APACT: phase III, multicenter, international, open-label, randomized trial of adjuvant *nab*-paclitaxel plus gemcitabine (*nab*-P/G) vs gemcitabine (G) for surgically resected pancreatic adenocarcinoma.

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Background: In metastatic pancreatic cancer (PC), *nab*-P/G demonstrated significantly longer overall survival (OS) vs G. APACT assessed efficacy & safety of *nab*-P/G vs G in surgically resected PC. **Methods:** Treatment (tx)-naive patients (pts) with histologically confirmed PC, macroscopic complete resection, ECOG PS 0/1, & CA19-9 $<$ 100 U/mL were eligible. Stratification factors: resection status (R0/R1), lymph node status (LN+/−), & geographic region. Tx was initiated $\leq$ 12 wks postsurgery. Pts received *nab*-P 125 mg/m^2 + G 1000 mg/m^2 or G 1000 mg/m^2 on days 1, 8, 15 of six 28-day cycles. Primary endpoint was disease-free survival (DFS) by independent reviewer (IR); IRs received baseline clinical data & scans. Secondary endpoints were OS & safety. ≈438 DFS events were needed for 90% power to detect an HR for disease recurrence or death of 0.73 with *nab*-P/G vs G at a 2-sided significance level of 0.05. **Results:** 866 pts were randomized. Median age was 64 y (range, 34 - 86); most pts had ECOG PS 0 (60%), LN+ (72%), & R0 (76%). 69% of pts completed 6 tx cycles (*nab*-P/G, 66%; G, 71%). Median follow up for OS was 38.5 mo. Median IR-assessed DFS (439 events) was 19.4 mo (*nab*-P/G) vs 18.8 mo (G) (HR, 0.88; 95% CI, 0.729 - 1.063; stratified log-rank $P = 0.1824$). Investigator-assessed DFS (571 events) was 16.6 mo (*nab*-P/G) vs 13.7 mo (G) (HR, 0.82; 95% CI, 0.694 - 0.965; nominal $P = 0.0168$). Interim OS (427 events) was 40.5 mo (*nab*-P/G) vs 36.2 mo (G) (HR, 0.82; 95% CI, 0.680 - 0.996; nominal $P = 0.045$). Grade $\geq$ 3 TEAEs were reported in 86% vs 68% of pts with *nab*-P/G vs G. The most common grade $\geq$ 3 hematologic & nonhematologic TEAEs with *nab*-P/G vs G were neutropenia (49% vs 43%) & fatigue (10% vs 3%). TEAEs led to death in 2 pts in each arm. **Conclusions:** IR DFS with *nab*-P/G was not significantly longer vs G; median DFS with G was longer than historical data. DFS by investigator (sensitivity analysis) and interim OS were improved with *nab*-P/G vs G (HR 0.82 for both). Adjuvant *nab*-P/G may be an option for pts who are ineligible for FOLFIRINOX. Additional OS follow-up may better support *nab*-P/G as an option in the adjuvant setting. Clinical trial information: NCT01964430.

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ARTIST 2: Interim results of a phase III trial involving adjuvant chemotherapy and/or chemoradiotherapy after D2-gastrectomy in stage II/III gastric cancer (GC).

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Background: Adjuvant chemotherapy and/or chemoradiotherapy have been the standard of care in GC for years, supported by randomized trials. We compared the efficacy of different chemotherapy regimens and chemoradiotherapy in patients with D2-resected, stage II/III, node-positive GC. **Methods:** From Feb 2013 through Nov 2018, we randomly assigned, in a 1:1:1 ratio, patients with pathologically-staged II or III, node-positive, D2-resected GC, to receive adjuvant S-1 (40-60 mg twice daily 4-weeks-on/2-weeks-off) for one year, S-1 (2-weeks-on/1-week-off) plus oxaliplatin 130 mg/m2 (SOX) for six months, or SOX plus chemoradiotherapy 45 Gy (SOXRT). Randomization was stratified according to the type of surgery (total or subtotal gastrectomy), stage (II or III), and Lauren histologic classification (diffuse or intestinal). The primary endpoint was disease-free survival (DFS). A total of 900 patients had to be enrolled to demonstrate superiority of SOX or SOXRT to S-1 (hazard ratio [HR] 0.667), with 90% power at a two-sided significance level of 5%. **Results:** A total of 538 patients were included for this interim efficacy analysis. Median age was 58 years, men constituted 65%, and stage II and III were 31% and 69%, respectively. Baseline tumor and patient characteristics were balanced between treatment arms. Adverse events were as anticipated in each arm, generally well-tolerated and manageable. DFS in the control arm (S-1) were significantly shorter than in SOX and SOXRT arms (stratified HR for recurrence): S-1 vs. SOX, 0.617 (P = 0.016) and S-1 vs. SOXRT, 0.686 (P = 0.057). The DFS at 3-years was found to be 65%, 78% and 73% in S-1, SOX and SOXRT arms, respectively. No difference in DFS between SOX and SOXRT was found (HR 0.910, P = 0.667). Based on the results after the observation of 145 recurrence events at the cutoff date of Dec 27, 2018, the independent data monitoring committee considered the results sufficient to meet the endpoint of the trial and recommended early stopping of the trial. **Conclusions:** In patients with curatively D2-resected, stage II/III, node-positive GC, adjuvant SOX or SOXRT was effective in prolonging DFS, when compared to S-1 monotherapy. Clinical trial information: NCT0176146.

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

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Background: Surgery (SUR) and radiofrequency ablation (RFA) are both known to be effective therapy for treating patients with small oligonodular hepatocellular carcinoma (HCC), however there is only insufficient evidence about which therapy is more preferred approach. This randomized controlled trial was designed to prospectively compare the efficacy of SUR and RFA as the first approach to primary HCC. **Methods:** In this open-label trial undertaken at 49 hospital in Japan, we recruited patients having primary HCC with tumor foci numbering less than 3, each measuring 3 cm or less, Child-Pugh score of 7 or less, ages between 20 and 79 year. Before randomization, technical and liver functional feasibility for both treatment arms were confirmed by joint chart review by surgeons and hepatologists. Patients were then randomly assigned in a 1:1 ratio to undergo SUR or RFA, stratified by age, infection of hepatitis-C virus, number of tumors, tumor size and institution. The primary endpoint was recurrence free survival (RFS) and overall survival (OS). **Results:** Between April 2009 and August 2015, total 308 patients were enrolled to this trial. Because of ineligibility 15 patients were excluded, therefore 145 patients underwent SUR and 148 patients underwent RFA finally. There was no perioperative mortality. Under the median follow-up of 5 years, the 3-year RFS of patients underwent SUR and RFA was 49.8%, 47.7%, respectively (hazard ration [HR] 0.96, 95% CI 0.72-1.28; p = 0.793). OS will be analyzed and published after two years. **Conclusions:** SUR and RFA were both safe therapeutic approaches and provided equally RFS for early stage HCC smaller than 3 cm. Clinical trial information: UMIN000001795.

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ABC-06 | A randomised phase III, multi-centre, open-label study of active symptom control (ASC) alone or ASC with oxaliplatin / 5-FU chemotherapy (ASC+mFOLFOX) for patients (pts) with locally advanced / metastatic biliary tract cancers (ABC) previously-treated with cisplatin/gemcitabine (CisGem) chemotherapy.

Angela Lamarca, Daniel H. Palmer, Harpreet Singh Wasan, Paul J. Ross, Yuk Ting Ma, Arvind Arora, Stephen Falk, Roopinder Gillmore, Jonathan Wadsley, Kinnari Patel, Alan Anthoney, Anthony Maraveyas, Justin S. Waters, Claire Hobbs, Safia Barber, David Ryder, John Ramage, Linda M Davies, John A. Bridgewater, Juan W. Valle, on behalf of the Advanced Biliary Cancer (ABC) Working Group; Department of Medical Oncology, The Christie NHS Foundation Trust / Institute of Cancer Sciences, University of Manchester, Manchester, United Kingdom; University of Liverpool, Liverpool, United Kingdom; Hammersmith Hospital, Department of Cancer Medicine, London, United Kingdom; Guy's Hospital, London, United Kingdom; University of Birmingham, Birmingham, United Kingdom; University Hospital of Nottingham NHS Trust, University of Nottingham, Nottingham, United Kingdom; Bristol Haematology and Oncology Centre, Bristol, United Kingdom; Royal Free, London, United Kingdom; Weston Park Hospital, Sheffield, United Kingdom; Oxford, Oxford, United Kingdom; Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; Castle Hill Hospital, HULL, United Kingdom; Kent Oncology Centre, Maidstone, United Kingdom; Swindon, Swindon, United Kingdom; University of Manchester Clinical Trials Unit, Manchester, United Kingdom; Hampshire Hospitals NHS Foundation Trust, Basingstoke, United Kingdom; University of Manchester Health Economics Department, Manchester, United Kingdom; University College London Cancer Institute, London, United Kingdom; University of Manchester/The Christie, Manchester, United Kingdom

Background: Level A evidence supports use of CisGem as first-line chemotherapy for ABC; no robust evidence is available for second-line chemotherapy. **Methods:** Pts diagnosed with ABC with disease progression after prior CisGem were randomised (1:1) to either ASC+mFOLFOX or ASC. Randomisation was stratified by serum albumin levels (< 35 vs ≥ 35 g/L), platinum sensitivity (determined from first-line CisGem) and disease extent (locally advanced vs metastatic). Pts with ECOG PS0-1, adequate haematological, renal and liver function, and adequate biliary drainage were eligible. Primary end-point was overall survival (OS) (multivariable Cox regression adjusted for stratification factors); sample size: 162 pts delivering 148 events were required (80% power; 5% two-sided alpha) for a hypothesised hazard ratio (HR) of 0.63. Assumed median survival for ASC was 4 months. **Results:** 162 pts (81 in each arm) were randomised (27 March '14 - 04 Jan '18); median age 65 yrs (range 26-84); sex: 80 (49%) male, 82 (51%) female; primary site: intrahepatic 72 (44%), extrahepatic 45 (28%), gallbladder 34 (21%) and ampullary 11 (7%). Baseline characteristics were balanced between arms except platinum sensitivity (ASC+mFOLFOX 27 pts (33%); ASC 34 pts (42%)). After 150 OS events, the adjusted HR was 0.69 (95% CI 0.50-0.97; p = 0.031; ASC+mFOLFOX vs ASC). Median OS (months (m)), 6m and 12m OS-rate (%) were 6.2m, 50.6% and 25.9% for the ASC+mFOLFOX and 5.3m, 35.5%, 11.4% for the ASC arm, respectively. Grade 3/4 toxicities were reported in 48 (59%) and 32 (39%) pts in the ASC+mFOLFOX and ASC arm, respectively; these were balanced between arms except for fatigue and neutropenia (more frequent in ASC+mFOLFOX arm); data cleaning is ongoing. No chemotherapy-related deaths were reported. **Conclusion:** Survival with ASC was greater than assumed; ASC+mFOLFOX improved OS after progression to CisGem with a clinically meaningful increase in 6m and 12m OS rate. ASC+mFOLFOX should become standard of care in second-line for ABC. Clinical trial information: NCT01926236.

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Results of KEYNOTE-240: phase 3 study of pembrolizumab (Pembro) vs best supportive care (BSC) for second line therapy in advanced hepatocellular carcinoma (HCC).

Richard S. Finn, Baek-Yeol Ryoo, Philippe Merle, Masatoshi Kudo, Mohamed Bouattour, Ho-Yeong Lim, Valeriy Vladimirovich Breder, Julien Edeline, Yee Chao, Sadahisa Ogasawara, Thomas Yau, Marcelo Garrido, Stephen Lam Chan, Jennifer J. Knox, Bruno Daniele, Scot Ebbinghaus, Erluo Chen, Abby B. Siegel, Andrew X. Zhu, Ann-Lii Cheng, for the KEYNOTE-240 Investigators; University of California, Los Angeles, Los Angeles, CA; Asan Medical Center, Seoul, South Korea; Lyon University, Lyon, France; Kindai University, Faculty of Medicine, Osaka, Japan; Service d'Oncologie Medicale, APHP, Clichy, France; Samsung Medical Center, Seoul, South Korea; Russian Oncological Research Center N.N. Blokhin of Ministry of Health, Moscow, Russian Federation; Centre Eugene Marquis, Rennes, France; Taipei Veterans General Hospital, Taipei, Taiwan; Chiba University Graduate School of Medicine, Chiba, Japan; The University at Hong Kong, Hong Kong, China; Pontificia Universidad Católica de Chile, Santiago, Chile; State Key Laboratory in Oncology of South China, The Chinese University of Hong Kong, Shatin, Hong Kong; Princess Margaret Cancer Centre and University of Toronto, Toronto, ON, Canada; Ospedale del Mare, Napoli, Italy; Merck & Co., Inc., Kenilworth, NJ; Massachusetts General Hospital Cancer Center and Harvard Medical School, Boston, MA; National Taiwan University Hospital, Taipei, Taiwan

Background: Pembro received accelerated approval based on results of KEYNOTE-224, a phase 2 trial in pts with advanced HCC in the second line setting. KEYNOTE-240 (NCT02702401) was a randomized, placebo (Pbo) controlled, phase 3 study of Pembro vs BSC in pts with previously treated advanced HCC. **Methods:** Eligible pts had a radiographic or pathologic diagnosis of HCC, radiographic progression on/intolerance to sorafenib, Child-Pugh A disease and ECOG PS 0-1. Pts were randomized 2:1 to receive Pembro 200 mg + BSC or Pbo + BSC IV every 3 wk, stratified by geographic region, macrovascular invasion and α-fetoprotein levels for ≤35 cycles or until confirmed PD/unacceptable toxicity. Response was assessed every 6 wk per RECIST v1.1 by central imaging review. Co-primary endpoints were OS and PFS. Secondary endpoints included ORR, DOR and safety. Data cutoff was Jan 2 2019 for OS; Mar 26 2018 for PFS and ORR. **Results:** 413 patients were randomized; 278 to Pembro and 135 to Pbo. After a median follow up of 13.8 mo, 10.1% of pts remained on Pembro and 3.0% on Pbo. Pembro improved OS (HR: 0.78; one sided p = 0.0238) and PFS (HR: 0.78; one sided p = 0.0209) vs Pbo; these differences did not meet significance per the prespecified statistical plan. ORR was 16.9% (95% CI 12.7-21.8%) for Pembro vs 2.2% (95% CI 0.5-6.4%) for Pbo (nominal one sided p = 0.00001); responses on Pembro were durable (median DOR: 13.8 mo [1.5-23.6+]). Off study, new therapy use was 42% for Pembro and 47% for Pbo. The safety profile including incidence of hepatitis and other immune mediated events was generally consistent with that previously reported in Pembro studies; no cases of HBV/HCV flare were identified. **Conclusions:** Pembro reduced the risk of death by 22% and improved PFS over Pbo in pts with advanced HCC, although significance was not reached per prespecified statistical criteria. ORR in the Pembro arm was consistent with that of KEYNOTE-224. Subsequent anticancer therapy in the Pbo arm likely impacted the OS results. The safety profile was comparable to that established for Pembro monotherapy. These results are overall consistent with those of KEYNOTE-224 further supporting second line therapy with Pembro in HCC pts. Clinical trial information: NCT02702401.

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4005 **Oral Abstract Session, Sun, 9:45 AM-12:45 PM**

Prospective randomized phase II trial of pazopanib versus placebo in patients with progressive carcinoid tumors (CARC) (Alliance A021202).

Emily K. Bergsland, Michelle R. Mahoney, Timothy R. Asmis, Nathan Hall, Priya Kumthekar, Michael L. Maitland, Donna Niedzwiecki, Andrew B. Nixon, Eileen Mary O'Reilly, Lawrence Howard Schwartz, Jonathan R. Strosberg, Jeffrey A. Meyerhardt; University of California San Francisco, San Francisco, CA; Mayo Clinic, Rochester, MN; Ottawa Hospital Cancer Centre, Ottawa, ON, Canada; University of Pennsylvania, Philadelphia, PA; Northwestern Memorial Hospital, Chicago, IL; Inova Center for Personalized Health and University of Virginia, Falls Church, VA; Duke University Medical Center, Durham, NC; Memorial Sloan Kettering Cancer Center, New York, NY; Columbia University Medical Center, New York, NY; Moffitt Cancer Center, Tampa, FL; Dana-Farber Cancer Institute/Partners CancerCare, Boston, MA

Background: Patients (pts) with progressive advanced well-differentiated neuroendocrine tumors arising outside of the pancreas have limited systemic treatment options. Pazopanib (PZ) is an oral multi-kinase inhibitor with activity against VEGFR-2,-3, PDGFR-α, and β, and c-KIT, with initial data suggesting efficacy in CARC. **Methods:** This was a multicenter, randomized, double-blind, phase II study of PZ (800 mg/day) versus placebo (PL) in progressive CARC. Key eligibility: low-intermediate grade CARC, radiologic progressive disease (PD) $<$ 12 months (mo), and adequate end-organ function. Prior somatostatin analog (SSA) mandated for midgut tumors. Concurrent SSA allowed if previous PD on SSA documented. Primary endpoint was progression-free survival (PFS), defined as time from randomization to PD by central review or death. Secondary endpoints included overall survival (OS), objective response rate (ORR) and safety. The trial had 85% power to detect a difference in median PFS of 14 v 9 mo (hazard ratio [HR] 0.64) at one-sided alpha = 0.1. A stratified log-rank test based on the intend-to-treat (ITT) principle was used. Unblinding and crossover were allowed if PD confirmed by central review. **Results:** 171 (97 PZ, 74 PL) pts were randomized between 6/2013-10/2015: median age 63; 56% female; 66% small bowel primary; 87% concurrent SSA. Median follow-up of 31 mo; 112 (56 PZ, 56 PL) PFS events observed. 6 pts (4 PZ, 2 PL) remain on initial treatment. Median PFS was 11.6 and 8.5 mo in PZ and PL, respectively (HR = 0.53, 1-sided 90% upper confidence limit [UCL] 0.69, p = 0.0005) which crossed the pre-specified protocol efficacy boundary. 49 PL pts received PZ after PD. Median OS was 41 and 42 mo in PZ and PL, respectively (HR = 1.13, 1-sided 90% UCL 1.51, p = 0.70). RR data will be presented. Notable grade 3+ adverse events were (PZ v. PL %) hypertension (35 v. 8), fatigue (11 v. 4), ALT (10 v. 0), AST (10 v. 0), and diarrhea (7 v. 4). **Conclusions:** PZ compared to PL was associated with significant improvement in PFS in patients with progressive CARC. The results confirm that VEGF signaling pathway is a valid target for therapy in CARC. Support: U10CA180821, U10CA180882 https://acknowledgments.alliancefound.org. Clinical trial information: NCT01841736.

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Optimizing chemotherapy for frail and elderly patients (pts) with advanced gastroesophageal cancer (aGOAC): The GO2 phase III trial.

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Background: Many pts with aGOAC are elderly and/or frail. We previously compared epirubin/ oxaliplatin/ capecitabine (EOCap) vs OCap vs Cap in a pick-the-winner study and found OCap best. GO2 was designed to find the optimum dose of OCap and to explore the use of an objective baseline geriatric assessment to individualize doses for maximum Overall Treatment Utility (OTU), a composite of clinical benefit, tolerability, QL and patient value. **Methods:** Pts with aGOAC were eligible if unsuitable for full-dose EOCap due to age or frailty, but fit for OCap; GFR $\geq$ 30, bili $<$2x ULN. Baseline assessment included global QL; symptoms; functional scales; comorbidity; frailty. Randomization was 1:1:1 to dose Level A (Ox 130 mg/m^{2}d1, Cap 625 mg/m^{2}bd d1-21, q21d), B (80% Level A doses) or C (60% Level A doses). Pts with GFR 30-50 ml/min or bili 1.5-2.0 xULN received 75% of the allocated dose of Cap. At 9 wks, pts were scored for OTU. Continuation thereafter was based on clinical judgement. Non-inferiority (vs A) was assessed using PFS censored at 12 months, with boundary HR 1.34 (based on discussion with pts and clinicians), needing 284 PFS events per 2-way comparison. Baseline fitness was assessed as predictive of OTU, overall and by interaction with dose level. **Results:** 514 pts were randomised, 2014-17, at 61 UK centres. Clinical trial information: 44687907. Non-inferiority of PFS is confirmed for Level B vs A (HR 1.09, CI 0.89-1.32) and for Level C vs A (HR 1.10, CI 0.90-1.33). Level C pts had less toxicity and better OTU outcomes than A or B. When analysed by baseline age, frailty and PS, Level C produced the best OTU even in younger, less frail and better PS patients; no group was identified who benefit more from the higher dose levels. **Conclusions:** This is the largest RCT to date specifically investigating frail and/or elderly aGOAC pts, and should guide future treatment. The lowest dose tested was non-inferior in terms of PFS and produced less toxicity and better overall treatment utility.

	Level A	Level B	Level C
Pts (PFS events)	170 (142).	171 (147).	173 (149)
Median age	76	76	77
% PS ≥2	31	32	31
% any Frailty; % very Frail	86; 61	82; 56	76; 58
% any Gr ≥3 non-haem adverse event	56	56	37
Median PFS mo	4.9	4.1	4.3
OTU (wk 9): % Good/intermed./poor	35/34/31	36/26/38	43/27/29
Median OS mo	7.5	6.7	7.6

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LBA4007 **Oral Abstract Session, Sun, 9:45 AM-12:45 PM**

Pembrolizumab with or without chemotherapy versus chemotherapy for advanced gastric or gastroesophageal junction (G/GEJ) adenocarcinoma: The phase 3 KEYNOTE-062 study.

Josep Tabernero, Eric Van Cutsem, Yung-Jue Bang, Charles S. Fuchs, Lucjan Wyrwicz, Keun Wook Lee, Iveta Kudaba, Marcelo Garrido, Hyun Cheol Chung, Hugo Raul Castro Salguero, Wasat Mansoor, Maria Ignez Freitas Melro Braghiroli, Eray Goekkurt, Joseph Chao, Zev A. Wainberg, Uma Kher, Sukrut Shah, SoonMo Peter Kang, Kohei Shitara; Vall d'Hebron University Hospital and Institute of Oncology, Barcelona, Spain; University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium; Seoul National University College of Medicine, Seoul, Korea, Republic of (South); Yale Cancer Center, New Haven, CT; M. Sklodowska-Curie Memorial Cancer Center, Warsaw, Poland; Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, South Korea; Riga East University Hospital, Riga, Latvia; Pontificia Universidad Catholica de Chile, Santiago, Chile; Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; Hospital de Enfermedad Comun Igss Zona 9, Guatemala, Guatemala; Christie NHS, Manchester, United Kingdom; Instituto do Câncer do Estado de São Paulo, Universidade de São Paulo, São Paulo, Brazil; Hematology Oncology Practice Eppendorf, and University Cancer Center Hamburg, Hamburg, Germany; City of Hope Comprehensive Cancer Center, Duarte, CA; David Geffen School of Medicine at UCLA, Los Angeles, CA; Merck & Co., Inc., Kenilworth, NJ; Merck & Co., Inc., Rahway, NJ; Department of Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa, Chiba, Japan

The full, final text of this abstract will be available at abstracts.asco.org at 7:30 a.m. ET on Saturday, June 1. Onsite at the Meeting, this abstract will be printed in the Sunday edition of ASCO Daily News.

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4009 Poster Discussion Session; Displayed in Poster Session (Board #114), Mon, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Mon, 3:00 PM-4:30 PM

Efficacy and safety of pembrolizumab (pembro) alone or in combination with chemotherapy (chemo) in patients (pts) with advanced gastric or gastroesophageal (G/GEJ) cancer: Long-term follow up from KEYNOTE-059.

Zev A. Wainberg, Harry H. Yoon, Daniel V.T. Catenacci, Shadia Ibrahim Jalal, Kei Muro, Marcelo Garrido, Talia Golan, Toshihiko Doi, Ravit Geva, Geoffrey Yuyat Ku, Jonathan Scott Bleeker, Yung-Jue Bang, Hiroki Hara, Hyun Cheol Chung, Jiang Dian Wang, Andrea Hazzard, Sukrut Shah, Charles S. Fuchs; David Geffen School of Medicine at UCLA, Los Angeles, CA; Mayo Clinic, Rochester, MN; University of Chicago Medicine, Chicago, IL; Indiana University School of Medicine, Indianapolis, IN; Aichi Cancer Center Hospital, Nagoya, Japan; Pontificia Universidad Católica de Chile, Santiago, Chile; The Oncology Institute, Sheba Medical Center at Tel-Hashomer, Tel Aviv University, Tel Aviv, Israel; National Cancer Center Hospital East, Kashiwa, Japan; Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; Memorial Sloan Kettering Cancer Center, New York, NY; Sanford Health, Sioux Falls, SD; Seoul National University College of Medicine, Seoul, South Korea; Saitama Cancer Center, Saitama, Japan; Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; Merck & Co., Inc., Kenilworth, NJ; Yale Cancer Center, New Haven, CT

Background: Interim analysis of a global, phase 2 KEYNOTE-059 study (NCT02335411) reported manageable safety and promising antitumor activity for pembro alone or pembro + chemo in pts with G/GEJ cancer. Here we report long-term efficacy and safety data of all cohorts. **Methods:** Pts with recurrent or metastatic G/GEJ adenocarcinoma were enrolled in 3 cohorts. Cohort 1 pts (PD-L1positive or negative) received pembro alone after ≥2 prior lines of therapy. Cohort 2 pts (PD-L1positive or negative) received pembro + cisplatin (80 mg/m^2 day 1) + 5-fluorouracil (800 mg/m^2 days 1-5 Q3W) or capecitabine (in Japan only, 1000 mg/m^2 twice daily) as first-line. Cohort 3 pts (PD-L1positive, combined positive score ≥1% using the PD-L1 IHC 22C3 pharmDx assay) received pembro alone as first-line. All pts received pembro 200 mg Q3W for up to 2 years. End points included safety, ORR, DOR, and OS. **Results:** At data cutoff (Aug 8, 2018), median (range) follow-up was 6 (1-38), 14 (2-40), and 21 (2-36) months for cohorts 1 (n = 259), 2 (n = 25), and 3 (n = 31), respectively. In cohort 1, confirmed ORR (95% CI) was 11.6% (8-16) overall, 15.5% (10-22) in PD-L1positive, and 6.4% (3-13) in PD-L1negative tumors. In cohort 2, confirmed ORR was 60.0% (39-79) overall, 73.3% (45-92) in PD-L1positive, and 37.5% (9-76) in PD-L1negative tumors. In cohort 3, confirmed ORR was 25.8% (12-45). Median (range) DOR in months was 16.1 (2-35+), 4.6 (3-37+), and not reached (2.1-32.5+) in cohorts 1, 2, and 3, respectively. OS at 1 year/2 years was 24.6%/12.5%, 52%/32%, and 63.6%/40.1% in cohorts 1, 2, and 3, respectively. In cohorts 1, 2, and 3, grade 3-5 treatment-related adverse event (TRAE) incidence was 46 (18%), 20 (80%), and 8 (26%) respectively. TRAEs led to discontinuation in 6 (2%) and 3 (12%) pts in cohorts 1 and 2, respectively, and to death in 2 (1%) pts in cohort 1. No TRAEs led to discontinuation or death in cohort 3. **Conclusions:** These updated results demonstrate manageable safety, durable clinically meaningful activity of pembro in heavily pretreated pts, and promising efficacy of first-line pembro (alone or + chemo) in pts with advanced G/GEJ cancer. Clinical trial information: NCT02335411.

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4010 Poster Discussion Session; Displayed in Poster Session (Board #115), Mon, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Mon, 3:00 PM-4:30 PM

Pembrolizumab versus chemotherapy as second-line therapy for advanced esophageal cancer: Phase 3 KEYNOTE-181 study.

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Background: The phase 3 KEYNOTE-181 study compared pembrolizumab (pembro) vs chemo as second-line therapy for patients (pts) with advanced/metastatic squamous cell carcinoma (SCC) and adenocarcinoma (ACC) of the esophagus (NCT02564263). **Methods:** Eligible pts were randomized 1:1 to pembro 200 mg Q3W for up to 2 years or choice of paclitaxel, docetaxel, or irinotecan. Randomization was stratified by histology (SCC vs adenocarcinoma) and region (Asia vs rest of world). Primary end points were OS in the SCC, PD-L1 combined positive score (CPS) ≥10, and the ITT. Secondary endpoints included PFS, ORR, safety; exploratory endpoints included health-related quality of life (HRQoL) in CPS ≥10. **Results:** 628 pts were randomized (401 with SCC; 222 with CPS ≥10). As of Oct. 15, 2018, median follow-up was 7.1 mo (pembro) vs 6.9 mo (chemo). In CPS ≥10, OS was superior with pembro vs chemo (median 9.3 vs 6.7 mo; HR 0.69; 95% CI 0.52-0.93; *P*= 0.0074). In CPS ≥10 SCC, median OS was 10.3 mo vs 6.7 mo and in CPS ≥10 ACC, median OS was 6.3 mo vs 6.9 mo; 12-mo OS rates were higher with pembro vs chemo (Table). In SCC, median OS was 8.2 mo vs 7.1 mo; HR 0.78; 95% CI 0.63-0.96; *P*= 0.0095. In the ITT, median OS was 7.1 mo vs 7.1 mo; HR 0.89; 95% CI 0.75-1.05; *P*= 0.0560. Updated OS will be presented. Grade 3-5 drug-related AEs (≥10% incidence in either arm) included decreased white blood cells (0% vs 10%), decreased neutrophils (0.3% vs 10%). In CPS ≥10, HRQoL improved with pembro vs chemo only for EQ-5D VAS (difference in LS mean change from baseline 5.57; 95% CI 0.58-10.56). **Conclusions:** Pembro significantly improved OS vs chemo as second-line therapy for advanced esophageal cancer with PD-L1 CPS ≥10, with a more favorable safety profile and stable and similar QOL. These data support pembro as a new second-line standard of care for esophageal cancer with PD-L1 CPS ≥10. Clinical trial information: NCT02564263.

	CPS ≥10					
	Total		SCC		ACC	
	Pembro N = 107	Chemo N = 115	Pembro N = 85	Chemo N = 82	Pembro N = 22	Chemo N = 33
12-mo OS, %	43	20	48	23	23	15
Median PFS (95% CI), mo	2.6 (2.1-4.1)	3.0 (2.1-3.7)	3.2 (2.1-4.4)	2.3 (2.1-3.4)	2.1 (1.9-3.5)	3.7 (2.0-5.7)
12-mo PFS, %	21	7	23	7	14	7
ORR, %	21.5	6.1	22	7	18	3
Median DOR (range), mo	9.3 (2.1+ to 22.6+)	7.7 (4.3 to 16.8+)	9.3 (2.1+ to 18.8+)	7.7 (4.3 to 16.8+)	Not reached (6.5 to 22.6+)	4.4 (4.4-4.4)

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4011 Poster Discussion Session; Displayed in Poster Session (Board #116), Mon, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Mon, 3:00 PM-4:30 PM

First-line pembrolizumab (P), trastuzumab (T), capecitabine (C) and oxaliplatin (O) in HER2-positive metastatic esophagogastric adenocarcinoma.

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Background: Trastuzumab stimulates HER2-specific T cell responses and increases tumor PD-L1 expression, and anti-PD-1 antibody can help enhance T cell-specific immunity of trastuzumab. We conducted a phase II trial of pembrolizumab with chemotherapy/trastuzumab. **Methods:** Patients (pts) with previously untreated HER2 IHC 3+ or FISH+ tumors irrespective of PD-L1 status received intravenous P 200 mg flat dose, T 6 mg/kg (after 8 mg/kg load), O 130 mg/m2 every 3 weeks and oral C 850 mg/m2 2 weeks on/1 week off. 22 pts received 1 cycle of induction P/T prior to initiation of chemotherapy. The primary endpoint was 6-months PFS; with target accrual of 37 pts. Secondary endpoints included safety, OS, ORR, and biomarker analysis. **Results:** Accrual completed and 100% of the 32 evaluable pts had tumor regression (ranging from -20% to -100%). The RECIST 1.1 ORR was 87% (25 PR, 3 CRs), and 12 (52%) of pts that received induction P/T x 1 cycle showed reduction in target lesions. Median PFS was 11.3 months (mo), with 67% 6 mo PFS. Median follow up was only 6.6 mo. In pts with available material, 14/36 (40%) had PD-L1 CPS >1 and median TMB was 4.4 mut/Mb (0-10.6). There was no correlation between PD-L1 status and PFS or OS. *ERBB2* amplification was evident by tissue-NGS in 17/29 (61%) and ctDNA-NGS in 17/30 (58%) pre-treatment, while the remaining pts were ERBB2- by NGS likely due to tumor heterogeneity or low tumor content. CtDNA maxVAF decreased in 16/24 tested pts after 1 cycle of induction T/P alone. irAEs included interstitial nephritis Gr4 (3%), transaminitis Gr3 (11%), Gr4 (3%), colitis Gr3 (3%). **Conclusions:** Most pts (51%) remain on therapy, and so the primary endpoint should be reached by 6/19. Updated survival, correlative studies and will be presented. These promising preliminary safety and efficacy results led to initiation of a definitive phase III Keynote 811 trial. Clinical trial information: NCT02954536.

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4012 Poster Discussion Session; Displayed in Poster Session (Board #117), Mon, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Mon, 3:00 PM-4:30 PM

Nivolumab (NIVO) + ipilimumab (IPI) combination therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC): Results from CheckMate 040.

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Background: NIVO monotherapy (mono) is approved for sorafenib (SOR)-treated pts with HCC based on data from CheckMate 040 (NCT01658878), which reported an objective response rate (ORR) of 14% and median overall survival (mOS) of 16 months (mo). This is the first report of efficacy and safety of the NIVO + IPI combination in SOR-treated pts with aHCC. **Methods:** Pts were randomized to 3 arms: [A] NIVO 1 mg/kg + IPI 3 mg/kg Q3W (4 doses) or [B] NIVO 3 mg/kg + IPI 1 mg/kg Q3W (4 doses), each followed by NIVO 240 mg Q2W, or [C] NIVO 3 mg/kg Q2W + IPI 1 mg/kg Q6W. Treatment continued until intolerable toxicity or disease progression. Primary endpoints included safety and tolerability. Secondary endpoints included ORR (BICR per RECIST v1.1), duration of response (DOR), disease control rate (DCR), and OS. Cutoff was 25 Sep 2018. **Results:** 148 SOR-treated pts were randomized. Minimum follow-up for OS from last pt randomization date to data cutoff was 24 mo. At baseline: 88% had vascular invasion or extrahepatic spread, 91% had BCLC stage C, 84% discontinued SOR due to disease progression and 14% due to toxicity. Overall, ORR was 31% (7 had a complete response [CR]) with a median DOR of 17 mo; DCR was 49% and 24-mo OS rate was 40%. Pts in arm A had a mOS of 23 mo and 4 pts had a CR. The table shows additional efficacy results by arm. Overall, NIVO + IPI was well tolerated; 37% of pts had a grade 3–4 treatment-related adverse event (TRAE; most common: pruritus and rash); 5% had grade 3–4 TRAEs leading to discontinuation. **Conclusions:** NIVO + IPI led to clinically meaningful responses and had an acceptable safety profile in SOR-treated pts, with an ORR twice that of NIVO mono (31% and 14%, respectively). Pts in arm A had the most promising mOS of 23 mo. Clinical trial information: NCT01658878.

	[A] NIVO1/IPI3 Q3W (n = 50)	[B] NIVO3/IPI1 Q3W (n = 49)	[C] NIVO3 Q2/IPI1 Q6W (n = 49)
ORR, n (%)	16 (32)	15 (31)	15 (31)
Complete response	4 (8)	3 (6)	0
Partial response	12 (24)	12 (24)	15 (31)
Stable disease	9 (18)	5 (10)	9 (18)
Progressive disease	20 (40)	24 (49)	21 (43)
DCR, % (95% CI)	54 (39–68)	43 (29–58)	49 (34–64)
mOS, mo (95% CI)	23 (9–NA)	12 (8–15)	13 (7–33)
12-mo OS rate, % (95% CI)	61 (46–73)	56 (41–69)	51 (36–64)
24-mo OS rate, % (95% CI)	48 (34–61)	30 (18–44)	42 (28–56)

NA, not available.

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4014 Poster Discussion Session; Displayed in Poster Session (Board #119), Mon, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Mon, 3:00 PM-4:30 PM

Randomized phase II study of second-line modified FOLFIRI with PARP inhibitor ABT-888 (Veliparib) (NSC-737664) versus FOLFIRI in metastatic pancreatic cancer (mPC): SWOG S1513.

E. Gabriela Chiorean, Katherine A Guthrie, Philip Agop Philip, Elizabeth M. Swisher, Florencia Jalikis, Michael J. Pishvaian, Jordan Berlin, Marcus Smith Noel, Jennifer Marie Suga, Ignacio Garrido-Laguna, Dana Backlund Cardin, Danika L. Lew, Andrew M. Lowy, Howard S. Hochster; University of Washington and Fred Hutchinson Cancer Research Center, Seattle, WA; SWOG Statistics and Data Management Center, and Fred Hutchinson Cancer Research Center, Seattle, WA; Karmanos Cancer Institute, Detroit, MI; University of Washington School of Medicine, Seattle, WA; University of Washington Medical Center, Seattle, WA; Georgetown University Medical Center, Washington, DC; Vanderbilt University, Nashville, TN; University of Rochester James P. Wilmot Cancer Institute, Strong Memorial Hospital, Rochester, NY; Kaiser Permanente, Vallejo, CA; University of Utah Huntsman Cancer Institute, Salt Lake City, UT; Vanderbilt-Ingram Cancer Center, Nashville, TN; SWOG Statistical Center, Fred Hutchinson Cancer Research Center, Seattle, WA; UCSD Moores Cancer Center, La Jolla, CA; Rutgers Cancer Institute of New Jersey, New Brunswick, NJ

Background: PC is characterized by DNA Damage Repair (DDR) deficiencies, including in *BRCA1/2*, *ATM*, and *FANC* genes. Given preclinical synergism between veliparib with irinotecan, safety and preliminary efficacy, we designed a randomized phase II study of mFOLFIRI (no 5-FU bolus) + veliparib vs FOLFIRI alone for 2nd line mPC patients (pts). **Methods:** Eligible pts had mPC, adequate organ function, ECOG PS 0-1, and 1 prior non-irinotecan systemic therapy.143 pts were to be randomized (1:1) to veliparib vs control. Primary endpoint was overall survival (OS). All pts had blood and tumor biopsies at baseline to assess germline and somatic *BRCA1/2* mutations (integrated), and homologous recombination (HR) or DDR biomarkers (exploratory). **Results:** 123 pts were accrued between 09/2016 to 12/2017, and 108 were included in this analysis. 117 pts were biomarker evaluable: 109 blood/106 tumors. 11 cancers (9%) had HR deficiency (HRD), including 4 germline (*BRCA1*, *BRCA2*, *ATM*) and 7 somatic mutations (*BRCA2*, *PALB2*, *ATM*, *CDK12*). Additional 24 cancers (20%) had germline (n = 11, e.g., *FANC*, *BLM*, *SLX4*, *CHEK2*) or somatic mutations (n = 13, e.g., *FANC*, *BLM*, *POLD1*, *RIF1*, *MSH2*, *MSH6*) in other DNA repair genes, not classified as HRD. A planned interim futility analysis at 35% of expected PFS events determined the veliparib arm was unlikely to be superior to control. Most common grade 3/4 treatment related toxicities were neutropenia (33% vs 20%), fatigue (19% vs 4%), and nausea (11% vs 4%), for veliparib vs control. Treatment exposure was similar for veliparib vs control: median 4 cycles (range 1-31 vs 1-32). Median OS was 5.1 vs 5.9 mos (HR 1.3, 95%CI 0.9-2.0, p = 0.21), and median PFS was 2.1 vs 2.9 mos (HR 1.5, 95%CI 1.0-2.2, p = 0.05) for veliparib vs control arms, respectively. Correlations of gene mutations and signatures with efficacy outcomes will be presented. **Conclusions:** Nearly 30% of mPC pts had DNA repair gene abnormalities, including 9% with HRD. Veliparib increased toxicity and did not improve OS when added to mFOLFIRI in biomarker unselected pts. *BRCA1/2* and DDR biomarkers will be correlated with efficacy to inform patient selection for future PARP inhibitor clinical trials. Clinical trial information: NCT02890355.

