unresectable MUC17-positive (as determined by IHC using a central laboratory assay) gastric adenocarcinoma or gastroesophageal junction adenocarcinoma ineligible for curative surgery and relapsed or treatment-refractory following $\geq$2 lines including a platinum, a fluoropyrimidine, taxane or irinotecan, and an approved vascular endothelial growth factor receptor antibody or tyrosine kinase inhibitor. Patients eligible for human epidermal growth factor receptor 2 (HER2) directed therapy should have received an approved HER2 targeting antibody. Primary endpoints include: dose-limiting toxicities, treatment-emergent or -related adverse events, vital signs, electrocardiogram (ECG), and laboratory changes. Secondary endpoints include: pharmacokinetics of AMG 199, objective response, duration of response, time to progression, 6-month and 1-year progression-free survival, and 1-year and 2-year overall survival. The dose exploration (n = 30) will estimate the maximum tolerated dose and/or recommended phase 2 dose; this will be followed by a dose expansion (n = 40) and evaluation of the benefit/risk profile of AMG 199. The study began enrolling patients in January 2020 and is ongoing. This is the first clinical trial to investigate MUC17 as a potential anti-tumor target. For more information, please contact Amgen Medical Information: medinfo@amgen.com. Clinical trial information: NCT04117958. Research Sponsor: Amgen.

TPS4650 **Poster Session (Board #258), Fri, 8:00 AM-11:00 AM**

A randomized phase II/III study of paclitaxel/cisplatin versus cisplatin/5-fluorouracil in neoadjuvant chemoradiotherapy (CRT) followed by surgery for patients with locally advanced esophageal squamous cell carcinoma (ESCC).

Ta-Chen Huang, Chih-Hung Hsu, Jason C. Cheng, Chia-Chi Lin, Jhe-Cyuan Guo, Hung-Yang Kuo, Feng-Ming Hsu, Pei-Ming Huang, Kuan-Yin Ko, Jang-Ming Lee; National Taiwan University Hospital, Taipei, Taiwan; National Taiwan University Cancer Center, Taipei City, Taiwan; National Taiwan University Hospital, Taipei City, Taiwan; Department of Nuclear Medicine, National Taiwan University Hospital, Taipei, Taiwan

Background: Meta-analyses have shown the survival benefit of cisplatin/5-fluorouracil (PF) neoadjuvant CRT over surgery alone for patients with locally advanced ESCC. The CROSS study has demonstrated the statistically significant survival benefit of paclitaxel/carboplatin neoadjuvant CRT for patients with locally advanced esophageal cancer, especially ESCC. A network meta-analysis based on published phase III trials suggested that paclitaxel/platinum might be superior to PF as neoadjuvant CRT in patients with ESCC (Huang et al: Jpn J Clin Oncol. 2015;45:1023–8). However, a direct comparison of two CRT regimens in a prospective randomized clinical trial has not been performed in ESCC. We designed this clinical trial to test the hypothesis that paclitaxel-platinum is superior to PF as neoadjuvant CRT in patients with locally advanced ESCC. **Methods:** This single center open-label phase 2/3 study randomizes patients with histologically confirmed ESCC, T3/4aN0M0 or T1-3N1-3M0 (AJCC 7th edition), in 1:1 ratio, to receive TP (paclitaxel, 50 mg/m2/week; cisplatin 30 mg/m2/week; for 5 weeks) or PF (cisplatin 75 mg/m2, d1; 5-FU 1,000 mg/m2, d1-4; on week 1 and week 5)-neoadjuvant CRT (180 cGy/d, 5 days/week, for 5 weeks). Esophagectomy will be performed 6 to 10 weeks after completing CRT. All patients must be eligible to esophagectomy, with tumor length $\leq$8cm and tumor radial $\leq$5cm, with adequate organ functions, and have ECOG performance status of 0-2. In the phase 2 stage, 128 patients will be enrolled, assuming the pathologic complete response (pCR) rate of TP and PF as 45% and 25%, respectively, with a power of 80% and one-sided 10% significance level. If the primary endpoint of pCR is met, additional 120 patients will be enrolled for the phase III stage with overall survival as the primary endpoint, assuming the hazard ratio of TP versus PF as 0.65 with a power of 80% and a 5% significance level. The trial started patient enrollment in May, 2017. As of Jan of 2020, 52 of planned 128 patients for phase II part have been enrolled. Clinical trial information: NCT03623737. Research Sponsor: Grant for investigator initiated clinical trials.

TPS4651 **Poster Session (Board #259), Fri, 8:00 AM-11:00 AM**

A phase II/III study of perioperative nivolumab and ipilimumab in patients (pts) with locoregional esophageal (E) and gastroesophageal junction (GEJ) adenocarcinoma: A trial of the ECOG-ACRIN Cancer Research Group (EA2174).

Jennifer Rachel Eads, Michelle Weitz, Michael K. Gibson, Lakshmi Rajdev, Onkar V Khullar, Steven H. Lin, Constantine Gatsonis, Ignacio Ivan Wistuba, Aravind Sanjeevaiah, Al Bowen Benson, Nathan Bahary, Kristen Renee Spencer, Nabil F. Saba, Stanley R. Hamilton, Charles A. Staley, Anuradha Bapsi Chakravarthy, Terence Z. Wong, Peter J. O'Dwyer; University of Pennsylvania, Philadelphia, PA; Dana-Farber Cancer Institute, Boston, MA; Vanderbilt University Ingram Cancer Center, Nashville, TN; Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY; Winship Cancer Institute of Emory University, Atlanta, GA; The University of Texas MD Anderson Cancer Center, Houston, TX; Brown University, Providence, RI; The University of Texas Southwestern Medical Center, Dallas, TX; Northwestern Medicine, Chicago, IL; UPMC Hillman Cancer Center, University of Pittsburgh School of Medicine, Pittsburgh, PA; Rutgers Cancer Institute of New Jersey, New Brunswick, NJ; City of Hope National Medical Center, Duarte, CA; Duke University Medical Center, Durham, NC; University of Pennsylvania, Division of Medical Oncology, Philadelphia, PA

Background: E/GEJ adenocarcinoma has a high mortality rate despite curative intent treatment. A pathologic complete response (pCR) is associated with better overall survival (OS) but occurs in less than 30% of pts. Immunotherapy is effective in the metastatic setting. Here we aim to evaluate the contribution of immunotherapy in the neoadjuvant and adjuvant settings in pts with locoregional E/GEJ cancer. **Methods:** This is a multi-center, randomized phase II/III trial. Surgical candidates with locoregional E/GEJ adenocarcinoma receive carboplatin AUC 2 IV and paclitaxel 50 mg/m2 IV, both weekly x 5 during concurrent radiation (50.4 Gy) either with or without nivolumab 240 mg IV during weeks 1 and 3, followed by surgery. Pts with no post-operative disease receive nivolumab 240 mg IV every 2 weeks for 12 cycles either with or without ipilimumab 1 mg/kg IV every 6 weeks for 4 cycles. Eligibility criteria include pts with T1-N1-3M0 or T2-3N0-2M0 disease whom are candidates for surgery, no prior chemotherapy or radiation for this disease, no prior immunotherapy, no significant autoimmune disease. Pts must be disease free for adjuvant treatment. Primary neoadjuvant endpoint is pCR rate; primary adjuvant endpoint is disease free survival (DFS). Secondary endpoints include toxicity, DFS and OS. Pre- and mid-treatment diffusion weighted imaging MRI will be conducted during the neoadjuvant portion of the study. A neoadjuvant safety run in of 30 pts is underway. Overall, 278 pts will be needed to detect an absolute improvement of 15% in pCR rate in pts receiving and not receiving neoadjuvant nivolumab and 236 pts will be needed to detect a HR of 0.65 in favor of adjuvant ipilimumab/nivolumab over nivolumab (90% power, one sided alpha of 0.10). Accrual is expected over 34 months at a rate of 8 patients per month. If favorable at interim analysis. Clinical trial information: NCT03604991. Research Sponsor: U.S. National Institutes of Health.

TPS4652 **Poster Session (Board #260), Fri, 8:00 AM-11:00 AM**

A phase II study of selective HDAC6 inhibition with KA2507 for second-line treatment of advanced biliary tract cancer (ABC-11).

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Background: The ABC-02 trial provided Level A evidence supporting the use of cisplatin plus gemcitabine as first-line chemotherapy for advanced biliary tract cancer (ABC) [Valle, 2010]. In second line therapy oxaliplatin and 5FU and ivosedinib for IDH1 mutated cancers are options [Lamarca, 2019; Abou-Alfa, 2019] however there remains significant unmet need for patients without actionable alterations. Histone deacetylase 6 (HDAC6) is over-expressed in cholangiocarcinoma, reducing primary cilia. This is mediated through increased resorption in normal human cholangiocytes via tubulin deacetylation in the ciliary axoneme. Inhibition of HDAC6 elicits both cell intrinsic and extrinsic anti-cancer activity. HDAC6 inhibition reversed oncogenic loss of ciliation and demonstrated preclinical efficacy in a syngeneic rat orthotopic biliary cancer model [Gradilone, 2013]. KA2507 is a potent and selective small molecule inhibitor of HDAC6. Phase I dose escalation study identified an oral dose of 800mg bid for further development, being well tolerated and showing evidence of selective target engagement. **Methods:** ABC-11 is a Phase II multi-centre, open-label study of KA2507 in 40 evaluable patients with advanced biliary tract cancer previously treated with standard of care chemotherapy. The study follows a single-arm single-stage design using A'Hern's methodology. Eligible patients receive continuous 28-day cycles of fixed daily oral dose of KA2507 until death, disease progression or other pre-defined reason for study drug discontinuation. Tumour assessment is made at baseline and at 8-weekly intervals using RECIST 1.1 criteria until disease progression; primary endpoint is PFS at 4 months. Independent Data Monitoring Committee will review 4 month PFS and other data after first six patients, after a total of 17 patients (futility analysis, corresponding to cut-off of the Simon's minimax 2-stage design; 33% was set as the target 4-month PFS rate expected with KA2507) and at least annually thereafter. Subject to availability of adequate tissue, mandatory pre-treatment and on-study tumour biopsy samples will undergo multiparameter flow cytometry of immune cell subsets, immunofluorescence analysis of immune cell subsets (activation status and topology) and T cell repertoire studies. The study received regulatory and ethical approval to proceed in January 2020 and enrolment is in progress. Clinical trial information: NCT04186156. Research Sponsor: Karus Therapeutics Ltd.

TPS4653 **Poster Session (Board #261), Fri, 8:00 AM-11:00 AM**

Neoadjuvant chemotherapy with gemcitabine plus cisplatin followed by radical liver resection versus immediate radical liver resection alone with or without adjuvant chemotherapy in incidentally detected gallbladder carcinoma after simple cholecystectomy or in front of radical resection of BTC (ICC/ECC): A phase III study utilizing the German Registry of Incidental Gallbladder Carcinoma Platform (GR)—The AIO/CALGP/ACO-GAIN-Trial.

Thorsten Oliver Goetze, Ulli Simone Bankstahl, Sven A. Lang, Steffen Heeg, Wolf Otto Bechstein, Andreas Schnitzbauer, Ursula Pession, Daniel Reim, Sylvie Lorenzen, Tobias Keck, Alfred Königsrainer, Pompiliu Piso, Arndt Vogel, Claudia Pauligk, Salah-Eddin Al-Batran; Institute of Clinical Cancer Research, Krankenhaus Nordwest, UCT University Cancer Center, Frankfurt am Main, Germany and Institute of Clinical Cancer Research (IKF) GmbH at Krankenhaus Nordwest, Frankfurt, Germany; Institute of Clinical Cancer Research (IKF) at Krankenhaus Nordwest, UCT-University Cancer Center, Frankfurt, Germany; Department of General, Visceral and Transplantation Surgery, RWTH Aachen University Hospital, Aachen, Germany; Klinik für Allgemein- und Viszeralchirurgie, Universitätsklinikum Freiburg, Freiburg, Germany; Department of General and Visceral Surgery, University Hospital Frankfurt, Frankfurt, Germany; Department of General and Visceral Surgery, University Hospital Frankfurt, Frankfurt am Main, Germany; Klinik und Poliklinik für Chirurgie, Klinikum rechts der Isar, Technische Universität München, Munich, Germany; Third Department of Internal Medicine (Hematology/Medical Oncology), Klinikum Rechts der Isar, Technische Universitat Munchen, Munich, Germany; University of Luebeck, Luebeck, Germany; University Hospital Tübingen, Tübingen, Germany; University Medical Center, Regensburg, Germany; Hannover Medical School, Hannover, Germany; University Cancer Center Frankfurt, Institut für Klinisch-Onkologische Forschung and IKF Klinische Krebsforschung GmbH am Krankenhaus Nordwest, Frankfurt, Germany; Institute of Clinical Research (IKF) at Krankenhaus Nordwest, UCT-University Cancer Center, Frankfurt, Germany

Background: Currently, complete surgical resection represents the only potentially curative treatment option for Biliary Tract Cancer (BTC) including Gallbladder Cancer (GBC). Even after curative resection, 5-year OS is only 20–40%. GBC is relatively rare, but still the fifth most common neoplasm of the digestive tract and even the most frequent cancer of the biliary system. Gallbladder carcinoma is suspected preoperatively in only 30% of all pts, while the majority of cases are discovered incidentally by the pathologist after cholecystectomy for a benign indication. 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 of GBC management and even in intrahepatic and extrahepatic cholangiocarcinoma. Especially because data regarding pure adjuvant chemotherapy in BTC`s are conflicting. **Methods:** This is a multicenter, randomized, controlled, open-label phase III study including pts with incidentally discovered GBCs after simple cholecystectomy in front of radical liver resection and pts with resectable/borderline resectable cholangiocarcinomas (ICC/ECC) scheduled to receive perioperative chemotherapy (Gemcitabine + Cisplatin 3 cycles pre- and post-surgery) or surgery alone followed by a therapy of investigator's choice. 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 6, 2020. EudraCT number: 2017-004444-38. Clinical trial information: NCT03673072. Research Sponsor: Deutsche Forschungsgesellschaft (DFG).

TPS4654 **Poster Session (Board #262), Fri, 8:00 AM-11:00 AM**

Multicenter phase II study of trastuzumab deruxtecan (DS-8201) for HER2-positive unresectable or recurrent biliary tract cancer: HERB trial.

Akihiro Ohba, Chigusa Morizane, Makoto Ueno, Satoshi Kobayashi, Yasuyuki Kawamoto, Yoshito Komatsu, Masafumi Ikeda, Mitsuhito Sasaki, Naohiro Okano, Junji Furuse, Nobuyoshi Hiraoka, Hiroshi Yoshida, Aya Kuchiba, Gakuto Ogawa, Kenichi Nakamura, Naoko Matsui, Yoshiaki Nakamura, Wataru Okamoto, Takayuki Yoshino, Takuji Okusaka; National Cancer Center Hospital, Tokyo, Japan; Kanagawa Cancer Center, Yokohama, Japan; Hokkaido University Hospital, Sapporo, Japan; National Cancer Center Hospital East, Kashiwa, Japan; Kyorin University Faculty of Medicine, Tokyo, Japan; Kyorin University School of Medicine, Tokyo, Japan; National Cancer Center, Tokyo, Japan; Hiroshima University Hospital, Hiroshima, Japan

Background: Biliary tract cancer (BTC) is one of the most lethal cancers with limited treatment options. Early clinical trials showed a hint of activity of HER2 blockade for HER2 positive BTC, the prevalence of which was reported to be from 5% to 20%. Trastuzumab deruxtecan (DS-8201) is an antibody-drug conjugate composed of an anti-HER2 antibody, cleavable terapeptide-based linker, and a topoisomerase I inhibitor, which showed durable response in HER2 positive breast cancer as well as in a wide spectrum of cancer subtypes in a phase I study. In addition, preclinical research demonstrated the effectiveness of trastuzumab deruxtecan for HER2 positive BTC patient derived xenograft model. This phase II study is being conducted to evaluate the efficacy and safety of trastuzumab deruxtecan for HER2 positive BTC. **Methods:** The main inclusion criteria are unresectable or recurrent BTC, histologically diagnosed as adenocarcinoma or adenosquamous carcinoma, confirmed HER2-expressing status by central pathological examination, refractory or intolerant to treatment including gemcitabine, and adequate organ function. Patients are registered and receive 5.4 mg/kg trastuzumab deruxtecan every 3 weeks until disease progression or unacceptable toxicities. Primary endpoint is the overall response rate (ORR) in HER2 positive (defined as IHC3+, or IHC2+/ISH+; ISH+ defined as *HER2*/*CEP17* $\geq$2.0) patients by central imaging review. The ORR in all HER2-expressing patients (including HER2 low expressing defined as IHC/ISH status of 0/+, 1+/-, 1+/+, or 2+/-), progression-free survival, overall survival, and incidence of adverse events are assessed as secondary endpoints. Thirty-two patients will be enrolled, including 24 with HER2 positive BTC as primary cohort and 8 with HER2 low expressing BTC. The study has 80% power for primary endpoint in HER2 positive BTC patients, with one-sided alpha error of 5%; threshold ORR of 15% and expected ORR of 40%. Pharmacokinetics and circulating tumor DNA analyses serially are performed. The study was initiated in May 2019 with enrollment ongoing. A total of 15 patients were enrolled as of January 2020. Funding: Japan Agency for Medical Research and Development, and Daiichi Sankyo. Clinical trial information: JMA-IIA00423. Research Sponsor: Japan Agency for Medical Research, Pharmaceutical/Biotech Company.