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4015 Poster Discussion Session; Displayed in Poster Session (Board #120), Mon, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Mon, 3:00 PM-4:30 PM

Final report of a phase I/II study of veliparib (Vel) in combination with 5-FU and oxaliplatin (FOLFOX) in patients (pts) with metastatic pancreatic cancer (mPDAC).

Michael J. Pishvaian, Hongkun Wang, Sarah Parenti, Aiwu Ruth He, Jimmy J. Hwang, Lisa Ley, Holly Difebo, Brandon George Smaglo, Sunnie S. Kim, Benjamin Adam Weinberg, Louis M. Weiner, John Marshall, Jonathan Robert Brody; Georgetown University, Washington, DC; Levine Cancer Institute, Carolinas Health Care System, Charlotte, NC; Dan L Duncan Comprehensive Cancer Center at Baylor College of Medicine, Houston, TX; The Sidney Kimmel Cancer Center at Thomas Jefferson University, Philadelphia, PA

Background: 17 – 25% of mPDACs harbor DNA damage response (DDR) mutations, the presence of which can be predictive of a response to platinum and PARP inhibitor-based therapy. The PARP inhibitor, Vel is a potent sensitizing agent for, and has been safely combined with DNA-damaging chemotherapies. **Methods:** We initiated a Phase I/II trial of Vel + FOLFOX in pts with mPDAC. Pts received standard mFOLFOX6 except without the 5FU bolus, Q2 weeks. For the Phase I portion, a 3+3 dose escalation of Vel identified a recommended Phase II dose of 200mg orally BID, days 1-7, Q2 weeks. For the Phase II portion, we enrolled two cohorts: 1) Untreated pts; 2) Previously treated pts. Also, for Phase II, pts were pre-selected if they had either a pathogenic germline or somatic DDR mutation (e.g. *BRCA1/2, PALB2, ATM*), and/or a family history suggestive of a breast or ovarian cancer syndrome (labelled FH+). Objective response rate (ORR) was the primary objective of the Phase II cohorts; key secondary endpoints were median progression-free survival (PFS) and overall survival (OS). **Results:** Between 01-2011 and 12-2018, 64 pts received treatment, 31 in Phase I, and 15 untreated and 18 previously treated in Phase II. The combination was well tolerated, with the main Grade 3/4 AEs being myelosuppression (16%) and nausea/vomiting (6%). Of the 64 pts, 55% were male; median age was 64; 95% had an ECOG PS of 1; 78% were platinum-naïve; 69% were FH+; and 27% had a known DDR mutation. 57 pts were evaluable for response, and the ORR, PFS, and OS for the different pt subgroups are detailed below. The Phase II cohorts achieved the primary endpoint of an ORR $\geq$ 25%. Most notably, plat-naïve, FH+, and DDR mutation+ pts had an ORR of 58%. **Conclusions:** The combination of Vel + FOLFOX is safe, well tolerated, and shows promising efficacy particularly in plat-naïve pts who are FH+ and/or harbor DDR mutations. A randomized trial to assess the contribution of Vel to the regimen is warranted. Clinical trial information: NCT01489865.

Category (n)	ORR (%)	mPFS (mos)	mOS (mos)
All pts (57)	26	3.7	8.5
Plat-Naïve (43)	33	5.3	9.4
Prior Plat (14)	7	1.9	5.0
FH+ (43)	30	4.3	10.1
No FH (14)	14	3.5	5.5
DDR mutation+ (16)	50	7.2	11.1
No mutation (41)	17	3.5	6.8
Plat-Naïve, FH+, DDR+ (12)	58	8.7	11.8

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4016 Poster Discussion Session; Displayed in Poster Session (Board #121), Mon, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Mon, 3:00 PM-4:30 PM

Rivaroxaban thromboprohylaxis in ambulatory patients with pancreatic cancer: Results from a prespecified subgroup analysis of the CASSINI study.

Saroj Vadhan-Raj, Mairead Geraldine McNamara, Marino Venerito, Hanno Riess, Eileen Mary O'Reilly, Michael J. Overman, Xiao Zhou, Ujjwala Vijapurkar, Simrati Kaul, Peter Wildgoose, Alok A. Khorana; The University of Texas MD Anderson Cancer Center, Department of Sarcoma Medical Oncology, Section of Cytokines and Supportive Oncology, Houston, TX; Department of Medical Oncology, The Christie NHS Foundation Trust, Manchester, United Kingdom; Klinik für Gastroenterologie, Hepatologie und Infektiologie Universitätsklinikum, Magdeburg, Germany; Charité Universitätsmedizin Berlin, Berlin, Germany; Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY; The University of Texas MD Anderson Cancer Center, Houston, TX; Janssen Research & Development, Raritan, NJ; Janssen Scientific Affairs, LLC, Titusville, NJ; Department of Hematology and Medical Oncology, Cleveland Clinic, Cleveland, OH

Background: Rivaroxaban thromboprophylaxis has been shown to reduce venous thromboembolism (VTE) on-treatment in ambulatory cancer patients in a recent randomized trial. Pancreatic cancer patients are at substantial risk for VTE; value of thromboprophylaxis has not been definitively established. **Methods:** CASSINI was a double-blind placebo-controlled trial of cancer patients initiating a new regimen, at high risk for VTE (Khorana score $\geq$2), randomized to rivaroxaban 10 mg daily or placebo up to 180 days. Patients were stratified by presence or absence of pancreatic cancer. Patients had screening ultrasound and blood drawn at baseline and every 8 wks. Primary efficacy endpoint was a composite of symptomatic DVT, asymptomatic proximal DVT, any PE and VTE-related death. Primary safety endpoint was International Society on Thrombosis and Hemostasis (ISTH)-defined major bleeding. **Results:** Of 1080 patients enrolled, 49 (4.5%) failed screening due to baseline VTE, with even higher rates [24/362 (6.6%)] in patients with pancreatic cancer. Of 841 randomized patients, 273 (32.6%) had pancreatic cancer with median age 66 y; 57% male and 155/273 (57% in each arm) completing the double-blind period. During intervention (on-treatment) period, 5/135 (3.7%) pancreatic cancer patients in the rivaroxaban arm and 14/138 (10.1%) in placebo arm had primary endpoint events [HR 0.35; 95%CI (0.13, 0.97), p = 0.03; number needed to treat, NNT = 16]. Major bleeding was not increased, occurring in 2 (1.5%) patients in rivaroxaban arm and 3 (2.3%) in placebo arm. Further benefit with rivaroxaban was observed when including primary and secondary endpoints (arterial/visceral events): 6/135 (4%) events in rivaroxaban vs 17/138 (12%) in placebo [HR, 0.34; 95%CI (0.14, 0.87), P = 0.02; NNT = 13]. Correlative biomarker studies demonstrated significant decline in D-dimer values over time (weeks 8 and 16) in patients without VTE randomized to rivaroxaban prophylaxis compared to placebo ($P < 0.01$), supporting clinical findings. **Conclusions:** Rivaroxaban substantially reduced VTE in pancreatic cancer patients during intervention period. Given no increase in major bleeding, our findings suggest benefit to rivaroxaban thromboprophylaxis in pancreatic cancer patients initiating systemic therapy. Clinical trial information: NCT02555878.

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4017 **Oral Abstract Session, Sun, 9:45 AM-12:45 PM**

S-1 plus oxaliplatin versus S-1 plus cisplatin as first-line treatment for advanced diffuse-type or mixed-type gastric/gastroesophageal junction adenocarcinoma: A randomized, phase 3 trial.

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Background: Diffuse-type or mixed-type gastric adenocarcinoma is associated with poor prognosis, and more effective treatment is needed. In Asia, S-1 plus cisplatin (SP) is the standard first-line chemotherapy regimen for advanced gastric cancer. Nevertheless, some clinical data suggested that oxaliplatin-based chemotherapy might be more efficacious and more tolerant than cisplatin-based chemotherapy. **Methods:** This trial is a multicenter, randomized, parallel-group, open-label, phase 3 trial in China. Patients aged 18-75 years, with PS 0-2, adequate organ function, histology confirmed, unresectable, advanced diffuse-type or mixed-type gastric adenocarcinoma/GEJA were randomized 1:1 to S-1 plus oxaliplatin group (SOX) (S-1: 40-60mg bid on d1-14, q3w; oxaliplatin: 130 mg/m2 on d1, q3w) or SP group (S-1: 40-60mg bid on d1-14, q3w; cisplatin: 60 mg/m2 d1, q3w). The primary endpoint was overall survival (OS) in the full analysis set (FAS). The secondary endpoints were progression-free survival (PFS), time to treatment failure (TTF) and safety. **Results:** Between Jul 2013 and Jul 2018, 576 patients were randomized and 558 initiated treatment (279 patients/group). The median number of chemotherapy cycles was four in each group. In the FAS, the SOX group showed improved OS (13.0 vs. 11.8 months, HR = 0.764, 95% CI: 0.636-0.918), PFS (5.7 vs. 4.9 months, HR = 0.752, 95%CI: 0.632-0.895), and TTF (5.2 vs. 4.7 months, HR = 0.763, 95%CI: 0.641-0.909) compared with the SP group. In terms of grade$\geq$3 adverse events, SOX showed lower occurrences of neutropenia (10.0% vs. 22.9%), leukopenia (9.7% vs. 21.9%), anemia (4.3% vs. 14.3%),vomiting (3.9% vs. 10.4%), nausea (2.2% vs. 10.4%), anorexia (2.2% vs. 6.8%), and febrile neutropenia (2.5% vs. 6.8%) than SP (all $P < 0.05$). The occurrence of grade$\leq$2 sensory neuropathy(41.6% vs. 12.2%, $P < 0.001$)was higher with SOX than with SP. **Conclusion:** Compared with SP, SOX was more effective and less toxic (except neurosensory toxicity) in patients with previously untreated advanced diffuse-type or mixed-type gastric adenocarcinoma/GEJA. Clinical trial information: NCT01824459.

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4018 Poster Discussion Session; Displayed in Poster Session (Board #123), Mon, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Mon, 3:00 PM-4:30 PM

PET-directed combined modality therapy for gastroesophageal junction cancer: First results of the prospective MEMORI trial.

Sylvie Lorenzen, Michael Quante, Isabel Rauscher, Julia Slotta-Huspenina, Karl Friedrich Becker, Wilko Weichert, Marcus Feith, Helmut Friess, Stephanie E Combs, Wolfgang Weber, Bernhard Haller, Martin K Angele, Markus Albertsmeier, Christiane Blankenstein, Stefan Kasper, Jens Peter Zimmermann, Hana Algül, Roland M. Schmid, Markus Schwaiger, Jens T Siveke; Third Department of Internal Medicine (Hematology/Medical Oncology), Klinikum rechts der Isar, Technische Universitat Munchen, Munich, Germany; Technical University Munich, Klinikum rechts der Isar, II. Medizinische Klinik und Poliklinik, Munich, Germany; Rechts der Isar University Hospital, Technical University of Munich, Munich, Germany; Technical University Munich, Institute of Pathology, Munich, Germany; Technical University Munich, Klinikum rechts der Isar, Surgical Clinic and Policlinic, Munich, Germany; German Cancer Consortium (DKTK) Core Center Heidelberg and DKTK Partner Site Munich (TUM), Munich, Germany; Technical University Munich, Klinikum rechts der Isar, Department of Nuclear Medicine, Munich, Germany; Institute for Medical Statistics and Epidemiology, Technische Universität München, Munich, Germany; Department of Surgery, University Hospital Grosshadern, Munich, Germany; Ludwig Maximilian University, Department of General, Visceral and Transplantation Surgery, Munich, Germany; Technical University Munich, Muenchener Studienzentrum, Munich, Germany; University Hospital Essen, Essen, Germany; Klinikum rechts der Isar, Department of Internal Medicine II, Technische Universität München, Munich, Germany; University Hospital Essen, West German Cancer Center, Essen, Germany

Background: We evaluated a PET-guided treatment stratification for improvement in obtaining negative surgical margins (R0) in resectable gastroesophageal junction (GEJ) adenocarcinoma. According to sequential ^{18}F-FDG PET, only 40–50% of patients (pts) respond to neoadjuvant chemotherapy (CTX). Early PET non-responders (P-NR) after induction CTX might benefit from changing to chemoradiation (CRT). **Methods:** 75 pts with resectable GEJ adenocarcinomas were enrolled in this interventional, prospective, non-randomized multicenter trial. Pts underwent baseline ^{18}F-FDG PET scan followed by 1 cycle of CTX (physicians' choice, e.g. EOX, XP, mFOLFOX6). PET was repeated at day 14-21 and responders (P-R), defined as $\geq$ 35% decrease in SUVmax from baseline, continued with CTX. P-NR switched to CRT (41.4 Gy/23 fractions with weekly carboplatin/paclitaxel). Pts underwent surgery 4-6 weeks post-CTX/CRT. Primary objective was an improvement of R0 resection rates in P-NR above a proportion of 70% based on results from the MUNICON1/2 trials. Secondary endpoints include disease-free survival (DFS), overall survival (OS), measured from randomization to death from any cause, and translational endpoints. **Results:** Between 12/2014 and 07/ 2018 160 pts with resectable GEJ adenocarcinomas were prospectively screened with PET in three German university centers. Overall, 85 pts (53%) could not be included due to previously undetectable metastases (40/25%), no or too low FDG uptake of the primary tumor (21/13%), other reasons (24/15%). 75 eligible pts were enrolled in the study and 69 were evaluable. Based on PET criteria, 47 (68%) and 22 (32%) were P-R and P-NR, respectively. R0 resection rates were 94% (44/47) for P-R and 91% (20/22) for P-NR. Pathologic complete remission (pCR; $<$ 10% vital tumor cells), was 33% (15/46) in P-R and 55% (12/22) in P-NR. With a median follow-up time of 19 months (mo), estimated 18 mo DFS was 71%/61% for P-R/P-NR, respectively. Observed median 18 mo OS was 95% for P-R and 75% for P-NR. **Conclusions:** Alternative CRT for GEJ adenocarcinoma improved R0- and pCR rates among pts who were P-NR after induction CTX. PET response was prognostic for a prolonged OS and DFS. Clinical trial information: 2014-000860-16.

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4019 Poster Discussion Session; Displayed in Poster Session (Board #124), Mon, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Mon, 3:00 PM-4:30 PM

Adjuvant chemotherapy versus perioperative chemotherapy (CTx) for resectable gastric signet ring cell (SRC) gastric cancer: A multicenter, randomized phase II study (PRODIGE 19).

Clarisse Eveno, Antoine Adenis, Olivier Bouche, Karine Le Malicot, Vincent Hautefeuille, Roger Faroux, Anne Thirot Bidault, Joëlle Egreteau, Bernard Meunier, May Mabro, Nicolas Carrere, Nicolas Barriere, Meher Ben Abdelghani, François Mauvais, Frédéric Di Fiore, David Malka, Sylvain Manfredi, Guillaume Piessen; CHRU Lille, Lille, France; Institut du Cancer de Montpellier, Montpellier, France; CHU Robert Debre, Reims, France; FFCD and INSERM U1231, Dijon, France; Amiens University Hospital, Amiens, France; Centre Hospitalier Departemental Les Oudairies, La Roche-Sur-Yon, France; Hôpital Privé d'Antony, Antony, France; Centre Hospitalier Bretagne Sud, Lorient, France; Pontchaillou University Hospital, Rennes, France; Hôpital Foch, Suresnes, France; Department of Digestive Surgery, Purpan University Hospital, Toulouse, France; Hôpital Européen, Marseille, France; Centre Paul Strauss, Strasbourg, France; CH Beauvais, Beauvais, France; Digestive Oncology Unit, Department of Hepato-Gastroenterology, Rouen University Hospital, Rouen, France; Gustave Roussy, Université Paris-Saclay, Département de Médecine Oncologique, Villejuif, France; CHU Le Bocage HGE, Dijon, France; University Hospital of Lille, Lille, France

Background: The incidence of SRC gastric cancers is markedly increasing in Western countries. SRC cancers may harbor intrinsic resistance to chemotherapy (CTx) leaving many clinicians unsure of the benefits of delaying surgery to pursue a neoadjuvant approach. The primary objective of this study was to assess whether upfront surgery plus adjuvant CTx would provide enough survival benefit for study in a phase III trial when compared to perioperative CTx. **Methods:** Patients with stage IB-III SRC gastric cancer were randomly assigned to receive upfront surgery plus adjuvant CTx (epirubicin, cisplatin and 5-fluorouracil [ECF regimen], 6 cycles; experimental arm [SurgFirst]) or perioperative CTx (ECF, 3 cycles before and 3 cycles after surgery; control arm [CTxFirst]). Randomization (1:1) was stratified by tumor stage, tumor location, performance status and center. The primary endpoint was overall survival (OS) at 2 years (OS2; target (H_1): OS2 $>$ 26%). **Results:** 83 eligible patients were included in 27 centers from 11/12 to 09/16 (median age, 61 years (range: 32-80 years); male, 59%; ECOG PS 0-1, 99%). Results were (CTxFirst/SurgFirst): full completion of CTx, 87%/77%; surgical resection, 82.5%/90%; major postoperative complications (Clavien Dindo III-IV), 24%/23%; R0 resection rate, 88%/78%; OS2, 60%/53.5%; and median OS, 39/28 months (exploratory hazard ratio, 0.71 [95%CI: 0.40-2.64]). **Conclusions:** This trial met its primary endpoint (OS2 $>$ 26% in the experimental arm). With OS2 rates $>$ 50%, both CTx modalities deserve further evaluation in Phase III studies in stage IB-III SRC gastric cancer. Clinical trial information: NCT01717924.

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4020 Poster Discussion Session; Displayed in Poster Session (Board #125), Mon, 8:00 AM-11:00 AM, Discussed in Poster Discussion Session, Mon, 3:00 PM-4:30 PM

Randomized phase III trial of laparoscopy-assisted versus open distal gastrectomy with nodal dissection for clinical stage IA/IB gastric cancer (JCOG0912).

Hitoshi Katai, Junki Mizusawa, Hiroshi Katayama, Shinji Morita, Takanobu Yamada, Etsuro Bando, Kazunari Misawa, Masakazu Takagi, Akinori Takagane, Shin Teshima, Keisuke Koeda, Souya Nunobe, Takaki Yoshikawa, Masanori Terashima, Mitsuru Sasako, Stomach Cancer Study Group of Japan Clinical Oncology Group; National Cancer Center Hospital, Tokyo, Japan; Japan Clinical Oncology Group Data Center/Operations Office, National Cancer Center Hospital, Tokyo, Japan; Division of Gastric Surgery, National Cancer Center Hospital, Tokyo, Japan; Department of Gastrointestinal Surgery, Kanagawa Cancer Center, Yokohama, Japan; Division of Gastric Surgery, Shizuoka Cancer Center, Shizuoka, Japan; Department of Gastroenterological Surgery, Aichi Cancer Center Hospital, Nagoya, Japan; Shizuoka General Hospital, Shizuoka, Japan; Department of Surgery, Hakodate Goryoukaku Hospital, Hakodate, Japan; Dept. of Surgery, NHO Sendai Medical Center, Sendai, Japan; Department of Medical Safety Science, Iwate Medical University School of Medicine, Morioka, Japan; Department of Gastroenterological surgery, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; Kanagawa Cancer Center, Kanagawa, Japan; Division of Upper Gastrointestinal Surgery, Department of Surgery, Hyogo College of Medicine, Nishinomiya, Japan

Background: The number of patients undergoing laparoscopy-assisted distal gastrectomy (LADG) has been increasing worldwide. Several retrospective studies have demonstrated equivalent survival after LADG compared to open distal gastrectomy (ODG). However, no confirmatory randomized controlled trials has been published in a peer review journal to evaluate the efficacy of LADG compared with ODG, ensuring strict surgical skill and quality control of surgery. We conducted phase III study to confirm that LADG is not inferior to ODG in efficacy. **Methods:** Eligibility criteria included histologically proven adenocarcinoma in the middle or lower third of the stomach; clinical stage I tumor (T1N0, T1N1, T2(MP)N0). Patients were preoperatively randomized to ODG or LADG. LADG was performed by accredited surgeon. The extent of nodal dissection was decided according to Japanese gastric cancer treatment guidelines. The primary endpoint is relapse-free survival (RFS) and the secondary endpoints are overall survival (OS), short-term clinical outcomes, and postoperative quality of life. Planned sample size was 920 patients in total, which was determined with at least 80% power, a one-sided alpha of 5%, and a non-inferiority margin for a hazard ratio of 1.54. Before the 1st interim analysis, the primary endpoint was amended from OS to RFS in 2015 because the surrogacy of RFS for OS was demonstrated and the predicted number of events for OS was smaller than expected. **Results:** A total of 921 patients were randomized (ODG 459, LADG 462) between Mar. 2010 and Nov. 2013. Among 921 patients, 912 patients (99%) underwent assigned surgery. Conversion to ODG was needed for 16 patients (3.5%) in LADG arm mainly due to advanced disease. 5-year RFS was 94.0% (95% CI: 91.4-95.9%) in ODG and 95.1% (92.7-96.8%) in LADG. LADG was non-inferior to ODG for RFS. (HR: 0.84 [90% CI: 0.56-1.27 ($<$ 1.54)], p for non-inferiority = 0.008). 5-year OS was 95.2% (92.7-96.8) in ODG and 97.0% (94.9-98.2) in LADG (HR: 0.83 [95% CI: 0.49-1.40]). **Conclusions:** The non-inferiority of LADG to ODG in RFS was confirmed. LADG has been established as one of the standard treatments for clinical stage I gastric cancer. Clinical trial information: UMIN000003319.

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4021 **Poster Session (Board #126), Mon, 8:00 AM-11:00 AM**

Tumor mutational burden identifies chemorefractory gastric cancer with overall survival advantage after receiving toripalimab, a PD-1 antibody.

Rui-Hua Xu, Feng Wang, Xiao-Li Wei, Fenghua Wang, Nong Xu, Lin Shen, Guanghai Dai, Xianglin Yuan, Ye Chen, Shujun Yang, Jianhua Shi, Xi-Chun Hu, Xiaoyan Lin, Qingyuan Zhang, Ji Feng Feng, Yi Ba, Yunpeng Liu, Hai Wu, Hui Feng, Sheng Yao; Sun Yat-sen University Cancer Center, Guangzhou, China; Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Guangzhou, China; The First Affiliated Hospital , Zhejiang University, Hangzhou, China; Department of Gastrointestinal Oncology, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital and Institute, Beijing, China; Chinese People's Liberation Army (PLA) General Hospital, Beijing, China; Department of Oncology, Tongji Hospital, Huazhong University of Science and Technology, Wuhan, China; West China Hospital, Sichuan University, Chengdu, China; Henan Cancer Hospital, Zhengzhou, China; Shandong Linyi Tumor Hospital, Linyi, China; Fudan University Shanghai Cancer Center, Shanghai, China; Fujian Medical University Union Hospital, Fuzhou, China; Harbin Medical University Cancer Hospital, Harbin, China; Jiangsu Cancer Hospital and Jiangsu Institute of Cancer Research and Nanjing Medical University Affiliated Cancer Hospital, Jiangsu, China; Department of Medical Oncology, Tianjin Cancer Hospital, Tianjin, China; The First Hospital of China Medical University, Shenyang, China; Topalliance Biosciences, Shanghai, China; TopAlliance Bioscience Inc, Maryland, MD; Shanghai Junshi Bioscience Co., LTD, Rockville, MD

Background: Tumor mutational burden (TMB) is correlated with enhanced objective response rate (ORR) and progression-free survival for certain cancers receiving immunotherapy. This study aimed to investigate the safety and activity of toripalimab, a humanized PD-1 antibody, in advanced gastric cancer (AGC), and the efficacy predictive value of biomarkers including TMB and PD-L1. **Methods:** This study was a part of phase Ib/II trial evaluating the safety and activity of toripalimab as a single agent therapy or in combination with chemotherapy in chemo-refractory or treatment-naïve AGC, esophageal squamous cell carcinoma, nasopharyngeal carcinoma and head and neck squamous cell carcinoma. This report focused on the chemo-refractory AGC cohort receiving toripalimab (3 mg/Kg d1, Q2W) as a single agent therapy. Primary endpoint was ORR. Biomarkers including tumor PD-L1 expression, TMB, microsatellite instability (MSI) and Epstein-Barr virus (EBV) infection status were evaluated for their correlation with clinical efficacy as preplanned. Tumor PD-L1 expression was assessed with the SP142 immunohistochemistry assay, and the other biomarkers were assessed with whole exome sequencing based on tumor samples. **Results:** There were 58 subjects included in this cohort. The ORR was 12.1% and the disease control rate was 39.7%. Only 1 subject was MSI-H and achieved partial response. One out of 4 EBV positive subjects achieved partial response. Significant higher ORR was observed in subjects with positive PD-L1 expression (ORR 37.5%, 3/8) or TMB $\geq$12 Mutations/Mb (ORR 33.3%, 4/8) than those with negative PD-L1 expression (ORR 8.5%) or TMB $<$ 12 Mutations/Mb (ORR 7.0%). The TMB-high subgroup showed significant superior OS than the TMB-low subgroup (HR = 0.48 [96% CI 0.24 to 0.96], p = 0.038), while PD-L1 expression status failed to differentiate OS. **Conclusions:** Toripalimab demonstrated promising anti-tumor activity in chemo-refractory AGC patients. TMB might serve as a better predictive marker for OS than PD-L1 expression for chemo-refractory AGC patients receiving PD-1 blockade immunotherapy. Clinical trial information: NCT02915432.

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4022 **Poster Session (Board #127), Mon, 8:00 AM-11:00 AM**

Impact of age and sex on chemotherapy (CTx) efficacy, toxicity and survival in early oesophagogastric (OG) cancer: A pooled analysis of 3265 patients from four large randomised trials (OE02, OE05, MAGIC & ST03).

Avani Athauda, Matthew Guy Nankivell, Ruth E Langley, Derek Alderson, William H. Allum, Heike I Grabsch, Ian Chau, Naureen Starling, Stephen Falk, Adrian Crellin, Wasat Mansoor, Fareeda Coxon, Suzanne Darby, Joyce Thompson, Sebastian J. Cummins, Erica Beaumont, Nicholas West, Rupert Langer, Susan Pritchard, David Cunningham; The Royal Marsden Hospital, Surrey, United Kingdom; University College London, London, United Kingdom; Medical Research Council Clinical Trials Unit at University College London, London, United Kingdom; Queen Elizabeth Hospital, Birmingham, United Kingdom; Royal Marsden Hospital, London & Sutton, United Kingdom; Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, United Kingdom; The Royal Marsden NHS Foundation Trust, London & Sutton, United Kingdom; Royal Marsden Hospital NHS Foundation Trust, London & Sutton, United Kingdom; Bristol Haematology and Oncology Centre, Bristol, United Kingdom; St James Institute of Oncology, Leeds, United Kingdom; Christie NHS, Manchester, United Kingdom; Newcastle Hospitals NHS Foundation Trust, Newcastle, United Kingdom; Weston Park Hospital, Sheffield, United Kingdom; Birmingham Heartlands Hospital, Birmingham, United Kingdom; Royal Surrey County Hospital, W. Sussex, United Kingdom; Yeovil District Hospital, Yeovil, United Kingdom; Pathology & Data Analytics, Leeds Institute of Medical Research at St. James's, University of Leeds, Leeds, United Kingdom; Institute of Pathology, University of Bern, Bern, Switzerland; Manchester University NHS Foundation Trust, Manchester, United Kingdom; The Royal Marsden Hospital, Sutton, United Kingdom

Background: No large scale randomised data exists evaluating the impact of age and sex in patients (pts) undergoing potentially curative surgery and CTx for OG cancer. However, differences in age and sex may be contributing factors to variability in CTx dose-response and toxicity which could also impact survival. **Methods:** Data from four prospective randomised controlled trials were pooled using a two-stage meta-analysis. For survival data, hazard ratios were calculated for pts <70 and ≥ 70 years and between males and females. Pts were allocated to receive neoadjuvant platinum and fluoropyrimidine +/- anthracycline and bevacizumab. Mandard tumour regression grade (TRG) and prevalence of $\geq$G3 toxicities were compared according to the same subgroups using Chi-squared test. **Results:** 3265 pts were included for survival analysis (2668 (82%) M, 597 (18%) F; 2626 (80%) <70, 639 (20%) ≥ 70). A significant improvement in disease specific survival (DSS) (HR 0.78; $p<0.001$) and OS (HR 0.78; $p<0.001$) was observed in females vs males. Although OS was worse in older vs younger pts (HR 1.15; p=0.01) no significant difference in DSS was observed (HR 1.04; p=0.52). For those pts who underwent resection following neoadjuvant CTx, older patients (19 vs 13%; p=0.01) and female patients (19% vs 13%, p=0.02) were more likely to achieve more favourable Mandard TRG 1&2 scores. Older pts experienced significantly more $\geq$G3 neutropaenia (30 vs 22%; p=0.004). Females experienced significantly more $\geq$G3 nausea (12 vs 7%; p=0.006), vomiting (10 vs 5%; $p\leq 0.001$) and diarrhoea (9 vs 4%; p=0.001). **Conclusions:** This study represents the largest pooled analysis of age and sex differences on safety of neoadjuvant CTx and survival in early OG cancer. Females had significantly improved survival while experiencing more GI toxicities. Older pts achieved comparable DSS and thus, dependent on fitness, should be offered the same treatment paradigm as younger pts.

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4023 **Poster Session (Board #128), Mon, 8:00 AM-11:00 AM**

FOLFIRI plus ramucirumab versus paclitaxel plus ramucirumab for patients with advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction as second-line therapy: Interim safety and efficacy results from the phase II RAMIRIS Study (AIO-STO-0415) of the German Gastric Group at AIO.

Sylvie Lorenzen, Peter C. Thuss-Patience, Claudia Pauligk, Eray Goekkurt, Thomas Jens Ettrich, Florian Lordick, Michael Stahl, Peter Reichardt, Martin Soekler, Daniel Pink, Stephan Probst, Hana Algül, Axel Hinke, Thorsten Oliver Goetze, Salah-Eddin Al-Batran; Klinikum Rechts der Isar der TU München, Munich, Germany; Charité–University Medicine Berlin, Department of Haematology, Oncology and Tumorimmunology, Berlin, Germany; University Cancer Center Frankfurt, Institut für Klinisch-Onkologische Forschung and IKF Klinische Krebsforschung GmbH am Krankenhaus Nordwest, Frankfurt, Germany; Hämatologisch-Onkologische Praxis Eppendorf (HOPE), Facharztzentrum Eppendorf, Hamburg, Germany; Ulm University Hospital, Ulm, Germany; University Cancer Center Leipzig, Leipzig, Germany; Evang. Kliniken Essen-Mitte, Essen, Germany; HELIOS Klinikum Berlin-Buch, Berlin, Germany; University Hospital, Tübingen, Germany; Helios Klinikum Bad Saarow, Bad Saarow, Germany; Klinikum Bielefeld, Bielefeld, Germany; Klinikum rechts der Isar, Department of Internal Medicine II, Technische Universität München, Munich, Germany; CCRC, Düsseldorf, Germany; Institute of Clinical Research (IKF) at Krankenhaus Nordwest, UCT-University Cancer Center, Frankfurt, Germany

Background: Ramucirumab as monotherapy and in combination with paclitaxel is a proven second-line option for advanced gastroesophageal adenocarcinoma (GEA). More and more patients (pts) are pre-treated with docetaxel in the perioperative or first-line setting. For those pts, the benefit of a combination of ramucirumab and paclitaxel is unclear, and physicians would choose an irinotecan-based regimen as second line treatment. This provides a rationale for the evaluation of FOLFIRI + ramucirumab. **Methods:** This is a multicenter, randomized, investigator initiated, phase II trial, planned to include 111 pts with advanced GEA to receive 2:1 either FOLFIRI plus ramucirumab every two weeks (Arm A) or paclitaxel (days 1, 8, 15 of a 28-day cycle) plus ramucirumab every two weeks (Arm B). Primary endpoint is 6-months OS rate. This abstract displays interim results of safety and overall objective response (ORR) in docetaxel pre-treated group from up to 65 randomized pts. The results were needed to decide on conducting a subsequent phase III study. **Results:** 58 (A, 36; B, 22) pts were included in the safety analysis and 50 pts with tumor assessment in the response analysis. Main ≥ grade 3 adverse events were respectively in arms A/B: neutropenia (20%/22%), fatigue (6%/0%), diarrhea (8%/3%), and related SAEs (14% v 23%). Twenty-nine of 50 pts (58%) were pre-treated with docetaxel. In these pts, ORR was 30% in Arm A (5/17) and 8% (1/12) in Arm B. Disease control rate (DCR) was 65% and 50% for Arm A and B respectively. **Conclusions:** The interim safety analysis of the RAMIRIS trial has demonstrated feasibility of the combination of FOLFIRI and ramucirumab. Docetaxel pre-treated pts had higher ORR and DCR when ramucirumab is combined with FOLFIRI, instead of paclitaxel. EudraCT: 2015-005171-24. Clinical trial information: NCT03081143.

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4024 **Poster Session (Board #129), Mon, 8:00 AM-11:00 AM**

Tumor mutation burden and immunogenicity in gastric cancer with HER2 alterations.

Bo Wei, Xiaojing Xing, Ziyu Li, Quanli Han, Yingxue Hao, Jing Zhou, Yuzi Zhang, Jing Zhao, Shangli Cai, Yanhong Gu, Tufeng Chen; The Third affiliated hospital, Sun Yat-Sen University, Guangzhou, China; Liaoning Cancer Hospital and Institute, Shenyang, China; Peking University Cancer Hospital and Institute, Beijing, China; Chinese PLA General Hospital, Beijing, China; Southwest Hospital, Chongqing, China; Peking University People's Hospital, Beijing, China; The Medical Department, 3D Medicines Inc., Shanghai, China; The First Affiliated Hospital of Nanjing Medical University, Nanjing, China; Department of Gastrointestinal Surgery, The Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, China

Background: Human epidermal growth receptor 2 (HER2) is considered as an oncogenic driver gene in gastric cancer (GC). Immunotherapy has been proven to be effective in GC patients. Previous studies indicated that patients harboring driver mutations were considered as poor candidate for immunotherapy. But the efficacy of immunotherapy for HER2 positive GC has not been defined. We therefore analyzed the immunogenicity of HER2 alterations in GC. **Methods:** Genomic profiling of DNA from 448 GC was performed using next-generation sequencing on 381 cancer associated genes. The expression of PD-L1 protein was evaluated in 192 GC with the use of an automated immunohistochemical assay (Ventana, SP263). Whole-exome sequencing, copy number variations, RNA-seq and clinical data of 443 GC from The Cancer Genome Altas (TCGA) were also analyzed to further evaluate the immunogenicity of HER2 alterations. TMB was defined as number of somatic non-synonymous mutations in coding regions. HER2 amplification in TCGA was defined as "2" derived from the copy-number analysis algorithms GISTIC. **Results:** HER2 alterations including amplification, missense and fusion were present in 19.2% (85/443) of TCGA cohort and 11.4% (51/448) of clinical cohort. 14.0% (62/443) of TCGA cohort and 6.0% (27/448) of clinical cohort harbored HER2 amplification. Higher TMB was observed in MSS/MSI-L patients carrying any HER2 alterations in TCGA cohort ($P = 0.009$). On the contrary, HER2 alterations did not show a higher neoantigen level and HER2 alterations were associated with decreased immunogenicity in terms of immune-related gene mRNA expression and immune infiltrates. In clinical cohort, HER2 alterations was also significantly associated with higher TMB ($P = 0.001$). Meanwhile, a trend of shrinking proportion of PD-L1 expression was observed in HER2 alteration subgroup (2/23, 8.7%) than HER2 wild-type subgroup (47/169, 27.8%, $P = 0.071$). Furthermore, HER2 amplification had significant positive associations with HRD score ($P = 0.0169$) in TCGA cohort which indicated an increased degree of genome instability. **Conclusions:** Although HER2 alterations in GC were associated with increased TMB, HER2 alterations exhibited poor immunogenicity. These findings indicated that HER2 alterations might confer resistance to immune monotherapy.

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4025 **Poster Session (Board #130), Mon, 8:00 AM-11:00 AM**

Treatment patterns and outcomes in Chinese gastric cancer by HER2 status: A non-interventional registry study (EVIDENCE).

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Background: Gastric cancer (GC) is the second leading cause of cancer-related deaths in China. Trastuzumab (TRA) has been used to treat HER2+ metastatic gastric cancer (mGC) in China since 2012. However, real-world data on effectiveness and safety in Chinese patients are limited. **Methods:** This prospective, multicenter (85 hospitals), real-world noninterventional registry study evaluated the effectiveness and safety of TRA in five cohorts of Chinese GC patients with different HER2 statuses from April 2013 to June 2018. Effectiveness analysis was conducted in three cohorts: Cohort I (HER2+ mGC with TRA), Cohort II (HER2+ mGC untreated with TRA) and Cohort IV (HER2− mGC untreated with TRA). Safety outcomes of TRA-related adverse events (AEs) were analyzed in Cohort I. **Results:** Cohorts I, II and IV included 709 patients (174, 113 and 422, respectively; mean age 57.8 years; 72% male); 64.9% of patients were ECOG 0–1, 93.7% had a primary GC tumor and 42.3% were at stage T4. Progressive disease was the cause of death in 32.8%, 27.4% and 29.9% in Cohorts I, II and IV, respectively. Respective mean duration of follow-up was 422.5, 287.5 and 277.5 days. Median overall survival (OS) was 22.3, 17.2 and 17.4 months, respectively. After excluding patients who had surgery, the respective median OS was 19.9, 15.3, and 12.6 months. For the first-line treatment, the median OS in Cohort I was 22.1 months, and the median progression free survival (PFS) was 8.2, 6.9 and 6.2 months in Cohorts I, II and IV, respectively. Response rates (RR) for first-line treatment in Cohorts I, II and IV were 51.7%, 18.4% and 32.8%, respectively. After propensity score matching, OS, PFS and RR were all significantly better in Cohort I versus II (all $P<0.05$). The most common regimen, TRA+XELOX (capecitabine+ oxaliplatin), was estimated to have the longest median OS at 34.6 months. Grade ≥ 3 AEs were reported in 33.9% (59/174) of patients in Cohort I; anemia was the most common AE (12.1%). **Conclusions:** TRA improved OS and PFS in Chinese HER2+ mGC patients compared with chemotherapy alone and was well tolerated and effective when combined with a range of other therapies in a real-world setting. Clinical trial information: NCT01839500.

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4026 **Poster Session (Board #131), Mon, 8:00 AM-11:00 AM**

A phase II study of S-1, oxaliplatin, and nab-paclitaxel, and itraconazole aimed at conversion surgery for advanced and recurrent gastric cancer.

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Background: Preclinical and clinical studies demonstrated that itraconazole, a common anti-fungal agent, has anticancer activity. The purpose of this study was to evaluate the efficacy of the chemotherapy with itraconazole on unresectable, metastatic, and recurrent gastric cancer. **Methods:** All patients were referred to our clinic with a clinical diagnosis of unresectable gastric cancer. The regimen consisted of 160 mg/m2 nab-paclitaxel IV on day 1, 100 mg/m2 oxaliplatin IV on day 1, 60 mg/m2 S-1 orally on days 1-7, and 400mg itraconazole orally on days -1 to 3, repeated every 3 weeks. Conversion surgery was allowed. The primary endpoint was overall survival (OS). **Results:** Between 2015 and 2018. 23 patients were enrolled. Their median age was 68 years (range 40-80 years); stomach/gastroesophageal junction: 21/2; Stage IIIA/IIIB/IV: 2/1/20. Among 10 patients who had liver metastases, 2 had simultaneous lung metastases. Nine patients had peritoneal dissemination. Five patients with stage IV had recurrent disease after primary surgery followed by adjuvant S-1. The other 18 patients had no history of surgery or chemotherapy. Response rate was 70% (CR/PR: 2/14). Among 12 patients (67%) who had conversion surgery, R0 resection was conducted in 8 and no residual tumor was observed in 2. Among enrolled 23 patients, median OS was 22 months (95%CI: $>$ 12 months) and 1-year OS rate was 81.8% (95%CI: 46.7% –95.5%). Grade 3/4 neutropenia in 5 (22%), no grade 3/4 thorombocytopenia, grade 2 peripheral sensory neuropathy in 6 (26%). **Conclusions:** The addition of itraconazole to chemotherapy showed promising efficacy with high conversion surgery rate and with acceptable toxicities. Clinical trial information: UMIN000021340.