TPS4655 **Poster Session (Board #263), Fri, 8:00 AM-11:00 AM**

Perioperative MVT-5873, a fully human monoclonal antibody against a CA 19-9 epitope, for operable CA 19-9 producing pancreatic cancers, cholangiocarcinomas, and metastatic colorectal cancers.

Shreya Gupta, James D McDonald, Reed I Ayabe, Tahsin M Khan, Lauren A Gamble, Alexander J Rossi, Surajit Sinha, Cathleen Hannah, Donna Mabry-Hrones, M. Cecilia Monge B., Andrew M. Blakely, Tim F. Greten, Jeremy L. Davis, Jonathan M Hernandez; National Cancer Institute, Bethesda, MD; National Institutes of Health, Bethesda, MD; National Cancer Institute, National Institutes of Health, Bethesda, MD

Background: Operable hepatopancreatobiliary (HPB) cancers continue to pose significant challenges. Radical resections are rarely curative, and chemotherapy is able to reduce tumor recurrence for only a fraction of patients. Despite the obvious advantages of extirpation of the identifiable tumor(s), the inflammatory milieu that accompanies surgery and the obligate time off cytotoxic agents allows for activation of remote quiescent disseminated tumor cells, leading to metastatic recurrence. We are conducting a study to determine the safety and efficacy of immediate peri-operative MVT-5873, a cytotoxic monoclonal antibody targeting Carbohydrate Antigen 19-9 (CA 19-9), in patients undergoing resections pancreatic cancer, cholangiocarcinoma or metastatic colorectal cancer to the liver. MVT-5873 is a human IgG1 antibody isolated from a patient following immunization with a sLe^a-KLH vaccine. MVT-5873 has demonstrated cell surface binding in sLe^a positive human tumor lines and has been shown to be potent in complement-dependent cytotoxicity assays and antibody-dependent cell mediated cytotoxicity assays. In patients with CA 19-9-producing cancers, MVT-5873 treatment has been shown to decrease serum CA 19-9 levels and prevent tumor progression. This trial may open the door for investigation of additional and/or synergistic agents in the immediate peri-operative period and usher in a new paradigm in the management of surgically treated cancers. **Methods:** This is a prospective, Phase II trial designed to determine the efficacy (increase in 1-yr DFS) and safety of peri-operative MVT-5873 for subjects with operable pancreatic, liver and bile duct cancers with elevated CA 19-9 levels. Patients may receive any standard neoadjuvant regimen prior to enrollment at the NIH Clinical Center in Bethesda, Maryland. Eligible patients will receive a pre-operative dose of MVT-5873 three days prior to the planned operation to remove all demonstrable disease. Following the operation, patients will receive a total of four doses of MVT-5873; the first two doses on postoperative days four and ten. The third dose will be administered on the normally scheduled postoperative clinic visit, followed by a final dose one month after discharge from the hospital and prior to the start of adjuvant treatment. Clinical trial information: NCT03801915. Research Sponsor: U.S. National Institutes of Health.

TPS4656 **Poster Session (Board #264), Fri, 8:00 AM-11:00 AM**

Phase II study of nivolumab (anti-PD1), tadalafil, and oral vancomycin in patients with refractory primary hepatocellular carcinoma or liver dominant metastatic cancer from colorectal or pancreatic cancers.

M. Cecilia Monge B., Changqing Xie, Donna Mabry-Hrones, Bradford J. Wood, Seth M. Steinberg, David E Kleiner, Tim F. Greten; National Cancer Institute, National Institutes of Health, Bethesda, MD; National Cancer Institute, Bethesda, MD; National Institutes of Health, Bethesda, MD; Biostatistics and Data Management Section, National Cancer Institute, NIH, Bethesda, MD

Background: Treatment options for advanced hepatocellular carcinoma (HCC) and liver dominant metastatic disease from colorectal or pancreatic cancers are limited with poor overall survival. Tadalafil has shown to increase anti-tumor immunity by decreasing myeloid derived suppressor cells (MDSC) and impair tumor growth in preclinical HCC models. Oral vancomycin affects bile acid metabolizing gut commensal bacteria leading to increased CXCL16 expression in the liver resulting in NKT mediated liver-selective anti-tumor effects. This study combines immune checkpoint inhibition (ICI) treatment with nivolumab in combination with tadalafil and oral vancomycin. We aim to evaluate the synergy of the antitumor effect induced by the change in gut microbiome with oral vancomycin and the immunomodulatory effect of PDE5 inhibition combined with ICI with nivolumab in advanced liver cancer or liver metastasis. Correlative Studies: Paired liver tumor biopsies are analyzed for genomic analysis (WES, RNA-seq), immune cell infiltration, proteomics and metabolomic studies (bile acids) and chemokine expression. Stool samples are analyzed for microbiota. Blood samples are analyzed for immune monitoring, cytokine profiles and pharmacokinetics of study drugs. Serum bile acid levels are determined in blood in the 2 hour period after test meal ingestion. **Methods:** This is a single-arm study of nivolumab, oral vancomycin and tadalafil. Treatment is delivered in 4-week cycles (C) and continues until off treatment. Imaging is done every 8 weeks. Biopsies are done at baseline and during week 3 of C2. Nivolumab is administered on day (D)1 of each C at a dose of 480 mg IV. Tadalafil is administered orally (PO); 10 mg daily starting on D1 of C1 and continues daily until off study. Vancomycin administration starts on D1 of C1 at 125 mg PO every 6 hours for a total daily dose of 500 mg. Patients will be on vancomycin 3 weeks on, 1 week off per regimen. The study is currently enrolling without DLT. Clinical trial information: NCT03785210. Research Sponsor: U.S. National Institutes of Health.

TPS4657 **Poster Session (Board #265), Fri, 8:00 AM-11:00 AM**

An exploratory study of fruquintinib as second-line treatment for patients with advanced or metastatic biliary tract cancer.

Qiu Li, Pengfei Zhang; West China Hospital , Sichuan University, Chengdu, China; The Department of Medical Oncology, Cancer Center, State Key Laboratory of Biotherapy, West China Hospital, Sichuan University, Chengdu, China

Background: Biliary tract cancer (BTC) is a relatively uncommon but highly fatal malignancy and most patients with BTC are diagnosed at advanced stages. Currently, no standard second-line treatment has been established following recurrence from the first-line treatment. VEGF is highly expressed in more than 50% of BTC, which indicates anti-angiogenesis might be a potentially effective method to improve the outcome in BTC. Fruquintinib is a novel small molecule tyrosine kinase inhibitor targeting VEGFR1, VEGFR2, and VEGFR3 and is currently being evaluated in clinical trials for multiple cancers including lung cancer, gastric cancer and colorectal cancer, and showed strong anti-tumor activity. However, the effect and safety of fruquintinib has not been investigated in the setting of second-line treatment for BTC. **Methods:** The study is a multicenter, single-arm, phase 2 trial of fruquintinib (5 mg, po, for 3 weeks, followed by 1 week off, 4 weeks for a cycle) for patients with advanced or metastatic BTC who have failed to first-line chemotherapy. The primary endpoint is progression-free survival (PFS) with the null hypotheses of 8 weeks, and the median PFS$\geq$15 weeks as evidence of the study drug activity (α=0.05, 80% power, one-sided). The number of patients required to complete the study is 27. Allowing for 20% expulsion rate, the study needs 33 patients. The secondary endpoints include objective response rate (ORR), disease control rate (DCR), overall survival (OS), safety and quality of life (QoL). Meanwhile, the study also set an exploratory objective to evaluate the mutation status of related genes in plasma (cfDNA) and tumor tissue and explore the interplay between mutation patterns with efficacy. Major eligibility requirements: Age $\geq$18 years; Histologically or cytologically confirmed diagnosis of advanced or metastatic biliary tract adenocarcinoma; First-line chemotherapy failed (tumor progression or intolerable adverse events); No less than 3 months of expected survival; ECOG PS$\leq$1; At least one measurable lesion according to RECIST 1.1 criteria; Adequate organ function. Eligible patients with advanced or metastatic BTC refractory to first-line chemotherapy will be enrolled at 7 medical centers in China. The study is open and actively enrolling at time of submission. Clinical trial information: NCT04156958. Research Sponsor: None.

TPS4658 **Poster Session (Board #266), Fri, 8:00 AM-11:00 AM**

An exploratory study of sorafenib plus toripalimab for unresectable hepatocellular carcinoma with portal vein tumor thrombus.

Yu Yang, Qiu Li; Department of Medical Oncology, Cancer Center, West China Hospital, Sichuan University, Chengdu, China

Background: Portal vein tumor thrombosis (PVTT) is common among advanced hepatocellular carcinoma (HCC), resulting in poor prognosis. As the standard first-line treatment, the efficacy of Sorafenib is not satisfactory in HCC with PVTT. Although immune checkpoint inhibitors have made a breakthrough in treatment of advanced HCC, objective response rate (ORR) of anti-PD-1 monoclonal antibody monotherapy is only 17-20%. Recently, PD-1/PD-L1 inhibitors combined with anti-angiogenesis therapy have shown good efficacy in the clinical studies. However, the data on immunotherapy for HCC with PVTT are still limited. Toripalimab is the first Chinese-produced anti-PD-1 monoclonal antibody marketed. We designed the study to evaluate the efficacy and safety of Sorafenib plus Toripalimab as the first-line treatment for unresectable HCC with PVTT. **Methods:** The study is a multicenter, single-arm, phase Ib/II trial. The primary objectives are 6-month progression-free survival (PFS) rate and safety. Secondary objectives include ORR, disease control rate, PFS, overall survival. The escalation stage includes two dose cohorts: Sorafenib 400 mg po qd or 400 mg bid combined with Toripalimab 240 mg iv d1 q3w. 6-12 patients are estimated to evaluate the dose-limiting toxicity within the first 42 days of administration. In the expansion stage, patients are treated with the recommended dose based on the escalation stage, until progressive disease or intolerable toxicity. Assuming Sorafenib plus Toripalimab can improve the 6-month PFS rate to 40% (Sorafenib:20%, $\beta = 0.2$, $\alpha = 0.05$) and dropout is 10%, this stage need 39 patients. A total of 45-51 patients are enrolled. Major eligibility requirements include: unresectable HCC with diagnoses confirmed histologically or cytologically, or confirmed clinically in accordance with Chinese guideline for HCC diagnosis and treatment (v2017); radiographic evidence of PVTT; age $\geq$18 and $<$ 75 years; at least one measurable lesion according to RECIST 1.1; a predicted life expectancy $\geq$ 3 months; ECOG PS$\leq$1, Child-Pugh class A or B ($\leq$7); no any prior systemic anti-cancer treatment; adequate organ function. Patients with hepatitis B treated with antiviral therapy (viral load $<$ 100 IU/mL) or patients with chronic hepatitis C can be included. The study is open and actively enrolling at time of submission. Clinical trial information: NCT04069949. Research Sponsor: Shanghai Junshi Biosciences Co., Ltd.

TPS4659 **Poster Session (Board #267), Fri, 8:00 AM-11:00 AM**

Phase II study of pembrolizumab plus olaparib in the treatment of patients with advanced cholangiocarcinoma.

Aiwu Ruth He, Benjamin Adam Weinberg, Marcus Smith Noel, Violeta P Milic, Petra Prins, Hongkun Wang, Marion L. Hartley, John Marshall; Georgetown University Lombardi Comprehensive Cancer Center, Washington, DC; Georgetown University, Washington, DC; James P. Wilmot Cancer Institute, University of Rochester, Rochester, NY; Medstar Georgetown University Hospital, Washington, DC; The Ruesch Center for the Cure of Gastrointestinal Cancers, Washington, DC

Background: Lack of an effective second-line treatment of patients (pts) with advanced cholangiocarcinoma (CC) necessitates the development of new therapies. Preclinical studies suggest CC susceptibility to PARP inhibition (PARPi): *ERCC1* is underexpressed in 74% of CCs, and olaparib is selective for *ERCC1* deficiency, profoundly inhibiting DNA repair. Additionally, PARPi exploits *IDH* mutation-related DNA damage repair deficiency, which is found in about 25% of CCs. Unfortunately, PARPi also upregulates PD-1-PD-L1 receptor-ligand binding, which attenuates anticancer immunity and counteracts the efficacy of PARPi. However, this can be prevented by PD-1 inhibition—blockade of PD-1-PD-L1 acts to re-sensitize cancer cells to T-cell killing. Hence, we hypothesize that the combination of olaparib and pembrolizumab will produce a durable anti-tumor response against CC by synergistically inducing DNA damage and increasing immune response. **Methods:** Thirty-six pts with advanced CC, who either failed to respond to or progressed on first-line therapy, will be enrolled to receive olaparib (300 mg PO bid) daily plus pembrolizumab (200 mg IV Q3 weeks) for 12 months, unless unacceptable toxicities or cancer progression occur, in which cases therapy will cease. MRI or CT tumor assessment will occur just before therapy, every 6 weeks for the first 6 months of therapy, and then every 9 weeks for the next 6 months of therapy (total, 12 months). Three tumor biopsies will be collected: at baseline; at week 4; and at time of progression. In each biopsy, ERCC1, PD-1, and PD-L1 expression, *IDH1/2* mutation status, and immune cell (CD3 and CD8) response will be assessed. The total study duration will be 20-36 months. The primary endpoint will be overall response rate; the secondary endpoints will be PFS, OS, duration of response, and safety and tolerability. It is hypothesized that in pts with advanced CC, second-line therapy with olaparib plus pembrolizumab will improve the response rate from 17.5% to 35%, as well as increase PFS and OS compared to cytotoxic chemotherapy. Study enrollment began in Q1 2020. NCI number pending at time of abstract submission. Clinical trial information: pending at time of submission. Research Sponsor: Merck.

TPS4660 **Poster Session (Board #268), Fri, 8:00 AM-11:00 AM**

Etctn 10388: A phase I trial of triapine and lutetium Lu 177 dotatate in well-differentiated somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs).

Aman Chauhan, Charles Kunos, Riham El Khouli, Jill Kolesar, Heidi Weiss, William Edgar Carson, Mark B Evers, Mark S. Kidd, Jan Hendrik Beumer, Susanne M. Arnold, Elise C. Kohn, Lowell Brian Anthony; University of Kentucky, Division of Medical Oncology, Lexington, KY; SUMMA Physicians, Akron, OH; University of Kentucky, Lexington, KY; University of Kentucky and Markey Cancer Center, Lexington, KY; The Ohio State University Comprehensive Cancer Center, Department of Surgery, Columbus, OH; Yale School of Medicine, New Haven, CT; NSABP Foundation and University of Pittsburgh Cancer Institute, Pittsburgh, PA; Markey Cancer Center, University of Kentucky, Lexington, KY; Women's Malignancies Branch, Center for Cancer Research, National Cancer Institute, Bethesda, MD