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4027 **Poster Session (Board #132), Mon, 8:00 AM-11:00 AM**

A phase II trial of preoperative chemoradiotherapy and pembrolizumab for locally advanced esophageal squamous cell carcinoma (ESCC).

Min Hee Hong, HyeRyun Kim, Seong Yong Park, Dae Joon Kim, Chang Geol Lee, Jaeho Cho, Jong Hoon Kim, Hyeong Ryul Kim, Yong-Hee Kim, Sook Ryun Park, Byoung Chul Cho; Division of Medical Oncology, Department of Internal Medicine, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; Department of Thoracic and Cardiovascular Surgery, Yonsei University College of Medicine, Seoul, South Korea; Department of Radiation Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; Department of Radiation Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; Department of Thoracic and Cardiovasular Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

Background: Even though preoperative chemoradiotherapy (CRT) showed survival improvement in patients with resectable ESCC in a randomized trial over upfront surgery, ESCC still has a dismal prognosis. With the potential benefit of combining PD-1 blockade to CRT, we conducted a phase II trial which assessed the efficacy, feasibility, and safety of the combination of preoperative CRT and pembrolizumab (PEM) in ESCC. **Methods:** Patients (pts) with histologically confirmed ESCC (clinical stage Ib to III according to the American Joint Committee on Cancer 7^{th} staging system) were enrolled. Pts received concurrent neoadjuvant chemotherapy (weekly paclitaxel and carboplatin), radiotherapy (44.1 Gy in 21 fractions), and PEM (every 3 week, 200 mg) during 5 weeks followed by surgery. After surgery, pts were treated with PEM during 2 years or until progression, unacceptable toxicity, death, or pts' refusal, which came first. The primary endpoint was pathologic complete response (pCR) rate in the primary tumor and secondary endpoints were overall survival (OS), disease-free survival (DFS), the incidence of adverse events, and etc. **Results:** In a total of 28 enrolled pts (median age 60), 26 pts received esophagectomy. Two pts did not undergo surgery due to death (hematemesis) and consent withdrawal. There were two in-hospital mortality cases after surgery, which were resulted from acute lung injury. The pCR in primary tumor was achieved in 46.1% of pts who underwent resection (95% CI: 28.8 – 64.6). With a median follow-up of 11.7 months, median OS was not reached. Six-month and 12-month OS rates were 89.3% and 82.1%, respectively. There was a trend toward better DFS in the pCR group (n = 12) compared with the non-pCR group (n = 14) (HR = 0.33, p = 0.1). Most common treatment-related adverse events were neutropenia (50.0%) and liver enzyme elevation (30.8%) in the neoadjuvant and adjuvant period, respectively. **Conclusions:** The addition of PEM to preoperative CRT in ESCC demonstrated promising efficacy with acceptable toxicity. Based on the results, further investigation is warranted in a phase III clinical trial. The exploratory endpoints including biomarkers analyses are ongoing. Clinical trial information: NCT02844075.

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4028 **Poster Session (Board #133), Mon, 8:00 AM-11:00 AM**

Perioperative chemotherapy alone versus preoperative chemoradiotherapy for locally advanced distal esophageal and gastroesophageal junction cancer: A 10-year review of the British Columbia (BC) Cancer Registry.

Shiru Lucy Liu, Irene S. Yu, Sally CM Lau, Yizhou Zhao, Devin Schellenberg, Sharlene Gill, Howard John Lim; BC Cancer, Vancouver, BC, Canada; Princess Margaret Cancer Center, Toronto, ON, Canada; BC Cancer Surrey Centre, Surrey, BC, Canada; British Columbia Cancer Vancouver, Vancouver, BC, Canada

Background: The optimal treatment strategy for resectable cancer of the distal esophagus (ESOPH) and gastroesophageal junction (GEJ) remains controversial. This study evaluates patterns of practice in BC, rates of complete surgical resection, and survival outcomes of patients treated with perioperative chemotherapy alone (CA), per MAGIC or FLOT4 protocol, versus preoperative chemoradiotherapy (CRT), per CROSS protocol. **Methods:** We undertook a provincial analysis of initially resectable, locally advanced, cancer of the ESOPH and/or GEJ who underwent surgery in BC, from 2008 to 2018. Baseline patient, tumor, treatment, and clinical outcome data were collected from the BC Cancer Registry. Kaplan-Meier survival and multivariate regression analyses were conducted. **Results:** Among 575 patients, 468 underwent surgery and were included (Table). More surgeries were aborted intraoperatively in the CA cohort compared to CRT (12% vs 2%, $p<0.001$). There was no difference in age, sex, or ECOG performance status among the cohorts, and 83% were adenocarcinoma. While 82% of ESOPH involving GEJ (N = 251, 54%) is treated with CRT, only 53% of GEJ alone (N=217, 46%) is treated with CRT ($p<0.001$). CRT is associated with a higher rate of complete or partial pathologic response compared to CA (59% vs 39%, p=0.002). R0 resection rate was 90% and 94% in the CA and CRT cohort, respectively (p=0.383). There is no statistically significant difference in overall survival, with medians of 29.6 and 26.0 months for patients treated with CA and CRT, respectively (p=0.723). Cancer-specific survival is also not significantly different (p=0.565). In the CA cohort, 37% of patients complete all 8 cycles of FLOT and 52% of patients complete all 6 cycles of MAGIC (p=0.396). **Conclusions:** Patients treated with CRT have higher rates of complete resection and pathologic response, but their survival is not significantly different compared to those treated with CA.

	Total	Surgery attempted	Surgery completed	Pathologic response rate
CRT	420	322	316	156
CA	155	146	128	47
Total	575	468	444	203

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4029 **Poster Session (Board #134), Mon, 8:00 AM-11:00 AM**

Clinicopathological features of Epstein–Barr virus associated gastric carcinoma with submucosal invasion.

Hiroki Osumi, Hiroshi Kawachi, Toshiyuki Yoshio, Satoshi Ida, Yusuke Horiuchi, Akiyoshi Ishiyama, Toshiaki Hirasawa, Tomohiro Tsuchida, Noriko Yamamoto, Kensei Yamaguchi, Souya Nunobe, Kengo Takeuchi, Junko Fujisaki; Department of Gastroenterology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; Department of Pathology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; Department of Gastroenterological surgery, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan

Background: The incidence of lymph node metastasis (LNM) in pathological T1b (pT1b) gastric cancer (GC) is around 20% and the majority of them have no LNM. The Cancer Genome Atlas Research Network proposed the concept of molecular phenotype classifying GC into 4 phenotypes including Epstein-Barr virus-CIMP (EBV). EBV positive gastric cancer (EBVGC) is associated with a low prevalence of LNM; however, EBV status is not considered in the present indication of endoscopic resection (ER). We aimed to clarify the implication of EBV status for ER of pT1b GC. **Methods:** Consecutive cases of pT1b GCs treated with curative surgery between 2005 and 2014 were retrospectively analyzed. Tissue microarray was made and EBV-encoded RNA in situ hybridization was performed for evaluation of EBV status. Clinicopathological factors and LNM status were compared between EBVGC and non-EBVGC groups. **Results:** Among the 1221 pT1b GCs that underwent gastrectomy with regional lymph node dissection, 898 pT1bGCs were eligible in this study. EBVGC accounted for 7.9% (71 of 898) cases. Compared to non-EBVGC, EBVGC was more frequent in males ($p = 0.0055$), the upper third region ($p < 0.0001$), showed elevated growth features ($p = 0.0059$), and was associated with a lower frequency of accompanying ulceration ($p = 0.002$), greater depth of submucosal invasion ($p = 0.017$), and lower frequency of lymphatic invasion ($p < 0.0001$). Frequency of LNM was significantly lower in EBVGC than in non-EBVGC (4.2% vs. 21.9%, $p < 0.0001$). In EBVGC, tumors without lymphovascular invasion showed significantly lower frequency of LNM than those with lymphovascular invasion (0 of 50, 0%; vs 3 of 21, 14.3%; $p = 0.023$). Histologically, 84.5% (60 of 71) of EBVGC included carcinomas with lymphoid stroma and/or lace pattern components. **Conclusions:** pT1b EBVGC is a convincing candidate for ER, regardless of risk factors other than lymphovascular invasion.

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4030 **Poster Session (Board #135), Mon, 8:00 AM-11:00 AM**

A phase Ib study of IMU-131 HER2/neu peptide vaccine plus chemotherapy in patients with HER2/neu overexpressing metastatic or advanced adenocarcinoma of the stomach or gastroesophageal junction.

Yee Chao, Thomas Yau, Marina Maglakelidze, Iurie Bulat, Suebpong Tanasanvimon, Chaiyut Charoentum, Wichit Arpornwirat, Jedzada Maneechavakajorn, Arunee Dechaphunkul, Teerapat Ungtrakul, Chia-Jui Yen, Li-Yuan Bai, Wen-Chi Chou, Ursula Wiedermann, Anthony J Good, Nick Ede, Leslie Mi Ok Chong; Taipei Veterans General Hospital, Taipei, Taiwan; Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong, Hong Kong; ARENSIA Exploratory Medicine LLC, Tbilisi, Georgia; ARENSIA Exploratory Medicine Research Unit, Institute of Oncology, Chisinau, Moldova, The Republic of; King Chulalongkorn Memorial Hospital, Bangkok, Thailand; Maharaj Nakorn Chiang Mai Hospital, Mueang Chiang Mai District, Thailand; National Cancer Institute, Bangkok, Thailand; Rajavithi Hospital, Bangkok, Thailand; University of Alberta, Edmonton, AB, Canada; Faculty of Medicine and Public Health, HRH Princess Chulabhorn College of Medical Science, Bangkok, Thailand; National Cheng Kung University Hospital, Tainan, Taiwan; China Medical University Hospital, Taichung, Taiwan; Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan; Medical University Vienna, Vienna, Austria; Imugene, Sydney, Australia; Genentech, South San Francisco, CA

Background: Gastric cancer is the 5th most common cancer and the 3rd leading cause of cancer deaths. HER2/neu is overexpressed in 15% - 25% of patients with gastric cancer. Monoclonal antibodies against HER2/neu are effective but alternatives are needed due to cost and global availability. IMU-131 is a B-cell peptide vaccine composed of a fusion of 3 epitopes from the extracellular domain of HER2/neu conjugated to CRM197 with the adjuvant Montanide. Polyclonal antibodies against IMU-131 peptides elicit antitumor activity in vitro and a phase I study demonstrated safety and immunogenicity in Her-2 +/++ breast cancer patients. **Methods:** IMU-131 was given to patients with HER2/neu overexpressing gastric or gastroesophageal junction (GEJ) adenocarcinoma in an international open-label Phase 1b dose escalation trial performed in 14 Asian and Eastern European sites assessing safety, tolerability, and immunogenicity. Each patient received IMU-131 on Days 0, 14, and 35, accompanied by cisplatin and 5-fluorouracil or capecitabine every 21 days. **Results:** 14 patients were enrolled with advanced stage IIIb or IV with 10 HER2 overexpressing tumors (7 x HER2+++, 3 x HER2++ FISH positive) and 4 HER2++ expressing tumors. Mean age was 57 yo (range of 21 - 79) with ECOG scores of 0 or 1 in 7 patients each. There were 9 Asian and 5 Caucasian patients with 5 females and 9 males. Dose levels were 0.1, 0.3 and 0.5 mg with 3, 6, and 5 patients receiving those dose levels each. 11 patients received all 3 doses with 3 patients who received only 2 doses due to disease progression and 2 patients received a dose on day 182. Of the 14 patients dosed 11 were evaluable for tumor progression at day 56 and later. Of those patients, the best response was 1 CR, 4 PR,5 SD and 1 PD. In the 0.1 mg dose group the best response was 1 CR and 2 SD, with 2 PR, 2 SD and 1 PD in the 0.3 mg group and 2 PR and 1 SD in the 0.5 mg group. In patients with HER2 overexpression there was 1 CR, 4 PR, 2 SD and 1 PD, and in patients with HER2++ expression there was 3 SD. There were no SAEs related to IMU-131 and 1 patient had a mild injection site reaction. **Conclusions:** IMU-131 is a promising B-Cell vaccine against HER2. Further work in a controlled phase 2 trial is ongoing. Clinical trial information: NCT02795988.

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4031 **Poster Session (Board #136), Mon, 8:00 AM-11:00 AM**

Camrelizumab combined with capecitabine and oxaliplatin followed by camrelizumab and apatinib as first-line therapy for advanced or metastatic gastric or gastroesophageal junction cancer: Updated results from a multicenter, open label phase II trial.

Lin Shen, Zhi Peng, Yan-Qiao Zhang, Jia Wei, Feng Wang, Jieer Ying, Yanhong Deng, Kangsheng Gu, Ying Cheng, Xianglin Yuan, Juxiang Xiao, Linna Wang, Jianjun Zou; Beijing Cancer Hospital, Beijing, China; Department of Gastrointestinal Oncology, Peking University Cancer Hospital & Institute, Beijing, China; Department of Gastrointestinal Medical Oncology, Harbin Tumor Hospital, Harbin, China; The Comprehensive Cancer Centre of Drum Tower Hospital, Medical School of Nanjing University & Clinical Cancer Institute of Nanjing University, Nanjing, China; Department of Oncology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; Department of Medical Oncology, Zhejiang Cancer Hospital, Hangzhou, China; Department of Medical Oncology, The Sixth affiliated hospital of Sun Yat-Sen University, Guangzhou, China; Department of Oncology, The First Affiliated Hospital of Anhui Medical University, He Fei, China; Department of Oncology, Jilin Province Cancer Hospital, Changchun, China; Department of Cancer, Tongji Hospital of Tongji Medical College, Huazhong University of Science & Technology, Wuhan, China; Department of Oncology, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China; Jiangsu Hengrui Medicine Co. Ltd, Shanghai, China

Background: Capecitabine plus oxaliplatin (CAPOX) is one of the standard first-line treatments for advanced or metastatic gastric cancer. Camrelizumab (SHR-1210, an anti–PD-1 antibody) shows promising anti-tumor activity in patients (pts) with advanced or metastatic gastric or gastroesophageal junction (G/GEJ) cancer. Camrelizumab combined with CAPOX for untreated G/GEJ cancer was assessed as a part of an ongoing multicenter, open-label phase 2 trial (cohort 1), and encouraging preliminary results were reported. Here, we present the updated safety and efficacy data. **Methods:** In this cohort, systemic treatment naïve pts with $HER2^-$ advanced or metastatic G/GEJ adenocarcinoma were given camrelizumab 200 mg on Day 1, capecitabine 1000 mg/m^2 bid on Days 1–14 and oxaliplatin 130 mg/m^2 on Day 1 of each 21-day-cycle for 4 to 6 cycles followed by camrelizumab 200 mg every 3 weeks plus apatinib 375 mg qd until disease progression or intolerable toxicity. The primary endpoint was objective response rate. **Results:** At data cutoff (Jan 20, 2019), 43 of the 48 enrolled pts were evaluable. Partial response was observed in 28 pts (65%), and 19 (44%) were confirmed. Stable disease in 14 pts and progressive disease in 10 pts were reported. Median estimates for duration of response and progression-free survival were not reached. Grade ≥3 treatment-related adverse events (TRAEs) occurred in 9 pts (21%), included neutropenia, diarrhea, rash and elevated ALT, whereas none of the TRAEs was fatal. Ten pts without progression after 4–6 cycles of camrelizumab and CAPOX combination therapy all received camrelizumab plus apatinib as sequential therapy, and no new safety signals were observed. **Conclusions:** The updated results confirmed that camrelizumab plus CAPOX followed by camrelizumab plus apatinib was well tolerated with noteworthy responses as first-line therapy in advanced or metastatic G/GEJ cancer pts. Expansion of this cohort in a phase 3 study are under way. Clinical trial information: NCT03472365.

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4032 **Poster Session (Board #137), Mon, 8:00 AM-11:00 AM**

Pembrolizumab in previously treated metastatic esophageal cancer: Longer term follow-up from the phase 2 KEYNOTE-180 Study.

Ken Kato, Takashi Kojima, Daniel Hochhauser, Jaafar Bennouna, Antoine Hollebecque, Florian Lordick, Sung-Bae Kim, Masahiro Tajika, Heung Tae Kim, Haeseong Park, Nabil F. Saba, Susan Urba, Anjali Desai, Qi Liu, Sandra Cruz, Manish A. Shah; Department of Gastrointestinal Medical Oncology, National Cancer Center Hospital, Tokyo, Japan; National Cancer Center Hospital East, Kashiwa, Japan; University College London Cancer Institute, London, United Kingdom; Institut de Cancérologie de l'Ouest, Nantes, France; Gustave Roussy, Villejuif, France; University Cancer Center Leipzig, Leipzig, Germany; Asan Medical Center, Seoul, South Korea; Department of Endoscopy, Aichi Cancer Center Hospital, Nagoya, Japan; National Cancer Center, Goyang, South Korea; Washington University School of Medicine, St. Louis, MO; Winship Cancer Institute of Emory University, Atlanta, GA; University of Michigan Cancer Center, Ann Arbor, MI; Merck & Co., Inc., (under contract with Execupharm, King of Prussia, PA, USA), Kenilworth, NJ; Merck & Co., Inc., Kenilworth, NJ; Weill Cornell Medicine, New York-Presbyterian Hospital, New York, NY

Background: In the phase 2, open-label, KEYNOTE-180 (NCT02559687) study, after a median follow-up of 5.8 months, pembrolizumab (pembro) provided antitumor activity with durable responses in pts with previously treated, advanced/metastatic adenocarcinoma (EAC) including Siewert type 1 adenocarcinoma of the gastroesophageal junction or squamous cell carcinoma (ESCC) of the esophagus. Here we present results of an additional 10 months of follow-up. **Methods:** Eligible pts with metastatic esophageal cancer, ≥2 prior lines of therapy, and tumor samples evaluable for biomarker expression, received pembro 200 mg Q3W for up to 2 years, or until disease progression, unacceptable toxicity, or withdrawal. Tumor response was assessed Q9W (RECISTv1.1, central review). PD-L1+ pts had combined positive score ≥10 using IHC (22C3 antibody). Primary endpoint was objective response rate (ORR). Secondary endpoints included safety, DOR, PFS, and OS. **Results:** Of 121 pts enrolled, 63 (52%) had ESCC and 58 (48%) had PD-L1+ (combined positive score ≥10) tumors. As of July 30, 2018, median follow-up duration, from randomization to data cutoff, was 5.8 mo (range, 0.2 mo to 27.8+ mo). ORR (CR+PR) was 10% (95% CI, 5%-17%); 2 (2%) CR,10 (8%) PR, 25 (21%) SD. Median DOR was not reached ([NR] range, 2.1 mo to 25.1+ mo). Median PFS was 2 mo (95% CI, 1.9%-2.1%) with 9-mo PFS rate of 9%. Median OS was 5.8 mo (4.5-7.2) with 12 mo OS rate of 27%. In ESCC, ORR was 14% (95% CI, 7%-25%); 2 (3%) CR, 7 (11%) PR, with median DOR NR (range, 4.2 mo to 25.1+ mo). In EAC, ORR was 5% (95% CI, 1-14); 3 PR, with median DOR NR (range, 2.1 mo to 15.6+ mo). In PD-L1+ pts, ORR was 14% (95% CI, 6%-25%); 1 (2%) CR, 7 (12%) PR with median DOR NR (range, 4.2 mo to 25.1+ mo). In PD-L1- pts ORR was 6% (95% CI, 2%-16%); 1 (2%) CR, 3 (5%) PR; median DOR NR (range, 2.1 mo to 17.3+ mo). Overall, 19 (16%) pts had treatment-related grade 3-5 AEs. Seven (6%) pts discontinued due to a treatment-related AE. There was one treatment-related death from pneumonitis. **Conclusions:** Pembro continued to provide durable clinical benefit with a manageable safety profile for pts with heavily pretreated esophageal cancer, with conversions of PR to CR observed. Clinical trial information: NCT02559687.

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4033 **Poster Session (Board #138), Mon, 8:00 AM-11:00 AM**

Phase 2 study of camrelizumab (anti-PD-1 antibody) combined with apatinib and chemotherapy for the first-line treatment of advanced esophageal squamous cell carcinoma.

Bo Zhang, Ling Qi, Xi Wang, Jun Jiang, Xin Zhang, Yun Liu, Lan Mu, Jing Huang; Department of Medical Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; Department of Diagnostic Radiology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Background: Both anti-PD-1 antibodies and molecular antiangiogenic agents have shown promising anti-tumor activities in patients with advanced esophageal cancer. We conducted this single-center phase 2 study to evaluate the efficacy and safety of camrelizumab (anti-PD-1 antibody) plus apatinib (VEGFR2-TKI) in combination with liposomal paclitaxel and nedaplatin in the first-line treatment of patients with esophageal squamous cell carcinoma (ESCC). **Methods:** Patients with unresectable locally advanced or metastatic ESCC received camrelizumab 200mg d1, liposomal paclitaxel 150mg/m^2 d1, nedaplatin 50mg/m^2 d1 and apatinib 250mg d1-14. Treatments were repeated every 14 days for up to 6-9 cycles, followed by maintenance therapy with camrelizumab, apatinib, or both. The primary end point was progression-free survival (PFS) in the intention-to-treat population. Secondary end points included objective response rate (ORR), disease control rate (DCR), overall survival (OS) and safety. PD-L1 positivity, defined as a combined positive score (CPS) $\geq$1, was evaluated by immunohistochemistry (IHC). **Results:** Between Aug 6th 2018 and Feb 6th 2019, a total of 29 patients were enrolled. The median age was 62 years (43-70). Most patients were male (22/29, 75.9%) with metastatic disease (25/29, 86.2%). Response evaluation by independent central review was available in 26 patients, with 19 achieving a best response of PR, 6 with SD, and 1 with PD. The ORR and DCR were 73.1% (19/26) and 96.2% (25/26), respectively. Data for PFS and OS were not matured. The most common grade 3/4 adverse events were leucopenia (21/29, 72.4%) and neutropenia (15/29, 51.7%). Two cases of treatment-related SAEs occurred, both led to hospitalization: one patient developed grade 3 febrile neutropenia, grade 4 leucopenia and grade 3 anorexia; another patient developed grade 4 toxic epidermal necrolysis. **Conclusions:** Camrelizumab plus apatinib in combination with liposomal paclitaxel and nedaplatin could be a new treatment option for patients with unresectable locally advanced or metastatic ESCC. Clinical trial information: NCT03603756.

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4034 **Poster Session (Board #139), Mon, 8:00 AM-11:00 AM**

Prognostic value of serum soluble programmed death-ligand 1 (sPDL1) and dynamics during chemotherapy in advanced gastric cancer patients.

Woochan Park, Ju-Hee Bang, Ah-Rong Nam, Ji Eun Park, Mei Hua Kim, Kyoung Seok Oh, Yung-Jue Bang, Do-Youn Oh; Seoul National University Hospital, Seoul, South Korea; Cancer Research Institute, Seoul National University College of Medicine, Seoul, South Korea; Seoul National University College of Medicine, Seoul, South Korea; Cancer Research Institute, Seoul National University College of Medicine, Seoul, Korea, Seoul, South Korea; Seoul National University Hospital, Seoul National University College of Medicine, Seoul, South Korea

Background: The soluble form Programmed Death-Ligand 1(sPDL1) is suggested to have immunosuppressive activity and under investigation as candidate biomarker for immuno-oncology drug development. In this study, we measured the serum sPDL1 at pre-and post-chemotherapy and evaluated its prognostic implication and dynamics during chemotherapy in advanced gastric cancer (GC). **Methods:** We prospectively enrolled 68 GC patients who were candidates for palliative standard 1st-line chemotherapy, and blood was serially collected at pre-and post-one cycle of chemotherapy, at best response and disease progression. sPDL1 was measured using an enzyme-linked immunosorbent assay. Response to chemotherapy, overall survival (OS), progression-free survival (PFS) and other prognostic factors including neutrophil-lymphocyte ratio (NLR) were obtained. The cut-off values of sPDL1 levels and changes for survivals were found using C-statistics. **Results:** The median baseline sPDL1 was 0.8ng/mL(range, 0.06 - 6.06ng/mL). The median OS and PFS were 14.9 months (95% CI: 7.33-22.47) and 8.0 months (95% CI: 5.96-10.0), respectively. sPDL1 and NLR showed a positive correlation. Patients with low levels of sPD-L1 at diagnosis ($<$ 1.92 ng/mL) showed a better OS and PFS than the patients with a high sPDL1 (OS: 18.3 vs. 95 months, P = 0.057, PFS: 8.9 vs. 6.0 months, P = 0.04). The baseline sPDL1 before treatment were higher in the PD group than in the SD and PR groups (mean:2.91, 1.17, 1.19, P = 0.019). Patients whose sPDL1 increased after 1st cycle of chemotherapy showed the tendency of worse PFS and OS. When disease progressed, sPDL1 increased compared with baseline (mean:1.31, 1.45, P = 0.029). **Conclusions:** sPDL1 at pre-chemotherapy confers the prognostic value for PFS and OS in GC patients under palliative 1st-line chemotherapy. The dynamics of sPDL1 during chemotherapy correlates with disease courses.

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4035 **Poster Session (Board #140), Mon, 8:00 AM-11:00 AM**

POF (paclitaxel plus FOLFOX) versus IP PAC (intraperitoneal paclitaxel plus FOLFOX) versus FOLFOX as a first-line treatment in advanced gastric cancer (AGC): Update from a multicenter, randomized phase II trial, FNF-004 trial.

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Background: The PFS with POF was statistically significantly improved and IP PAC was trending to improve compared to FOLFOX in first-line setting in AGC were reported in 2019 ASCO-GI (abstract 6). Update and subgroup analysis were released herein. **Methods:** The patients with AGC were randomized to three groups. The POF or IP PAC was paclitaxel 135 mg/m^{2}intravenously (POF) or paclitaxel 80 mg/m^2 intraperitoneally (IP PAC) followed by mFOLFOX6 omitted 5-Fu bolus. Every 14 days repeated for all three regimens. Up to 9 cycles of treatment were administered, followed by S-1 until disease progression. The primary endpoint was PFS. **Results:** Between Nov 2015 and May 2018, 89 pts (30 POF, 29 IP PAC, 30 FOLFOX) were randomly allocated. PFS, OS and RR were seen in the table below. Either POF or IP PAC was statistically significantly better than FOLFOX in PFS. In subgroup with female, peritoneal metastasis, ascites, lymphadenopathy in peritoneal cavity, number of organs involved > 2, POF was statistically significantly better than FOLFOX in PFS. In subgroup with female, gastrium of primary tumor site, peritoneal metastasis, ascites, no lymphadenopathy out of peritoneal cavity, IP PAC was statistically significantly better than FOLFOX in PFS. Intravenously docetaxel plus S-1 still saw response after IP PAC. **Conclusions:** either POF or IP PAC improved survival compared to FOLFOX, especially in patients with female or peritoneum metastasis. Only POF, not IP PAC, improved response rate compared to FOLFOX. Clinical trial information: NCT02845908.

	POF (n=30)	IP PAC (n=29)	FOLFOX (n=30)	P value (HR, 95%CI)	
				POF vs FOLFOX	IP PAC vs FOLFOX
PFS (m, 95% CI)	6.148 (3.898 -8.398)	6.214 (4.191–8.237)	4.405 (1.803–7.008)	0.042 (0.603, 0.354-1.026)	0.027 (0.510, 0.291-0.894)
OS (m, 95% CI)	9.534 (8.034-11.034)	10.882 (8.839 - 12.925)	6.641 (4.788 - 8.494)	0.180 (0.679, 0.386-1.195)	0.094 (0.598, 0.332-1.077)
CR (n, %)	4 (13.3%)	2 (6.9%)	2 (6.7%)		
PR (n, %)	13 (43.3%)	9 (31.0%)	9 (30.0%)		
RR (n, %)	17 (56.7%)	11(37.9%)	11(36.6%)	0.121	0.920
SD (n, %)	9 (30.0%)	12 (41.4%)	12 (40%)		
PD (n, %)	4 (13.3%)	6 (20.7%)	7 (23.3%)		

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4036 **Poster Session (Board #141), Mon, 8:00 AM-11:00 AM**

Association of frequent amplification of chromosome 11q13 in esophageal squamous cell cancer with clinical benefit to immune check point blockade.

Feng Wang, Chao Ren, Qi Zhao, Nong Xu, Lin Shen, Guanghai Dai, Xianglin Yuan, Ye Chen, Shujun Yang, Jianhua Shi, Xichun Hu, Xiaoyan Lin, Qingyuan Zhang, Jifeng Feng, Yi Ba, Yunpeng Liu, Wei Li, Yongqian Shu, Fenghua Wang, Rui-hua Xu, Shanghai Junshi Biosciences Co., LTD; Sun Yat-sen University Cancer Center, Guangzhou, China; Sun Yat-Sen University Cancer Center, Guangzhou, China; The First Affiliated Hospital, Zhejiang University, Hangzhou, China; Department of Gastrointestinal Oncology, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital and Institute, Beijing, China; Chinese People's Liberation Army (PLA) General Hospital, Beijing, China; Department of Oncology, Tongji Hospital, Huazhong University of Science and Technology, Wuhan, China; West China Hospital, Sichuan University, Chengdu, China; Henan Cancer Hospital, Zhengzhou, China; Linyi Tumor Hospital, Linyi, China; Fudan University Shanghai Cancer Center, Shanghai, China; Fujian Medical University Union Hospital, Fuzhou, China; Harbin Medical University Cancer Hospital, Harbin, China; Jiangsu Cancer Hospital, Nanjing, China; Department of digestive oncology, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; Department of Medical Oncology, the First Hospital of China Medical University, Shenyang, China; The Cancer Center, The First Hospital of Jilin University, Jilin, China; Jiangsu Province Hospital, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China

Background: Esophageal squamous cell carcinoma (ESCC) is the predominant histological subtype of esophageal cancer in South America and East Asian countries and remains an unmet medical need worldwide. Previous studies have shown the efficacy of programmed cell death 1 (PD-1) targeted therapy in a subset of patients with metastatic ESCC. However, robust predictive biomarkers to PD-1 antibody-based immunotherapy remain undefined. **Methods:** Patients included in this analysis were part of multi-center, phase Ib/II trial (NCT02915432) evaluating the safety and activity of toripalimab, a humanized PD-1 antibody in solid tumors. To identify molecular determinants of response, we performed whole exome sequencing (WES), messenger RNA sequencing and immunohistochemistry on patients' samples and evaluated genomic and transcriptional biomarkers, PD-L1 expression and tumor mutational burden (TMB) for correlation with clinical efficacy. **Results:** Sixty advanced chemo-refractory ESCC patients were enrolled and 59 were treated with toripalimab. 94.9% (56/59) patients experienced at least one treatment related adverse event after 16 months; mostly grade 1 or grade 2. Treatment-related grade 3 or higher AEs occurred in 30.5% (18/59) of subjects. By the data cutoff date, 11 (18.6%; 95%CI 9.7 to 30.9) patients achieved an objective response, while the disease control rate was 47.5% (95%CI 34.3 to 60.9). Copy number analysis identified 24 out of 50 (48%) patients with amplifications of chromosome 11q13 region, which was consistent with elevated mRNA expression of amplified genes, including *CCND1*(Cyclin D1) and fibroblast growth factor family members (*FGF3/4/19*). Patients without 11q13 amplification, had significantly better objective response rate (ORR 30.8% versus 4.2%, p= 0.024) and progression free survival (3.7 versus 2.0 months, HR = 0.47 [95%CI 0.24 to 0.91], p= 0.025) when compared with 11q13 amplified individuals. In contrast, patients with high TMB (≥12 Mutations/Mb; 11/47, 23.4%) or positive PD-L1 expression (TC or IC 1%; 19/57, 33.3%) showed no significant advantage in ORR or survival. **Conclusions:** Toripalimab has demonstrated a manageablesafety profile and promising anti-tumor activity in chemo-refractory ESSC patients. Genomic amplification of 11q13 region may serve as a negative predictive marker for advanced ESSC patients receiving anti-PD-1 based immunotherapy. Further interrogation of putative resistance genes that lie within this region is under study. Clinical trial information: NCT02915432.

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4037 **Poster Session (Board #142), Mon, 8:00 AM-11:00 AM**

Trifluridine/tipiracil (FTD/TPI) in patients (pts) aged ≥65 years with metastatic gastric/gastroesophageal junction cancer (mGC/mGEJC): Subgroup analysis from TAGS.

Kohei Shitara, Toshihiko Doi, Hisashi Hosaka, Peter C. Thuss-Patience, Armando Santoro, Paula Jiménez-Fonseca, Federico Longo, Ozgur Ozyilkan, Irfan Cicin, David Park, Mohamedtaki Abdulaziz Tejani, Aziz Zaanan, Domenico Bilancia, Carles Pericay, Mustafa Ozguroglu, MARIA ALSINA, Lukas Makris, Sandra McGuigan, David H. Ilson; National Cancer Center Hospital East, Chiba, Japan; Gunma Prefectural Cancer Center, Gunnma, Japan; Charité–University Medicine Berlin, Department of Haematology, Oncology and Tumorimmunology, Berlin, Germany; Humanitas Research Hospital, Rozzano (MI), Italy; Hospital Universitario Central de Asturias, Asturias, Spain; Hospital Universitario Ramon y Cajal, Madrid, Spain; Baskent University Adana Practice and Research Centre Kisla, Adana, Turkey; Trakya Universitesi, Edirne, Turkey; St Jude Crosson Cancer Institute/St Joseph Heritage Healthcare, Fullerton, CA; University of Rochester Medical Center, Rochester, NY; AP-HP–Hôpitaux Universitaires Paris Ouest, Paris, France; Azienda Ospedaliera Regionale–Potenza, Potenza, Italy; Corporación Sanitaria Parc Tauli, Barcelona, Spain; Istanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine, Istanbul, Turkey; Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; Stathmi, Inc,, New Hope, PA; Taiho Oncology, Princeton, NJ; Memorial Sloan Kettering Cancer Center, New York, NY

Background: 60% of newly diagnosed GC pts are > 65 y of age, a proportion that is increasing. The global phase 3 study TAGS (NCT02500043) demonstrated the efficacy and safety of FTD/TPI in previously treated pts with mGC/mGEJC. Here we report results in the pt subgroup aged ≥65 in TAGS. **Methods:** Pts with mGC/mGEJC treated with ≥2 prior chemotherapy regimens were randomized (2:1) to receive FTD/TPI (35 mg/m^2 BID on days 1–5 and 8–12 of each 28-day cycle) or placebo, plus best supportive care. A preplanned efficacy/safety analysis was performed in pts aged ≥65 y. **Results:** Of 507 randomized pts, 228 (45%) were aged ≥65 y (range 65–89). The pt subset aged ≥65 y was similar to the overall population, except for a higher incidence of moderate renal impairment in the elderly subgroup (31% vs 17%). For pts aged ≥65 y, baseline characteristics were generally balanced across the treatment groups, although more pts treated with FTD/TPI than with placebo had ECOG PS 1 (69% vs 59%). FTD/TPI had an efficacy benefit in pts aged ≥65 y, and the FTD/TPI safety profile was similar in this subgroup vs the overall population (table). Treatment-related deaths (one in each treatment group) did not occur in pts aged ≥65 y. No drug-related deaths associated with cardiotoxicity were reported in pts aged ≥65 y. Although dose modifications were used more often in this subgroup, there was no increase in discontinuations vs the overall population. **Conclusions:** FTD/TPI was safe and effective in pts aged ≥65 y, who had a higher incidence of moderate renal impairment vs the overall population. Clinical trial information: NCT02500043.

	Overall population[1]		Age ≥65 y	
	FTD/TPI	Placebo	FTD/TPI	Placebo
ITT population, n	337	170	154	74
Median OS, mo	5.7	3.6	6.2	5.4
HR (95% CI)	0.69 (0.56–0.85)		0.73 (0.52–1.02)	
Median PFS, mo	2.0	1.8	2.2	1.8
HR (95% CI)	0.57 (0.47–0.70)		0.44 (0.32–0.61)	
Safety population, n	335	168	153	72
Grade ≥3 AEs of any cause, %				
Any	80	58	80	51
Most common[a]				
Neutropenia[b]	34	0	40	0
Anemia[c]	19	8	18	8
Actions taken for any-cause/grade AEs, %				
Dose modification	58	22	61	22
Treatment discontinuation	13	17	12	14

[a]Occurring in ≥10% of pts in any group. [b]Includes decreased neutrophil count. [c]Includes decreased hemoglobin level. 1. Shitara K, et al. *Lancet Oncol* 2018.

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Trifluridine/tipiracil (FTD/TPI) in patients (pts) with metastatic gastroesophageal junction cancer (mGEJC): Subgroup analysis from TAGS.

Wasat Mansoor, Hendrik-Tobias Arkenau, MARIA ALSINA, Kohei Shitara, Mohamedtaki Abdulaziz Tejani, Peter C. Thuss-Patience, Sinead Cuffe, Mikhail Dvorkin, David Park, Takayuki Ando, Marc Van Den Eynde, Giordano D. Beretta, Alberto Zaniboni, Toshihiko Doi, Josep Tabernero, David H. Ilson, Lukas Makris, Sandra McGuigan, Eric Van Cutsem; Christie NHS, Manchester, United Kingdom; Sarah Cannon Research Institute, Cancer Institute, University College London, London, United Kingdom; Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; National Cancer Center Hospital East, Chiba, Japan; University of Rochester Medical Center, Rochester, NY; Charité–University Medicine Berlin, Department of Haematology, Oncology and Tumorimmunology, Berlin, Germany; St. James's Hospital, Dublin, Ireland; Omsk Regional Clinical Centre of Oncology, Omsk, Russia; St Jude Crosson Cancer Institute/St Joseph Heritage Healthcare, Fullerton, CA; Third Department of Internal Medicine, University of Toyama, Toyama, Japan; Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium; Humanitas Gavazzeni, Bergamo, Italy; Fondazione Poliambulanza–Istituto Ospedaliero, Brescia, Italy; Memorial Sloan Kettering Cancer Center, New York, NY; Stathmi, Inc,, New Hope, PA; Taiho Oncology, Princeton, NJ; University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium

Background: The incidence of GEJC is increasing in North America and Europe, especially among white men. Many pts present with metastatic disease or relapse locally or systemically after resection of early-stage disease. The global phase 3 study TAGS (NCT02500043) demonstrated the efficacy and safety of FTD/TPI in previously treated pts with metastatic gastric cancer (mGC)/mGEJC. Here we report results in the mGEJC subgroup from TAGS. **Methods:** Pts with mGC/mGEJC treated with ≥2 prior chemotherapy regimens were randomized (2:1) to receive FTD/TPI (35 mg/m^2 BID on days 1–5 and 8–12 of each 28-day cycle) or placebo, plus best supportive care. A preplanned efficacy and safety analysis was performed in pts with mGEJC. **Results:** Of 507 randomized pts, 145 (29%) had GEJC as the sole primary disease site (FTD/TPI, 98/337; placebo, 47/170). Of pts with mGEJC, 85% were male and 83% were white (overall population, 73% and 70%). Baseline characteristics were generally balanced for pts with mGEJC across treatment groups, except for fewer pts having prior gastrectomy (40% vs 55%) and more pts having received ≥3 prior regimens (74% vs 66%) in the FTD/TPI group than in the placebo group. FTD/TPI had an efficacy benefit in pts with mGEJC, and the FTD/TPI safety profile was similar in this subgroup and the overall population (table). **Conclusions:** FTD/TPI showed a manageable safety profile and efficacy benefit in pts with mGEJC in the TAGS trial, despite heavier pretreatment of the FTD/TPI than the placebo group. Clinical trial information: NCT02500043.