Background: Radiolabeled somatostatin analogues provide a means of delivering targeted radiation with a high therapeutic index to NETs that express somatostatin receptors (SSTRs). Radiolabeled somatostatin analogue Lutetium Lu 177 Dotatate (Lutathera) is a beta-emitting radionuclide, recently FDA approved for use in SSTR positive gastroenteropancreatic neuroendocrine tumors (GEPNETS) in the US based on the NETTER-1 Phase III trial. Despite favorable PFS and safety profile, the drug has limited cytoreductive capability with a 17% ORR. We hypothesize that addition of an effective radiation sensitizer could help improve antitumor activity of Lutathera. Ribonucleotide reductase (RNR) is the only enzyme responsible for conversion of ribonucleoside diphosphate to deoxyribonucleotide diphosphate (dNDP), the key building blocks for DNA synthesis. Radiation is a potent inducer of DNA double-strand breaks (DSBs), and RNR is the rate-limiting enzyme in the repair of DNA in this setting. Triapine is an inhibitor of RNR. This study will test the hypothesis that radiation sensitizer triapine can be safely combined with peptide receptor radionuclide therapy and ultimately may improve antitumor activity of Lutetium Lu 177 Dotatate. **Methods:** This study is an investigator initiated, NCI sponsored, multicenter phase 1 trial of triapine and Lutetium Lu 177 Dotatate in well-differentiated somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumor (GEP-NETs) after the failure of at least one line of prior systemic cancer treatment. A total of 29 patients will be enrolled in the dose escalation with help of Bayesian optimal interval design (BOIN) and dose expansion cohorts. The study will be open through the NCI ETCTN (National Cancer Institute Experimental Therapeutics Clinical Trials Network) program. Patients will be treated with 177 lutetium dotatate in combination with triapine. Triapine will be administered orally (100 mg once a day starting dose) from D1-14 with each dose of PRRT [200 mCi]. Primary endpoint is to evaluate recommended phase II dose (RP2D). Secondary endpoints are to evaluate safety, pharmacokinetics, and clinical activity (ORR and PFS). We are also evaluating NETEST, a novel blood based test that evaluates levels of 51 neuroendocrine tumor gene transcripts. In addition, the study will correlate clinical outcome with baseline somatostatin receptor density, somatic tumor mutations and germline mutations. Clinical trial information: 04234568. Research Sponsor: NCI CTEP.

TPS4661 **Poster Session (Board #269), Fri, 8:00 AM-11:00 AM**

NAPOLI-3: An open-label, randomized, phase III study of first-line liposomal irinotecan + 5-fluorouracil/leucovorin + oxaliplatin versus nab-paclitaxel + gemcitabine in patients with metastatic pancreatic ductal adenocarcinoma.

Zev A. Wainberg, Tanios S. Bekaii-Saab, Richard Hubner, Teresa Macarulla, Andrew Scott Paulson, Eric Van Cutsem, Fiona Maxwell, Yan Moore, Haofei Tiffany Wang, Bin Zhang, Eileen Mary O'Reilly; University of California, Los Angeles, Medical Center, Los Angeles, CA; Mayo Clinic, Scottsdale, AZ; Christie NHS Foundation Trust, Manchester, United Kingdom; Vall d'Hebrón University Hospital and Vall d'Hebrón Institute of Oncology, Barcelona, Spain; Texas Oncology/The US Oncology Network, Dallas, TX; University of Leuven, Leuven, Belgium; Ipsen, Abingdon, United Kingdom; Ipsen Bioscience, Boston, MA; Memorial Sloan Kettering Cancer Center, New York, NY

Background: Liposomal irinotecan administered with 5-fluorouracil/leucovorin (5-FU/LV) is approved in the USA for metastatic pancreatic ductal adenocarcinoma (mPDAC) following progression with gemcitabine-based therapy. A phase 1/2 study in previously untreated locally advanced/metastatic PDAC showed promising anti-tumor activity with liposomal irinotecan 50 mg/m^2 free base + 5-FU 2400 mg/m^2 + LV 400 mg/m^2 + oxaliplatin (OX) 60 mg/m^2 on days 1 and 15 of a 28-day cycle (Wainberg *et al. Ann Oncol* 2019;30 Suppl 4: SO-005). Herein, we present the design of the phase 3 NAPOLI-3 study investigating the efficacy and safety of this regimen as first-line therapy in patients with mPDAC. **Methods:** NAPOLI-3 (NCT04083235) is a phase 3, open-label, randomized, global study in adults with histologically/cytologically confirmed pancreatic adenocarcinoma not previously treated in the metastatic setting. Patients are required to have one or more metastatic tumors measurable with computed tomography/magnetic resonance imaging and an Eastern Cooperative Oncology Group performance status score of 0–1. Site activation began in Dec 2019 and enrollment is ongoing. Random allocation (1:1) of 750 patients is planned to liposomal irinotecan + 5-FU/LV + OX (regimen as per phase 1/2 study) or nab-paclitaxel 125 mg/m^2 + gemcitabine 1000 mg/m^2 on days 1, 8 and 15 in a 28-day cycle. The primary endpoint is overall survival (OS). Secondary endpoints (progression-free survival [PFS] and overall response rate assessed with Response Evaluation Criteria in Solid Tumors v1.1 criteria) will be compared only if the primary endpoint shows superiority for liposomal irinotecan + 5-FU/ LV + OX over nab-paclitaxel + gemcitabine. Safety assessments include adverse-event monitoring. Patients will continue treatment until disease progression, unacceptable toxicity or study withdrawal, and will then be followed for survival every 2 months until death or study end (when all patients have died, withdrawn consent or are lost to follow-up). Clinical trial information: NCT04083235. Research Sponsor: Ipsen.

TPS4662 **Poster Session (Board #270), Fri, 8:00 AM-11:00 AM**

A phase II trial of PD-1 inhibition with INCMGA00012 in patients with previously treated unresectable or metastatic adenosquamous pancreatic cancer.

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Background: Adenosquamous pancreatic cancer (ASQ) constitutes 1-5% of all pancreatic cancers and compared to pancreatic adenocarcinoma (PDAC) has a worse survival. ASQ has glandular and squamous histologic components and given its rarity and aggressiveness, in practice there is no current standard regimens for ASQ. Unfortunately, checkpoint blockade has had an overall disappointing impact on survival in PDAC. In an effort to identify a patient subgroup most likely to respond to immunotherapy, the immune tumor microenviroment (TME) in ASQ was evaluated. Tissue microarrays from archived ASQ samples were first created. Then immunocytochemistry (IHC) staining for immune cells and immune checkpoint proteins was performed. PD-L1 expression and the combined presence of PD-L1+, IDO+, LAG3+, and VISTA+ was seen. All ASQ cases had some degree of tumor infiltrating lymphocytes (TIL, including CD8+ T-cells). Furthermore, PD-L1 and other checkpoint positivity correlated with increased TIL. These findings suggest the presence of adaptive immune resistance. This is in contrast to standard PDAC, in which the expression of immune checkpoints is rarely accompanied by increased effector T-cells. **Methods:** We are conducting a multiple-center, single arm, phase II clinical trial to evaluate PD-1 inhibition with INCMGA00012 in locally advanced unresectable and metastatic ASQ patients. INCMGA00012 is a humanized monoclonal antibody antagonistic to PD-1. The primary objective is to determine the disease control rate at 4 months using RECIST 1.1. The study is planned with 21 evaluable subjects and allows early termination for lack of efficacy. Patients have a pre-treatment biopsy followed by INCMGA00012 500 mg on Day 1 of each cycle (every 4 weeks). A second biopsy will occur eight weeks later. Eligibility criteria includes histologically- or cytologically-proven adenosquamous carcinoma of the pancreas by central pathologic review and patients must have received (or been intolerant to or ineligible for) at least 1 prior line of cytotoxic chemotherapy and received no more than 2 prior systemic treatments. Patients with known MSI-H/dMMR status are excluded. Exploratory objectives include examining changes in the TME checkpoint expression and immune cell infiltrate in the biopsies via IHC and RNA expression studies. The clinical study was activated in February 2020. Clinical trial information: NCT04116073. Research Sponsor: None.

TPS4663 **Poster Session (Board #271), Fri, 8:00 AM-11:00 AM**

Phase I study of proton therapy in adjuvant pancreatic cancer (PROTON-PANC).