	Overall population[1]		mGEJC	
	FTD/TPI	Placebo	FTD/TPI	Placebo
ITT population, n	337	170	98	47
Median OS, mo	5.7	3.6	4.8	3.5
HR (95% CI)	0.69 (0.56–0.85)		0.75 (0.50–1.11)	
Median PFS, mo	2.0	1.8	1.9	1.8
HR (95% CI)	0.57 (0.47–0.70)		0.60 (0.41–0.88)	
Safety population, n	335	168	97	46
Grade ≥3 AEs of any cause, %				
Any	80	58	77	59
Most common[a]				
Neutropenia[b]	34	0	25	0
Anemia[c]	19	8	13	4
Fatigue	7	6	10	0
Abdominal pain	4	9	4	15
AEs of any grade or cause, %				
Leading to dosing modification	58	22	54	24
Leading to treatment discontinuation	13	17	9	11

[a]Occurring in ≥10% of pts in any group. [b]Includes decreased neutrophil count. [c]Includes decreased hemoglobin level. 1. Shitara K, et al. *Lancet Oncol* 2018.

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4039 **Poster Session (Board #144), Mon, 8:00 AM-11:00 AM**

Pooled safety analysis from phase 3 studies of trifluridine/tipiracil (FTD/TPI) in patients (pts) with metastatic gastric/gastroesophageal junction cancer (mGC/mGEJC) and metastatic colorectal cancer (mCRC).

Eric Van Cutsem, Howard S. Hochster, Kohei Shitara, Robert J. Mayer, Atsushi Ohtsu, Alfredo Falcone, Takayuki Yoshino, Toshihiko Doi, David H. Ilson, Hendrik-Tobias Arkenau, Ben George, Sandra McGuigan, Lukas Makris, Josep Tabernero; University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium; Rutgers Cancer Institute, New Brunswick, NJ; National Cancer Center Hospital East, Chiba, Japan; Dana-Farber Cancer Institute, Boston, MA; Azienda Ospedaliero Universitaria Pisana, Pisa, Italy; National Cancer Center Hospital East, Kashiwa, Japan; Memorial Sloan Kettering Cancer Center, New York, NY; Sarah Cannon Research Institute, Cancer Institute, University College London, London, United Kingdom; Medical College of Wisconsin, Milwaukee, WI; Taiho Oncology, Princeton, NJ; Stathmi, Inc,, New Hope, PA; Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain

Background: FTD/TPI was approved in 2015 for pretreated pts with mCRC based on the phase 3 RECOURSE trial. FTD/TPI recently demonstrating significantly improved overall survival vs placebo in pretreated pts with mGC/mGEJC in the phase 3 TAGS trial. **Methods:** We evaluated the pooled safety of FTD/TPI in TAGS and RECOURSE in all pts who received ≥1 dose of FTD/TPI (safety population). Pts were required to have ECOG PS 0/1 and to have received ≥2 previous chemotherapy lines. **Results:** FTD/TPI and placebo were administered to 335 and 168 pts, respectively, in TAGS, and 533 and 265 pts in RECOURSE. Baseline characteristics were balanced across treatment groups and reflected the disease populations. In the pooled population, 66% of pts were men and 75% had received ≥3 prior systemic treatments. The safety profile of FTD/TPI was comparable between studies (table). In TAGS and RECOURSE, the most common any-cause grade (gr) ≥3 AEs in FTD/TPI-treated pts were neutropenia (34%; 35%), anemia (19%; 17%), and leukopenia (9%; 13%). Gr ≥3 febrile neutropenia occurred in 2% and 4% of pts and gr ≥3 GI AEs in 21% and 12%. Gr ≥3 cardiac AEs were reported in 1% of FTD/TPI-treated pts (both studies), in contrast to results obtained with other third-line agents. Similar proportions of FTD/TPI-treated pts in both studies had AEs leading to dosing delay, dose reduction, or treatment discontinuation. Dosing delay was used more often than dose reduction to manage AEs. TRAEs leading to death occurred in one FTD/TPI-treated pt (< 1%) in each trial. **Conclusions:** In a pooled analysis, FTD/TPI was well tolerated with a consistent safety profile in pts with mGC/mGEJC or mCRC. The most frequent AEs were hematologic and GI, which were managed with dosing delays/dose reductions. Clinical trial information: NCT02500043; NCT01607957.

	TAGS (mGC/mGEJC)				RECOURSE (mCRC)			
	FTD/TPI (n = 335)		Placebo (n = 168)		FTD/TPI (n = 533)		Placebo (n = 265)	
	Any gr, %	Gr ≥3, %	Any gr, %	Gr ≥3, %	Any gr, %	Gr ≥3, %	Any gr, %	Gr ≥3, %
Any-cause AEs	97	80	93	58	98	69	93	52
TRAEs	81	53	57	13	86	49	55	10
Actions taken for any-cause AEs								
Dosing delay	57	41	21	16	52	35	13	8
Dose reduction	11	7	1	1	14	12	1	1
Treatment discontinuation	13	11	17	12	10	8	14	11

TRAEs, treatment-related AEs.

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4040 **Poster Session (Board #145), Mon, 8:00 AM-11:00 AM**

Homologous recombination deficiency as prognostic marker in metastatic gastric cancer.

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Background: Gastric cancer is the 5th cancer diagnosis and 3rd cause of cancer death worldwide. Metastatic gastric cancer (mGC) has a median survival of 11 months. mGC is an heterogeneous disease and different biologic characteristics may justify differential therapeutic opportunities. Tumors with homologous recombination (HR) deficiency may benefit with treatment with PARP inhibitors or immune checkpoint inhibitors. The purpose of this study was to evaluate the prevalence and prognostic impact of altered expression of HR proteins as surrogates for homologous recombination deficiency (HRD) in mGC. **Methods:** Multicenter retrospective cohort of mGC treated with platinum-based chemotherapy. HRD defined as absence of at least one of the following proteins: ATM, ATR, CHK2, RAD51, RAD52, BRCA1, BRCA2, MRE11 by immunohistochemistry. Survival time calculated as the difference between first cycle of platinum-based chemotherapy and death or last observation. Association between HRD and survival examined with log-rank test. **Results:** 440 patients included, of which 70% male, with mean age of 58 years (SD: 11). 75% of patients had mGC at diagnosis, 43% had 2 or more organs involved and 63% were registered as ECOG 0 or 1 at the start of first line chemotherapy. The most common histologic subtype was tubular adenocarcinoma (44%) followed by diffuse carcinoma (32%). HRD was noted in 196 (45%) cases (95%CI: 40%-49%). The most commonly altered proteins were ATM (21%) and BRCA2 (18%). In HRD tumors, 99 (51%) had altered expression of only one HR protein; 47 (24%) had altered expression of two HR proteins; the remaining cases had altered expression of 3 or more proteins. After a median follow up of 11 months, median survival for the cohort was 11 months (95% CI 9-12). HRD was associated with an improved survival, HR = 0.61 (95%CI: 0.48-0.78, $p < 0.001$), that remained significant after adjustment for sex, age, performance status and disease status (HR = 0.63; 95%CI: 0.48-0.82; $p < 0.001$). **Conclusions:** HRD phenotype was present in 45% of mGC cases and is associated with improved prognosis for mGC treated with platinum-based first line chemotherapy.

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4041 **Poster Session (Board #146), Mon, 8:00 AM-11:00 AM**

Safety of neoadjuvant chemoradiation (CRT) in combination with avelumab (A) in the treatment of resectable esophageal and gastroesophageal junction (E/GEJ) cancer.

Nataliya Volodymyrivna Uboha, James D. Maloney, Daniel McCarthy, Dustin A. Deming, Noelle K. LoConte, Kristina Matkowskyj, Jens C. Eickhoff, Philip Emmerich, Malcolm M. DeCamp, Sam Joseph Lubner, Anita Ahmed Turk, Michael Frederick Bassetti; University of Wisconsin, Carbone Cancer Center, Madison, WI; Department of Surgery, Division of Cardiothoracic Surgery, University of Wisconsin, Madison, WI; University of Wisconsin, Madison, WI; University of Wisconsin Carbone Cancer Center, Madison, WI; Department of Biostatistics, University of Wisconsin, Madison, WI

Background: Neoadjuvant CRT followed by surgery is the standard of care (SOC) for patients (pts) with stage II/III E/GEJ cancer. However, recurrence rates are high. Immunotherapy has demonstrated promising activity in advanced E/GEJ cancer. This trial evaluates safety and efficacy of perioperative A with CRT in resectable E/GEJ cancer. **Methods:** This is a 2-part phase I/II trial. Part 1 is a run-in phase with 6 pts for safety evaluation. Part 2 will enroll additional 18 pts in the expansion cohort. Pts with E/GEJ cancer of any histology receive CRT (41.4 Gy in 23 fractions) with carboplatin and paclitaxel as per SOC. Three doses of A (10 mg/kg, q14 days) are administered starting on day 29 of treatment, to coincide with the last chemotherapy dose. Surgery is performed ~8 weeks after CRT completion. Pts receive 6 doses of A after resection. Dose-limiting toxicity (DLT) evaluations are completed on the first post-operative clinic visit, 2-4 weeks post resection. **Results:** Between 6/2018 and 2/2019, 6 pts (all male, median age 62) enrolled in part 1: 6 adenocarcinoma (100%); 1 E, 3 Siewert 1, 2 Siewert 2; 1 cT2N0, 2 cT3N0, 3 cT3N1. All pts underwent successful resection with negative surgical margins. 1/6 pts had R1 resection due to tumor extension to inked adventitial surface without invasion of surrounding structures. There were no unexpected surgical complications. At resection, 2 pts had ypT0N0, 2 ypT1N0, 1 ypT2N0, and 1 ypT3N1 disease. Combination of CRT and A had an acceptable toxicity profile. No DLTs were seen in the first 5 pts, so expansion cohort is open to enrollment. No grade $\geq$3 immune-related AEs were observed. Immune-related hypothyroidism was seen in 1 patient (grade 2). 6/6 pts had reversible grade 3 or 4 lymphopenia; 1/6 had grade 3 neutropenia. Correlative studies are ongoing and will be presented at the meeting. **Conclusions:** Perioperative CRT with A is well tolerated with no unexpected toxicities. Additional safety and correlative data will be presented at the meeting. This study is actively enrolling pts to an expansion cohort at University of Wisconsin. Clinical trial information: NCT03490292.

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4042 **Poster Session (Board #147), Mon, 8:00 AM-11:00 AM**

Efficacy and safety of sintilimab in combination with XELOX in first-line gastric or gastroesophageal junction carcinoma (GC/GEJC).

Nong Xu, Lin Shen, Haiping Jiang, Yulong Zheng, Jiong Qian, Chenyu Mao, Hui Zhou, Shuyan Wang; The First Affiliated Hospital, Zhejiang University, Hangzhou, China; Beijing Cancer Hospital, Beijing, China; Innovent Biologics (Suzhou) Co., Ltd., Suzhou, China

Background: Immune checkpoint inhibitors have shown clinical benefit in advanced GC/GEJC. This phase 1b study evaluates the efficacy and safety of sintilimab, an anti-programmed cell death-1 antibody (PD-1 Ab) in combination with XELOX for GC/GEJC in first-line setting. **Methods:** This phase 1b study enrolled treatment-naïve unresectable locally advanced or metastatic GC/GEJC patients without HER2 amplification in cohort F. Patients received sintilimab 200mg IV q3w until disease progression, unacceptable toxicity or death, in combination with XELOX regimen (oxaliplatin 130mg/m^2 IV D1 and capecitabine 1000mg/m^2 PO BID D1-14) for up to 6 cycles. The primary objective was to evaluate the efficacy of the combination per RECIST v1.1 and safety and tolerability. **Results:** Totally 20 patients were enrolled in cohort F. As data cutoff (15 Jan 2019), median follow up was 5.8 months (range, 2.4 to 12.5). The median dose of sintilimab was 6.5 (range, 4 to 12). The objective response rate (ORR) was 85.0% (95%CI, 62.1 to 96.8) and disease control rate (DCR) was 100.0% (95%CI, 83.2 to 100.0). Among 17 patient with BOR of PR, two patients achieved a complete response (CR) of the target lesion. The median duration of response (DOR) and median progression free survival (PFS) had not been met. Three patients underwent resection of primary tumor after achieving a BOR of partial response (N=2) and stable disease (N=1). The incidence of treatment emergent adverse events (TEAEs) was 85.0%. Treatment-related AEs (TRAEs) occurred in 14 (70.0%) patients. The incidence of TRAE $\geq$ Grade 3 was 15%. AEs of immune-related etiology, occurred in 6 patients (30.0%). There were no AEs that resulted in death. As data cutoff, 12 patients were still in treatment and 8 had discontinued treatment and were under survival follow up. The biomarker analysis including PD-L1 expression in tumor specimen was ongoing. **Conclusions:** Sintilimab in combination with XELOX in first-line GC/GEJC shows promising anti-tumor efficacy and a tolerable safety profile. The further randomized, phase 3 study of Sintilimab in combination with XELOX in this setting is ongoing (NCT03745170). Clinical trial information: NCT02937116.

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4043 **Poster Session (Board #148), Mon, 8:00 AM-11:00 AM**

Analysis of symptoms and functional HRQoL scales in TAGS, a phase III trial of trifluridine/tipiracil (FTD/TPI) in metastatic gastric cancer (mGC).

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Background: The phase 3, randomized, double-blind, placebo-controlled study (TAGS) evaluated the efficacy and safety of FTD/TPI (35 mg/m^2 given orally twice a day on days 1–5 and 8–12 of a 28-day cycle) in mGC patients who had previously received≥2 prior regimens for advanced disease and demonstrated a clinically relevant and statistically significant benefit in OS and PFS with a predictable and manageable safety profile. HRQoL data and association between QoL and time to ECOG status deterioration (2 or more) are reported here. **Methods:** HRQoL was evaluated using EORTC QLQ-C30 and the gastric-specific module (QLQ-STO22) questionnaires at baseline and at every 4 weeks thereafter until treatment discontinuation. Prespecified key HRQoL were changes from baseline and time to deterioration. Changes ≥10 points were deemed clinically relevant. A time-dependent Cox-regression analysis was performed to evaluate the association of 10-point Global Health Status deterioration with worsening ECOG status. **Results:** Of 507 patients randomized, 332/337 (98.5%) of FTD/TPI and 164/170 (96.5%) of placebo had baseline QoL data. Overall compliance was 84% for both questionnaires. Demographic and disease were generally balanced between the two groups; QoL scores were also similar between groups. HRQoL was largely maintained during treatment in both arms for most items; mean changes from baseline remained under the 10-point threshold. Clinically relevant changes from baseline were observed only for pain relief at cycle 2 (favouring FTD/TPI); and improved role functioning at cycle 3 (favouring placebo). In a sensitivity analysis including death or progression as an event, FTD/TPI was associated with a positive trend suggesting a reduced risk of QoL deterioration across all scales compared to placebo (HRs ranged from 0.57 to 0.74. A 10-point Global Health Status deterioration was associated with a worsening ECOG status (HR, 95% CI, 1.5, 1.2 to 1.86). **Conclusions:** During the treatment period, HRQoL remained stable for most functional and symptom scales in both arms, suggesting that HRQoL is largely maintained with FTD/TPI. Treatment with FTD/TPI was associated with a positive trend toward a lower risk of QoL deterioration than placebo across all scales. Changes in QoL were informative for patients 'expected ECOG status. Clinical trial information: NCT02500043.

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4044 **Poster Session (Board #149), Mon, 8:00 AM-11:00 AM**

Recurrence risk evaluation in stage IB gastric cancer with *TP53* codon 72 polymorphism.

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Background: Post-operative adjuvant chemotherapy is not currently indicated for Stage IB gastric cancer. However, about 10% of these patients experience recurrence and metastasis. Our previous study on a panel of gastric cancer cell lines indicated that *TP53* codon 72 polymorphisms may affect the degree of biological malignancy. Hence, we hypothesized that the *TP53* codon 72 polymorphisms may have been associated with post-operative survival without adjuvant chemotherapy. In this study, we investigated the risk of recurrence after treatment of Stage IB gastric cancer patients carrying the *TP53* codon 72 polymorphism and attempted to identify a subpopulation that should receive post-operative adjuvant chemotherapy. **Methods:** Among 658 gastric cancer patients who received gastrectomy with curative-intent, 130 Stage IB patients were enrolled in the present study. The *TP53* codon 72 polymorphisms of formalin-fixed paraffin-embedded cancer tissue sections were assessed by direct sequencing using originally designed primers. Overall survival rate (OS) and relapse-free survival rate (RFS) were analyzed based on the status of *TP53* codon 72 polymorphism "Arg/Arg", "Arg/Pro" and "Pro/Pro". The hazard ratio for each subgroup was compared by *TP53* codon 72 polymorphism. All interaction *p* values were calculated using the likelihood test. **Results:** Of the 125 patients for whom polymorphism analysis results were available, the 5- and 10-year OS was 84.5% and 63.9%, respectively. The 5- and 10-year RFS was 82.2% and 64.3%, respectively. When the study cohort was divided into two groups according to polymorphism status (i.e., Arg/Arg and Arg/Pro vs. Pro/Pro), both the OS (hazard ratio [HR], 1.968; 95% confidence interval [CI], 0.770-7.430, $p = 0.045$) and RFS (HR, 1.976; 95% CI, 0.778-7.515, $p = 0.033$) of the Pro/Pro group across the entire observation period were significantly lower than those for the Arg/Arg and Arg/Pro group. The majority of recurrences in Pro/Pro occurred within three years from the operation. **Conclusions:** Among Stage IB gastric cancer patients that underwent gastrectomy with curative-intent, post-operative adjuvant chemotherapy may be considered immediately after surgery for patients carrying the *TP53* codon 72 Pro/Pro polymorphism.

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4045 **Poster Session (Board #150), Mon, 8:00 AM-11:00 AM**

A phase II feasibility trial of neoadjuvant chemoradiotherapy combined with atezolizumab for resectable esophageal adenocarcinoma: The PERFECT trial.

Tom van den Ende, Nicolien C. de Clercq, Mark I. van Berge Henegouwen, Suzanne S. Gisbertz, Sybren L. Meijer, Sandor Schokker, Jacques J.G.H.M. Bergman, Nadia Haj Mohammad, Jelle P. Ruurda, Richard van Hillegersberg, Stella Mook, Max Nieuwdorp, Tanya T.D. Soeratram, Bauke Ylstra, Nicole C.T. van Grieken, Tanja D. de Gruijl, Maarten F. Bijlsma, Maarten C.C.M. Hulshof, Hanneke W.M. Van Laarhoven; Amsterdam UMC, University of Amsterdam, Department of Medical Oncology, Cancer Center Amsterdam, Amsterdam, Netherlands; Amsterdam UMC, University of Amsterdam, Department of Internal and Vascular Medicine, Amsterdam, Netherlands; Amsterdam UMC, University of Amsterdam, Department of Surgery, Cancer Center Amsterdam, Amsterdam, Netherlands; Amsterdam UMC, University of Amsterdam, Department of Pathology, Cancer Center Amsterdam, Amsterdam, Netherlands; Amsterdam UMC, University of Amsterdam, Department of Gastroenterology, Cancer Center Amsterdam, Amsterdam, Netherlands; Utrecht UMC, Utrecht University, Department of Medical Oncology, Utrecht, Netherlands; Utrecht UMC, Utrecht University, Department of Surgery, Utrecht, Netherlands; Utrecht UMC, Utrecht University, Department of Radiotherapy, Utrecht, Netherlands; Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Pathology, Cancer Center Amsterdam, Amsterdam, Netherlands; Amsterdam University Medical Centers, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Medical Oncology, Cancer Center Amsterdam, Amsterdam, Netherlands; Amsterdam UMC, University of Amsterdam, Laboratory for Experimental Oncology and Radiobiology, Cancer Center Amsterdam, Amsterdam, Netherlands; Amsterdam UMC, University of Amsterdam, Department of Radiotherapy, Cancer Center Amsterdam, Amsterdam, Netherlands

Background: The CROSS study demonstrated the superiority of neoadjuvant chemoradiotherapy (nCRT) over surgery alone (van Hagen et al. NEJM. 2012). However, for resectable esophageal adenocarcinoma (rEAC) 5y survival is only 43%. PD1/PDL1 checkpoint inhibitors have shown promising efficacy for several cancer types, including esophageal cancer. To further improve outcomes in rEAC, we performed a phase II trial of nCRT combined with atezolizumab, a PD-L1 inhibitor. **Methods:** Pts with rEAC received standard dose CROSS regimen (5 cycles of IV: carboplatin AUC2, paclitaxel 50 mg/m^2 and concurrent 23 fractions of 1.8 Gy on weekdays) with atezolizumab (5 cycles: 1200 mg IV, 3 weekly). Primary endpoint was the percentage of pts completing treatment with atezolizumab. Secondary endpoints included: toxicity, post-operative complications (Clavien-Dindo), Mandard score, R0 resection rate, PFS and OS. In total 40 pts will be enrolled. **Results:** Since July 2017, 39 pts have been enrolled (87% males, median age 63). Neoadjuvant treatment was completed by 31 pts and is ongoing in 8 pts. All cycles/fractions of nCRT were administered in 29/31 pts; 26 pts completed all cycles of atezolizumab, 24 pts finished complete neoadjuvant treatment. Reasons for missing any cycle of chemotherapy/atezolizumab included: toxicity (6 pts, in 3/6 pts immune-related adverse events (irAE)) and progression (1 pt). Grade 3-4 toxicity was observed in 15/31 pts (6/31 irAEs of any grade) which did not delay surgery. Thus far 23/31 pts were resected, 3 pts are planned for surgery, 3 pts had interval metastases preoperatively, 1 pt died during treatment (pulmonary embolism), and 1 pt declined surgery. Clavien-Dindo grade 3-4 complications were seen in 11/23 pts with no surgery related mortality. A pathological complete response (pCR), Mandard 1 was seen in 9/23 (39%) pts. All patients underwent an R0 resection. Updated results will be presented at the meeting. **Conclusions:** Based on data thus far, atezolizumab added to nCRT is feasible. A pCR was observed in 39% of patients, which is promising compared to 23% in the CROSS study. Treatment is associated with irAE which are manageable. Biomarker research will be performed on blood (circulating tumor DNA), tissue (immune microenvironment) and feces (microbiome). Clinical trial information: NCT03087864.

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4046 **Poster Session (Board #151), Mon, 8:00 AM-11:00 AM**

Total neoadjuvant chemo (ctx; TNT) for locally advanced gastric cancer (GC): The Memorial Sloan Kettering Cancer Center experience.

Megan Greally, Vivian E. Strong, Sam S. Yoon, Daniel G. Coit, Joanne F Chou, Marinela Capanu, David Paul Kelsen, Yelena Yuriy Janjigian, David H. Ilson, Geoffrey Yuyat Ku; Memorial Sloan Kettering Cancer Center, New York, NY; Memorial Sloan Kettering Cancer Center, New York City, NY

Background: Peri-op chemo (ctx) and surgery is a standard in the treatment of GC, based on the MAGIC (NEJM 2006; 355:11) and FLOT4 (J Clin Oncol 35:4004 [abstr]) studies. However, less than half of patients (pts) completed ctx in the MAGIC and FLOT4 studies, mainly from issues delivering post-op therapy. We assessed safety and feasibility of TNT, where all ctx is given pre-op. **Methods:** We reviewed GC pts who received TNT or peri-op ctx and had surgery; decision for TNT was by physician preference, based on clinical or radiographic benefit to justify completing ctx pre-op. Pt characteristics were compared using Fisher's exact and Wilcoxon Rank Sum tests. Post-op length of stay (LOS) was calculated from date of surgery (DOS) to date of discharge and surgical morbidity was determined using the Clavien-Dindo classification. Progression free survival (PFS) and overall survival (OS) were calculated from DOS using Kaplan-Meier methods and compared between groups using the log-rank test. **Results:** 120 pts were identified, median age 63, 62.5% male, 98% ECOG 0/1. 93 pts (77.5%) received peri-op ctx and 27 (22.5%) received TNT. In peri-op pts, 19%, 43% and 38% received FLOT, platinum/fluropyrimidine (FP) and ECF/EOX respectively. In TNT pts, 56%, 37% and 7% received FLOT, platinum/FP and ECF/EOX respectively. 57% had subtotal gastrectomy. Surgical outcomes were similar between groups; median LOS was 6 and 7 days ($p = 0.31$) in peri-op and TNT pts respectively. There was no significant difference in Clavien Dindo grade I-II or III-IV morbidity between groups ($p = 0.103$). There were no deaths. TNT pts received higher proportions of planned treatment than peri-op ctx pts: 90% vs. 60% FP (0.001); 85% vs. 41% platinum (< 0.001); 100% vs. 9% epirubicin (0.015) and 53% vs. 28% docetaxel ($p = 0.169$). At median follow-up of 19 months, median PFS and OS were not reached. There was no significant difference in PFS ($p = 0.089$) or OS ($p = 0.59$) between groups. **Conclusions:** TNT appears safe with no increase in post-op LOS or surgical morbidity observed. TNT pts had higher percentage drug delivery, suggesting potential benefit for administering all ctx before surgery. While longer survival follow-up is required, TNT may be considered in pts with locally advanced GC who are candidates for ctx.

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4047 **Poster Session (Board #152), Mon, 8:00 AM-11:00 AM**

Clinical and molecular factors predicting resistance to first-line (1L) FOLFOX in patients (pts) with advanced esophagogastric cancer (EGA) and patterns of subsequent therapy.

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Background: In the US, FOLFOX is the most widely used 1L treatment for advanced EGA. We evaluated if FOLFOX resistance (FR) impacted subsequent therapy and characterized the clinical and molecular factors that predict resistance to 1L FOLFOX. **Methods:** We reviewed pts with advanced Her2-negative EGA treated with 1L FOLFOX from Jan 2013 to Aug 2017. Response or stable disease (SD) at time of first restaging scan defined pts as FOLFOX sensitive (FS); progression defined FR. Pt characteristics were compared using Fisher's exact and Wilcoxon Rank-Sum tests. Outcomes were correlated with clinical variables and MSK-IMPACT data. Microsatellite instable (MSI) pts were excluded from gene and pathway analysis. Overall survival (OS) was calculated from start of FOLFOX using Kaplan-Meier methods. Landmark analysis (2 months [mo] after starting FOLFOX) was used to compare OS between groups. **Results:** We identified 311 pts, median age 62, 73% male, 82% ECOG 0/1. 246 pts (79%) were FS and 65 (21%) were FR. FR pts had a higher number of metastatic sites, $p = 0.001$. Median OS was 13.4 mo in FS pts vs 4.3 mo in FR pts ($p < 0.001$). At time of analysis, 213 pts (172 FS pts and 41 FR pts) and 110 pts (90 FS pts and 20 FR pts) had received 2^{nd}-line (2L) and 3^{rd}-line (3L) chemo respectively. In pts who received 2L chemo (ctx), there was no difference in ctx duration between FS and FR pts (2.1 vs 1.4 mo, $p = 0.67$). However, in pts who received 3L ctx, the duration was longer in FS vs FR pts (1.6 vs 0.5 months, $p = 0.002$). In IMPACT tested pts ($n = 130$), univariate analysis identified EGFR (33.3% vs 10.7%, $p = 0.032$) and WNT pathway (26.7% vs 4.9%, $p = 0.015$) alterations more frequently in FR pts vs FS pts. 12 pts were MSI, all were FS (3 SD, 8 PR, 1 CR). Of 63 pts who had IMPACT germline testing, 7 (11%) had germline mutations identified, including CDH1 ($n = 2$) and ATM ($n = 1$), all were FS. No pts were enrolled on genotype-matched trials as a result of IMPACT testing. **Conclusions:** From time of first restaging scan, FR pts have inferior OS to FS pts. The duration of 3L ctx was longer in FS vs FR pts. Higher number of metastatic sites and EGFR and WNT pathway alterations were associated with FR; MSI was not. IMPACT did not facilitate enrolment on genotype-matched studies.

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4048 **Poster Session (Board #153), Mon, 8:00 AM-11:00 AM**

Health-related quality of life (HRQoL) of pembrolizumab (pembro) versus physician choice single-agent paclitaxel, docetaxel, or irinotecan in subjects with advanced/metastatic adenocarcinoma (ACC) or squamous cell carcinoma (SCC) of the esophagus that has progressed after first-line standard therapy (KEYNOTE-181).

Antoine Adenis, Amit Kulkarni, Gustavo Colagiovanni Girotto, Christelle De La Fouchardiere, Helene Senellart, Hanneke W.M. Van Laarhoven, Daniel Hochhauser, Wasat Mansoor, Raed Al-Rajabi, Josephine Norquist, Shailaja Suryawanshi, Pooja Bhagia, Jean-Philippe Metges; Institut du Cancer de Montpellier, Montpellier, France; Merck & Co., Inc., Kenilworth, NJ; Hospital de Base de São Jose do Rio Preto, São Jose Do Rio Preto/SP, Brazil; Leon Berard Cancer Centre, Lyon, France; Centre Rene Gauducheau ICO, Saint-Herblain, France; Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, Netherlands; UCL Hospitals NHS Foundation Trust, London, United Kingdom; Christie NHS, Manchester, United Kingdom; University of Kansas Cancer Center, Kansas City, KS; Centre Hospitalier Regional Universitaire (CHRU) de Brest–Hopital Morvan, Brest, France

Background: KEYNOTE-181 (NCT02564263) is an open-label, randomized, phase 3 trial in ACC and SCC of the esophagus that evaluated IV pembro 200 mg Q3W for up to 2 years vs investigator choice of single-agent paclitaxel/docetaxel/irinotecan (control). Pembro was superior to control for OS in patients with PD-L1 CPS ≥10 (N = 222; median 9.3 vs 6.7 months; *P*= 0.0074). Here we present results of prespecified HRQoL analyses in this population. **Methods:** The EORTC QLQ-C30 and EORTC QLQ-OES18 were administered at baseline; weeks 2, 3, 4, 6, 9, 12, 18; every 9 weeks up to 1 year/end of treatment; and 30-day safety follow-up visit. Data from patients receiving ≥1 dose of study treatment and completing ≥1 HRQoL assessment were analyzed. Least squares mean (LSM) score change from baseline to week 9, 95% CI, and nominal *P* values were calculated. Time to deterioration (TTD) (≥10-point decline from baseline) was assessed by Kaplan-Meier method and Cox regression model. HRs, 95% CIs, and nominal *P* values are provided. **Results:** The HRQoL population included 218 PD-L1 CPS ≥10 patients (107 pembro, 111 control). QLQ-C30 compliance at week 9 was 88.9% for pembro and 83.9% for control. There was no significant difference in LSM between arms (3.68; 95% CI −2.28, 9.64; *P*= 0.2248) in global health status (GHS)/QoL score. Week 9 QLQ-OES18 compliance was 88.4% for pembro and 83.3% for control. QLQ-OES18 scores were not significantly different between arms. TTD for pain (HR 1.02; 95% CI 0.58, 1.81; *P*= 0.5282), reflux (HR 1.69; 95% CI 0.83, 3.47; *P*= 0.9254), and dysphagia (HR 1.81; 95% CI 0.97, 3.37; *P*= 0.9693) subscales were not significantly different between arms. **Conclusions:** Over 9 weeks, patients treated with pembro had stable GHS/QoL scores similar to those of patients treated with single-agent docetaxel/paclitaxel/irinotecan. Combined with the superior OS and lower rate of treatment-related AEs seen with pembro, these data support clinically meaningful benefit of pembro in esophageal cancer patients with PD-L1 CPS ≥10. Clinical trial information: NCT02564263.

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4049 **Poster Session (Board #154), Mon, 8:00 AM-11:00 AM**

Correlation between immune-related adverse events and prognosis in patients with gastric cancer treated with nivolumab.

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Background: Recent studies have shown that immune-related adverse events (irAEs) caused by immune checkpoint inhibitors were associated with clinical benefit in patients with melanoma or lung cancer. In advanced gastric cancer (AGC) patients, there have been few reports about the correlation between irAEs and efficacy of immune checkpoint inhibitors. Therefore, in this study, we retrospectively investigated the correlation between irAEs and efficacy in AGC patients treated with nivolumab. **Methods:** The subjects of this study were AGC patients that had received nivolumab monotherapy between January 2015 and August 2018. IrAEs were defined as those AEs having a potential immunological basis that required close follow-up, or immunosuppressive therapy and/or endocrine therapy. We divided the patients who received nivolumab into two groups based on occurrence of irAEs; those with irAEs (irAE group) or those without (non-irAE group). We assessed the efficacy in both groups**. Results:** Of the 65 AGC patients that received nivolumab monotherapy, 14 developed irAEs. The median time to onset of irAEs was 30.5 days (range 3–407 days). Median follow-up period for survivors was 32 months (95% CI, 10.8 to 34.5). The median progression-free survival was 7.5 months (95% CI, 3.6 to 11.5) in the irAE group and 1.4 months (95% CI, 1.2 to 1.6) in the non-irAE group (HR = 0.11, $p < 0.001$). The median overall survival was 16.8 months (95% CI, 4.4 to not reached) in the irAE group and 3.2 months (95% CI, 2.2 to 4.1) in the non-irAE group (HR = 0.17, $p < 0.001$). Multivariate analysis demonstrated that high ALP level (HR = 2.88; 95% CI, 1.51 to 5.51) and absence of irAEs (HR = 3.06, 95% CI, 3.06 to 23.46 for yes vs. no) were associated with a poor prognosis. The most frequent irAEs was diarrhea/colitis (n = 5). Grade 3 adverse events were observed in 6 patients; hyperglycemia (n = 2), diarrhea/colitis (n = 1), adrenal insufficiency (n = 1), increased aspartate aminotransferase increased (n = 1), peripheral motor neuropathy (n = 1). One of the 14 patients experienced the irAE after discontinuation of nivolumab due to progression of disease. There were no grade 4 or 5 adverse events related to nivolumab. **Conclusions:** Development of irAEs was associated with clinical benefit for AGC patients receiving nivolumab monotherapy.

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4050 **Poster Session (Board #155), Mon, 8:00 AM-11:00 AM**

Perioperative (P) UGT1A1 genotype guided irinotecan (iri) dosing 'gFOLFIRINOX' for gastroesophageal adenocarcinoma (GEA).

Daniel V.T. Catenacci, Leah Chase, Samantha Lomnicki, Theodore Karrison, Robert de Wilton Marsh, Murtuza M. Rampurwala, Sunil Narula, Lindsay Alpert, Namrata Setia, Shu-Yuan Xiao, John Hart, Uzma Siddiqui, Chih-Yi Liao, Blase N. Polite, Hedy L. Kindler, Kiran Turaga, Vivek N. Prachand, Kevin K. Roggin, Mark K. Ferguson, Mitchell C. Posner; University of Chicago Medical Center and Biological Sciences, Chicago, IL; University of Chicago Medicine, Chicago, IL; University of Chicago, Chicago, IL; The University of Chicago Medicine and Biological Sciences, Chicago, IL; Kellogg Cancer Center, NorthShore University Health System, Evanston, IL; University of Wisconsin, Madison, WI; University of Chicago Medicine Comprehensive Cancer Center at Silver Cross Hospital, Woodridge, IL; Department of Pathology, The University of Chicago, Chicago, IL; University of Chicago, Section of Gastroenterology, Chicago, IL; Barnes Jewish Hosp, St Louis, MO; The University of Chicago, Chicago, IL; University of Chicago, Department of Surgery, Chicago, IL; University of Chicago Medical Center, Chicago, IL; The University of Chicago Medical Center, Chicago, IL; The University of Chicago Hospital, Chicago, IL; The University of Chicago Medicine, Chicago, IL

Background: Complete resection (R0) and pathologic response grade (PRG) correlate with long-term GEA outcome. FOLFIRINOX demonstrated efficacy in advanced GEA; gFOLFIRINOX improved tolerability. We evaluated R0, PRG and tolerability in this pilot P study. **Methods:** Gastric body (GB) + esophagogastric (EGJ) GEA patients (pts) with ≥T3Nx or TxN+ were enrolled & treated with 4 pre + 4 postoperative biweekly cycles of gFOLFIRINOX (5-FU 2400mg/m2 over 46 hrs; oxaliplatin 85mg/m2; iri: 180mg/m2 for UGT1A1 genotype 6/6, 135mg/m2 for 6/7, 90mg/m2 for 7/7) (+ trastuzumab (T) 6mg/kg then 4mg/kg for HER2+) with prophylactic peg-filgastrim. 1°endpoint R0 resection required 36 pts to assess for a 90% R0 rate (intention to treat (ITT)) with 90% power + 0.05 alpha; ≥30/36 R0 considered positive. Co-1°endpoint was PRG (Becker); 36 pts provided 85% power with 0.05 alpha for a complete (pCR G1a) rate of 16%. 2° endpoints were safety/toxicity, PET response, & R0/PRG by tumor site, histologic subtype, HER2 status, & UGT1A1 genotype. We report efficacy and toxicity data from the neoadjuvant (Neo) portion of the study; postop data & survival outcomes will be presented at the meeting. **Results:** 4 sites enrolled 36 ITT pts between 2/2014-8/2018; 75% male, median age 66 (range 27-85). All pts completed all 4 cycles of Neo therapy: 10% had any dose reduction of iri (16%/0%/25% by genotype 6/6, 6/7, 7/7); any G3+ toxicity occurred in 35% of pts (32% 6/6, 29% 6/7, 75% 7/7). G3+ toxicity in ≥5% of pts: diarrhea (17.5%; 6/6 21%, 6/7 11%, 7/7 25%), anemia (5%), vomiting (5%). Efficacy is shown in the Table. Of pts going to surgery, both R1 resections were GB linitus. PRG1(a+b) was achieved in 36% of ITT pts, 46% of intestinal type histology. **Conclusions:** Neo gFOLFIRINOX was tolerable with surrogate efficacy comparable to FLOT. Clinical trial information: NCT02366819.

			PRG ITT (%)					PET response >-35% SUV (%)
gFOLFIRINOX +/-T	Incidence (%)	R0 ITT (%)	1a+b	1a	1b	2	3	*In evaluable pts
ITT	N = 36	89	36	8	28	22	42	24/27 (89)
Primary:								
EGJ	72	92	38	8	31	27	35	91
GB	28	80	30	10	20	10	60	75
Histology:								
Intestinal	67	92	46	13	33	17	38	90
Mixed/Diffuse	33	83	17	0	17	33	50	86
HER2:								
+ve	17	100	50	17	33	33	17	100
-ve	83	87	33	7	27	20	47	86
Genotype:								
6/6	50	83	33	17	17	28	39	93
6/7	44	94	44	0	44	19	38	83
7/7	6	100	0	0	0	0	100	--
PET Response*:	89	92	100	100	100	100	63	

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4051 **Poster Session (Board #156), Mon, 8:00 AM-11:00 AM**

Best supportive care (BSC) with or without low-dose chemotherapy (chemo) in frail elderly patients with advanced gastroesophageal cancer (aGOAC): The uncertain randomization of the GO2 phase III trial.

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Background: Before 2000, trials comparing BSC +/- chemo for aGOAC showed overall survival (OS) benefit, but in predominantly fit patients (pts). We have revisited this question in a modern context, using low-dose chemo in a frail population, with comprehensive baseline health and frailty assessment. **Methods:** In the GO2 trial, elderly and/or frail aGOAC pts with a "certain" indication for chemo were randomised between 3 chemo doses. In this GO2 substudy, pts with an "uncertain" indication for chemo were instead randomised to BSC ± the lowest dose chemo. Pts were eligible if clinician and pt agreed the indication for chemo was uncertain. There was no PS threshold, but eGFR ≥30 and bili < 2xULN were required. Baseline assessment included global QL, symptom & functional scales, frailty and comorbidity. Randomisation was 1:1 to BSC alone, or with oxaliplatin 78 mg/m2 d1, capecitabine 375 mg/m2 bd d1-21 (modified if eGFR 30-50 ml/min or bili 1.5-2.0 xULN), q21d. QL was reassessed after 9 and 18 wks. The primary endpoint analysis was OS, adjusted for baseline factors. The sample size for this exploratory sub-study was not pre-set, but around 60 pts were anticipated. **Results:** 558 pts entered GO2 at 61 centres 2014-17, of whom only 45 pts (8%) at 21 centres entered this uncertain randomisation. This would provide 80% power at p = 0.05 (2-tailed) to detect an OS HR of 0.3. OS was shorter in pts with worse baseline PS ($p<0.01$) or distant mets ($p<0.05$). OS was not significantly improved with chemo; however we cannot exclude HR >0.32. QL deteriorated less with BSC+chemo than with BSC alone. **Conclusions:** In this frail, poor PS population, we observed a small survival benefit with chemo but this did not reach statistical significance. Clinicians should carefully consider BSC alone as a valid treatment option for aGOAC pts with poor PS and/or frailty. Clinical trial information: 44687907.

	BSC alone	BSC + chemo
Pts (deaths)	22 (20)	23 (17)
Median age	78.5	79
% PS ≥2	68	57
% frail; % very frail	96; 68	91; 70
Mean baseline EQ5D QL (scale 0-1)	0.64	0.61
Median OS mo unadjusted	3.0	6.1
OS adjusted Cox model	HR= 0.69 [95%CI: 0.32-1.48], p=0.34	
Mean QL @ 9wks	0.37	0.45

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4052 **Poster Session (Board #157), Mon, 8:00 AM-11:00 AM**

The quality of life in neoadjuvant versus adjuvant therapy of esophageal cancer treatment trial (QUINTETT).

Richard Malthaner, Edward Yu, Michael Susmoy Sanatani, Debra Lewis, Andrew Warner, A. Rashid Dar, Brian P Yaremko, Joel Bierer, David A. Palma, George Rodrigues, Dalilah Fortin, Richard Inculet, Eric Frechette, Jacques Raphael, Steward Gaede, Sarah Kuruvilla, Jawaid Younus, Mark David Vincent; London Health Sciences Centre, London, ON, Canada; London Regional Cancer Centre, London, ON, Canada; LHSC London Regional Cancer Program, London, ON, Canada; Department of Radiation Oncology, London Regional Cancer Program, London, ON, Canada; London Regional Cancer Program, University of Western Ontario, London, ON, Canada; Richard Malthaner, London, ON, Canada; London Regional Cancer Program, London, ON, Canada; Charles-Lemoyne Hospital, Longueuil, QC, Canada; Western University, London Regional Cancer Program, London, ON, Canada

Background: We compared the health-related quality-of-life (HRQOL) of standard neoadjuvant cisplatin and 5-FU chemotherapy plus radiotherapy (N) followed by surgical resection to adjuvant cisplatin, 5-FU, and epirubicin chemotherapy with concurrent extended volume radiotherapy (A) following surgical resection for resectable esophageal carcinoma. **Methods:** 96 patients with stage I to III resectable cancer of the esophagus were enrolled into a prospective randomized trial (NCT00907543) from April 2009 to November 2016. Patients were randomized into 2 groups: N (47 cases) and A (49 cases). The primary end point was HRQOL using the FACT-E at one year. The secondary endpoints included other HRQOL measures, overall survival (OS), disease-free survival (DFS), and adverse events. **Results:** The median follow-up was 5.0 years [95% CI :4.6 to 5.5]. The majority of patients had adenocarcinomas of the distal esophagus/gastroesophageal junction (80.9% vs 87.8%). The stage distribution was: I 9%; II 22%; III 58%; TxN0-1 10%. Using an intention-to-treat analysis there was no significant difference in the FACT-E total scores between arms at one year ($p = 0.759$), with 35.5% vs. 41.2% respectively showing an increase of ≥ 15 points (*a priori* minimal clinical difference) compared to pre-treatment ($p = 0.638$). The HRQOL was temporarily significantly inferior at 2 months in the N arm for FACT-E, EORTC OG25, and EQ-5D-3L in the dysphagia, reflux, pain, taste, and coughing domains ($p < 0.05$). There were no 30-day mortalities but 2.1% vs. 10.2% 90-day mortalities ($p = 0.204$). There were no significant differences in either 5-year OS (37.9% vs 28.9%, $p = 0.321$) or DFS (34.0% vs 25.5%, $p = 0.551$. 48.9% of patients required chemotherapy to be modified or stopped in the N arm compared to 57.1% in the A arm ($p = 0.421$). 51.1% of patients were able to complete the prescribed N arm chemotherapy without modification compared to only 14.3% in the A arm ($p < 0.001$). Chemotherapy related adverse events significantly more frequent in the neoadjuvant arm ($p < 0.05$). Surgery related adverse events were significantly more frequent in the neoadjuvant arm ($p < 0.05$). **Conclusions:** Trimodality therapy is challenging for patients with resectable esophageal cancer regardless if it is given before or after surgery. Less toxic protocols are needed. Clinical trial information: 00907543.

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4053 **Poster Session (Board #158), Mon, 8:00 AM-11:00 AM**

Molecular comparison between peritoneal metastases (PM) and primary gastric (GC) and gastroesophageal junction (GEJ) cancer.

Matthew K Stein, Joanne Xiu, Michael Gary Martin, Axel Grothey, Philippe Prouet, Jeffrey Owsley, Forrest W Williard, Evan Scott Glazer, Paxton Vandiver Dickson, David Shibata, Danny Yakoub, Richard M. Goldberg, W. Michael Korn, Anthony Frank Shields, Jimmy J. Hwang, Heinz-Josef Lenz, Jeremiah Lee Deneve; West Cancer Center, U Tennessee, Memphis, TN; Caris Life Sciences, Phoenix, AZ; West Cancer Center, University of Tennessee, Germantown, TN; College of Medicine, University of Tennessee Health Science Center, Memphis, TN; University of Tennessee Health Science Center, Memphis, TN; West Virginia University Cancer Institute, Morgantown, WV; Karmanos Cancer Institute, Wayne State University, Detroit, MI; Levine Cancer Institute, Carolinas Health Care System, Charlotte, NC; University of Southern California, Los Angeles, CA

Background: PM from GC or GEJ portend a poor prognosis and molecular differences are ill defined. **Methods:** We compared genomic profiles of primary (P) GC and GEJ with PM patients (pts) and other metastases (OM) sent to Caris Life Sciences. Testing comprised immunohistochemistry (IHC) including programmed death ligand 1 (PD-L1) combined positive score (CPS), copy number alterations (CNA), 592-gene next-generation sequencing (NGS), microsatellite instability (MSI) and tumor mutational burden (TMB). **Results:** 1366 cases were identified: 1041 GC (707 P, 98 PM, 236 OM) and 325 GEJ (248 P, 5 PM, 72 OM). PM were increased in GC versus GEJ (9% v. 2%, $p < 0.0001$). 91% GC and 93% GEJ were adenocarcinoma (AD); GC were more likely signet ring (SR) histology versus GEJ (11% v. 3%, $p < 0.0001$) and GC PM were more likely SR versus other OM or P (13% v. 12% v. 7%, $p = 0.067$). The mean age of PM pts (57 years) was younger than primary GC (63, $p = 0.002$) and OM (61; $p = 0.044$). More PM GC pts were female than P or OM (48% v. 35% v. 34%, $p = 0.03$). No molecular profiling differences were seen between GEJ and GC pts and they were combined for analysis; findings from 1246 AD pts are shown below (see Table). OM (9%, $p = 0.041$) had more CNA in *CCNE1* than PM (2%, $p = 0.041$) or P (5%, $p = 0.002$). **Conclusions:** Compared to P and OM GC, PM pts were younger, more likely female and had a higher incidence of SR histology. PD-L1, HER2 IHC and *ERBB2* CNA were reduced in PM versus P, suggesting novel therapeutic targets are needed.

Characteristic	PM (N = 87)	P (N = 893)	*p*-value (PM v. P)	OM (N = 266)	*p*-value (OM v. P)
TMB ≥10 mutations/Mb (%)	18/87 (21)	220/885 (25)	0.388	65/261 (25)	0.988
PD-L1 CPS 1+ (%)	26/83 (31)	412/855 (48)	*0.003*	98/256 (38)	*0.005*
PD-L1 CPS ≥10 (%)	10/83 (12)	120/855 (14)	0.617	35/256 (14)	0.883
MSI-high (%)	3/86 (3)	72/889 (8)	0.125	10/266 (4)	*0.016*
No. genes mutated ≥1% (%)	46/592 (8)	43/592 (7)	0.635	42/592 (7)	0.874
CDH1-mutated (%)	11/86 (13)	53/883 (6)	*0.016*	18/265 (7)	0.640
MUTYH-mutated (%)	3/87 (3)	4/891 (0)	*0.002*	5/266 (2)	*0.020*
ERBB2-mutated (%)	2/87 (2)	28/893 (3)	0.665	2/266 (1)	*0.032*
HER2-positive IHC (%)	2/81 (2)	70/796 (9)	*0.048*	15/236 (6)	0.232
ERBB2 CNA (%)	1/85 (1)	69/837 (8)	*0.019*	19/255 (7)	0.684

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4054 **Poster Session (Board #159), Mon, 8:00 AM-11:00 AM**

Comparison of efficacy and safety of second-line palliative chemotherapy with paclitaxel plus raltitrexed and paclitaxel alone in patients with metastatic gastric adenocarcinoma: A randomized phase II trial.

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Background: Paclitaxel is a microtubule stabilizing agent that has been the standard second line chemotherapy in the treatment of advanced gastric cancer. This study was designed to find out the clinical outcome of paclitaxel plus raltitrexed regimen as second line treatment in MGC patients. **Methods:** In an open, randomized, multi centers phase II clinical trial , 148 patients were randomly assigned and treated with either RP (raltitrexed 3 mg/m2 d1 and paclitaxel 135mg/m2 d1,3w) or P (paclitaxel 135mg/m2 d1,3w) as second-line palliative chemotherapy. The primary endpoint is PFS, secondary endpoint is ORR, OS and safety. **Results:** In 148 randomly assigned and treated patients (RP = 73; P = 75), the majority of patients were males (94 vs. 54). Progression free survival has a tendency to be prolonged with RP versus P (2.7m vs. 1.7m, p = 0.148). Overall survival also has a tendency to be prolonged with RP versus P (10.2m vs. 6.1m, p = 0.140). Overall response rate was equal with RP versus P (6.8% vs.4.0%, p = 0.72). DCR in the RP group was 56.2%, P group was 36.0%. Grade 3 to 4 treatment-related adverse events occurred in 36.2% (RP) v 28.2% (P) of patients. Frequent grade 3 to 4 toxicities for RP v P were: neutropenia (11.0% v 4.0%), anemia (1.4% v 4.0%), thrombocytopenia (1.4% v 5.3%), and all grade peripheral neurotoxicity (12.3% v 17.3%),all grade elevated aminotransferase (27.4% v 14.1%). Subgroup analysis shows if the disease combined with ascites or peritoneal involved , OS of RP regimen is more longer (p = 0.05). **Conclusions:** Second-line palliative chemotherapy with paclitaxel plus raltitrexed provides a tendency to prolong PFS and OS, and the patients with ascites or peritoneal involved may get benifits from combined chemotherapy, which needs to be confirmed by larger sample studies. Clinical trial information: NCT02072317.

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4055 **Poster Session (Board #160), Mon, 8:00 AM-11:00 AM**

Safety 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 (ESO-Shanghai 2).

Dashan Ai, Yun Chen, Qi Liu, Xiangpeng Zheng, Yunhai Li, Shihong Wei, Jinjun Ye, Jialiang Zhou, Qin Lin, Hui Luo, Jianzhong Cao, Jiancheng Li, Guang Huang, Kailiang Wu, Min Fan, Huanjun Yang, Zhengfei Zhu, Weixin Zhao, Ling Li, Kuaile Zhao; Fudan University Shanghai Cancer Center, Shanghai, 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; Jiangsu Cancer Hospital, Nanjing, China; Affiliated Hospital of Jiangnan University, Wuxi, 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; Fujian Cancer Hospital, Fuzhou, 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) 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/m^2/d, d1-3, PTX 175 mg/m^2, d1, q28d). Patients in TF group were treated with 6 cycles of TF (5-Fu 300 mg/m^2, civ 96h, PTX 50 mg/m^2, d1, qw) in CCR followed by 2 cycles of TF (5-FU 1800 mg/m^2, civ 72h, PTX 175 mg/m^2, d1, q28d) in consolidation chemotherapy. Patients in TC group were treated with 6 cycles of TC (CBP AUC = 2, d1, PTX 50 mg/m^2, d1, qw) in CCR followed by 2 cycles of TC (CBP AUC = 5, d1, PTX 175 mg/m^2 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 and the secondary endpoints were progression-free survival and adverse events. **Results:** Between July 2015 and January 2018, 321 ESCC patients in 11 centers were enrolled. TP group had a significant higher incidence of acute grade 3/4 neutropenia (59.7% vs. 16.8%(TF) or 32.4%(TC)), thrombocytopenia (12.7% vs. 3.5%(TF) or 6.2%(TC)), anemia (6.4% vs. 4.4%(TF) or 4.4%(TC)), fatigue (10.0% vs. 0.9%(TF) or 0.9%(TC)) and vomiting (5.5% 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 (13.1% vs. 1.8%(TP) or 5.3%(TC)) and pneumonitis (4.4% vs. 0%(TP) or 1.8%(TC)) than other two groups ($P < 0.05$). One patient in TF group died of acute pneumonitis. One patient in TF group and one in TC group died of acute esophagitis. **Conclusions:** TP and TF regimen showed different severe AEs in CCR in ESCC patients and TC showed mild AEs. Clinical trial information: NCT02459457.

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4056 **Poster Session (Board #161), Mon, 8:00 AM-11:00 AM**

Phase I trial of hyperthermic intraperitoneal chemoperfusion (HIPEC) with cisplatin, mitomycin, and paclitaxel in patients with gastric adenocarcinoma and carcinomatosis or positive cytology.

Brian D. Badgwell, Mariela A. Blum, Naruhiko Ikoma, Xuemei Wang, Jeannelyn Estrella, Sinchita Roy-Chowdhuri, Prajnan Das, Bruce D. Minsky, Shumei Song, Paul F. Mansfield, Jaffer A. Ajani; University of Texas MD Anderson Cancer Center, Houston, TX; The University of Texas MD Anderson Cancer Center, Houston, TX; Univ of Texas MD Anderson Cancer Ctr, Houston, TX

Background: This phase I trial evaluated the safety and toxicity of laparoscopic hyperthermic intraperitoneal perfusion with chemotherapy (HIPEC) combining mitomycin, cisplatin, and paclitaxel for patients with gastric cancer metastatic to the peritoneum. **Methods:** A Bayesian optimal interval design was used to identify the maximum tolerated dose (MTD) of escalating doses of paclitaxel (starting dose of 20 mg/m2 to maximum dose of 60 mg/m2) in combination with flat doses of mitomycin (30 mg) and cisplatin (200 mg) during laparoscopic HIPEC for patients with gastric adenocarcinoma metastatic to the peritoneum. The primary endpoint was MTD. Secondary endpoints included surgical complications and overall survival (OS). **Results:** A total of 27 patients were treated from November 2017 through November 2018. No dose-limiting toxicities were found. Treatment-related grade 1-2 side effects were leukopenia (11%), oral dysesthesia (4%), arthralgia (4%), and diarrhea (4%). Treatment-related grade 3-4 side effects included leukopenia (4%) and neutropenia (4%). The MTD was 60 mg/m2. Clavien-Dindo surgical complications were grade I (all representing electrolyte deficiencies requiring replacement) in 96% of patients, grade II in 4%, grade III in 0%, grade IV in 0%, and grade V in 4%. At a median follow-up of 15 months, the median OS from diagnosis of metastatic disease and the date of surgery has not been reached. One- and 2-year OS rates from the date of metastatic disease were 74% and 58%, respectively. The 1-year OS rate from the date of HIPEC was 51%. **Conclusions:** Laparoscopic HIPEC with mitomycin, cisplatin, and paclitaxel appears safe at intraperitoneal doses of 30 mg, 200 mg, and 60 mg/m2, respectively. Although electrolyte abnormalities are common, systemic toxicity of this therapy is modest. Survival rates are promising, supporting further research into intraperitoneal therapy for stage IV gastric cancer. Clinical trial information: NCT03330028.

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4057 **Poster Session (Board #162), Mon, 8:00 AM-11:00 AM**

A pilot study of neoadjuvant FOLFIRINOX followed by chemoradiation for gastric and gastroesophageal cancer: Preliminary results.

Jennifer Yon-Li Wo, Jeffrey William Clark, Jill N. Allen, Lawrence Scott Blaszkowsky, Florence Keane, Lorraine C. Drapek, David P. Ryan, Ryan Bruce Corcoran, Eric Roeland, Aparna Raj Parikh, Melin Janardan Khandekar, Rebecca Suk Heist, Christopher Morse, Beow Y. Yeap, Christine A Ulysse, Benjamin Christopher, Michael Lanuti, David L. Berger, John Thomas Mullen, Theodore S. Hong; Massachusetts General Hospital, Boston, MA; Harvard University/ Massachusetts General Hospital, Boston, MA; University of California, San Francisco, San Francisco, CA; Harvard Rad Onc Prog, Boston, MA; Massachusetts General Hospital Cancer Center, Boston, MA; Division of Thoracic Surgery, Massachusetts General Hospital, Boston, MA; NRG Oncology and Massachusetts General Hospital, Boston, MA

Background: We performed a single-arm pilot study of total neoadjuvant approach including FOLFIRINOX and chemoradiation (CRT) with concurrent carboplatin/taxol (C/T) followed by surgery in patients with locally advanced gastric or gastroesophageal junction (GEJ) cancer. **Methods:** Patients were enrolled on a NCI sponsored, prospective, single arm study (NCT03279237). Key eligibility criteria included: histologically confirmed T3/4 or lymph node (LN) positive gastric or GEJ cancer, ECOG PS $\leq$1, age 18+, life expectancy $>$ 3 months. Exclusion criteria included: visceral metastases, prior chemotherapy or RT, or prior targeted therapy. Extensive LN disease beyond the surgical field (supraclavicular or paraaortic) was permitted if deemed feasible to be encompassed within a RT field. Laparoscopy was not required. Pts were treated with neoadjuvant FOLFIRINOX x 8, restaging, CRT (45 Gy for gastric, 50.4 Gy for GEJ) with concurrent C/T, restaging, followed by surgical resection. Dose reductions were at discretion of the treating physician. The primary objective was to determine the rate of completion of FOLFIRINOX x 8 followed by CRT delivered in the preoperative setting. Secondary endpoints included: 1) acute toxicity and 2) pathologic complete response (pCR). **Results:** From Oct 2017 to June 2018, 25 pts were enrolled. Median age was 60 (range:30-76), 17 pts were male (68%). All pts started FOLFIRINOX; 23 (92%) pts completed all 8 planned cycles. Two pts did not complete the planned 8 cycles due to metastatic progression. Rates of grade 3+ overall, gastrointestinal, and hematologic toxicities were 28%, 12%, and 28% respectively. Of the entire cohort, 23 (92%) pts started chemoRT and 22 (88%) pts completed chemoRT (1 pt died during CRT due to pulseless electrical activity arrest). All 22 pts (88%) who completed CRT went for surgical exploration, of whom 2 pts were found with intraoperative metastases. Therefore, 20 (80%) pts underwent surgical resection. At time of abstract, 1 pt's pathology is in process; 7 pts had a pCR (37% in resected cohort, 28% in ITT cohort), all with R0 resection. **Conclusions:** Total neoadjuvant FOLFIRINOX followed by CRT is feasible with acceptable rates of treatment completion and grade 3+ toxicity. In our small series, the rate of pCR is promising and a follow-up study is currently planned. Clinical trial information: NCT03279237.

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4058 **Poster Session (Board #163), Mon, 8:00 AM-11:00 AM**

Safety and efficacy of durvalumab following multimodality therapy for locally advanced esophageal and GEJ adenocarcinoma: 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. No adjuvant tx has been shown to improve survival in these pts. Immune checkpoint inhibitors have activity in metastatic PD-L1 positive EAC. Preclinical studies have shown upregulation of PD-1/PD-L1 pathway with RT +/- chemotherapy. **Methods:** We conducted a phase II trial evaluating safety and efficacy of durvalumab (durva), a monoclonal antibody against PD-L1, in pts with LA-EAC and GEJ adenocarcinoma who have viable tumor in surgical specimen after neoadjuvant CRT and R0 resection. Pts received durva 1500mg IV every 4 weeks for up to 1yr. **Results:** 24 pts were enrolled from 4/2016-1/2018 (median age: 60yrs (range, 43-70). 18 received carbo/paclitaxel and 6 received cis/5-FU concurrently with radiation. Staging at diagnosis: T2N0 (n=3, 12.5%), T2N2 (n=3, 12.5%),T3N0 (n=6, 25%), T3N1 (n=6, 25%), T3N2 (n=4, 17%), T3N3 (n=1, 4%), T3Nx (n=1, 4%).19 pts (79%) had positive lymph nodes (LNs) at the time of surgery following CRT. 12 pts completed 1yr of tx, 12 came off tx before 1yr because of relapse(6), AEs(5), and consent withdrawal (1). Median number of tx cycles was 12.5 (range, 2-13). Most common AEs were fatigue (n=8, 33.3%) and nausea (n=6, 25%). 3pts (12.5%) developed grade 3 irAEs: pneumonitis (1), hepatitis (1), colitis (1). At median follow up of 14.5 mo (range, 1.7-24mo), 17 are disease free (including 5 who came off tx before 1yr). 7pts (29%) have relapsed (3 alive, 4 died). 6/7pts had distant relapse (lung, brain, bone, cervical LNs) and 1 had locoregional relapse. 1-yr RFS and OS were 79.2% and 95.5%, respectively. 2-yr OS was 59.2%. RFS probability at 26 mo was 67.9%. Median survival after relapse was 11.1 mo (range, 0.1-11.3mo). **Conclusions:** Adjuvant durvalumab following trimodality therapy for LA-EAC and GEJ adenocarcinoma was safe and feasible with improvement in 1-yr RFS to 79.2% compared to historical rate of 50%. OS results are encouraging in this high risk pt population. Clinical trial information: NCT02639065.

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4059 **Poster Session (Board #164), Mon, 8:00 AM-11:00 AM**

Prospective evaluation of metabolic intratumoral heterogeneity using ^{18}F-FDG-PET-CT in patients with advanced gastric cancer receiving palliative chemotherapy.

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Background: Metabolic intratumoral heterogeneity (ITH) gives important information on treatment response and prognosis. However, temporal changes in metabolic ITH and their associations with treatment outcome have not been reported yet in gastric cancer (GC). We aimed to evaluate the early changes in metabolic ITH and their predictive roles in advanced GC patients receiving palliative chemotherapy. **Methods:** Unresectable locally advanced or metastatic GC patients were prospectively enrolled before the first-line palliative chemotherapy and underwent ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG-PET-CT) at baseline (T1) and at the first response evaluation follow-up (T2). SUVs (Standardized uptake values), volumetric parameters, and textural features including entropy$_{Histo}$ and contrast$_{GLCM}$ were extracted from the primary gastric tumor at T1, T2, and ΔT (T2-T1) was evaluated. Associations of these parameters with treatment response, progression-free survival (PFS), and overall survival (OS) were analyzed. **Results:** 87 patients were analyzed. Of 86 evaluable patients, 44 obtained partial response, 33 stable disease, and 8 progressed. The objective response rate was 51.8% (95% confidence interval [CI], 40.7% to 62.7%). The median PFS and OS were 7.3 months (95% CI, 5.4 to 8.2 months) and 11.5 months (95% CI, 10.1 to 14.3 months), respectively. From T1 to T2, metabolic ITH was significantly reduced ($P < 0.01$), and the degree of decrease was greater in responders than in non-responders ($P < 0.01$). By multiple Cox regression analyses adjusted for clinical variables, low entropy$_{Histo}$ at T2 (P= 0.001), larger decreases in coefficient of variance (P= 0.003) and contrast$_{GLCM}$ (P= 0.017) were associated with better PFS. Low SUV$_{peak}$ at T2 (P= 0.001), larger decreases in coefficient of variance (P= 0.032) and being a responder were associated with better OS. **Conclusions:** Early reduction in metabolic ITH is useful to predict response to palliative chemotherapy, PFS and OS in advanced GC patients.

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4060 **Poster Session (Board #165), Mon, 8:00 AM-11:00 AM**

Phase I study of fluzoparib, a PARP1 Inhibitor in combination with apatinib and paclitaxel in patients (pts) with advanced gastric and gastroesophageal junction (GEJ) adenocarcinoma.

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Background: Fluzoparib (SHR3162) is an oral, selective PARP1 inhibitor. In our gastric cancer PDX model, fluzoparib + apatinib + paclitaxel demonstrated significant tumor growth inhibition as compared to apatinib alone, and fluzoparib + paclitaxel. In this phase I study, we hypothesized that the combination of fluzoparib+apatinib+paclitaxel should be safe and active in pts with advanced gastric and GEJ cancer. **Methods:** Dose-escalation phase (P1) explored 4 dose levels of fluzoparib with a 3+3 design to identify a recommended phase II dose (RP2D) for further study. Pts received fluzoparib (20, 30, 40, 60 mg/twice daily)+apatinib (250mg/day)+paclitaxel (60mg/m2, Day1, 8, 15). Dose-expansion phase (P2) was to assess safety and efficacy. Pts received RP2D of fluzoparib+apatinib+paclitaxel until progression or intolerant toxicity. Treatment was repeated every 4 weeks. Pts had to have progressive disease after standard platinum-based regimen treatment. Adverse events (AE), PK, and response per RECIST 1.1 (every 8 wks in pts with measurable disease) were assessed. **Results:** 39 pts (median age 58) have been treated in P1 and P2, including fluzoparib 20mg (n=4), 30mg (n=27; 6 pts in P1, 21 pts in P2), 40mg (n=6), and 60mg (n=2). The median treatment duration for this study was 2.8 months. No DLTs were reported in 20mg cohort. One DLT occurred in 30 mg cohort (grade 3 [G3] hypophosphatemia), 1 DLTs (1 grade 4 [G4] febrile neutropenia) occurred and 1 G4 neutropenia occurred and recovered in 3 days in 40mg cohort, 2 DLTs (1 G4 neutropenia, 1 G4 febrile neutropenia) in 60mg cohort. Therefore, 40 mg dose was deemed the MTD. There were no treatment-related deaths on study. The most common AEs≥G3 were neutropenia, febrile neutropenia, and hypertension. 1 treatment-related discontinuation was observed. Of 36 evaluable pts, 12 (30.0%) had confirmed partial response and 13 had stable disease (36.1%). Median progression-free survival was 4.9 months. PK analysis will be presented. **Conclusions:** The RP2D of combination of fluzoparib + apatinib + paclitaxel is well tolerated and has activity in pts with advanced gastric and EGJ cancer who have failed to platinum-based regimen. Clinical trial information: NCT 03026881.

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4061 **Poster Session (Board #166), Mon, 8:00 AM-11:00 AM**

Phase 1 open label trial of intraperitoneal paclitaxel (IPP) in combination with intravenous cisplatin (C) and oral capecitabine (X) in patients with advanced gastric cancer and peritoneal metastases.

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Background: IPP is a potential treatment option in patients with gastric cancer with peritoneal metastasis. IPP with a dose of 20 mg/m2 is well tolerated in combination with S1; however, this has been achieved in a specific genetic pool (Japanese population), and S1 is not available in some countries. We investigated the Maximum Tolerated Dose (MTD) of IPP in addition to a standard chemotherapy combination in an Australian population. **Methods:** Study population included synchronous or metachronous metastatic HER-2 non-amplified gastric adenocarcinoma with histologically/cytologically proven peritoneal involvement and adequate organ function. Intra-peritoneal catheter was placed surgically. 3 + 3 standard dose-escalation design was used. MTD was defined as the highest dose level at which $\leq$ 33% of patients had Dose Limiting Toxicity (DLT). DLT was defined within the first 3 cycles. Recommended Phase-2 Dose was defined as equal to the MTD, or cohort-3 dose if MTD was not reached. Treatment: maximum of six 21-day cycles of C (80mg/m2 IV day 1) + X (1000mg/m2 PO BD days 1-14) + IPP (days 1 and 8). IPP doses for Cohort-1, 2 and 3 were 10, 20 and 30mg/m2 respectively. Primary endpoint was the MTD of IPP. Secondary endpoints included safety, tolerability, overall response rate, ascites response rate, progression free survival and overall survival. **Results:** 15 patients were recruited in 3 cohorts: 9 males (60%), median age at study entry: 61y (range 32-82). All had synchronous metastatic disease and were chemo-naïve. Cohort-1 expanded to 6 patients due to 1 DLT (grade 3 diarrhea), cohort-2 included 3 patients (no DLT) and cohort-3 was expanded to 6 patients as planned and 1 DLT occurred (febrile neutropenia). MTD was not reached and Recommended Phase 2 Dose was determined as 30mg/m2. 8 patients (53%) completed all 6 cycles of treatment. The last patient on the study has completed 3 cycles and is expected to complete 6 cycles by April 2019. No grade 4 or 5 toxicity was recorded. **Conclusions:** MTD of IPP was not reached. IPP is safe in combination with C + X and the Recommended Phase 2 Dose is 30 mg/m2. Survival data will be presented when available. Clinical trial information: ACTRN12614001063606.

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4062 **Poster Session (Board #167), Mon, 8:00 AM-11:00 AM**

A digital pathology demonstration of an "immune hot" ICOS+/CD45RO+ immunephenotype and the impact on survival in patients with esophageal adenocarcinoma.

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Background: Therapies targeting immune checkpoints are changing our understanding of the biology and treatment of cancer. Analysing the immune landscape in esophageal adenocarcinoma (EA) may help future prognostication and therapeutic decision-making. **Methods:** We assembled 310 EA cases in a tissue microarray format with associated clinicopathological information, including a discovery cohort of 156 EA from Northern Ireland and a 154 EA validation cohort from Aberdeen. We carried out validated immunohistochemistry (IHC), stained for range of adaptive immune (CD3, CD4, CD8 and CD45RO) and immune checkpoint biomarkers (ICOS and IDO-1). Slides were digitised and assessed using QuPath image analysis software program to quantify their expression and correlate them with outcome. **Results:** In the discovery cohort we identified a group of patients highly expressing several immune biomarkers, conferring a significant positive survival advantage ($p = 0.022$). CD3, CD4, CD8, CD45RO, and ICOS were individually prognostic for better overall survival (Log rank $p = 0.0003$; $p = 0.0292$; $p = 0.0015$; $p = 0.0008$; $p = 0.0051$ and $p = 0.0264$ respectively). Multivariate and correlation analysis identified a subgroup of CD45RO+/ICOS+ patients with significantly improved overall survival ($p = 0.0002$). The co-expression of CD45RO+/ICOS+ immunophenotype was investigated in the validation cohort and a confirmed survival advantage was seen ($p = 0.042$). Additionally, the Opal Multiplex IHC technology revealed the much higher frequency of single-cell, dual labelling of CD45RO+/ICOS+ in immune hot cases. **Conclusions:** These data demonstrate the advantage of immune markers other than the traditional CD3/CD4/CD8 in EA prognostication. The fact that one of these biomarkers is an immune checkpoint inhibitor may have therapeutic implications.

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4063 **Poster Session (Board #168), Mon, 8:00 AM-11:00 AM**

Landscape of innate and adaptive immunity targets in oesophagogastric adenocarcinoma (OGA).

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Background: Anti-PD-1 therapy modestly improves survival in chemorefractory OGA. Combining PD-1 blockade with novel checkpoint inhibitors, T-cell co-stimulatory molecules, or myeloid suppressors could enhance PD-1 inhibition. Herein, we explore the landscape of known targetable immune markers in non-Asian OGA. **Methods:** OGA patient biopsies were prospectively collected and clinically annotated from 19 UK cancer centres (Oesophageal Cancer Clinical and Molecular Stratification – OCCAMs network). Genomic (WGS) and transcriptomic (bulk-RNA seq) data were generated using Illumina and processed using a validated in-house pipeline (Frankell, Nat Genetics 2019). Gene expression was computed in transcripts per kilobase. Using unsupervised clustering patient clusters were selected according to the expression of gene targets for immune therapy - PD-L1, LAG3, TIM3, TIGIT, ICOS, CCR2, CCR5, CXCR4, and CSF1R. Immune cell infiltration was extrapolated using GSVA gene set enrichment analysis. **Results:** RNAseq data were available for 251 patients; 96% had operable tumours (Stage I: 6%, II: 63%, III: 22%, IV: 4%). In untreated patients (n = 156) 3 subgroups were identified: immune low (83, 53%) with low level expression of all 9 markers, immune high (14, 9%) with high expression of all or majority of markers and intermediate (59, 38%) with heterogenous marker expression. Clinicopathological variables (sex, age, smoking, tumour location (gastric/GEJ/esophagus) and tumour regression grade) were similarly distributed across subgroups. In a cohort of 114 patients with matched WGS and RNAseq data tumour mutation burden was not different between subgroups. In post-chemotherapy biopsies (n = 95) a similar co-expression pattern was observed. Gene enrichment analysis supported infiltration by cells of innate and adaptive immune system in immune high patients. Neoantigen results, phenotypic immunohistochemistry and optimised survival outcomes according to lymphoid and myeloid target expression will be presented. **Conclusions:** High level co-expression of immune regulatory targets in OGA patients may limit the efficacy of anti-PD-1 monotherapy. Combination immune directed therapies may be required in this patient group.

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4064 **Poster Session (Board #169), Mon, 8:00 AM-11:00 AM**

Comprehensive molecular characterization of clinical response in ramucirumab-treated gastric cancer patients: Phase II trial with integrated genomic profiling.

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Background: The absence of tumor cells enables an enriched stromal environment to generate RNA signatures and through assembling genes involved in tumor stroma, four distinct stromal signatures that reflected biological processes such as signature vascular mature (VM), vascular mature/inflammatory (VMI), vascular immature/noninflammatory (VINI) and inflammatory alone (I) depending on mature of vasculature. We hypothesized that these stromal specific signatures may provide additional information to the pre-existing TCGA/ACRG subtypes when predicting response to anti-angiogenesis agent such as ramucirumab. **Methods:** We conducted a single-center phase II trial in which we treated 61 unselected patients with metastatic GC with ramucirumab plus paclitaxel as second line therapy and performed pre-planned integrated genomic profiling. **Results:** Sixty-two patients were enrolled in this study between May 2014 and June 2017. The cut-off date for treatment outcome analysis was January 2, 2019, at which time response evaluations were available for 57 patients with a median follow-up of 30.2months. In an intent-to-treat analysis cohort, there was no CR and 22 patients achieved confirmed PRs resulting in an ORR of 35.5% (95% CI: 23.6 – 47.4). The response rate to ramucirumab was considerably enriched in VM/VMI group (29.2%) (P = 0.0003) when compared to I ($<$ 10%) or VINI group ($<$ 10%). The strongest response defined by maximal response to ramucirumab was shown in GC patients with VM/VMI signatures. Of note, VM/VMI patients had prolonged duration of response to ramucirumab/paclitaxel demonstrating that these patients not only respond to ramucirumab but also had durable response. **Conclusions:** This is the first study to demonstrate a clinically robust correlation between stromal-based signature and response to anti-angiogenesis inhibitor in GC. Clinical trial information: 02628951.

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4065 **Poster Session (Board #170), Mon, 8:00 AM-11:00 AM**

Prospective validation of a serum miRNA panel for early detection of gastric cancer.

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Background: High mortality from gastric cancer is related to the late manifestation of its symptoms. A blood-based non-invasive biomarker with the ability to detect all stages of gastric cancer could significantly improve patient outcomes. We aimed to develop a novel serum miRNA assay for diagnosis of gastric cancer. **Methods:** We conducted a multi-center study involving 892 gastric cancer and control subjects from Singapore and Korea to develop a multi-target miRNA assay. Using RT-qPCR, we quantified the expressions of 578 serum miRNAs and constructed a 12-miR biomarker panel through multi-variant data analysis. The results were generated with the use of a logistic-regression algorithm, with the value of 40 or more considered to be positive. We subsequently validated this multi-miR assay in a large prospective cohort involving 4566 subjects and compared its performance with traditional markers such as H.Pylori and Pepsinogen. All participants underwent gastroscopy independent of the assay results. **Results:** Of the 4566 subjects that underwent gastroscopy and histopathological examination in the prospective cohort, 125 were diagnosed with gastric cancer. The 12-miR assay achieved an Area-Under-Curve (AUC) of 0.84, significantly outperforming (p-value < 0.01) that of H.Pylori (AUC of 0.64) and Pepsinogen (AUC of 0.62). The sensitivity of the miRNA assay in detecting early (stage 0-2) and late (stage 3-4) stage gastric cancer was 82.6% (95% CI, 68.6% to 92.2%) and 88.4% (95% CI, 78.4% to 94.9%) respectively at a specificity of 70.0% (95% CI, 67.8% to 71.9%). In comparison, H.Pylori showed a sensitivity of 80.4% at a specificity of 44.3% whereas the Pepsinogen showed sensitivity of 9.52% at a specificity of 95.3%. Using the miRNA assay as a pre-screening tool could potentially reduce number of endoscopy needed by 62% in detecting one case of gastric cancer. **Conclusions:** Our serum miRNA panel is a useful, non-invasive screening test for gastric cancer. It is cost-effective as it can reduce unnecessary diagnostic endoscopy.

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4066 **Poster Session (Board #171), Mon, 8:00 AM-11:00 AM**

Neoadjuvant epirubicyn, oxaliplatin, capecitabine and radiation therapy (NEOX-RT) followed by surgery for locally advanced gastric cancer (LAGC): A phase II multicentric study.

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Background: This study evaluates the feasibility, safety and efficacy of a trimodality treatment, with surgery postponed after neoadjuvant chemotherapy (CT) and chemoradiotherapy (CRT), in LAGC. **Methods:** Patients (pts) with cT3-4 and/or N+ LAGC were eligible. Staging included endoscopic ultrasound, PET-CT and laparoscopy. Three cycles of EOX (Epirubicyn 50mg/m2,q21 days, Oxaliplatin 130mg/m2,q21 days, and Capecitabine 625mg/m2 bid, by continuous oral administration (c.a.), followed by IMRT with 45Gy/25 frs, concurrent Capecitabine 625mg/m2 bid c.a. and weekly Oxaliplatin 30mg/m2 for 5 wks, was planned. Early PET-CT was performed after the 2nd EOX cycle to assess response or disease progression. Restaging was repeated after CT and CRT. Surgery was planned 4-6 wks after CRT, 22 wks from the start of NEOX-RT. Pathologic complete response (pCR) was the primary endpoint. **Results:** From November 2008 to March 2016, 51 pts (5 G-E Junction, 17 Cardia, 15 Corpus, 14 Antrum) entered the study. The NEOX-RT program was completed in 46 pts (90%) who proceeded to surgery and are assessable. Grade 3-4 toxicity (NCI-CTC criteria v.3) occurred in 13/51 pts (25%) during EOX, including 1 toxic death, and 9.5% CT cycles required dose modification, resulting in a CT compliance of 90%. No pts had progression during CT. Persistent G2-G3 toxicity occurred in 32/46 pts (69%) during CRT. However, 41/46 pts (89%) received the planned 45Gy with Capecitabine at dose $\geq$75% and 4-5 cycles of weekly Oxaliplatin in 52% pts. Curative resection (R0) rate was 89%; 4 pts (8.7%) had peritoneal carcinomatosis at surgery done after a median of 23 wks. pCR was reported in 9/46 pts (19.6%). Major postop complications occurred in 5 pts (11%). At median f-up of 62 mos (23-109), 5-yr OS and DFS in all and pCR pts were 58%, 100% and 51%, 75%, respectively. **Conclusions:** This trimodality program was feasible and safe. Most pts completed the planned treatment. The pCR rate of 19.6% was remarkable and met the hypothesis of pCR = 20%. A high R0 rate was also reported and delayed surgery didn't increase complications. The notable survival rates are available to be compared with ongoing phase III trials. Clinical trial information: 2008-002715-40.