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Background: Pancreatic adenocarcinoma (PAC) has a poor prognosis, with a 5-year survival rate of 10%. The current standard of care for patients with resectable disease is surgical resection followed by 6 months of adjuvant modified FOLFIRINOX (FFX, leucovorin, fluorouracil, irinotecan, and oxaliplatin). As survival outcomes and distant recurrence improve with the use of FFX, locoregional recurrence remains a cause of morbidity and mortality. We seek to integrate adjuvant short-course proton radiation therapy (PRT) to the surgical bed in between cycles of FFX. While there is limited literature on the combination of short course PRT and FFX, there are analogous experiences using 5 fraction SBRT or IMRT following FFX in routine clinical practice. The ongoing Alliance 021501 trial of preoperative chemotherapy vs. chemotherapy plus radiation (IMRT using 5 Gy X 5 or SBRT 6.6 X 5) in borderline resectable pancreatic cancer mandates that radiation starts 5 days or more following the last dose of FFX. Additionally, at the Lombardi Comprehensive Cancer Center, we routinely combine 5 fraction SBRT after a 10-14 day interval from FFX. **Methods:** This is a phase I, single-arm, open-label study. Eligible pts are $\geq$ 18 years old, have histologically confirmed, resected PAC of the pancreatic head (R0 or R1) on adjuvant FFX, an ECOG performance status of 0-1, and adequate normal bone marrow and hepato-renal function. Exclusion criteria are prior radiation to the upper abdomen (neoadjuvant chemotherapy is allowed). This study will use a 3+3 dose-escalation design to determine the safety and feasibility of combining 5 fractions of adjuvant PRT with FFX using different intervals between cycle 6 of FFX and PRT: dose level 1 uses a 12 day interval, and dose level 2 uses a 5 day interval. The primary endpoint is to determine the RP2D between the 2 proposed schedules. Using a 3+3 dose-escalation schema, 2-12 patients will be required to determine the RP2D. Enrollment began in Q4 2019. Clinical trial information: NCT03885284. Research Sponsor: The Ruesch Center for the Cure of Gastrointestinal Cancers.

TPS4664 **Poster Session (Board #272), Fri, 8:00 AM-11:00 AM**

A randomized phase II study of second-line treatment with liposomal irinotecan, and S-1 versus liposomal irinotecan and 5-fluorouracil in gemcitabine-refractory metastatic pancreatic cancer patients.

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Background: Pancreatic ductal adenocarcinoma (PDAC) is the deadliest form of cancer with a 5-year survival of less than 5% for patients with metastatic disease. Despite improvements over the past years, with the introduction of FOLFIRINOX and gemcitabine plus nab-paclitaxel, the majority has disease progression within 6 months after start of first line treatment. The NAPOLI trial was the first phase III study showing that patients with metastatic pancreatic cancer that progressed after treatment with gemcitabine-based chemotherapy benefitted from second line treatment. Patients received liposomal irinotecan (nal-IRI) either as a single agent or in combination with 5-fluorouracil/leucovorin (5-FU/LV), or 5-FU/LV alone. Patients treated with both nal-IRI and 5-FU/LV experienced a median overall survival (mOS) of 6.1 months versus 4.2 months for the 5-FU/LV group. Recently, two Japanese studies (GEST and JASPAC 01) reported on the use of S-1 in patients with PDAC. In patients with locally advanced or metastatic PDAC, S-1 was non-inferior compared to gemcitabine in terms of mOS (8.8 months for gemcitabine versus 9.7 months for S-1). In the adjuvant setting, S-1 showed superior mOS compared to gemcitabine, 46.5 and 25.5 months respectively, HR for mortality of S-1 compared with gemcitabine was 0.57 (95% CI 0.44–0.72). In view of these results, the objective of this NAPAN study is to compare the progression free survival (PFS) of nal-IRI plus S-1, with nal-IRI plus 5-FU/LV in a Western study population for second line treatment of PDAC. **Methods:** This is a multi-center, open label, randomized phase II trial. Patients $\geq$ 18 years of age with histologically or cytologically confirmed PDAC, previously treated with gemcitabine (-based) therapy, or progression within 6 months of adjuvant gemcitabine-based treatment are eligible. After a safety run-in of the nal-IRI plus S-1 regimen, patients will be randomized between nal-IRI plus S-1 and nal-IRI plus 5-FU/LV. Primary endpoint of the run-in phase is to determine dose limiting toxicity (DLT) and maximum tolerated dose (MTD) of nal-IRI when co-administered with fixed dose S-1. The primary endpoint of the phase II part is to determine the efficacy of the treatment arms in terms of PFS. Secondary endpoints include OS, response rate according to RECIST 1.1, adverse events according to CTC version 5.0 and Quality of life. Until now 2 of the planned 120 patients have been enrolled. Clinical trial information: NCT03986294. Research Sponsor: Servier and Nordic Pharma.

TPS4665 **Poster Session (Board #273), Fri, 8:00 AM-11:00 AM**

PD-1 antibody combined with paclitaxel (albumin bound) and gemcitabine as first-line therapy in patients with metastatic pancreatic cancer.

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Background: Pancreatic cancer is a malignant tumor with limited therapeutic strategies and poor prognosis. About 60% of the patients have metastasis disease at time of diagnosis and lose the opportunity for surgery. Thus, therapy based on drugs becomes a vital part in pancreatic cancer. In 2013, MPACT showed that albumin-bound paclitaxel combined with gemcitabine in the treatment of metastatic pancreatic cancer could increase the mOS from 6.6 months to 8.7 months (HR = 0.72, 95% CI: 0.62-0.83; $P < 0.001$). Nowadays, the immunosuppressive checkpoint inhibitors acting on PD-1/PD-L1 pathway have shown a significant efficacy in enhancing tumor immune surveillance and anti-tumor immune response. In 2018, two studies reported in ASCO showed the preliminary efficacy of albumin paclitaxel, gemcitabine and PD-1 inhibitor in the treatment of advanced pancreatic cancer. Among patients who have not received treatment before, the disease control rate was even up to 100%. Therefore, this study will further explore the domestic PD-1 antibody combined with albumin-bound paclitaxel and gemcitabine as the first-line treatment of advanced pancreatic cancer among Chinese pancreatic cancer patients. **Methods:** This is a prospective, single-armed, exploratory, investigator initiated trial to explore the efficacy and safety of PD-1 antibody combined with albumin-bound paclitaxel and gemcitabine as first-line treatment of metastatic pancreatic cancer. This study is, to our knowledge, the first one to test the efficacy and safety of PD-1 antibody on metastatic pancreatic cancer patients among Chinese population. Survival index is median survival estimated by Kaplan-Meier and draw the survival curve. The response rate was compared by χ 2 test / Fisher test. All primary and secondary outcomes will be analyzed on the full analysis set. PD-1 antibody, 200mg, D1 administration; paclitaxel (albumin binding type), 125mg/m2, D1, 8 days administration; gemcitabine, 1000mg/m2, D1, 8 days administration, every 21 days as a cycle and PD-1 antibody (200mg, D1, every 21 days) single drug maintenance treatment is given after the completion of 6 cycle chemotherapy. Major eligibility criteria is that each participant must have metastatic pancreatic cancer confirmed by histology or cytology and has never received systemic anti-tumor therapy before. So far, 11 of planned 20 patients have been enrolled. Clinical trial information: NCT04181645. Research Sponsor: HENGRUI MEDICINE.

TPS4666 **Poster Session (Board #274), Fri, 8:00 AM-11:00 AM**

TRYbeCA-1: A randomized, phase III study of eryaspase in combination with chemotherapy versus chemotherapy alone as second-line treatment in patients with pancreatic adenocarcinoma (NCT03665441).

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Background: Second-line treatment options for advanced pancreatic adenocarcinoma are currently limited. 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. We have recently reported the outcome of a randomized Phase 2b study inpatients with advanced pancreatic cancer whose disease progressed following first-line treatment(NCT02195180). 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. The results of this Phase 2b study provided a rationale for initiating this confirmatory Phase 3 pivotal trial (TRYbeCA-1). **Methods:** TRYbeCA-1 is a randomized, open-label Phase 3 trial (N = ~500) of eryaspase combined with chemotherapy in patients with adenocarcinoma of the pancreas who have failed only one prior line of systemic anti-cancer therapy for advanced pancreatic cancer and have measurable disease. Patients are randomized in a 1:1 ratio to receive gemcitabine/Abraxane or irinotecan-based therapy (FOLFIRI [FOLinic acid-Fluorouracil-IRInotecan regimen] or irinotecan liposome injection/5-fluorouracil/leucovorin) with or without eryaspase, administered as IV infusion on Day 1 and Day 15 of each 4-week cycle. Key eligibility criteria include performance status 0 or 1; stage III-IV disease; documented evidence of disease progression; available tumor tissue; and adequate organ function. The primary endpoint is OS. Key secondary endpoints include PFS and objective response rate, safety, quality of life, pharmacokinetics and pharmacodynamics, and biomarker research. A hazard ratio in OS of 0.725 is being targeted which represents a conservative estimate based on the Phase 2b data and is viewed as being highly clinically relevant. An IDMC is established to review safety at regular intervals andto review efficacy data at the planned interim and final analyses. IDMC last reviewed the trial in October 2019 and suggested the trial continue as planned. Clinical trial information: NCT03665441. Research Sponsor: Erytech.