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4067 **Poster Session (Board #172), Mon, 8:00 AM-11:00 AM**

The impact of postoperative complications on survival outcomes in patients with cT3/4a gastric cancer.

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Background: Recently, the negative impact of postoperative complications on long-term survival outcomes has been reported in patients with gastric cancer. However, most are single center, retrospective studies with different definitions of postoperative complications. The objective of this study was to evaluate the impact of postoperative complications on long-term outcomes using the data of a multicenter randomized controlled trial (JCOG1001). **Methods:** This study included 1191 out of all 1204 patients enrolled in JCOG1001 which was aimed to confirm the superiority of bursectomy for patients with cT3/4a locally advanced gastric cancer. Complications were graded by Clavien-Dindo classification. The relationships between the grade (≥grade II or ≥grade III) or type (all or intraabdominal infectious (pancreatic fistula, anastomotic leakage, and intra-abdominal abscess.)) of complications and survival outcomes were evaluated. **Results:** The incidences of ≥grade II and ≥grade III all complications were 23.0% and 9.7%, and those of ≥grade II and ≥grade III intraabdominal infectious complications were 13.4% and 6.9%, respectively. The hazard ratios for overall survival (OS) of patients with ≥grade II and ≥grade III all complications and those of patients with ≥grade II and ≥grade III intraabdominal infectious complications were shown in Table. With whichever definition we adopted, postoperative complications were significantly associated with OS in both univariable and multivariable analysis. **Conclusions:** Postoperative complication was identified as an independent prognostic factor in patients with cT3/4a gastric cancer. Hazard ratios for overall survival by univariable and multivariable Cox proportional hazard model. Clinical trial information: UMIN000003688.

		Hazard ratio [95% CI]	
		Univariable	**Multivariable**
All complications	≥CD II (vs. <CD II)	1.47 [1.10-1.96]	1.42 [1.05-1.92]
	≥CD III (vs. <CD III)	1.72 [1.18-2.51]	1.72 [1.17-2.52]
Intraabdominal infectious complication	≥CD II (vs. <CD II)	1.46 [1.03-2.06]	1.49 [1.04-2.15]
	≥CD III (vs. <CD III)	1.64 [1.04-2.56]	1.67 [1.06-2.64]

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4068 **Poster Session (Board #173), Mon, 8:00 AM-11:00 AM**

Prognostic significance of sarcopenia in metastatic esophageal squamous cell carcinoma.

Kirsty Taylor, Osvaldo Espin-Garcia, Tina Romagnuolo, Frances Allison, Lucy Xiaolu Ma, Micheal McInnis, Aline Fusco Fares, Geoffrey Liu, Gail Elizabeth Darling, Rebecca Wong, Eric Xueyu Chen, Patrick Veit-Haibach, Raymond Woo-Jun Jang, Dmitry Rozenberg, Elena Elimova; Princess Margaret Cancer Centre, Toronto, ON, Canada; Joint Department of Medical Imaging (JDMI), Toronto, ON, Canada; Princess Margaret Hospital, Toronto, ON, Canada; Toronto General Hospital, Toronto, ON, Canada; Joint Division of Medical Imaging (JDMI), Toronto, ON, Canada

Background: Sarcopenia is defined as low skeletal muscle mass and represents a quantifiable marker of frailty. Disease related symptoms of anorexia, nausea and dysphagia, in addition to reduced physical activity contribute to muscle wasting in metastatic esophageal squamous cell cancer (MESCC) patients. This study set out to evaluate the prognostic utility of sarcopenia and its association with nutritional indices. **Methods:** MESCC patients (pts) with available abdominal CT imaging, attending Princess Margaret Cancer Centre between 2011 and 2016, were identified from the institutional database. Skeletal muscle index (SMI), normalized by height, was calculated at the third lumbar (L3) vertebra using SliceOMatic software. SMI cutoffs for sarcopenia were $34.4cm^2/m^2$ in females and $45.4cm^2/m^2$ in males based on previously established consensus. Nutritional risk index (NRI) was calculated using weight and albumin with malnutrition defined as < 97.5. **Results:** Of the 58 pts analyzed, 26 presented with de novo MESCC, median age was 64 (range 48-85), 30 pts were ECOG PS ≤ 1 and 45% received systemic therapy. 93% of pts experienced weight loss $> 5\%$ in the 3 months preceding diagnosis and median BMI was 20.4 (range 16.3-34.9). Twenty-four (41%) pts were sarcopenic (SP) with differences in BMI and NRI ($p < 0.05$) compared to non-sarcopenic (NSP) pts. Median BMI in SP pts was 18.9 (16.3-25.6), 46% had a BMI $<$ 18.5 and none were obese (BMI $\geq$ 30). By NRI, 58% of SP pts were malnourished. Males comprised 71% of SP pts ($p = 0.03$) but no difference from NSP MESCC pts was identified with age, race, ECOG PS or smoking status with univariate analysis. Median overall survival (OS) was 6 months; 4.2 in SP pts and 6.2 in NSP pts. Significant difference was identified with NRI ($p = .0.009$) but not sarcopenia ($p = 0.247$) or BMI ($p = 0.393$). With a multi-variate Cox model for NRI and sarcopenia, including age, sex, race, and ECOG PS, only ECOG PS was a significant predictor of mortality, HR for 2-3 vs 0-1 of 5.4 (2.5-11.9) $p <$ 0.001. **Conclusions:** Sarcopenia at diagnosis was not associated with OS. NRI was superior to BMI alone with respect to discriminating pt outcomes, however ECOG PS was the only measure significantly associated with survival.

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4069 **Poster Session (Board #174), Mon, 8:00 AM-11:00 AM**

Impact of adjuvant therapy in patients with a microscopically positive margin after resection for gastroesophageal cancer.

Lucy Xiaolu Ma, Osvaldo Espin-Garcia, Charles Henry Lim, Peiran Sun, Di Maria Jiang, Hao-Wen Sim, Akina Natori, Bryan Anthony Chan, Daniel Yokom, Stephanie Moignard, Chihiro Suzuki, Eric Xueyu Chen, Geoffrey Liu, Carol Jane Swallow, Gail Elizabeth Darling, Rebecca Wong, Sara Hafezi-Bakhtiari, James Conner, Elena Elimova, Raymond Woo-Jun Jang; Princess Margaret Cancer Centre, Toronto, ON, Canada; Ontario Cancer Institute, Princess Margaret Cancer Centre, Toronto, ON, Canada; University of Toronto, Toronto, ON, Canada; Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; The Kinghorn Cancer Centre, St Vincent's Hospital Sydney, Sydney, Australia; St Lukes Int'l Hosp, Koto-Ku, Japan; Royal Brisbane and Women's Hospital, Brisbane, ON, Canada; Princess Margaret Hospital, Toronto, ON, Canada; Princess Margaret Cancer Centre/ Mount Sinai Hospital, Toronto, ON, Canada; Toronto General Hospital, University Health Network, Toronto, ON, Canada; Mount Sinai Hospital, Toronto, ON, Canada; University of Texas MD Anderson Cancer Center, Houston, TX

Background: A microscopically positive (R1) resection margin following resection for gastroesophageal (GE) cancer has been documented to be a poor prognostic factor. The optimal strategy and impact of different modalities of adjuvant treatment for an R1 resection margin remain unclear. **Methods:** A retrospective analysis was performed for patients (pts) with GE cancer treated at the Princess Margaret Cancer Centre from 2006-2016. Electronic medical records of all pts with an R1 resection margin were reviewed. Kaplan-Meier and Cox proportional hazards methods were used to analyze recurrence free survival (RFS) and overall survival (OS) with stage and neoadjuvant treatment as covariates in the multivariate analysis. **Results:** We identified 78 GE cancer pts with an R1 resection. 11% had neoadjuvant chemotherapy, 14% chemoradiation (CRT), 75% surgery alone. 28% had involvement of the proximal margin, 13% distal, 56% radial, 3% had multiple positive margins. By the American Joint Committee on Cancer 7th edition classification, 88% had a pT3-4 tumour, 66% pN2-3 nodal involvement, 64% grade 3, 68% with lymphovascular invasion. 3% were pathological stage I, 21% stage II and 74% stage III. Adjuvant therapy was given in 46% of R1 pts (24% CRT, 18% chemotherapy alone, 3% radiation alone, 1% reoperation). Median RFS for all pts was 12.6 months (95% CI 10.3-17.2). Site of first recurrence was 71% distant, 16% locoregional, 13% mixed. Median OS was 29.3 months (95% CI 22.9-50) for all pts. The 5 year survival rate was 23% (95% CI 12%-43%). There was no significant difference in RFS (log-rank test $p = 0.63$, adjusted $p = 0.14$) or OS (log-rank test $p = 0.68$, adjusted $p = 0.65$) regardless of adjuvant therapy. **Conclusions:** Most pts with positive margins after resection for GE cancer had advanced pathologic stage and prognosis was poor. Our study did not find improved RFS or OS with adjuvant treatment and only one pt had reresection. The main failure pattern was distant recurrence, suggesting that pts being considered for adjuvant RT should be carefully selected. Further studies are required to determine factors to select pts with good prognosis despite a positive margin, or those who may benefit from adjuvant treatment.

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4070 **Poster Session (Board #175), Mon, 8:00 AM-11:00 AM**

A landscape of circulating tumor DNA in esophageal adenocarcinoma and squamous cell carcinoma.

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Background: Esophageal cancer (EC) is a lethal malignancy with limited treatment options. Genomic analyses have led to the elucidation of numerous dysregulated genes in esophageal adenocarcinoma (AC) and squamous cell carcinoma (SCC), and the potential for advancement of targeted therapies in this disease. Data regarding circulating tumor DNA (ctDNA) plasma analysis in EC in real-world clinical practice is limited. **Methods:** We performed ctDNA next-generation sequencing (NGS) analysis in patients (pts) with EC (January 2015- February 2018). ctDNA analysis was performed using Guardant 360 (Guardant Health, CA) which detects single nucleotide variants and insertion/deletion mutations, and specific amplifications and fusions, in up to 73 different genes. The mutant allele fraction (MAF) for detected alterations was calculated relative to wild type in ctDNA. Therapeutic relevance was defined as alterations within OncoKB levels 1-3B and R1. **Results:** Among 450 pts, 487 total samples were analyzed (77% AC, 31% SCC). ctDNA NGS revealed at least one genomic alteration (excluding variants of uncertain significance and synonymous mutations) in 81% of pts (90% AC, 88% SCC). Median number of alterations per AC patient was 4 [range, 1-59] and a median MAF of 0.84% (range, 0.02% - 83.7%); SCC was 5 [range, 1-26], with a median MAF of 0.99% (range, 0.01% - 85.2%). The total number of unique alterations was 1,162. The most commonly altered genes in AC: *TP53* (70%), *KRAS* (20%), *ERBB2* (18%), *EGFR* (16%), *PIK3CA* (16%); in SCC: *TP53* (88%), *PIK3CA* (24%), *CCND1* (23%), *KRAS* (21%), *EGFR* 15%). Therapeutically relevant alterations will be described. **Conclusions:** ctDNA plasma profiling of pts with EC is a feasible alternative and non-invasive method to gather comprehensive genomic data. Further large comparison studies to assess landscape of genomic alterations observed through ctDNA versus tissue-based assays, in addition to studies of targeted therapy outcomes based on ctDNA-detected alterations, are needed.

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4072 **Poster Session (Board #177), Mon, 8:00 AM-11:00 AM**

First-line avelumab + axitinib in patients with advanced hepatocellular carcinoma: Results from a phase 1b trial (VEGF Liver 100).

Masatoshi Kudo, Kenta Motomura, Yoshiyuki Wada, Yoshitaka Inaba, Yasunari Sakamoto, Masayuki Kurosaki, Yoshiko Umeyama, Yoichi Kamei, Junichiro Yoshimitsu, Yosuke Fujii, Mana Aizawa, Paul B. Robbins, Junji Furuse; Kindai University, Faculty of Medicine, Osaka, Japan; Aso Iizuka Hospital, Fukuoka, Japan; Kyushu Medical Center, Fukuoka, Japan; Aichi Cancer Center Hospital, Nagoya, Japan; National Cancer Center Hospital, Tokyo, Japan; Musashino Red Cross Hospital, Tokyo, Japan; Pfizer R&D Japan, Tokyo, Japan; Pfizer Japan Inc., Tokyo, Japan; Pfizer Inc., San Diego, CA; Kyorin University Faculty of Medicine, Tokyo, Japan

Background: Combining an immune checkpoint inhibitor with a targeted antiangiogenic agent may leverage complementary mechanisms of action for treatment of advanced/metastatic (a/m) hepatocellular carcinoma (HCC). Avelumab is a human anti–PD-L1 IgG1 antibody with clinical activity in various tumor types; axitinib is a tyrosine kinase inhibitor selective for VEGF receptors 1/2/3. VEGF Liver 100 (NCT03289533) is a phase 1b study evaluating safety and efficacy of avelumab + axitinib in treatment-naive patients (pts) with HCC; interim results are reported here. **Methods:** Eligible pts had confirmed a/m HCC, ≥1 measurable lesion, a fresh or archival tumor specimen, ECOG PS ≤1, and Child-Pugh class A. Pts received avelumab 10 mg/kg IV Q2W + axitinib 5 mg orally BID until progression, unacceptable toxicity, or withdrawal. Endpoints included safety and objective response (RECIST v1.1; modified [m] RECIST for HCC). **Results:** Interim assessment was performed after a minimum follow up of 6 months based on the released study data set (clinical cut-off date: Aug 1, 2018). As of the cut-off date, 22 pts (median age: 68.5 y) were treated with avelumab (median: 20.0 wk) and axitinib (median: 19.9 wk). The most common grade 3 treatment-related adverse events (TRAEs) (≥10% of patients) were hypertension (50.0%) and hand-foot syndrome (22.7%); no grade 4/5 TRAEs were reported. Immune-related AEs (irAEs) (≥10% of pts) were hypothyroidism (31.8%) and hyperthyroidism (13.6%). No grade ≥3 irAEs were reported; no pts discontinued treatment due to TRAEs or irAEs. Based on Waterfall plot calculations, tumor shrinkage was observed in 15 (68.2%) and 16 (72.7%) pts by RECIST and mRECIST, respectively. ORR was 13.6% (95% CI, 2.9%-34.9%) and 31.8% (95% CI, 13.9%-54.9%) by RECIST and mRECIST, respectively. OS data were immature at data cutoff. **Conclusions:** The preliminary safety of avelumab + axitinib in HCC is manageable and consistent with the known safety profiles of avelumab and axitinib when administered as monotherapies. This study demonstrates antitumor activity of the combination in HCC. Follow-up is ongoing. Clinical trial information: NCT03289533.

	RECIST N = 22	mRECIST N = 22
Confirmed ORR, % (n)*	13.6 (3)	31.8 (7)
95% CI	2.9-34.9	13.9-54.9
Median PFS, mo*	5.5	3.8
95% CI	1.9-7.3	1.9-7.3
6-mo PFS rate, %*	35.1	30.9
95% CI	15.3-55.8	12.5-51.5

*per investigator assessment.

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4073 **Poster Session (Board #178), Mon, 8:00 AM-11:00 AM**

Ramucirumab (RAM) for sorafenib intolerant patients with hepatocellular carcinoma (HCC) and elevated baseline alpha fetoprotein (AFP): Outcomes from two randomized phase 3 studies (REACH, REACH2).

Josep M Llovet, Chia-Jui Yen, Richard S. Finn, Yoon-Koo Kang, Masatoshi Kudo, Peter R. Galle, Eric Assenat, Marc Pracht, Ho Yeong Lim, Kun-Ming Rau, Christophe Borg, Jean-Baptiste Hiriart, Bruno Daniele, Thomas Berg, Hyun Cheol Chung, Nathalie Godinot, Chunxiao Wang, Yanzhi Hsu, William R. Schelman, Andrew X. Zhu; Icahn School of Medicine at Mount Sinai, New York, NY; National Cheng Kung University Hospital, Tainan, Taiwan; University of California, Los Angeles, Los Angeles, CA; Department of Oncology, Asan Medical Center, Seoul, South Korea; Kindai University, Faculty of Medicine, Osaka, Japan; University Medical Center, Mainz, Germany; CHU de Montpellier, Montpellier, France; Centre Eugène Marquis, Rennes, France; Samsung Medical Center, Sungkyunkwan University, Seoul, South Korea; E-Da Cancer Hospital and Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan; University Hospital of Besançon, Besançon, France; CHU de Bordeaux, Pessac, France; Ospedale del Mare, Napoli, Italy; University of Leipzig, Section of Hepatology, Department of Gastroenterology and Rheumatology, Leipzig, Germany; Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; Eli Lilly and Company, Indianapolis, IN; Eli Lilly and Company, New York, NY; Massachusetts General Hospital Cancer Center, Harvard Medical Center, Boston, MA

Background: Oral multikinase inhibitors that have shown improvements in overall survival (OS) in HCC are associated with clinically important toxicities that commonly require dose adjustment or discontinuation (D/C) due to intolerance. REACH and REACH-2 studied RAM in patients (pts) with HCC who progressed on or were intolerant to sorafenib (SOR), and REACH-2 only enrolled pts with baseline AFP ≥400 ng/mL. In REACH-2 RAM treatment (trt) improved OS compared to placebo (P), supporting findings in REACH pts with baseline AFP ≥400 ng/mL. An exploratory analysis of outcomes by reason for D/C of SOR was performed. **Methods:** Pts had advanced HCC, Child-Pugh A, ECOG PS 0-1, and prior SOR. Pts were randomized to RAM 8 mg/kg or P Q2W. A pooled independent pt data analysis (stratified by study) of REACH-2 and REACH pts (AFP ≥400 mg/mL) was performed. Results are reported by reason for SOR D/C (intolerance or disease progression). OS and PFS were evaluated using Kaplan-Meier method and Cox proportional hazard model. Objective response rate (ORR), disease control rate (DCR) and safety are reported. **Results:** Baseline characteristics in the pooled population were generally balanced between trt arms in each subgroup. Median durations of prior SOR were 2.5 mo for SOR intolerant (n = 70) and 4.0 mo for SOR progressors (n = 472). Median OS (RAM v P) was 10.2 v 6.7 mo for SOR intolerant and 8.0 v 4.7 mo for SOR progressors (Table). Rates of D/C due to trt-related adverse events (AEs) (Table) (7% in each subgroup), and Grade ≥3 AEs (most frequently hypertension) were consistent with those observed in each study. **Conclusions:** Acknowledging limitations of sample size, the RAM trt benefit in SOR intolerant pts was consistent with that in the ITT population. RAM was well tolerated in SOR intolerant pts with low rates of D/C due to related-AEs. Clinical trial information: NCT01140347, NCT02435433.

Analysis Population (RAM v P)	SOR intolerant N = 70 (RAM 42, P 28)	SOR progressors N = 472 (RAM 274, P 198)
OS median, mo	10.2 v 6.7	8.0 v 4.7
HR (95% CI)	0.59 (0.34, 1.02)	0.71 (0.58, 0.88)
PFS median, mo	4.4 v 1.4	2.7 v 1.6
HR (95% CI)	0.32 (0.19, 0.55)	0.64 (0.52, 0.79)
ORR, %	12 v 0	4 v 1
DCR, %	79 v 21	53 v 39
D/C due to related AEs any grade, %	12 v 0	9 v 4

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4074 **Poster Session (Board #179), Mon, 8:00 AM-11:00 AM**

A phase II study of anti–PD-1 antibody camrelizumab plus FOLFOX4 or GEMOX systemic chemotherapy as first-line therapy for advanced hepatocellular carcinoma or biliary tract cancer.

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Background: Advanced hepatocellular carcinoma (HCC) and biliary tract cancer (BTC) patients (pts) have very limited treatment options. Considering the immunogenic effects of oxaliplatin, combination of camrelizumab with oxaliplatin-based chemotherapy might bring a better clinical benefit. **Methods:** That was an ongoing single-arm, multicenter phase 2 trial. Advanced HCC or BTC pts naive to systemic treatment were given camrelizumab (3 mg/kg i.v., every 2 weeks) plus typical FOLFOX4 (infusional fluorouracil, leucovorin and oxaliplatin) or GEMOX (gemcitabine and oxaliplatin) regimen. Primary endpoints were confirmed objective response rate (ORR) per RECIST v1.1 and safety per CTC AE 4.03. **Results:** From Apr 27, 2017 to Oct 31, 2018, 34 Chinese HCC and 47 BTC pts were treated, in which 27 (79.4%) HCC and 17 (36.2%) BTC pts were HBV-infected. In the 34 evaluable HCC pts, confirmed ORR was 26.5% and disease control rate (DCR) was 79.4%. Median time to response (TTR) was 2.0 mo (range 1.5–5.7). Six of the 9 responses were still ongoing, and median duration of response (DoR) was not reached (range 3.3–11.5^{+} mo). Median progression-free survival (PFS) was 5.5 mo. At data cutoff, 61.7% BTC pts were still receiving study drug. In the 43 evaluable BTC pts, with a median duration of exposure of 2.9 mo, confirmed ORR was 7.0% and DCR was 67.4%. Median TTR was 1.9 mo (range 1.8–2.1). Median DoR was 5.3 mo (range 3.7–7.0). Median PFS was not reached yet. Median estimates for overall survival in both HCC and BTC were also not reached. Grade ≥3 treatment-related adverse events (TRAEs) occurred in 85.3% of HCC and 57.4% of BTC pts, most commonly neutrophil count decreased (HCC: 55.9%; BTC: 29.8%), white blood cell decreased (HCC: 38.2%; BTC: 21.3%), platelet count decreased (HCC: 17.6%; BTC: 12.8%), and anaphylaxis (BTC: 19.1%). Only one BTC pt stopped treatment due to a TRAE (recurrent Grade 2 anemia related to FOLFOX4). Grade ≥3 immune-related AEs occurred only in 5.9% of HCC (lipase increased) and 3.8% of BTC pts (anaphylaxis). **Conclusions:** Camrelizumab plus FOLFOX4 or GEMOX chemotherapy was tolerable and might offer a new promising choice for advanced HCC and BTC pts. Clinical trial information: NCT03092895.

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4075 **Poster Session (Board #180), Mon, 8:00 AM-11:00 AM**

Multicentric prospettive study of validation of angiogenesis-related gene polymorphisms in hepatocellular carcinoma patients treated with sorafenib: Interim analysis of INNOVATE study.

Andrea Casadei Gardini, Giorgia Marisi, Vincenzo Dadduzio, Luca Faloppi, Luca Ielasi, Caterina Vivaldi, Mario Domenico Rizzato, Lorenzo Fornaro, Sara Lonardi, Laura Gramantieri, Irene Pecora, Giuseppe Francesco Foschi, Nicola Silvestris, Francesca Fornari, Giulia Orsi, Giulia Rovesti, Daniele Santini, Vittorina Zagonel, Stefano Cascinu, Mario Scartozzi; IRST-IRCCS, Meldola, Italy; Biosciences Laboratory, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy; Istituto Oncologico Veneto-IRCCS, Padova, Italy; Medical Oncology Department, University Hospital, University of Cagliari, Cagliari, Italy; UNIBO, Bologna, Italy; Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy; IVO Veneto, Padova, Italy; Department of Clinical and Experimental Oncology, Medical Oncology 1 Unit, Istituto Oncologico Veneto IOV-IRCCS, Padua, Italy; Center for Applied Biomedical Research (CRBA), S.Orsola-Malpighi Hospital, Bologna, Italy; Internal Medicine, Faenza, Italy; Medical Oncology Unit, Cancer Institute Giovanni Paolo II, Bari, Italy; UNIMORE, Modena, Italy; Unimore, Modena, Italy; Department of Medical Oncology, Campus Bio-Medico - University of Rome, Rome, Italy; University Hospital of Modena, Modena, Italy

Background: In the ePHAS study we analyzed three *eNOS*polymorphisms and at univariate analysis, patients with *eNOS*-786-TTgenotype had significantly shorter median Progression Free Survival (PFS) and Overall Survival (OS) compared to those with other genotypes. On the basis of these preliminary results, our aim is to validate in a prospective study this data in patients with HCC treated with sorafenib. **Methods:** This is a prospective Italian multicenter study, that includes 141 HCC patients receiving sorafenib. We analyzed *eNOS-786*and itwas analyzed by Real Time PCR in relation to the primary end point (OS). Event-time distributions were estimated using the Kaplan-Meier method and survival curves were compared using the log-rank test. **Results:** 141 HCC patients (122 males and 19 females), prospectively treated with sorafenib from May 2015 to September 2018 were included. Median age was 69 years (range 28-88 years). 120 patients had Child-Pugh A and 21 had Child-Pugh B7. 43 had BCLC-B and 98 patients had BCLC-C. Atunivariate analysis, we confirmed that *eNOS*-786 TT genotype were significantly associated with a lower median OS than the other genotypes (8.8 vs 15.7 months, HR 1.69, 95% CI 1.02-2.83 p=0.0424). Following adjustment for clinical covariates (age, gender, etiology, BCLC stage, serum α-FP level, MELD score), multivariate analysis confirmed *eNOS*- 786 and BCLC stage as the independentsprognostic factors predicting OS (TTvsTC+CC; HR: 2.39, 95% CI 1.14-5.03 p=0.0211; C vs B;2.23, 95% CI 1.44-4.77 p=0.039). **Conclusions:** Our prospective study confirms the prognostic role of *eNOS*-786 in advanced HCC patients treated with sorafenib. Clinical trial information: NCT02786342.

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4076 **Poster Session (Board #181), Mon, 8:00 AM-11:00 AM**

IGF-Child-Pugh score as a predictor of treatment outcome in advanced hepatocellular carcinoma patients treated with sorafenib.

Yehia I. Abugabal, Manal Hassan, Roberto Pestana, Lianchun Xiao, Lauren Girard, Kanwal Pratap Singh Raghav, Jeffrey Morris, Reham Abdel-Wahab, Robert A. Wolff, James C. Yao, Hesham M. Amin, Ahmed Omar Kaseb; University of Texas MD Anderson Cancer Center, Houston, TX; The University of Texas - MD Anderson Cancer Center, Houston, TX; MD Anderson Cancer Center, Sao Paulo, Brazil; GI Medical Oncology Department, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Gastrointestinal Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX; Assiut University Hospital, Faculty of Medicine, Assiut, Egypt; Department of GI Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Our recent published studies concluded that Lower levels of Insulin like growth factors-I (IGF-I) is correlated with shorter overall survival (OS) in HCC, and IGF-CP scores assigned based on serum bilirubin, serum albumin level, prothrombin time, and plasma IGF-1 provides better prognostic stratification. Sorafenib is the first frontline drug approved for the treatment of CP class A patients with advanced HCC. CP class A is the standard criterion for active therapy and trials entry in HCC. In this study we aimed at evaluating the predictive ability of IGF-CP to sub-stratify old CP classes and better predict sorafenib outcomes. **Methods:** Total of101 patients were prospectively enrolled from MD Anderson Cancer Center (MDACC). Blood sample were collected and tested for IGF-I and IGF-CP was calculated into class A, B and C. Median OS and progression free survival (PFS) were analyzed, and log rank test was used to compare PFS and OS between subgroups of IGF-CTP score of patients. **Results:** Among CP class, patients who were reclassified as IGF-CP (B) (Old A/new B) had significantly shorter OS in months (m) was 7.6m (95% CI= 5.23-26.51m) and PFS of 2.99m (95% CI=2.53-5.26m) with ($P<0.001$) in both, as compared to patients' who classified as class A by both scoring systems (AA), who had OS of 15.43m (95% CI=12.3-31.18m) and PFS of 4.97m (95% CI=3.26-7.2m), ($P<0.001$) in both. **Conclusions:** IGF-CTP score sub-stratified CP A class, and provided better prognostic stratification and accuracy than CP score in predicting sorafenib survival outcomes in HCC. This approach may lead to a paradigm shift in predicting efficacy and toxicity of systemic HCC therapies and in stratifying patients for active therapy and selection in HCC clinical trials.

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4077 **Poster Session (Board #182), Mon, 8:00 AM-11:00 AM**

Randomized clinical trial of transcatheter arterial chemoembolization plus radiofrequency ablation versus transcatheter arterial chemoembolization for hepatocellular carcinoma with intermediate stage (BCLC stage B) hepatocellular carcinoma beyond Milan criteria.

Xin Yin, Bei Tang, Yu-Hong Gan, Yan-hong Wang, Yi Chen, Ning-lin Ge, Rongxin Chen, Lan Zhang, Boheng Zhang, Zhenggang Ren; Liver Cancer Institute & Zhong Shan Hospital, Fudan University, Shanghai, China; Liver Cancer Institute & Zhong Shan Hospital, Fudan University, Shagnhai, China; Department of Medical Oncology, Zhongshan Hospital, Fudan University, Shanghai, China

Background: To determine treatment efficacy and safety of transarterial chemoembolization (TACE) combined with radiofrequency ablation (RFA) (hereafter, TACE+RFA) in patients with intermediate stage (BCLC stage B) hepatocellular carcinoma (HCC) beyond Milan criteria. **Methods:** In this randomized clinical trial, 110 patients with intermediate stage HCC beyond Milan criteria (single tumor with diameter 5-7cm, median; 3-5 multiple nodules with diameter less than 5cm) were included and randomly assigned to TACE+RFA group (n=55) and TACE group (n=55) at liver cancer institute, Zhongshan hospital. The primary endpoint was overall survival (OS). The secondary end point was progression-free survival (PFS) , time to progress (TTP) and best objective response (BOR). **Results:** The median OS in TACE+RFA and TACE group were 29 and 18 months, respectively. The median TTP and BOR were 15.7 months and 69.1 % in TACE+RFA group and 12.4 months and 40.0 % in TACE group (P=0.004). The 1-, 3-, and 4-year overall survivals for TACE+RFA group and TACE group were 97.2%, 67.9% and 59.4% versus 84.0%, 46.7% and 37.3% , respectively (P = 0.008). The corresponding PFS were 47.3%, 27.2% and 21.7% versus 35.6%,15.3% and 11.4% , respectively (P = 0.04).The incidences of major complications in TACE+RFA group were comparable to those in TACE group (P=0.14). **Conclusions:** TACE+RFA was superior to TACE in improving tumor response and overall survival for patients with intermediate stage (BCLC stage B) hepatocellular carcinoma beyond Milan criteria. Clinical trial information: NCT03636620.

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4078 **Poster Session (Board #183), Mon, 8:00 AM-11:00 AM**

DNA damage repair (DDR) gene alterations as a predictive biomarker for response to platinum-containing chemotherapy in advanced biliary tract cancer (BTC).

Heejung Chae, Changhoon Yoo, Deokhoon Kim, Jae Ho Jeong, Heung-Moon Chang, Kyu-Pyo Kim, Baek-Yeol Ryoo; Asan Medical Center, Seoul, South Korea; Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; Department of Pathology, Asan Institute for Life Sciences, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, Seoul, South Korea; Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

Background: Although many studies using whole-exome sequencing or targeted sequencing have reported the molecular profile of BTC, its clinical implications remains unclear. In this study, we assessed a predictive role of DDR gene mutations in advanced BTC patients treated with platinum-containing regimen. **Methods:** Eighty-eight patients with pathologically-confirmed BTC who received first-line gemcitabine-cisplatin combination (n = 69) or fluoropyrimidine-oxaliplatin combination (n = 19) were included in this analysis. Targeted exome sequencing was performed using Foundation Medicine T7 assay or in-house OncoPanel AMC. Germline or somatic mutations in *ATM*, *ATR*, *BAP1*, *BARD1*, *BRCA1*, *BRCA2*, *BRIP1*, *CHEK2*, *FAM175A*, *GEN1*, *MLH1*, *MSH2*, *MSH6*, *MRE11A*, *NBN*, *PALB2*, *PMS2*, *RAD50*, *RAD51*, *RAD51C*, *RAD51D*, and *XRCC2* were classified as DDR gene mutations. Data regarding baseline characteristics and treatment outcomes were retrospectively obtained from medical records. **Results:** The median age was 62 years (range, 25-78), with male comprising 64.8% (n = 57). By primary tumor site, 21 patients with GBC (23.9%), 44 with ICC (50.0%) and 23 with ECC (26.1%) were included. Most patients received palliative chemotherapy for their initially metastatic (50.0%) or recurred (44.3%) disease; the rest 5.7% had locally advanced disease. The median PFS and OS of overall patients were 7.1 and 16.1 months, respectively with median follow-up duration of 20.2 months. DDR gene mutations were found in 63.5% of patients. *BRCA2* (18.2%) was most frequently mutated, followed by *ATM* (13.6%), and *ATR* (8.0%). DDR gene mutations were significantly associated with prolonged PFS (presence vs. absence; median, 6.9 vs. 5.7 months; P = 0.013) and OS (median, 21.0 vs. 13.3 months, P = 0.009). The impact of DDR gene mutations remained significant in multivariate analyses for PFS that included other prognostic factors (hazard ratio, 0.51; P = 0.009), but not for OS. **Conclusions:** The presence of DDR gene mutations might be a promising predictive biomarker for response to platinum-based chemotherapies in advanced BTC. Future investigation using novel agents targeting DDR gene alteration in BTC are warranted.

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4079 **Poster Session (Board #184), Mon, 8:00 AM-11:00 AM**

Pembrolizumab (pembro) for advanced biliary adenocarcinoma: Results from the KEYNOTE-028 (KN028) and KEYNOTE-158 (KN158) basket studies.

Yung-Jue Bang, Makoto Ueno, David Malka, Hyun Cheol Chung, Adnan Nagrial, Robin Kate Kelley, Sarina Anne Piha-Paul, Willeke Ros, Antoine Italiano, Kazuhiko Nakagawa, Hope S. Rugo, Filippo G. De Braud, Andrea I. Varga, Aaron Richard Hansen, Chao Gao, Suba Krishnan, Kevin Norwood, Toshihiko Doi; Seoul National University College of Medicine, Seoul, South Korea; Kanagawa Cancer Center, Yokohama, Japan; Gustave Roussy, Université Paris-Saclay, Département de Médecine Oncologique, Villejuif, France; Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; Blacktown Hospital and University of Sydney, Sydney, NSW, Australia; University of California San Francisco, San Francisco, CA; The University of Texas MD Anderson Cancer Center, Houston, TX; Antoni van Leeuwenhoek Ziekenhuis, Amsterdam, Netherlands; Institut Bergonié, Bordeaux, France; Kindai University Hospital, Osaka, Japan; University of California San Francisco Comprehensive Cancer Center, San Francisco, CA; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Gustave Roussy, Université Paris-Saclay, Villejuif, France; Princess Margaret Cancer Centre, Toronto, ON, Canada; Merck & Co., Inc., Kenilworth, NJ; National Cancer Center Hospital East, Kashiwa, Japan

Background: Antitumor activity with pembro, an anti–PD-1 antibody, has been observed in patients (pts) with advanced/metastatic biliary tract cancers (BTC), who have limited treatment options. We present follow-up data from pts with advanced BTC treated with pembro in the KN158 (NCT02628067; phase 2) and KN028 (NCT02054806; phase 1) studies. **Methods:** Eligible pts ≥18 y in the KN158/KN028 BTC cohorts had histologically/cytologically confirmed incurable advanced BTC that progressed after/failed any number of prior standard treatment regimens, measurable disease per RECIST v1.1, ECOG PS of 0/1, and no prior immunotherapy. PD-L1–positivity (membranous PD-L1 expression in ≥1% of tumor and associated inflammatory cells or positive staining in stroma) was required for eligibility in KN028, but not KN158. Pts received pembro 200 mg Q3W (KN158) or 10 mg/kg Q2W (KN028) for up to 2 y. Radiographic imaging occurred Q9W for 12 mo (KN158) or Q8W for 6 mo (KN028) and Q12W thereafter. Primary efficacy endpoint in both studies was ORR by RECIST 1.1. Response assessed by independent central review is reported. **Results:** Median (range) follow-up was 7.5 (0.6–29.5) mo in the 104 pts from KN158 and 6.5 (0.6–33.1) mo in the 24 pts from KN028 with BTC. All pts in KN028 and 61 in KN158 had PD-L1–positive tumors. No pt had MSI-H tumors (not assessed in KN028). In KN158, ORR was 5.8% (6/104, all PR [including 1 pt with PD-L1–negative tumor]; 95% CI, 2.1%–12.1%) and median duration of response (DOR) was not reached (NR; range, 6.2 to 23.2+ mo). Median OS and PFS were 7.4 mo (95% CI, 5.5–9.6) and 2.0 mo (95% CI, 1.9–2.1). 12-mo OS rate was 32.7%. In KN028, ORR was 13.0% (3/23, all PR; 95% CI, 2.8%–33.6%) and median DOR was NR (range, 21.5 to 29.4+ mo). Median OS and PFS were 6.2 mo (95% CI, 3.8–10.3) and 1.8 mo (95% CI, 1.4–3.7), respectively. 12-mo OS rate was 27.6%. Grade 3–5 treatment-related AEs occurred in 13.5% in KN158 (1 pt had grade 5 renal failure) and 16.7% of pts in KN028 (no grade 5). 18.3% in KN158 and 20.8% of pts in KN028 had an immune-mediated AE or infusion reaction. **Conclusions:** Pembro provides durable antitumor activity, regardless of PD-L1 expression, and manageable toxicity in a subset of pts with advanced BTC. Clinical trial information: NCT02054806 and NCT02628067.

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4080 **Poster Session (Board #185), Mon, 8:00 AM-11:00 AM**

Comprehensive genomic profiling in FIGHT-202 reveals the landscape of actionable alterations in advanced cholangiocarcinoma.

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Background: Genomic studies of cholangiocarcinoma (CCA) have identified actionable alterations in multiple genes including *IDH1*, *IDH2*, *FGFR2* and *BRAF*, but no targeted therapies have been approved for this indication. Pemigatinib (formerly INCB054828) is a selective FGFR1-3 inhibitor currently being evaluated in multiple tumor types, including advanced CCA harboring *FGFR2* rearrangements. Comprehensive genomic profiling (CGP) was used to identify and enroll advanced CCA patients with *FGFR2* rearrangements into FIGHT-202 (NCT02924376). Here we provide an overview of the genomic landscape of advanced CCA and identify actionable alterations. **Methods:** CGP was performed on tumor samples from 1104 patients with advanced CCA using FoundationOne, a broad-based genomic panel which identifies mutations, rearrangements, and amplifications in 315 cancer genes. **Results:** The most frequently altered genes in advanced CCA were *TP53* (38.1%), *CDKN2A/B* (28.8%), *KRAS* (21.9%), *ARID1A* (15.7%), *SMAD4* (11.3%), *BAP1* (10.6%), *IDH1* (10.5%), *PBRM1* (10.0%), *FGFR2* (9.4%), *ERBB2* (7.6%), *PIK3CA* (7.0%), *MDM2*/*FRS2* (5.8%), and *BRAF* (4.7%). *FGFR2*:*BAP1* was the most significantly co-occurring alteration pair (odds ratio = 8.5; q-value = 1.08×10^{-13}, Fisher's exact test). 42.9% of patients had at least one alteration for which a targeted agent has been either approved or is under investigation. 91 (8.2%) patients had *FGFR2* rearrangements, involving 44 unique partner genes, 37 (84.1%) of which were observed only once. The most prevalent *FGFR2* rearrangement partner, *BICC1*, occurred in only 28 (30.7%) *FGFR2* rearrangement positive patients. *FGFR2* activating point mutations were found in 13 (1.2%) patients. Of 1,091 evaluable patients for microsatellite instability (MSI) or tumor mutational burden (TMB), only 10 (0.9%) were MSI-H and 13 (1.2%) had high TMB ($\geq$ 20 mutations/megabase). None of the MSI-H or TMB-High patients had *FGFR2*, *IDH1* or *IDH2* activating alterations. **Conclusions:** The high frequency (42.9%) of patients with actionable alterations and myriad *FGFR2* rearrangement partners strongly support the use of fusion partner-agnostic CGP in advanced CCA.

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4081 **Poster Session (Board #186), Mon, 8:00 AM-11:00 AM**

CT-based radiogenomic signature to identify *isocitrate dehydrogenase (IDH)1/2* mutations in advanced intrahepatic cholangiocarcinoma.

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Background: *IDH1/2* mutations have a high prevalence (20%) in intrahepatic cholangiocarcinoma (iCCA) and can be associated with therapeutic benefit from IDH inhibitors. Radiomics, a developing field within imaging, has shown its ability to discriminate between tumors of distinct genomic profiles and mutational status. **Methods:** We developed a radiogenomic signature to robustly predict *IDH1/2* mutation status (mutated versus wild-type [WT]) in 22 patients with iCCA using the pretreatment CT scans. The triphasic hepatic CT scan was used to segment the lesion. After semiautomatic segmentation of the tumor, the extracted volume of interest (VOI) was imported into our in-house radiomic pipeline and 610 radiomic features were extracted. The least absolute shrinkage and selection operator regression (LASSO) and minimum redundancy and maximum relevance (mRMR) were used for feature selection. Selected features were used to build a classification model for prediction of *IDH1/2* mutation status (XGboost). The performance of the radiomics model was assessed using leave-one-out cross-validation (LOOCV). **Results:** Of 22 patients, 16 patients (male, 6; female, 10; average age, 55.5 years) had *IDH1* (N = 14) or *IDH2* (N = 2) mutations and 6 patients (male, 4; female, 2; average age = 55.5 years) had *IDH1/2* WT.The CT-derived radiomic signature robustly predicted presence of *IDH1/2* mutations versus WT with an area under the curve (AUC), sensitivity and specificity of 98.4%, 83.3% and 93.8%, respectively ($P = 0.037$) and in a subgroup analysis presence of *IDH1* mutation versus WT with an AUC, sensitivity and specificity of 98.2%, 83.3% and 92.8%, respectively ($P = 0.035$). **Conclusions:** To our knowledge, this is the first study investigating the ability of radiogenomics as a potential method to predict the *IDH1/2* mutation status in iCCA patients. Our data suggest that radiogenomic signature may correlate with *IDH1/2* mutations and represent a promising non-invasive tool to stratify the patients based on molecular alterations.

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4082 **Poster Session (Board #187), Mon, 8:00 AM-11:00 AM**

Efficacy and safety of pembrolizumab in patients with PD-L1 positive advanced biliary tract cancer (BTC): A prospective cohort study.

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Background: For patients with advanced BTC, standard chemotherapy has limited benefit and no molecular targeted agents have been approved. Pembrolizumab is an anti PD-1 immune checkpoint inhibitor which has shown modest activity for advanced BTC patients in prior single-arm phase I/II studies. Considering the heterogeneity of BTC, more data are needed to evaluate the clinical outcomes of pembrolizumab in unresectable or metastatic BTC. **Methods:** In this prospective cohort study, 39 patients with PD-L1 positive BTC who received pembrolizumab in Asan Medical Center, Seoul, Korea were included (ClinicalTrials.gov identifier, NCT03695952). PD-L1 expression was assessed using immunohistochemistry and PD-L1 positive tumors were defined as the expression of PD-L1 in $\geq$ 1% of tumor cells. Pembrolizumab was given at a fixed dose of 200 mg intravenously, every 3 weeks. **Results:** The median age was 61 years old (range, 41-76) and 22 (56.4%) patients were male. Intrahepatic cholangiocarcinoma (CCA) was the most common type (n = 18, 46.2%), followed by gallbladder cancer (n = 12, 30.8%) and extrahepatic CCA (n = 9, 23.1%). Most of the patients had distant metastasis (n = 37, 94.9%). Pembrolizumab was administered as 2nd-, 3rd- and 4th or greater line chemotherapy in 18 (46.2%), 16 (41.0%) and 5 (12.8%) patients, respectively, and median 2 cycles (range 1-10) of pembrolizumab were given. In 36 patients whose response was assessable, partial response (PR) and stable disease were achieved in 4 (11.1%) and 13 (36.1%), respectively. In 19 (52.8%) patients, progressive disease was the best response. In patients with PR, the median time to response was 2.1 months (95% confidence interval (CI), 0.4 – 3.9). With a median follow-up duration of 4.4 months (95% CI, 2.4 – 6.4), median progression-free survival and overall survival was 1.5 months (95% CI, 0.4 – 2.6) and 4.3 months (95% CI, 2.6 – 6.1), respectively. No grade 3/4 adverse events (AEs) were reported and grade 1/2 fatigue (n = 4, 10.3%) was the most common AE. **Conclusions:** In PD-L1 positive BTC, pembrolizumab showed modest efficacy with 11.1% of response rates although our patients were heavily pretreated. Considering the limited therapeutic options and poor survival for these patients, further evaluation of immunotherapy including biomarker analysis is needed.

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4083 **Poster Session (Board #188), Mon, 8:00 AM-11:00 AM**

Final analysis of phase II trial of regorafenib (REG) in refractory advanced biliary cancers (BC).

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Background: While gemcitabine plus cisplatin has demonstrated significant antitumor activity as 1st line therapy of BC, there is no effective treatment after failure of gemcitabine-based therapy. REG is an oral multi-kinase inhibitor that targets angiogenesis, oncogenesis and cancer proliferation/metastasis. We evaluated the efficacy of REG in BC. **Methods:** Patients (pts) with histologically proven BC who progressed on at least one line of systemic therapy received REG 160 mg daily 21 days on 7 days off, in 28 day cycles. The primary endpoint was 6-month (mo) overall survival (OS) and the secondary endpoints were median OS, progression free survival (PFS) and response rates (RR). Pre and post-treatment plasma were collected for cytokine evaluation. **Results:** A total of 39 pts received at least 1 dose of REG; 32 pts were evaluable for efficacy. Median age was 62 (range: 27-88) years and the primary sites of tumor were intrahepatic cholangiocarcinoma (68.8%), extrahepatic (18.8%), and gallbladder (12.5%). Pts were considered evaluable for efficacy if patients received more than 1 cycle of REG. For 32 evaluable pts, 6 mo OS was 52% with median PFS of 2.8 mo (95% CI: 1.1-4.5) and median OS of 7.9 mo (95% CI: 0-18.7). Median PFS and OS of the pts (n=20) failed 1 line of therapy were 3.7 mo (95% CI: 3.2-4.1) and 13.8 mo (95% CI: 1.8-25.8), respectively. Median PFS and OS of the pts (n=12) failed 2 lines were 1.8 mo (95% CI: 1.63-1.97) and 4.5 mo (95% CI: 2.6-6.3), respectively. RR was 9.4% (2 PR and 1 unconfirmed PR) and DCR was 62.5%. Total 71.8% of grade 3/4 adverse events (AE) were observed, and the most common AE were fatigue (56.4%) and hypertension (53.8%). Dose modification was required in 49% of the pts. Among the 23 cytokines analyzed, elevated baseline VEGF-A was associated with good prognosis (HR 0.62, p=0.01). Elevated baseline TIMP-1 (HR 1.79, p=0.04) and IL-6 (HR 1.33, p=0.05) were associated with poor prognosis. REG treatment decreased BMP-9, GP130, VEGF-R2 and VEGF-R3 and increased IL-6, PIGF, TIMP-1, VCAM-1 and VEGF-A significantly. **Conclusions:** The primary endpoint was met in this study. VEGF-A may be further evaluated as a predictive biomarker for REG in BC. Further randomized trials are warranted to confirm the efficacy and the correlative data. Clinical trial information: NCT02115542.

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4084 **Poster Session (Board #189), Mon, 8:00 AM-11:00 AM**

Clinical and molecular features of patients with cholangiocarcinoma harboring FGFR genetic alterations.

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Background: Genetic alterations (GAs) in the fibroblast growth factor receptor (FGFR) pathway are emerging as promising therapeutic targets in CCA. The clinical and molecular features of patients (pts) with CCA harboring FGFR GAs are reported here. **Methods:** A retrospective chart review was performed in pts with CCA who were found to have an FGFR GA on tumor molecular profiling as part of routine care. Data on demographics, risk factors, pathology, systemic therapy, radiographical response, progression free survival (PFS), and overall survival (OS) were collected. **Results:** Among 65 pts, the median age at diagnosis was 55 years old (range = 27-92), and 38 (58%) pts were female, 63 (97%) had intrahepatic CCA, and 5 (11%) had chronic HBV. At presentation, 37% of pts had resectable disease. Of 47 pts with a known CA 19-9 at the time of initial diagnosis, 21 (45%) had a value $<$ 35U/mL. FGFR2 fusions were the most common FGFR GA (78%), followed by FGFR2 mutations (14%), FGFR3 mutations (4%), FGFR3 fusion (2%) and FGFR1 amplification (2%). The most common fusion partners were BICC1 (20%), POC1B (6%), SORBS1 (6%), DBP (4%), and TACC2 (4%). The most common co-alterations were in *ARID1A, CDKN2A/B, TP53, BAP1, IDH1, HER2, BRCA2*, and *PTEN*. The median lines of palliative systemic therapies received was 3 (range = 0-8), and 9/65 (14%) pts had $>$ 1 FGFR inhibitor (FGFRi). For the 30 (46%) pts with FGFR2 fusions who received gemcitabine/platinum as first line palliative systemic therapy, the median PFS was 4.7 months (95% CI: 2.1-6.0). In the overall population, the median OS from time of initial diagnosis was 35.8 months (95% CI:29.7-52.7). Among 46 pts who received an FGFRi on a clinical trial and had $\geq$ 1 follow-up scan, the overall response rate (ORR) by RECIST v1.1 in pts with FGFR2 fusions, was 35.8% (14/39) on their first FGFRi; ORR was 16.7% (1/6) for pts with FGFR2 mutations. **Conclusions:** Pts with CCA harboring FGFR GAs were found to have a high rate of normal CA 19-9 and short median PFS on first line gemcitabine/platinum compared to historical controls but additional comparative studies are necessary to evaluate these findings.

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4085 Poster Session (Board #190), Mon, 8:00 AM-11:00 AM

Frequency of BRCA mutation in biliary tract cancer and its correlation with tumor mutational burden (TMB) and microsatellite instability (MSI).

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Background: Biliary tract cancers constitute ~3% of cancers worldwide with incidence increasing, especially for intrahepatic cholangiocarcinoma (IHC). The prognosis of these tumors remains dismal and novel treatment strategies are needed to improve overall survival. *BRCA* mutations occur in biliary tract cancers but their frequency in distinct sites of biliary tract cancer is unknown. Moreover, no data are available correlating *BRCA* mutation with immunogenic markers such as TMB, MSI, or PD-L1 expression. **Methods:** Tumor samples from 1288 primary biliary tract cancers, comprising IHC (n = 746), extrahepatic cholangiocarcinoma (EHC) (n = 189), gallbladder (GBC) (n=353) were profiled at Caris Life Sciences, Phoenix, AZ. Testing included NextGen SEQ (MiSeq on 47 genes, NextSeq on 592 genes) and PD-L1 IHC (SP142). TMB was calculated based on somatic nonsynonymous missense mutations, and MSI was evaluated by NGS of known MSI loci. **Results:** *BRCA* mutations were detected in 3.6% (N = 46) of samples (*BRCA1* 0.6%, *BRCA2* 3%), no differences were seen based on the site of the tumor. In GBC and IHC *BRCA2* mutations (4.0% and 2.7%) were more frequent than *BRCA1* (0.3% and 0.4, $p < 0.05$) while in EHC, similar frequency was observed (*BRCA1*: 2.1%; *BRCA2*: 2.6%). There was no significant association with gender or age. In *BRCA*-mutant biliary tract cancer the most frequently mutated genes were *TP53* (55.6%), *ARID1A* (52.2%) and *KRAS* (26.1%), *KMT2D/C* (20%, 13%) and *CDKN2A(13%)*. Overall, *BRCA* mutations were associated with a higher rate of MSI-H (19.5% vs 1.7%, $p = 0.001$) and higher TMB in both MSI-H and MSS tumors ($p<0.05$). When investigated separately, *BRCA* association with elevated TMB was seen in IHC and EHC, but not in GBC. No correlation was seen with PD-L1 expression. *TP53*, *KMT2D/C*, *RB1*, *PTEN*, *KDM6A* mutations and *FGFR1* amplifications were significantly higher in *BRCA* mutated tumors ($p < 0.05$). **Conclusions:** *BRCA* mutations are found in a significant subgroup of biliary tract tumors and are associated with an immunogenic tumor profile. These data provide rationale for trials testing PARP inhibitors in combination with immunotherapy and targeted therapies in patients with *BRCA*-mutant biliary tract cancers that are MSS.

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4086 **Poster Session (Board #191), Mon, 8:00 AM-11:00 AM**

Efficacy and safety of FOLFIRINOX in advanced biliary tract cancer after failure of gemcitabine plus cisplatin: A phase II trial.

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Background: Currently there is no established standard treatment after failure of gemcitabine plus cisplatin (GemCis) for advanced biliary tract cancer (BTC). Based on the efficacy of FOLFIRINOX in advanced pancreatic cancer, which has histological and prognostic similarities with BTC, a Phase 2 study was conducted to determine whether FOLFIRINOX is effective and safe in BTC. **Methods:** Patients with BTC and an ECOG PS of 0/1 who had disease progression or unacceptable adverse events (AEs) after at least 3 cycles of GemCis were included. Patients received oxaliplatin 85 ml/m^2, irinotecan 180 mg/m^2, leucovorin 400 mg/m^2, fluorouracil bolus at 400 mg/m2, followed by fluorouracil continuous infusion of 2400 mg/m^2 over 46-hour every 2 weeks. This phase 2 study was conducted according to the two-stage Simon's Design. Stage 2 was activated if at least 1 objective response rate (ORR) or 2 stable diseases were observed among 10 patients in stage 1 and a maximum of 3 patients had severe AEs within the first 6 weeks of treatment. If more than 4 patients required a dose reduction in stage 1, stage 2 was initiated with a standard dose reduction (fluorouracil bolus was omitted and irinotecan reduced to 140 mg/m^2). Primary outcome was ORR per RECIST 1.1 and secondary outcomes were overall (OS), progression free survival (PFS), and safety profile. **Results:** Forty patients were screened and 30 patients were included between May 2016 and July 2018. Median age was 60 years and 63% of patients were males. In stage 1, 5 patients required a dose reduction within the first 6 weeks due to AEs, leading to initiation of stage 2 with modified FOLFIRINOX after inclusion of 10 patients. The partial response rate was 10% (3/30), disease control rate 67% and median OS and, PFS were 10.7 and 6.2 months, respectively. Most common grade 3/4 adverse events include neutropenia (50%), anemia (17%), diarrhea (13%), thrombocytopenia (10%), and deviated liver function tests (10%). **Conclusions:** This is the first Phase 2 study with modified FOLFIRINOX in BTC showing promising disease control rate, OS, and PFS, with an acceptable safety profile. Modified FOLFIRINOX is currently tested as a first-line treatment for patients with BTC in the ongoing randomized prospective Phase 2/3 AMEBICA trial (NCT02591030). Clinical trial information: NCT02456714.

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4087 **Poster Session (Board #192), Mon, 8:00 AM-11:00 AM**

Profiling of 3,634 cholangiocarcinomas (CCA) to identify genomic alterations (GA), tumor mutational burden (TMB), and genomic loss of heterozygosity (gLOH).

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Background: The management of CCA has evolved as targeted and immune checkpoint inhibitor (ICPI) therapies have emerged. We used comprehensive genomic profiling (CGP) to characterize the genomic alterations (GA) that have potential to personalize therapy for CCA. **Methods:** 3634 CCA underwent hybrid capture based CGP on 0.8-1.1 Mb of the coding genome to identify GAs in exons and select introns in up to 404 genes, TMB, microsatellite status (MSI) and % monoallelic genome (gLOH). PD-L1 expression was determined by IHC (Dako 22C3). **Results:** 52% of CCA were female with a median age of 62 years (range 16 - > 89). The most common biopsy sites were liver (74%), lymph node (4%), bile duct (3.3%), and lung (2%). MSI-high was rare (1%), 118 and 47 cases had TMB > 10 and > 20 mut/mb respectively. Of the latter, 51% (24/47) were MSI-H. *PD-L1* amplification (AMP) was present in 0.27%. Of 490 CCA tested, 43 (9%) were positive for PD-L1 expression. 11% of cases had gLOH > 16%, only 2 cases had both TMB > 20 and gLOH > 16%. GA were most common in *TP53* (31%), *CDKN2A* (29%), *KRAS* (20%) and *ARID1A* (17%). Potentially targetable GAs included *FGFR2* (11%, 85% fusions), *BRAF* (5%, 50% V600E), *ERBB2* (5%, 72% AMP), *MET* (2%, 90% AMP), *EGFR* (0.52%) and rarer (< 0.5%) *FGFR3*, *RET*, *FGFR1*, *ALK*, and *ROS1* fusions. The *FGFR2* fusions had 128 unique 3' partner genes including *BICC1* (26%), *CCDC6* (3.2%), *AHCYL1* (2.6%) and *KIAA1217* (2.6%). *FGFR2* fusions occurred in a mutually exclusive fashion from high gLOH ($p < 0.002$), but not high TMB. GA in *IDH1* (15%) were mutually exclusive of *FGFR2* fusions ($p <$ 1e-13), but co-occurred with *PBRM1* GA (23%, $p <$ 1e-21), *ARID1A* (26% $p <$ 1e-10). IDH1 GA had gLOH similar to the overall CCA population but were enriched for low TMB ($p <$ 1e-3). **Conclusions:** Nearly 20% of CCA cases harbor targetable kinase GA, half of which were *FGFR2* fusions. Independently, an additional 10% (gLOH) and 1% (high TMB, MSI and/or *PD-L1* AMP) may benefit from PARP inhibitors and ICPI respectively. Independently, co-mutation of *IDH1* and *PBRM1/ARID1A* defines a class of CCA that warrants further investigation for sensitivity to PARP inhibitors and may serve as a paradigm for other tumors (ie. gliomas) with a similar co-occurrence landscape.

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4088 **Poster Session (Board #193), Mon, 8:00 AM-11:00 AM**

Association of adverse events (AEs) with efficacy outcomes for cabozantinib (C) in patients (pts) with advanced hepatocellular carcinoma (aHCC) in the phase III CELESTIAL trial.

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Background: Class-specific AEs occurring with tyrosine kinase inhibitors have been associated with improved efficacy outcomes in several tumor types including aHCC. In the phase 3 CELESTIAL trial (NCT01908426), C, an inhibitor of VEGFR, MET, and AXL, improved overall survival (OS) and progression-free survival (PFS) vs placebo (P) in pts with previously treated aHCC. Here, we retrospectively evaluate the association of palmar-plantar erythrodysaesthesia (PPE) and hypertension (HTN) with OS and PFS for C in the CELESTIAL trial. **Methods:** 707 pts with aHCC were randomized 2:1 to receive 60 mg C or P once daily. Eligible pts had Child-Pugh score A, ECOG PS $\leq$1, must have received prior sorafenib, and could have received up to two prior regimens of systemic therapy for HCC. OS and PFS with C were evaluated for pts with any grade PPE or grade $\geq$3 HTN within the first 8 weeks of study treatment. **Results:** Overall, 374 (80%) pts in the C arm and 179 (76%) pts in the P arm completed $\geq$8 weeks of treatment. In the first 8 weeks, 188 (40%) of C-treated pts developed any grade PPE vs 11 (5%) of P-treated pts, and 61 (13%) of C-treated pts developed grade $\geq$3 HTN vs 3 (1%) of P-treated pts. Median OS with C was 14.4 mo for pts with any grade PPE vs 8.4 mo for pts without PPE (HR 0.59, 95% CI 0.47-0.74), and median PFS with C was 6.5 mo vs 3.7 mo, respectively (HR 0.63, 95% CI 0.51-0.78). Median OS with C was 16.1 mo for pts with grade $\geq$3 HTN vs 9.5 mo for pts without grade $\geq$3 HTN (HR 0.56, 95% CI 0.39-0.80), and median PFS with C was 7.4 mo vs 4.4 mo, respectively (HR 0.59, 95% CI 0.43-0.82). Some imbalances in baseline characteristics were present. Pts with PPE had better ECOG PS (60% vs 47% ECOG 0), better liver function (48% vs 34% ALBI grade 1), and less macrovascular invasion (24% vs 30%) than those without. Likewise, pts with grade $\geq$3 HTN had better ECOG PS (61% vs 51% ECOG 0), better liver function (56% vs 37% ALBI grade 1), and less macrovascular invasion (20% vs 29%) than those without. **Conclusions:** The development of PPE or grade $\geq$3 HTN with C was associated with prolonged OS and PFS in pts with previously treated aHCC although some imbalances in baseline characteristics between comparator groups were present. Clinical trial information: NCT01908426.

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4089 **Poster Session (Board #194), Mon, 8:00 AM-11:00 AM**

Nab-paclitaxel plus S-1 as first line treatment for advanced or metastatic biliary tract adenocarcinoma: A phase 2 study.

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Background: Gemcitabine plus cisplatin or S-1 can be used as first-line treatment for advanced or metastatic biliary tract adenocarcinoma. Multiple phase 2 studies found that gemcitabine, oxaliplatin, capecitabine, S-1 were not superior to gemcitabine plus cisplatin. Nab-paclitaxel plus S-1 was effective and well-tolerated in pancreatic cancer. **Methods:** Patients with pathological confirmed advanced or metastatic biliary tract adenocarcinoma (gallbladder carcinoma, intrahepatic cholangiocarcinoma ICC, extrahepatic cholangiocarcinoma ECC) were treated with Nab-paclitaxel plus S-1(Nab-paclitaxel 120mg/m^2, d1 and d8; S-1 80-120mg/d, d1-14; q21d). Patients that received PR or SD (RECIST1.1)after 6 cycles were given S-1 maintenance treatment. The primary endpoint was ORR. The study used Simon's Two Stage design. **Results:** From March 2016 to September 2018, we recruited 54 patients, with 27 males (50%) . The median age was 58(34-73yrs). As of Dec 31 2018, the median treatment cycle was 4(1-6 cycles). 51 patients were evaluable for efficacy: PR 14(27.5%), SD 22 (DCR=PR+SD: 70.6%), PD 15 (29.4%). The median PFS was 6 months, and the median OS was 13.2 months. The response rate varied in different tumor location: gallbladder carcinoma 53.8% (7/13), ICC 18.2% (6/33), ECC 20% (1/5).Common grade 3/4 AEs were: leucopenia 17 (31.5%), hyperbilirubinemia 5(9.3%), Mucositis 4 (7.4%) , neurotoxicity 2 (3.7%), diarrhea 2 (3.7%), omit 1(1.9%), fatigue 1 (1.9%), thrombocytopenia 1 (1.9%), ALT increase 1 (1.9%). **Conclusions:** Nab-paclitaxel plus S-1 as first line treatment for advanced or metastatic biliary tract adenocarcinoma was effective and well-tolerated, especially for gallbladder carcinoma (ORR 53.8%). This regimen need further exploration. Clinical trial information: NCT03830606.

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4090 **Poster Session (Board #195), Mon, 8:00 AM-11:00 AM**

Cell-free junctional DNA fragment from hepatitis B virus integration in HCC for monitoring postresection recurrence and clonality.

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Background: About one-third of patients suffer tumor recurrence within the first year after surgical resection of HCC. Early recurrence compromised their overall survival. Timing detection of HCC recurrence and its clonality is required to implement therapeutic trials appropriately. This study examined the virus-host chimera DNA (vh-chimera DNA), generated from junctions of HBV integration in HCC chromosome and released into blood, as a potential circulating biomarker for this clinical setting. **Methods:** We established a capture-next generation sequencing (NGS) platform to identify the HBV integrations in 50 resected HBV-related HCC. For individual HCC, the major clonal HBV integration sites were chosen to design specific primers for droplet digital PCR (ddPCR) to detect and quantify the vh-chimera DNA in plasma samples, collected either just before surgery or two months after surgery. Levels of vh-chimera DNA were then correlated with baseline HCC size or recurrence in one-year follow up. **Results:** We succeeded in detecting HBV integrations in the HCC from 44 out of 50 HBV-related HCC patients (88%). The copy number of vh-chimera DNA in plasma at surgery from 42 patients correlated with tumor sizes, with the detection limit at 1.5-2 cm. Among the plasma collected 2 months after surgery, 26.2% of samples contained the same HCC signature vh-chimera DNA as baseline plasma, indicating a possible residual tumor. Consistently, 81.8% of them suffered HCC recurrence within one year. The signature vh-DNA in the plasma suggested the majority of recurrences coming from the original HCC clones, whereas 2 from de novo ones. **Conclusions:** This study supported vh-chimera DNA as a new circulation marker for detecting the existence of most HBV-related HCC. This new biomarker may complement AFP to help detect residual or recurrent HCC and their clonality after curative therapies.

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4091 **Poster Session (Board #196), Mon, 8:00 AM-11:00 AM**

Novel staging system using carbohydrate antigen (CA) 19-9 in extrahepatic cholangiocarcinoma (ECCC) and its implications on overall survival (OS).

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Background: Optimal management of ECCA patients with elevated CA19-9 remains undefined. We hypothesized CA 19-9 elevation as a marker of aggressive biology in ECCA and that inclusion of CA 19-9 in the staging may improve OS discrimination. **Methods:** Patients with ECCA with CA 19-9 levels reported to the National Cancer Database (years 2004-2015) were included. The patients were classified based on their CA19-9 levels and a new staging system was proposed. Based on the current knowledge, we considered 37 U/ml as our cut off. Kaplan Meier method was used to compare OS between the groups. The net reclassification improvement (NRI) model was used to assess the predictive improvement in the proposed survival model. **Results:** A total of 2100 patients met the inclusion criteria: 601 (32%) and 1436 (68%) had normal and elevated CA19-9 levels, respectively. Rates of chemo (p=0.16) and radiation therapy (p=0.07) were similar between groups, but patients with elevated CA19-9 were less likely to undergo resection. Resected patients with CA19-9 elevation had higher 30-day mortality (p=0.02) and lower median OS ($p<0.01$). Patients with elevated CA 19-9 levels had decreased stage-specific survival in all stages ($p<0.01$). On adjusted analysis, CA19-9 elevation independently predicted poor OS (HR: 1.67 [1.42-1.97]) with impact resembling nodal metastasis, positive resection margin, lymphovascular invasion, and non-receipt of surgery or chemotherapy ($p<0.01$). CA 19-9 included proposed staging system (Table) had a better OS discrimination over AJCC 7th edition. The new staging system had a concordance of 60% as opposed to 58% for the AJCC staging, leading to an improvement of 2% ($p<0.01$). NRI of 46% (95% CI: 39-57) indicates that the new staging system is substantially effective at re-classifying events at 12 months as compared to AJCC staging. **Conclusions:** Elevated CA19-9 was found to be an independent risk factor for mortality in ECCA and its inclusion in the newly proposed staging system markedly improved OS discrimination.

New proposed staging system.

New Stage	
Stage 1	AJCC Stage 1 or AJCC Stage 2
Stage 2	AJCC Stage 3 or AJCC Stage 1+r or AJCC Stage 2+r
Stage 3	AJCC stage 3+r
Stage 4	AJCC Stage 4

r= elevated CA 19-9 ≥ 38 U/ml.

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4092 **Poster Session (Board #197), Mon, 8:00 AM-11:00 AM**

SHR-1210 plus GEMOX as first line treatment in biliary tract cancer: Results from a single-arm exploratory study.

Xiaofeng Chen, Xiaofeng Wu, Hao Wu, Qianwen Shao, Feipeng Zhu, Xiaofeng Qian, Fengjiao Zhao, Jing Sun, Jian Wang, Gaohua Han, Dongqin Zhu, Liuqing Zhu, Yang Shao, Yanhong Gu, Xiangcheng Li, Yongqian Shu; The First Affiliated Hospital of Nanjing Medical University, Nanjing, China; Taizhou People's Hospital affiliated to Nantong University, Nanjing, China; Nanjing Geneseeq Technology Inc., Nanjing, China; Nanjing Geneseeq Technology Inc.; School of Public Health, Nanjing Medical University, Nanjing, China

Background: SHR1210 is a humanized anti-programmed cell death receptor 1 (PD-1) antibody. We conducted a single arm exploratory study to evaluate the efficacy and safety of SHR-1210 plus gemcitabine and oxaliplatin (GEMOX) as first line treatment in patients (pts) with biliary tract cancer (BTC). **Methods:** Pts received SHR-1210 (3mg/kg, total dose ≤200mg, ivd, D1/2W) combined with gemcitabine (800 mg/m2, ivd, D1/2W) and oxaliplatin (85mg/m2, ivd, D2/2W). Combined chemotherapy lasted for no more than 8-12 cycles. Once chemotherapy intolerance occurred or at end of 12-cycle combined chemotherapy, pts with stable disease or objective response would continue to take SHR-1210 as single agent until disease progression or intolerable toxicity. Response was assessed every 8 weeks. **Results:** From February 2018 to Dec 15, 2018, 32 eligible pts were recruited, and 27 pts who had been treated for more than 2 months were included in this analysis. Median age was 64 (range 47-75) years. 16 pts were bile duct cancer, while 11 pts were gallbladder cancer. 26 pts can be evaluated for efficacy. Twelve pts achieved partial response (46.15%), 12 pts stable disease (46.15%), and 2 pts progressive disease. Pts with gallbladder cancer had the trend of higher objective response (63.64% vs 33.33%, p = 0.23) than those with cholangiocarcinoma. 19 pts had tissue sample for next generation sequencing. Gallbladder cancer had the tendency of higher median tumor mutation burden (TMB) than cholangiocarcinoma (8.1mut/Mb vs 5.4mut/Mb, p=0.33). Pts with high TMB(>8.6 mut/Mb, based on geenseeq BTC database) had significantly higher objective response than low TMB (100% vs 26%, p=0.0294). The most common grade ≥3 adverse events were nausea (18.52%),increased GGT (gammaglutamyltransferase,18.52%) , hypokalemia(18.52%) and fatigue (18.52%). **Conclusions:** SHR-1210 plus GEMOX showed promising efficacy with tolerable adverse events for BTC pts. Gallbladder cancer pts seem to benefit more from this treatment. Tumor mutation burden may be a predictive factor for immunotherapy. Clinical trial information: NCT03486678.

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4093 **Poster Session (Board #198), Mon, 8:00 AM-11:00 AM**

Impact of tumor shrinkage pattern by biweekly triplet gemcitabine/cisplatin/s-1 for biliary tract cancers: Implication for neoadjuvant therapy (KHBO1401-1A study).

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Background: There have not been any new evidenced regimen for biliary tract cancers (BTC) after ABC-02 study, we conducted biweekly triplet gemcitabine/cisplatin/s-1 regimen (GCS) and compared with conventional doublet gemcitabine/cisplatin regimen (GC) as phase III (KHBO1401) study. Biweekly GCS was proved not only to prolong patients' survival (HR 0.791 (90% C.I. 0.628-0.996), one-sided P = 0.046) but also to achieve high response rate (42% versus 15%, P < 0.001) and good conversion rate (2.5% versus 0.0%), and would be good for neoadjuvant therapy. Herein, we investigated tumor shrinkage pattern to explore possibilities of neoadjuvant therapy. **Methods:** Totally 246 patients were enrolled in multi-center phase III KHBO1401 study between 2014 and 2016. Tumor shrinkage pattern (best response, timing, response at 100 days (14 weeks, approx. 6 cycles in GCS and 4 cycles in GC), etc.) and survival were investigated in the patients with measurable BTC (n = 183, 74%, 91 in GCS and 92 in GC) as sub-analysis. P < 0.05 was considered statistically significant. **Results:** Tumor shrinkage pattern could be divided to 4 categories by the response at 100 days after enrollment; category A (< -30% in size), B (-30% to 0%), C (0% to +20%), and D (> +20%). GCS arm contained more category A & B (61 (67%) vs. 33 (36%), P < 0.0001). Each category predicted best response and overall survival (p < 0.0001). Timing for maximum tumor response were different among categories, category A achieved maximum tumor shrinkage at 165 +/- 76 days in GCS and 225 +/- 190 days in GC, category B at 139 +/- 78 versus 154 +/- 82 days, and category C and D did not achieve tumor shrinkage. Maximum tumor shrinkage in category A was -53% in GCS versus -65% in GC (P = 0.0892), and 20% patients in GCS underwent tumor regrowth 154 +/- 143 days later. **Conclusions:** GCS provided faster and more tumor shrinkage with better survival in the comparison of GC, although it had 20% risk of re-growth after 6 cycles.

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4094 **Poster Session (Board #199), Mon, 8:00 AM-11:00 AM**

The prognostic role of soluble transforming growth factor-β related with soluble programmed death-ligand 1 in biliary tract cancer.

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Background: We previously reported that soluble programmed death-Ligand 1 (sPD-L1) at pre-chemotherapy indicated the prognostic value for overall survival (OS) and the dynamics of sPD-L1 during palliative chemotherapy correlated with disease burden in biliary tract cancer (BTC). Transforming growth factor (TGF) -β attenuates tumor response to PD1/PD-L1 inhibitors. Strategy of dual targeting of PD1/PD-L1 and TGF-β is now under investigation. This study aimed to evaluate the association between soluble TGF-β (sTGF-β) and sPD-L1, dynamics during chemotherapy and its prognostic role in BTC. **Methods:** Study population consisted of 90 BTC patients treated with first line chemotherapy. Blood samples at pre-and post-chemotherapy and at disease progression (PD) were prospectively collected. Plasma sTGF-β and sPD-L1 levels were measured by using an enzyme-linked immunosorbent assay. **Results:** The median progression free survival (PFS) and OS of all patients was 6.9 months (m) (95% CI, 5.2-8.6) and 11.5 m (95% CI, 9.4-13.6). The best response was CR in 7 (7.8%), PR in 20 (22.2%), SD in 52 (57.8%), and PD in 11 patients (12.2%). The mean baseline sTGF-β and sPD-L1 were 16.4 ng/ml and 1.3 ng/ml. There was a positive association between sTGF-β and sPD-L1 in terms of baseline levels and changes after chemotherapy (at pre-chemo, Pearson correlation = 0.578, $p < 0.001$; change after chemotherapy, Pearson correlation = 0.542, $p < 0.001$). Patients with higher pre-chemotherapy sPD-L1 (> 1.3 ng/ml) showed worse OS (9.2 vs 16.2 m, $p < 0.001$). Both sPD-L1 (1.8 vs 1.0 ng/ml, $p < 0.001$) and sTGF-β (20.5 vs 11.6 ng/ml, $p < 0.001$) were increased significantly at the time of PD compared with pre-chemotherapy. Regarding changes after chemotherapy, increased sTGF-β after chemotherapy ($\Delta > 3.2$ ng/ml) had worse prognosis (PFS: 5.1 vs 7.3 m, $p = 0.024$; OS: 9.2 vs 12.3 m, $p = 0.028$). This prognostic value of change of sTGF-β after chemotherapy was also significant in multivariable analysis with other clinical factors (PFS: HR = 1.78, $p = 0.022$; OS: HR = 1.86, $p = 0.018$). **Conclusions:** In BTC, there is a positive association between sTGF-β and sPD-L1 value in terms of baseline levels and changes after chemotherapy. sTGF-β could be associated with the survival, particularly, increased value after chemotherapy indicates worse prognosis.

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4095 **Poster Session (Board #200), Mon, 8:00 AM-11:00 AM**

A phase I study of H3B-6527 in hepatocellular carcinoma (HCC) or intrahepatic cholangiocarcinoma (ICC) patients (pts).

Teresa Macarulla Mercade, Victor Moreno, Binu John, John Charles Morris, Michael B. Sawyer, Wei Peng Yong, Martin Gutierrez, Thomas Benjamin Karasic, Bruno Sangro, Yang Sheng-Shun, Carleen Gentry, Amy Kim, Pavan Kumar, Crystal MacKenzie, Nathalie Rioux, Joanne Schindler, Anand Selvaraj, Richard S. Finn; Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; START Madrid - FJD, Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain; Hunter Holmes McGuire VA Medical Center, Richmond, VA; University of Cincinnati Cancer Institute, Cincinnati, OH; Cross Cancer Institute and University of Alberta, Edmonton, AB, Canada; National University Cancer Institute, Singapore, Singapore; Hackensack University Medical Center, Hackensack, NJ; University of Pennsylvania Abramson Cancer Center, Philadelphia, PA; Clinica Universidad de Navarra and Biomedical Research Network in Hepatic and Digestive Diseases, Pamplona, Spain; Taichung Veterans General Hospital, Taichung, Taiwan; H3 Biomedicine, Cambridge, MA; H3 Biomedicine, Inc., Cambridge, MA; University of California, Los Angeles, Los Angeles, CA

Background: FGF19 overexpression is hypothesized to hyperactivate FGFR4 and its downstream signaling pathway leading to enhanced tumor growth in HCC/ICC. Targeting FGFR4 may have therapeutic benefit in HCC/ICC with altered FGF19 signaling. A phase 1 study (NCT02834780) was initiated to assess H3B-6527, an investigational highly selective covalent FGFR4 inhibitor. **Methods:** Adult pts with advanced HCC or ICC, ECOG PS 0-1, well compensated liver function, and who progressed after at least one prior therapy, were administered H3B-6527 orally QD (once daily) on a 21-day cycle following a 3+3 design. Patients in the dose escalation phase were treated regardless of FGF19 status. Adverse events (AEs), pharmacokinetics (PK), and pharmacodynamics (PD) were assessed. Response was determined by RECIST 1.1 or modified RECIST every 6 weeks. **Results:** As of 06-Jan-2019, 37 pts have been treated with H3B-6527 at doses of 300 to 1400 mg QD (23 pts in escalation; 14 in expansion). In dose escalation, a total of 17 patients with HCC, Child-Pugh A received prior systemic therapy including 100% with prior TKI and 35% with prior IO. 12% had hepatitis B virus and 47% had hepatitis C virus. H3B-6527 plasma levels increased with dose from 300 to 1000 mg QD and plateaued. H3B-6527 was rapidly absorbed with a t_{max} of ~2-3 h and showed a terminal half-life of ~4-5 h, following administration of 1000 mg (fasted). No dose-limiting toxicities or $\geq$ Grade 3 treatment-related AEs (TRAE) have been observed in escalation. Most common TRAEs ($\geq$ 10%) were diarrhea, nausea, and vomiting. Based on safety, PK, and PD, 1000 mg QD was the recommended phase 2 dose. Durable stable disease and partial responses (PR) have been observed on the once daily fasted schedule; 2 of 17 pts with HCC achieved PRs and an additional 7 with stable disease were on treatment for $\geq$ 5 months. **Conclusions:** H3B-6527 is well tolerated and demonstrates early signs of clinical activity. Dose expansion on QD schedule and exploration of BID (twice daily) schedule is ongoing. Clinical trial information: NCT02834780.

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4096 **Poster Session (Board #201), Mon, 8:00 AM-11:00 AM**

Non-invasive detection of acquired resistance to FGFR inhibition in patients with cholangiocarcinoma harboring FGFR2 alterations.