TPS4667 **Poster Session (Board #275), Fri, 8:00 AM-11:00 AM**

Phase II, open-label, randomized study of first-line zolbetuximab plus gemcitabine and nab-paclitaxel (GN) in Claudin 18.2–positive metastatic pancreatic cancer (mPC).

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Background: Combinations of folinic acid, fluorouracil (5-FU), irinotecan, and oxaliplatin (FOLFIRINOX) along with GN are standard first-line treatment options for mPC. Despite treatment advances, mPC has a poor prognosis with a 5-year survival rate of $< 5\%$, emphasizing an urgent need for new targeted therapeutics. Claudin 18.2 (CLDN18.2) is a tight junction protein restricted to normal gastric mucosa cells; however, in the context of malignant transformation, CLDN18.2 is frequently expressed in carcinomas derived from organs that do not normally express it, such as pancreatic adenocarcinoma (50-70% express CLDN18.2). Zolbetuximab is a chimeric IgG1 monoclonal antibody that specifically binds to CLDN18.2, designed to mediate cancer cell death through antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity. **Methods:** This phase 2 study (NCT03816163) with a safety lead-in phase will assess safety and antitumor activity of zolbetuximab plus GN in patients (pts) with histologically confirmed mPC with high CLDN18.2 expression ($\geq$75% of tumor cells demonstrate moderate-to-strong IHC staining). The safety lead-in will assess safety/tolerability of zolbetuximab (n = 3 at 1,000 mg/m^2 on Cycle 1 Day 1 then 600 mg/m^2 Q2W then expand/de-escalate using a 3+3 design) plus GN and confirm the recommended phase 2 dose (RP2D). Dose-limiting toxicities (DLTs), defined as a specified toxicity that occurs during the DLT assessment period and is related to zolbetuximab, will be assessed after Cycle 1 (28 days). After determining the RP2D, approximately 129 pts will be randomly assigned 2:1 to receive either zolbetuximab RP2D Q2W on Days 1 and 15 plus GN on Days 1, 8, and 15 of each cycle (*Arm 1*), or GN alone on Days 1, 8, and 15 of each cycle (*Arm 2*). Randomization will be stratified by ECOG performance status (0 or 1) and liver metastasis (yes or no). Imaging (CT/MRI) will be performed at baseline and every 8 weeks until investigator-assessed disease progression (per RECIST v1.1 criteria) or the start of other systemic anticancer treatment, whichever comes earlier. Primary objectives are to confirm RP2D (safety lead-in), to assess antitumor activity measured by overall survival (randomization phase), and to establish the safety/tolerability profile of zolbetuximab plus GN across the study. Key secondary endpoints in the randomization phase are progression-free survival and objective response rate. As of January 2020, this study is recruiting pts at 74 centers. Clinical trial information: NCT03816163. Research Sponsor: Astellas Pharma, Inc.

TPS4668 **Poster Session (Board #276), Fri, 8:00 AM-11:00 AM**

HGCSG 1803: Single-arm phase II study evaluating efficacy of oxaliplatin, irinotecan and S-1 combination therapy (OX-IRIS) in metastatic pancreatic cancer as first-line treatment.

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Background: Combination chemotherapy with oxaliplatin, irinotecan, fluorouracil and leucovorin (FOLFIRINOX) showed improved survival compared to gemcitabine monotherapy for patients with metastatic pancreatic cancer and has become the one of the standard regimens. Despite of its clinical benefit, FOLFIRNIOX needs continuous infusion of 5-FU for 46 hours, which impairs quality of life. In other gastrointestinal cancer, infuser pomp free regimens, in which oral 5-FU drug replace the continuous infusion of 5-FU, have developed as alternative regimen. Therefore, we planned to develop new combination chemotherapy with oxaliplatin, irinotecan and S-1 (OX-IRIS) for advanced pancreatic cancer. We previously conducted the phase I study for assessing the safety and determining the recommended dose of OX-IRIS regimen. **Methods:** To evaluate efficacy and safety of OX-IRIS, HGCSG1803 study staeted as a multicenter, non-randomized, single arm, prospective, phase II study in December 2019. The patients with untreated metastatic or relapsed pancreatic cancer are eligible for this study. OX-IRIS is administered as follows; a 30-min intravenous infusion (IV) of antiemetic, a 2-h IV of oxaliplatin at 85 mg/m^2, a 1.5-h IV of irinotecan at 150 mg/m^2 on day 1 and day 15 of each 4-week cycle, and S-1 (40 mg/m^2) was taken orally twice daily, from after dinner on day 1 to after breakfast on day 15, followed by a 14-day rest, and to be repeated every 2 weeks until disease progression, unacceptable toxicity, or patient refusal. The primary endpoint is response rate, and the secondary endpoints are overall survival, progression-free survival, safety, and dose intensity for each drug. A total of 40 cases are planned for registration from 18 institutions in Japan within 2.5 years. Clinical trial information: jRCTs011190008. Research Sponsor: None.

TPS4669 **Poster Session (Board #277), Fri, 8:00 AM-11:00 AM**

EndoTAG-1 plus gemcitabine versus gemcitabine alone in patients with measurable locally advanced and/or metastatic adenocarcinoma of the pancreas failed on FOLFIRINOX treatment (NCT03126435).

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Background: Pancreatic cancer (PC) is the 3rd deadliest cancer in the United State surpassing breast cancer in 2016, with the overall survival rate of - 9% for those newly diagnosed individuals. The notorious disease is set to become the 2nd leading cause of death from cancer by 2020 in US (National Cancer Institute, NIH). FOLFIRINOX regimen is one of the standard 1st-line treatments for PC patients with good performance status; however, there is currently no standard of care in 2nd-line therapy after FOLFIRINOX failure. EndoTAG-1 is a novel formulation of cationic liposomes embedded with Paclitaxel, which specifically displays antivascular and antiangiogenic activities. By binding and internalizing at tumor endothelial cells after intravenous administration, the cytostatic activity of paclitaxel will be targeted to the activated tumor endothelial cells. **Methods:** Eligible patients with measurable locally advanced and/or metastatic adenocarcinoma of the pancreas failed on FILFIRINOX treatment will be screened and randomized (1:1) into one of the two arms in the study (n=218). The primary endpoint of the study is overall survival (OS), with secondary endpoints include progression-free survival (PFS), objective response rate (ORR), duration of response (DOR) and quality of life (QoL). Arm A: EndoTAG-1 plus Gemcitabine: Patients will receive intravenous injection with EndoTAG-1 (22 mg/m^2) twice weekly plus gemcitabine (1,000 mg/m^2) once weekly for consecutively 3 weeks followed by 1 week rest. The treatment will be repeated every 4 weeks, with 8 weeks per cycle. The treatment will be kept until any one of the following occurs: progressive disease or unacceptable toxicity or withdrawal of consent. Arm B: Gemcitabine: Patients will receive gemcitabine (1,000 mg/m^2) once weekly for consecutive 3 weeks followed by 1 week rest. The treatment will be repeated every 4 weeks, with 8 weeks per cycle. The treatment will be kept until any one of the following occurs: progressive disease or unacceptable toxicity or withdrawal of consent. The phase III trial began enrollment since November 2018. The trial will continue as planned from the last review in January 2020. Clinical trial information: NCT03126435. Research Sponsor: SynCore Biotechnology Co., Ltd., Other Government Agency

TPS4670 **Poster Session (Board #278), Fri, 8:00 AM-11:00 AM**

Adaptive dose optimization trial of stereotactic body radiation therapy (SBRT) with or without GC4419 (avasopasem manganese) in pancreatic cancer.

Elizabeth Charlotte Moser, Sarah E. Hoffe, Jessica Frakes, Todd Anthony Aguilera, Mona Karim, Lauren Elizabeth Colbert, Shalini Moningi, Ching-Wei David Tzeng, Peter F. Thall, Shubham Pant, Manoop S. Bhutani, Melissa Brookes, Jon Holmlund, Joseph M. Herman, Cullen M. Taniguchi; Galera Therapeutics, Malvern, PA; Department of Gastrointestinal Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; The University of Texas Southwestern Medical Center, Dallas, TX; Morristown Memor Hosp, Morristown, NJ; The University of Texas MD Anderson Cancer Center, Houston, TX; MDAnderson, Houston, TX; MD Anderson Cancer Center, Houston, TX; UT MD Anderson Cancer Center, Houston, TX; University of Texas MD Anderson Cancer Center, Houston, TX; Galera Therapeutics, Inc, Malvern, PA

Background: Local progression causes up to 30% of deaths from pancreatic cancer (PC) and is also a significant source of morbidity. Stereotactic body radiotherapy (SBRT) offers the potential for improved therapeutic index over standard fractionation, but current regimens of 5 fractions of 5-7 Gy/fraction are constrained by nearby organ tolerance and offer only palliation without improving survival. Safe dose escalation may be necessary to improve SBRT efficacy. Avasopasem, a superoxide dismutase mimetic, selectively converts superoxide (O2 • -) to hydrogen peroxide (H_2O_2) and oxygen. O2 • -initiates normal tissue damage due to RT. Avasopasem is in a Phase 3 trial (NCT03689712) to reduce RT-induced oral mucositis in head and neck cancer, based on positive results in a randomized Phase 2 trial for that indication (Anderson, JCO 2019). Avasopasem improved the survival of mice receiving 8.5 Gy x 5 to the upper abdomen. Cancer cells are less tolerant to elevated H_2O_2, and more tolerant to elevated O2 • -, than normal cells, and avasopasem demonstrated mechanism-dependent synergy with high dose-fraction RT in a human tumor xenograft with inducible expression of catalase (Sishc, AACR 2018). Thus, adding avasopasem to SBRT may increase both the efficacy and the safety of the latter. **Methods:** 48 patients with locally advanced PC, who have completed medically-indicated induction chemotherapy, are randomized 1:1 to placebo or avasopasem, 90 mg IV, prior to each of 5 consecutive daily (M-F) SBRT fractions. A phase I/II Late Onset Efficacy/ Toxicity tradeoff (LO-ET) based adaptive design adaptive model drives assignment of SBRT dose escalation in each arm based on a dual endpoint (Gr 3-4 GI toxicity or death; local stable disease or better) by 90 days post SBRT. The planned dose levels are 10, 11 and 12Gy x 5 fractions (BED10 = 100,112.5 and 132Gy, respectively) as an integrated boost to the gross tumor volume (GTV). Primary endpoint: Maximum tolerated dose of SBRT with avasopasem or placebo. Secondary endpoints progression-free survival, response rate, and acute (90 day) and late (12 month) radiation toxicity with avasopasem vs placebo. Exploratory correlative studies include ctDNA, tumor exome/transcriptome sequencing, and immune profiling. Clinical trial information: NCT03340974. Research Sponsor: Galera Therapeutics.

TPS4671 **Poster Session (Board #279), Fri, 8:00 AM-11:00 AM**

Phase I study of SEA-CD40, gemcitabine, nab-paclitaxel, and pembrolizumab in patients with metastatic pancreatic ductal adenocarcinoma (PDAC).

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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, 2719–32). An ongoing Phase 1 study (SGNS40-001) is evaluating SEA-CD40 as monotherapy and in combination with pembrolizumab in patients with advanced solid or hematologic malignancies. A new cohort is enrolling to evaluate the combination of SEA-CD40, gemcitabine, nab-paclitaxel, and pembrolizumab in PDAC. **Methods:** The cohort consists of patients with metastatic PDAC who have had no prior therapy for metastatic disease. Patients must be $\geq$18 years old, with (neo)adjuvant therapy completed $>$4 months prior to enrollment, ECOG status $\leq$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 antitumor activity; secondary objectives are safety and tolerability and SEA-CD40 and pembrolizumab pharmacokinetics. Efficacy endpoints are confirmed RECIST ORR per investigator (primary), disease control rate (response or stable disease $\geq$16 weeks), duration of response, PFS, and OS. Disease is assessed every 8 weeks using RECIST and immune-based RECIST (iRECIST). Treatment continues until occurrence of unacceptable toxicity, progressive disease per iRECIST, consent withdrawal, or study closure. Assessment of dose-limiting toxicity will occur initially in groups of 6 patients 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.

TPS4672 **Poster Session (Board #280), Fri, 8:00 AM-11:00 AM**

A phase II study of siG12D-LODER in combination with chemotherapy in patients with locally advanced pancreatic cancer (PROTACT).

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Background: KRAS alterations are the most frequent driver alterations identified in pancreas cancer; however, KRAS has remained an elusive therapeutic target. siG12D-LODER is a novel, miniature biodegradable polymeric matrix encompassing a novel small interfering RNA targeting KRAS G12D and all additional G12X mutations (G12C, G12V...). The siG12D-LODER is inserted directly into the pancreas tumor via endoscopic intervention. A Phase 1/2a dose escalation and expansion study of patients receiving a one-time dose of siG12D-LODER with ongoing chemotherapy demonstrated that the combination was well-tolerated and safe and exhibited promising potential efficacy with 10/12 patients achieving disease control and median overall survival 15.1 months (Golan, Oncotarget 2015). **Methods:** This phase 2 study was initially designed as a randomized, two arm, open label study of gemcitabine and nab-paclitaxel with or without siG12D-LODER for patients with locally advanced pancreas cancer with planned 40 patients in each arm and primary endpoint of progression-free survival. Eighteen patients were enrolled in the chemotherapy alone arm and 18 in the chemotherapy and siG12D-LODER arm. After an interim analysis, the study design has been amended and is now a single arm study in which patients (N=39) with both borderline resectable and locally advanced pancreas cancer will receive investigator's choice of chemotherapy (the combination of gemcitabine/nab-paclitaxel or modified FOLFIRINOX) and all patients will receive up to three doses of the siG12D-LODER administered once every 12 weeks. Primary endpoint is overall response rate after final siG12D-LODER insertion. Secondary endpoints include duration of response, progression-free survival, overall survival, time to response, percentage of patients proceeding to surgical resection, and percentage of patients receiving radiation therapy. Exploratory analyses include evaluation of KRAS mutation status and monitoring of circulating free DNA and circulating tumor cells. The amended protocol is now open for accrual and four patients having been enrolled to date. Trial accrual is anticipated to be completed by December 2020. Clinical trial information: NCT01676259. Research Sponsor: Silenseed.

TPS4673 **Poster Session (Board #281), Fri, 8:00 AM-11:00 AM**

Improving FOLFIRINOX safety in pancreatic cancer patients through multidimensional remote monitoring and proactive care using a domomedecine mobile platform.

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Background: Pancreatic cancer is a poor prognosis and fast-growing cancer, whose five-year survival is 6% in Europe and the US. FOLFIRINOX has been established as the reference medical treatment for this disease worldwide, yet it also causes leuko-neutropenia, thrombocytopenia, diarrhea, anorexia, asthenia, weight loss, and peripheral sensory neuropathy. Its indication is usually limited to patients having a WHO performance status of 0 or 1. This treatment is often interrupted once Grade 3-4 clinical or hematological toxicities occur, resulting in poor patient performance status and quality of life. Presently, no prospective study monitor and evaluate the qualitative and quantitative effects of FOLFIRINOX on the daily life of pancreatic cancer patients in real-time. Such monitoring would provide early warning signals for the identification of any improvement or deterioration of the patient condition. Whenever necessary, proactive interventions would be triggered to avoid emergency hospitalization for severe adverse events and to enhance treatment compliance. **Methods:** Our study involves the use of the mobile e-Health platform PiCADo (JMIR 2018) to track and analyse circadian rhythms, symptoms, and body weight in real time in 45 advanced pancreatic cancer patients at 4 centres. The patients are continuously telemonitored for rest-activity, temperature and 3D-orientation via a BLE sensor during the six weeks following the first FOLFIRINOX course. Patients weigh themselves daily on a BLE scale and self-rate their symptoms using a touchscreen on GPRS tablet. Alerts are generated according to preset yet modifiable thresholds of automatically computed critical parameters. From these data, we will evaluate the rate of emergency hospital admissions and the admission-free survival, the rates of severe adverse events, patients' symptoms dynamics, and their relations with the disruption of the patients' circadian rhythm. Patient satisfaction and research experience will also be assessed, since engagement is at the core of the success of the approach. The results will guide a future randomized trial comparing standard pancreatic cancer patient care with a personalized FOLFIRINOX approach, including chronotherapy delivery. Support: Ramsay-Sante, Altran. Research Sponsor: Ramsay Générale de Santé.