Anna M. Varghese, Juber Ahamad A Patel, Yelena Yuriy Janjigian, Fanli Meng, S Duygu Selcuklu, Catherine Zimel, David Michael Hyman, Gopa Iyer, Brian Houck-Loomis, Ghassan K. Abou-Alfa, Michael F. Berger, Maeve Aine Lowery; Memorial Sloan Kettering Cancer Center, New York, NY; Memorial Sloan-Kettering Cancer Center, Leukemia Service and Human Oncology and Pathogenesis Program, New York, NY; Trinity College Dublin, Dublin, Ireland

Background: FGFR2 alterations are present in 14% of cholangiocarcinomas (CCA) and are promising targets of investigational FGFR-directed therapies. Cell-free DNA profiling has emerged as a non-invasive approach to monitor disease and longitudinally characterize tumor evolution. We describe the use of circulating tumor DNA (ctDNA) among patients (pts) with FGFR2-altered CCA receiving FGFR-targeted therapy in the identification of acquired FGFR2 mutations (mut) at resistance. **Methods:** Serial blood samples were collected from 8 pts with FGFR-altered CCA for ctDNA isolation and next generation sequencing. Plasma ctDNA collected at baseline and resistance to FGFR-targeted therapy were sequenced using a custom ultra-deep coverage cfDNA panel, MSK-ACCESS, incorporating dual index primers and unique molecular barcodes to enable background error suppression and high-sensitivity mut detection. The assay was enhanced to include all protein-coding exons and relevant introns of FGFR2. In 5/8 pts, genomic profiling of an initial tumor biopsy was performed. **Results:** 8 pts with FGFR2-altered CCA (7 gene fusions, 1 amplification) were treated with FGFR-targeted therapies. 7/8 pts exhibited stable disease or partial response. 19 total acquired mut in FGFR2 were detected at resistance in 5/8 pts (between 1-9 unique mut identified in each sample). All mut were located in the kinase domain. **Conclusions:** Acquired mut in FGFR2 are seen in pts who have developed resistance to targeted therapy. CtDNA can be used to identify these mut at the time of acquired resistance. The multitude of FGFR2 mut observed within individual pts suggest heterogeneity and evolutionary convergence of resistance mechanisms. Our results illustrate the utility of ctDNA as a less invasive way to monitor for signs of resistance and to identify other potential targetable alterations.

Pt	Baseline FGFR2 Alteration	FGFR2 Acquired Resistance Mutations
1	FGFR2-KIAA1217	N549K, L550F
2	FGFR2-BICC1	
3	FGFR2 amplification	V564L
4	FGFR2-WAC	M538L, M537I, N549H, N549T, N549K, V564I, E565A, D650Y, K659Q
5	FGFR2-VCL	
6	FGFR2-NRAP	
7	FGFR2-KIAA1217	N549K, N549D, V564L, E565A, L617V, Q746L
8	FGFR2-DDX21	K659M

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4097 **Poster Session (Board #202), Mon, 8:00 AM-11:00 AM**

A phase II study of nivolumab in patients with advanced refractory biliary tract cancers (BTC).

Richard D. Kim, Dae Won Kim, Olatunji B. Alese, Daneng Li, Neal Shah, Michael J. Schell, Jun Min Zhou, Vincent Chung; H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; The University of Texas MD Anderson Cancer Center, Houston, TX; Winship Cancer Institute, Atlanta, GA; City of Hope National Medical Center, Duarte, CA; H. Lee Moffitt Cancer Center, Tampa, FL; Moffitt Cancer Center, Tampa, FL; City of Hope, Duarte, CA

Background: Biliary tract cancers (BTC) are often typically diagnosed at an advanced stage. There is no established second line option for patients with advanced BTC who have failed one prior systemic therapy. The phase II study evaluated safety and efficacy of nivolumab, anti PD-1 antibody in refractory BTC patients. **Methods:** Pts with histologically proven BTC who progressed on at least one line but no more than three lines of systemic therapy received nivolumab 240mg IV q2weeks for 16 weeks and then 480 mg IV every 4 weeks until disease progression or unacceptable toxicity. The primary endpoint of the study was objective response rate (ORR) by RECIST 1.1 every 8 weeks. The Simon two staged design was used to assess ORR.18 patients were accrued and if one response was seen, the plan was to accrue additional 34 patients. Secondary endpoints were PFS, OS and safety profile. **Results:** At data cutoff (Jan 14, 2018), 54 patients with BTC (female: 50%, Median age: 65 years) were enrolled. The primary sites of tumor were intrahepatic cholangiocarcinoma (63%) extrahepatic (11%), and gallbladder (26%). 30 pts (56%) failed 1 line of therapy and 24 (44%) failed more than one line of therapy. 45 pts (1 pt withdrew consent, 1pt just enrolled prior to data cutoff and 7 pts came off the study due to clinical progression) were evaluable for response rate. Out of 45 pts, 10 pts (22%) achieved PR (1 unconfirmed PR) and 17 pts (37.8%) achieved SD. DCR was 60%. All patients who responded were microsatellite stable. For evaluable 45 pts with median follow up of 13.34 months, median PFS was 3.98 months (95% CI: 2.33-5.98) and the median OS was 14.22 months (95% CI: 6.64-NA). 6 and 12month OS was 71.4 and 52.3% and 6 and 12 month PFS was 35.2% and 24.1% respectively. Most common treatment related AEs (TRAE) was alkaline phosphatase increased (24.5%). Grade III/IV TRAEs were seen in 11 pts (20.4%); most common were hyponatremia (3 pts) and elevated alkaline phosphatase (2 pts). No treatment related AEs led to discontinuation of the study drug. Tissue samples were collected in all pts with planned correlative studies underway including the PDL 1 status. **Conclusions:** Nivolumab was well tolerated and has shown promising efficacy in refractory BTC including durable responses lasting 2 years. Further randomized trial is warranted in refractory BTC. Clinical trial information: NCT02829918.

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4098 **Poster Session (Board #203), Mon, 8:00 AM-11:00 AM**

Randomized, open-label, perioperative phase II study evaluating nivolumab alone or nivolumab plus ipilimumab in patients with resectable HCC.

Ahmed Omar Kaseb, Roberto Carmagnani Pestana, Luis M. Vence, Jorge M. Blando, Shalini Singh, Naruhiko Ikoma, Kanwal Pratap Singh Raghav, Divya Sakamuri, Lauren Girard, Dongfeng Tan, Jean-Nicolas Vauthey, Ching-Wei David Tzeng, Thomas A. Aloia, Yun Shin Chun, James C. Yao, Robert A. Wolff, James Patrick Allison, Padmanee Sharma; The University of Texas MD Anderson Cancer Center, Houston, TX; University of Texas MD Anderson Cancer Center, Houston, TX; Department of Immunology, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Gastrointestinal Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; GI Medical Oncology Department, The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Pathology, University of Texas MD Anderson Cancer Center, Houston, TX; University of Kentucky, Lexington, KY; Department of GI Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: In HCC, surgical resection is associated with high recurrence rate, and no effective neoadjuvant or adjuvant therapies currently exist. On the basis of of previous reports on the efficacy and safety of anti–PD-1 (nivolumab) and anti–CTLA-4 (ipilimumab) antibodies against HCC, we initiated a randomized pilot trial of perioperative immunotherapy for resectable HCC. **Methods:** This is a randomized, phase II pilot trial of nivolumab (Arm A) or nivolumab + ipilimumab (Arm B) as pre-operative treatment for patients (pt) with HCC who are eligible for surgical resection. Pt are given nivolumab 240 mg every 2 weeks (wk) for a total of 6 wk. Pt in Arm B are treated concurrently with ipilimumab 1 mg/kg every 6 wk. Surgical resection occurs within 4 weeks after last cycle of therapy. Pt continue adjuvant immunotherapy for up to 2 years after resection. Primary objective is the safety and tolerability of nivolumab +/- ipilimumab. Secondary objectives include overall response rate, complete response rate and time to progression. Exploratory objectives include evaluating the pre- and post-treatment immunological changes in tumor tissues and peripheral blood. **Results:** 17 pt were enrolled at the time of interim analysis (8 in Arm A, 9 in Arm B) and 14 were evaluable. Most pt (53%) were 60-70yo, and males (70%). 6 pt were HCV-positive and 4 had chronic hepatitis B. 14 pt proceeded with resection as planned; surgery was aborted for 2 pt (1 for frozen abdomen and 1 for development of contralateral liver nodule). One is still receiving preoperative therapy. Pathologic complete response (pCR) was observed in 4/14 evaluable pt – 2 in Arm A and 2 Arm B (29% pCR rate). 4 pt in Arm B and 1 in Arm A experienced grade 3 or higher toxicity prior to surgery. **Conclusions:** We report a pCR rate of 29% in an interim analysis of a phase II pilot trial of perioperative immunotherapy for resectable HCC. Treatment was safe and surgical resection was not delayed. The study is ongoing and results may contribute to a paradigm shift in the perioperative treatment of HCC. Clinical trial information: NCT03222076.

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4099 **Poster Session (Board #204), Mon, 8:00 AM-11:00 AM**

Clinical and prognostic significance of serum levels of fatty acid binding proteins in hepatocellular carcinoma (HCC).

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Background: Limited data are available about the prognostic effect of fatty acid binding proteins (FABP) in viral and non-viral-related hepatocellular carcinoma (HCC). Previous studies suggested that selected FABP could be a potential target markers for HCC chemotherapy response and may correlated with presence of cirrhosis and poor outcome. We aimed to test the association between plasma levels of Liver (L)-FABP, Heart (H)-FABP, and Adipose (A) FABP and HCC. **Methods:** we enrolled 767 HCC patients from MD Anderson Cancer Center. Under IRB approval, baseline patients' characteristics were retrieved from medical records and blood samples were collected and tested form plasma levels of L-, A-, H-, FABPs. Descriptive statistics were performed and the median values of FABPs among 200 normal controls (NC) were used as cutoff values of FABPs. Overall survival (OS) was estimated by Kaplan Meier curve and log rank test. **Results:** FABPs were highly expressed in HCC cases than controls. Mean values ($\pm$SE) of AFABP, HFABP, and LFABP were significantly higher in cases [25.6 (.7), 10.8 (.5), and 47.8 (1.9)] than controls [19.1 (.8), 7.7 (2), 22. 9 (.5)], $P < .001$. All FABPs were significantly associated with cirrhosis, higher Child Pugh Score (CTP), advanced stage in Barcelona clinic liver cancer stage (BCLC), higher AFP levels, vascular invasion and thrombosis, and tumor nodularity. Median OS (months) (95%CI) were significantly short in patients with higher level of AFABP, HFABP, and LFABP [9.3 (6.8-11.9), 9.4 (6.8-11.9), and 11.1 (8.8-13.3)] as compared to patients with low levels [16.4 (13.8-18.9), 16.4 (14.2-18.6), and 17.9 (14.9-20.9) respectively ($P < .01$). The significance was observed in non-viral related HCC for LFABP and HFABP, but not AFBABP. **Conclusions:** To the best of our knowledge, we describe the largest study correlating FABPs levels with clinical and prognostic characteristics of HCC. Higher levels were associated with poor survival. These findings suggest that LFABP and HFABP may be used as potential prognostic biomarkers for non-viral-related HCC.

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4100 **Poster Session (Board #205), Mon, 8:00 AM-11:00 AM**

Predictors of poor outcome for transarterial chemoembolization (TACE) in hepatocellular carcinoma (HCC).

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Background: The use of TACE in select patients with BCLC stage B HCC has been shown to improve survival. Despite this, it remains unclear which patients will benefit from repeated TACE versus switching to systemic therapy upon disease progression. The purpose of this study is to identify prognostic factors that predict poor outcomes in patients who receive TACE. **Methods:** In this single-institutional retrospective analysis, patients with unresectable HCC were treated with TACE between 2007-2016. Relevant factors such as staging by BCLC stage B, Child-Pugh score, vascular invasion (VI), tumor thrombus (TT), AFP levels, and number of TACE treatments within six months from the initiation of TACE were analyzed using either Pearson's chi-square test or the student's t-test. The Kaplan-Meier method was used for survival analysis. **Results:** Patients (n = 176) underwent TACE; 45% had stage I-II disease, 42% were BCLC stage B prior to TACE, 71% were Child-Pugh A, 21% had extrahepatic spread, 34.7% had VI, and 26% had TT. The median number of TACE treatments was 2 (range, 1- 6). The median overall survival (mOS) was 43 months (m) (95% CI 31.3-54.7) and mOS from start of TACE was 34m (95% CI 26.2-41.8). Elevated AFP (>400) correlated with decreased mOS (25m vs. 35m, p=0.041). Similarly, the presence of TT correlated with poor outcomes (25m vs. 37m, p=0.015). The mOS was also negatively impacted by having 3 or more TACE treatments within a 6 m period (25m vs. 38m, p = 0.09). AFP >400, TT, and interval between TACE were all independent factors in this multivariate analysis, resulting in a shorter mOS of approx. 2 years compared to 3 years in patients without these negative prognostic factors. There was a strong association with both elevated AFP and TT (Chi square p=0.009). **Conclusions:** Elevated AFP (>400), the presence of TT, and a need for 3 or more TACE treatments within 6 months appear to be independent predictors for shorter mOS in patients receiving TACE. Patients with these poor prognostic factors tend to have more aggressive HCC, and earlier initiation of systemic therapy might provide benefit to these patients. A larger study is needed for confirmation of these findings.

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4101 **Poster Session (Board #206), Mon, 8:00 AM-11:00 AM**

An open label, single-arm, two-stage, multicenter, phase II study to evaluate the efficacy and safety of TLC388 as second-line treatment in subjects with poorly differentiated neuroendocrine carcinomas (TCOGT1Z14).

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Background: Therapeutic options for metastatic poorly differentiated neuroendocrine carcinoma (NEC) after prior platinum-based chemotherapy are unknown. Camptothecin analogs, like topotecan and irinotecan, are approved chemotherapy in small cell lung cancer (SCLC). NEC is considered to have similar biological behavior to SCLC. The aim of this study was to analyze the efficacy of TLC388 (Lipotecan) Hydrochloride, which is a novel camptothecin analog, in pretreated metastatic NEC patients. **Methods:** This single-arm, 2-stage, phase 2 clinical trial was conducted at 4 community and academic centers in Taiwan. Patients aged 20 years or older enrolled between July 2015 to May 2018 had confirmed metastatic NEC with prior systemic therapy with etoposide plus cisplatin. Patients received intravenous 40 mg/m^2 of TLC388 on Days 1, 8 and 15 of a 28-day cycle until disease progression or unacceptable toxic effects. **Results:** twenty-three patients with a median age of 61 (range, 44-73) years, including 18 men (78%), were enrolled. Patients received a median of 2 (range, 0-6) treatment cycles. Among 20 evaluable patients, three patients showed a stable disease and no patient a complete or partial remission, resulting in a disease control rate of 15%. Median PFS was 1.8 (95% CI, 0.4-15) months and median OS was 4.3 (95% CI, 1.7-15) months. The most common treatment-related hematologic adverse events at grade 3 or higher were leukopenia (22.7%), anemia (31.8%), and thrombocytopenia (18.2%), respectively. **Conclusions:** TLC388 shows modest antitumor activity in metastatic NEC. Clinical trial information: NCT02457273.

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4102 **Poster Session (Board #207), Mon, 8:00 AM-11:00 AM**

A phase I study of oncolytic immunotherapy of metastatic neuroendocrine tumors using intralesional rose bengal disodium: Cohort 1 results.

Timothy Jay Price, Gabby Cehic, Eric Andrew Wachter, Ian Kirkwood, Rubin Sebbon, Lisa Leopardi, Jessic Reid, Anas Alawawdeh, Susan J Neuhaus, Guy Maddern; Queen Elizabeth Hospital, University of Adelaide, Adelaide, Australia; The Queen Elizabeth Hospital, Adelaide, Australia; Provectus Biopharmaceuticals, Inc, Knoxville, TN; Department of Nuclear Medicine, Royal Adelaide Hospital, and The University of Adelaide, Adelaide, Australia; The Queen Elizabeth Hospital, Woodville, Australia; University of Adelaide and Royal Adelaide Hospital, Adelaide, Australia

Background: Metastatic neuroendocrine neoplasms (mNEN's) originating in the gastrointestinal tract are frequently slow growing yet both symptom and disease control remain important. Treatment options include resection, chemoablation, systemic somatostatin analogues (SSA) or peptide receptor radionuclide therapy (PRRT), but additional options are needed and one such option is hepatic intralesional (IL) rose bengal disodium (PV-10), an oncolytic immunotherapy under development for solid tumours. **Methods:** This phase 1 study is evaluating the safety, tolerability and reduction of biochemical markers and symptoms resulting from percutaneous administration of PV-10 in 12 subjects with progressive mNEN with hepatic lesions not amenable to resection or other potentially curative therapy. Target lesion(s) must be 1.0 - 3.9 cm in longest diameter. In Cohort 1 (n = 6) subjects receive PV-10 to a single hepatic lesion per treatment cycle, and can receive PV-10 to additional uninjected hepatic lesions $\geq$6 weeks after prior injection. Cohort 2 (n = 6) subjects may receive injection of multiple lesions per treatment cycle. The primary endpoint is safety. Secondary endpoints include objective response rate (ORR) assessed by contrast enhanced CT and ^{68}Ga-DOTATATE PET, biochemical response (CgA) and patient-reported outcome (EORTC QLQ-C30 and GI.NET21). **Results:** Cohort 1 has fully enrolled, with 4 of 6 subjects male, median age 65yrs, range 47-72. Primary sites were: small bowel 3, pancreas 2, caecal 1; grade: Gd1 = 5, Gd2 = 1. All patients received prior SSA and PRRT. Median CgA was 645 (range 30-2819). To date 1 subject has received 4 PV-10 treatment cycles, 1 has received 2 cycles, and 4 have received a single cycle. Toxicity has been acceptable, including pain post procedure, carcinoid flare and nausea. LFT's have remained stable. Overall QOL score was stable for 5 of 6 subjects. ORR in injected lesions is 50% (progression in 1 subject), with overall disease control of 84%. CgA response: 5 stable, 1 progression. One subject with "carcinoid pellagra" had rash resolution. Response follow-up is ongoing and additional efficacy and functional data will be presented. **Conclusions:** Hepatic IL PV-10 elicited no safety concerns with encouraging evidence of both local and systemic disease control. Enrolment to Cohort 2 is underway. Clinical trial information: NCT02693067.

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4103 **Poster Session (Board #208), Mon, 8:00 AM-11:00 AM**

A phase II, open label, multicenter trial of avelumab in patients with advanced, metastatic high-grade neuroendocrine carcinomas NEC G3 (WHO 2010) progressive after first-line chemotherapy (AVENEC).

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Background: High grade Neuroendocrine Neoplasias (NEN) are rare tumors with a poor prognosis and no established second line therapy when progressive after first line platinum-based chemotherapy resulting in a median overall survival (OS) of 5 months. This study aims to evaluate the efficacy and safety of the anti-programmed death ligand-1 (PD-L1) antibody Avelumab in patients (pts) with NEN G3 progressing after first-line chemotherapy. **Methods:** In a multicenter, national, single-arm, open-label, phase II trial the efficacy and safety of Avelumab was evaluated in patients with metastatic progressive Neuroendocrine Carcinomas (NEC G3) according to WHO 2010, excluding Merkel cell carcinoma and small cell lung cancer. **Results:** From 12/2017-11/2018 a total of 29 pts (20 male, 69%), were enrolled (16 NEC G3 and 11 moderately differentiated NETG3). Mean age was 59.2±10.2 ys (range 33-75), median follow up 16.5 weeks (3-48). Median Ki67 was 60% (range 20-95%). Site of origin included pancreas (12), genito-urinary tract (4), stomach-esophagus (3), colo-rectum (3), lung (2), ear-nose-throat (2), papilla of Vater (1). In an interim analysis the DCR (stable disease or partial remission according to irRECIST) after 8 weeks was 32% (4 SD, 2 PR). In responders, mean duration of disease control was 20 (±13.8) weeks, with 4 pts. showing stable disease or partial remission ≥6 months. Median OS was 4.2 months (range 1->12). Treatment-related adverse events occurred in 11 of 29 pts (38%) and were mainly mild to moderate (CTCAE-grade 1 [52%], 2 [44%] and 3 [4%]) and included fatigue (n=6; 20.6%), diarrhea (n=4; 13.7%), fever/chills after infusion (n=4; 13.7%), loss of appetite and nausea (n=4; 13.7%), skin rash (n=1; 3%), deterioration of preexisting psoriasis (n=1; 3%) and abdominal pain (n=1; 3%). **Conclusions:** Immune checkpoint blockade with avelumab in pretreated high grade NEN shows relevant activity in a subset of patients with excellent tolerability. Clinical trial information: NCT03352934.

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4104 **Poster Session (Board #209), Mon, 8:00 AM-11:00 AM**

Oxaliplatin and 5-fluorouracil (FOLFOX) in advanced well-differentiated digestive neuroendocrine tumors: A multicenter national retrospective study from the French Group of Endocrine Tumors (GTE).

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Background: Oxaliplatin-based regimens have shown promising antitumor activity in digestive neuroendocrine tumors (NETs), however the available data are limited. Our aim was to assess the tumor response and survival in a large series of patients treated with oxaliplatin and 5-fluorouracil (FOLFOX) for advanced digestive NETs.Oxaliplatin-based regimens have shown promising antitumor activity in digestive neuroendocrine tumors (NETs), however the available data are limited. Our aim was to assess the tumor response and survival in a large series of patients treated with oxaliplatin and 5-fluorouracil (FOLFOX) for advanced digestive NETs. **Methods:** All patients with advanced well-differentiated digestive NETs treated with at least 3 cycles of FOLFOX between 2004 and 2018 in 12 centers of the French GTE, were retrospectively included. Best response according to the RECIST 1.1 criteria, progression-free survival (PFS) and overall survival (OS) were evaluated. The prognostic factors for PFS were investigated by multivariate analysis using a Cox proportional hazard model including variables with a p value $\leqslant 0.20$ in univariate analysis. **Results:** One hundred and forty-nine patients were included. Primary tumor location was pancreas (n = 88), small intestine (n = 37), stomach (n = 7), rectum (n = 4) and unknown without lung tumor at CT scan (n = 13). Partial response rate was of 31% for pancreatic NETs, 13% for small intestine NETs, 14% for gastric NETs, 25% for rectal NETs and 38% for unknown primary NETs. Median PFS were, respectively, 9, 9, 14, 4 and 6 months, and median OS were 30, 28, 31, 25 and 15 months. Significant poor prognostic factors for PFS after FOLFOX in digestive NETs were: progressive disease (HR = 2.5, p = 0.018), hepatic involvement $>$ 50% (HR = 1.8, p = 0.009), prior targeted therapy (HR = 1.5, p = 0.048) and rectal primary tumor (HR = 4.2, p = 0.01). Among pancreatic NETs, the 9 insulinomas had a 22 months PFS versus 9 months for the others (p = 0.025), and serum glucose normalization was obtained in 8 out of 9 cases. **Conclusions:** FOLFOX has a promising clinical activity for gastroenteropancreatic NETs, especially in insulinomas.

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4105 **Poster Session (Board #210), Mon, 8:00 AM-11:00 AM**

The SUNEVO (GETNE-1408) trial to evaluate the activity and safety of thecombination of sunitinib with evofosfamide (TH-302) in patients with G1/G2 metastatic pancreatic neuroendocrine tumours (pNETs) naïve forsystemic treatment: A phase II study of the Spanish Task Force Group for Neuroendocrine and Endocrine Tumors (GETNE).

Enrique Grande, Carlos Lopez, Teresa Alonso-Gordoa, Marta Benavent, Jaume Capdevila, Alex Teule, Ana Custodio, Isabel Sevilla, Pablo Gajate, Javier Molina-Cerrillo, Jorge Hernando-Cubero, Rocio Garcia-Carbonero; MD Anderson Cancer Center Madrid, Madrid, Spain; Hospital Universitario Marqués de Valdecilla, Santander, Spain; Hospital Ramón y Cajal, Madrid, Spain; Hospital Universitario Virgen del Rocío, Sevilla, Spain; Hospital Universitari Vall d'Hebron, Barcelona, Spain; Institut Català d'Oncologia L'Hospitalet, Barcelona, Spain; Hospital Universitario La Paz, Madrid, Spain; Hospital Universitario Virgen de la Victoria, Málaga, Spain; Medical Oncology Department Hospital Universitario Ramón y Cajal, Madrid, Spain; Hospital Universitario 12 de Octubre, IIS imas12, UCM, CNIO, CIBERONC, Madrid, Spain

Background: Angiogenesis plays an important role in tumorigenesis and progression of pNETs. Evofosfamide (EVO) is a DNA alkylator prodrug that selectively activates under hypoxia. Sunitinib as monotherapy shows a wide range of responses (9-24%) in similar populations. We hypothesized that sunitinib-induced hypoxia might increase the cytotoxic activity of EVO in patients with metastatic pNETS and naïve for systemic treatment other than somatostatin analogues (SSA). **Methods:** This is a phase-II, single-arm, and multicenter trial of EVO (340mg/m2 on days 8, 15 and 22 every 4 weeks) and sunitinib (37.5mg/day continuously). Primary endpoint was Objective Response Rate (ORR) by RECIST v1.1 assessed every 8 weeks. A Simon two-stage optimal design was used, considering a minimum of 3 responses in the first 18 pts in order to start with the second stage (power = 0.80, alpha = 0.05). **Results:** Between May/2015 and May/2018, 17 pts were included (median age was 62.4 y.o). Prior SSA was reported in 7 (41.2%) pts and 8 (47.1%) had a Ki-67 $>$ 10%. There were 2 responders (11.8%; n = 1 complete and n = 1 partial response); stable disease was observed in 76.5%. Median (range) PFS and duration of response were 10.4 months (m) (2.9-17.9m) and, respectively 24.4m (13.7-35.2m), respectively. Grade 3 or 4 adverse events occurred in 11 (64.7%) pts, being neutropenia (33.3%), fatigue (16.7%), thrombocytopenia (11.1%), hand-foot syndrome (5.6%), and pancreatitis (5.6%) the most frequent. Toxicity led to treatment discontinuation in 5 (38.5%) pts. Dose reductions were reported in 20% (sunitinib) and 100 % (EVO) of pts. **Conclusions:** Combination of sunitinib and EVO failed to demonstrate activity in terms of tumor shrinkage as only two patients achieved response, therefore, second stage was not proceeded. While cross trial comparisons are difficult, response rate of 12% with the combination was disappointing. Concerns over toxicity arose; translational analysis are undergoing. Clinical trial information: NCT02402062.

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4106 **Poster Session (Board #211), Mon, 8:00 AM-11:00 AM**

Final results of the TALENT trial (GETNE1509): a prospective multicohort phase II study of lenvatinib in patients (pts) with G1/G2 advanced pancreatic (panNETs) and gastrointestinal (giNETs) neuroendocrine tumors (NETs).

Jaume Capdevila, Nicola Fazio, Carlos Lopez Lopez, Alex Teule, Juan W. Valle, Salvatore Tafuto, Ana B. Custodio, Nicholas Reed, Markus Raderer, Enrique Grande, Rocio Garcia-Carbonero, Paula Jiménez-Fonseca, Vicente Alonso, Lorenzo Antonuzzo, Andrea Spallanzani, Alfredo Berruti, Isabel Sevilla, Adelaida La Casta Munoa, Jorge Hernando-Cubero, Toni Ibrahim; Medical Oncology Department, Vall d'Hebron University Hospital; Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; European Institute of Oncology, IRCCS, Milan, Italy; Department of Medical Oncology, H. Marques de Valdecilla, Santander, Spain; Institut Català d'Oncologia, L'Hospitalet, Barcelona, Spain; University of Manchester/The Christie, Manchester, United Kingdom; Istituto Nazionale Tumori Fondazione G. Pascale, Naples, Italy; Hospital Universitario La Paz, Madrid, Spain; Beatson Oncology Centre, Glasgow, United Kingdom; Department of Internal Medicine I, Medical University of Vienna, Vienna, Austria; MD Anderson Cancer Center Madrid, Madrid, Spain; 12 de Octubre University Hospital, Madrid, Spain; Hospital Universitario Central de Asturias, Asturias, Spain; Medical Oncology Department, Hospital Universitario Miguel Servet, Zaragoza, Spain; Careggi University Hospital, Florence, Italy; Department of Oncology and Hematology, University Hospital of Modena, Modena, Italy; Medical Oncology, University of Brescia, Spedali Civili Hospital, Brescia, Italy; Hospital Universitario Virgen de la Victoria, Málaga, Spain; Hospital Universitario Donostia, San Sebastian, Spain; Vall Hebron University Hospital, Vall Hebron Institute of Oncology (VHIO), Bracelona, Spain; Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy

Background: Approved systemic therapies for advanced NETs have showed limited tumor shrinkage and no data of activity after progression to prior targeted agents (TA) is available. Lenvatinib, a potent VEGFR1-3 & FGFR1-4 inhibitor may increase efficacy and revert primary and acquired resistance to TA. We report the final results of the TALENT trial. **Methods:** Two independent cohorts were included: panNETs and giNETs. All pts had baseline documented progression disease (PD) by RECIST. For panNETs, PD to TA was mandatory, regardless of prior therapy with somatostatin analogs (SSAs) or chemotherapy (CHT); and for giNETs, PD on SSAs. Pts were treated with lenvatinib at 24 mg qd until PD or intolerable toxicity. The primary endpoint was overall response rate (ORR) by central radiology review. Progression-free (PFS) and overall survival (OS) were assessed by investigator. With 55 pts per arm, our study was powered to identify an ORR $\geq$25% (90% power, 5% α-error). **Results:** We recruited 111 pts: 55 panNETs and 56 giNETs (78% from small intestine). Prior therapies were CHT 32%, SSAs 87%, everolimus 70% and sunitinib 30% for panNETs. ORR was 29%, 42.3% for panNETs and 16.3% for giNETs. With a median follow-up of 19 m, PFS and OS for panNETs were 15.5 m (95% CI 11.3-not reached (NR)) and 29.2 m (95% CI 23.2-NR); and 15.4 m (95% CI 11.5-19.4) and NR for giNETs, respectively. Pts who obtained a response by RECIST had a significantly better PFS compared with non-responders (NR vs 11.2 m in panNETs (p=0.004); 37.2 m vs 14.9 m in giNETs (p=0.005). In the subgroup analyses, all pts obtained the same benefit in PFS and ORR, including tumor grade, prior therapies, hormone release, primary location and tumor burden. The most frequent G3/4 adverse events were hypertension (22%), fatigue (11%) and diarrhea (11%). Dose reductions/interruptions were needed in 91.8% with a median dose of 20 mg qd. **Conclusions:** To our knowledge, we report the highest ORR by central radiology assessment with a TA in this setting. Lenvatinib showed a promising PFS and OS in a pretreated population with benefit across subgroups. Further development in advanced NETs is warranted. Clinical trial information: NCT02678780.

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4107 **Poster Session (Board #212), Mon, 8:00 AM-11:00 AM**

Molecular characterization of the tumour microenvironment in neuroendocrine malignancy.

David James Pinato, Anu Vallipuram, Joanne Evans, Clement Wong, Hua Zhang, Matthew Brown, Roberto Dina, Pritesh Trivedi, Ayse Akarca, Teresa Marafioti, Francesco A Mauri, Rohini Sharma; Imperial College London, London, United Kingdom; Department of Surgery & Cancer, Imperial College London, London, United Kingdom; Imperial College Healthcare NHS Trust, London, United Kingdom; Department of Histopathology, Imperial College London, London, United Kingdom; University College London, London, United Kingdom; Department of Cellular Pathology, University College London Hospital, London, United Kingdom; Department of Pathology, Imperial College London, London, United Kingdom

Background: A comprehensive characterization of the tumour microenvironment is lacking in neuroendocrine tumors (NETs), where immunotherapy is undergoing efficacy testing. We investigated drivers of cancer-related immunosuppression across NETs of various sites and grade using multi-parameter immunohistochemistry and targeted transcriptomics. **Methods:** Tissue microarrays (n = 102) were stained for PD-L1 & 2, Indoleamine-deoxygenase-1 (IDO-1) and evaluated in relationship to functional characteristics of tumor-infiltrating T-lymphocytes (TILs) and biomarkers of hypoxia/angiogenesis including VEGF-A, Hif-1α and Carbonic Anhydrase-IX. PD-L1 expression was tested in circulating tumour cell (CTCs, n = 12) to evaluate its relationship with metastatic dissemination. **Results:** PD-L1 expression was highest in lung NETs (n = 30, p = 0.007), whereas PD-L2 was highest in pNETs (n = 53, $p < 0.001$) with no correlation with grade, stage or biomarkers of hypoxia. Incubation of QGP-1 and BON-1 NET cells in 1% O2 did not induce PD-L1 expression confirming transcriptional independence from hypoxia. PD-L1$^+$ NETs (n = 26, 25%) had frequent IDO-1 co-expression (p = 0.03), greater CD4$^+$/FOXP3$^+$ and CD8$^+$/PD1$^+$ TILs ($p < 0.001$) and necrosis (p = 0.02). CD4$^+$/FOXP3$^+$ infiltrate was highest PD-L1/IDO-1 co-expressing tumours (p = 0.006). Survival was predicted by tumour grade ($p < 0.001$) and necrosis ($p < 0.001$) but not PD-L1, PD-L2 nor IDO-1. High-grade NETs had lower CD4$^+$/FOXP3$^+$ and CD8$^+$/PD1$^+$ TILs density ($p < 0.001$) and Nanostring immune-profiling revealed enrichment of macrophage-related transcripts in cases with poorer prognosis. We identified PD-L1(+) CTC subpopulations in 75% of evaluated patients (n = 12). **Conclusions:** PD-L1 expression correlates with T-cell exhaustion independent of tumour hypoxia and is enhanced in a subpopulation of CTCs, suggesting its relevance to the progression of NETs. These findings support a potential therapeutic role for PD-L1/IDO-1 inhibitors in a subset of NETs.

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4108 **Poster Session (Board #213), Mon, 8:00 AM-11:00 AM**

Long-term survival and safety from a multi-center, open-label, pivotal phase 2 study of iobenguane I 131 in patients (Pts) with unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma (PPGL).

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Background: PPGL, rare neuroendocrine tumors with a 5-yr survival rate as low as 12%, have a high unmet need for effective treatment options. AZEDRA, a high-specific-activity iodine-131 meta-iodobenzylguanidine (HSA I-131-MIBG), is the first and only FDA- approved therapeutic radiopharmaceutical agent indicated for the treatment of adult and pediatric pts with iobenguane scan positive, unresectable, locally advanced or metastatic PPGL who require systemic anticancer therapy. **Methods:** Pts with advanced disease who were heavily pre-treated and were ineligible for curative surgery or chemotherapy received a dosimetric dose followed by up to two therapeutic doses (each at 296 MBq/kg to a max of 18.5 GBq). The primary endpoint, defined as the proportion of pts with at least 50% reduction of all antihypertensive medication(s) lasting ≥6 months, was met and previously reported. Updated secondary endpoints including overall survival (OS) and safety are reported. **Results:** A dosimetric dose of HSA I-131-MIBG was administered to 74 pts. Of those, 68 pts received one therapeutic dose and 50 received two doses of HSA I-131-MIBG. Clinical benefit rates (objective tumor responses *defined by RECIST 1.0* and stable disease) were observed in 71.4% and 98.0% of pts receiving one and two therapeutic doses, respectively. As of Jan 25, 2019, median OS for all pts was 41.1 months (95% CI 31.1, 91.2). Median OS was 17.5 months (95% CI 4.0, 31.5) and 48.7 months (95% CI 33.2, 91.2) in pts receiving one and two doses, respectively. A tail of survival was observed, with OS of 73.1% at 2 yrs and 44.2% at 4 yrs. The most common (≥50%) adverse events were nausea, fatigue, and myelosuppression. Myelosuppressive events resolved within 4-8 wks without requiring stem cell transplantation. Late radiation toxicity included 8 pts with secondary malignancies (myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), colon cancer, and lung carcinoma) of which MDS, ALL and AML were considered related to I-131 radiotherapy. **Conclusions:** Updated results from this pivotal phase 2 study suggest that HSA I-131-MIBG is an efficacious and safe treatment for advanced PPGL. Clinical trial information: NCT00874614.

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4109 **Poster Session (Board #214), Mon, 8:00 AM-11:00 AM**

Impact of gender on multikinase inhibitors (MKIs) toxicity in patients (pts) with advanced pancreatic and gastrointestinal neuroendocrine tumors (NETs): A pooled analysis of two phase II trials with pazopanib and lenvatinib.

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Background: Retrospective data in some cancer types suggested a possible different toxicity profile with chemotherapy and targeted therapies according to gender. However, data from prospective studies are still very limited, especially in infrequent tumors such as NETs. **Methods:** Pts with advanced pancreatic and gastrointestinal NETs treated with pazopanib or lenvatinib in the multicenter open-label phase II studies PAZONET and TALENT respectively, were included in the analysis. Both studies were performed by Spanish Task Force Group for Neuroendocrine Tumors (GETNE). All toxicity grades with an incidence higher than 5% were considered for univariate review. Additionally, all grade 3-4 toxicities were analyzed separately. **Results:** 155 pts (47.7% female) with 1213 adverse events (AEs) (20% G3-4) divided in 121 categories were included. In female patients, liver toxicity, headache, pyrexia, nausea/vomiting, hair/skin disorders and dizziness were significantly more common (table). The only toxicity with higher incidence in men was dysphonia (OR 0.42, 95% CI 0.2-0.9, p 0.02). There were no gender differences in grade 3-4 toxicities. **Conclusions:** We observed significant differences in toxicity AEs by gender in two prospective phase II studies with MKIs in NETs patients. Potential different approach to manage toxicity may be adopted based on gender.

Toxicity (all grades)	Women (%)	Men (%)	Difference (%)	Odds Ratio (95% CI)	p
Liver toxicity	64.9	41.9	23	2.97 (1.54-5.73)	0.001
Headache	32.4	17.6	14.9	2.5 (1.16-5.4)	0.01
Pyrexia	21.6	8.1	13.5	3.44 (1.26-9.36)	0.01
Nausea/Vomiting	70.3	58.1	12.2	2.08 (1.07-4.05)	0.02
Hair disorders	23	10.8	12.2	2.72 (1.09-6.75)	0.03
Skin disorders	56.8	44.6	12.2	1.9 (1.007-3.61)	0.04
Dizziness	20.3	9.5	10.8	2.68 (1.02-7.02)	0.04
Dysphonia	17.6	36.5	18.9	0.42 (0.2-0.9)	0.02

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4110 **Poster Session (Board #215), Mon, 8:00 AM-11:00 AM**

Blood-based next-generation sequencing analysis of neuroendocrine tumors.

Walid Labib Shaib, Ali Roberts, Katerina Mary Zakka, Mehmet Akce, Christina Wu, Olatunji B. Alese, Bassel F. El-Rayes, Pashtoon Murtaza Kasi, Jason Scott Starr; Winship Cancer Institute, Emory University, Atlanta, GA; Guardant Health, Inc., Redwood City, CA; Winship Cancer Institute of Emory University, Atlanta, GA; Winship Cancer Institute, Atlanta, GA; Ohio State University Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, Columbus, OH; Mayo Clinic, Jacksonville, FL; University of Florida Health Cancer Center, Jacksonville, FL

Background: Neuroendocrine tumors (NET) comprise around 2% of all malignant tumors of the gastrointestinal system. The genomic landscape of NET has not been well studied. The aim of this study was to confirm the feasibility of next generation sequencing (NGS) using ctDNA in NET and characterize common alterations in the genomic profile. **Methods:** Molecular alterations in 114 plasma samples from 114 patients with NET using clinical-grade NGS of ctDNA (Guardant360^{O}) across multiple institutions were evaluated. The test detects single nucleotide variants in 54-73 genes, copy number amplifications, fusions, and indels in selected genes. **Results:** A total of 114 NET patients were evaluated, of which 64 (56.1%) were female. Mean age was 59.7 years with a range between 23-89 years. ctDNA NGS testing was performed on 114 plasma samples; 1 patient had testing performed twice. Genomic alterations were defined in 94 (n = 94/114, 82.5%) samples with a total of 289 alterations identified after excluding variants of uncertain significance (VUSs) and synonymous mutations. Alterations were identified in at least one sample from 83 patients; TP53 associated genes were most commonly altered (n = 83/289, 28.7%), followed by KRAS (n = 22, 7.6%), PI3CA (n = 15, 5.2%), CCNE1 (n = 15, 5.2%), BRAF (n = 13, 4.5%), MYC (n = 12, 4.1%), ERBB2 (n = 11, 3.8%), APC (n = 10, 3.5%), EGFR (n = 10, 3.5%), MET (n = 10, 3.5%), PTEN (n = 9, 3.1%), RB1 (n = 9, 3.1%), CDK6 (n = 7, 2.4%), AR (n = 5, 1.7%), ARID1A (n = 5, 1.7%), FGFR1 (n = 5, 1.7%), and PDGFRA (n = 5, 1.7%). Other genomic alterations of low frequency, but clinical relevance included: CDK4 (n = 4, 1.3%), NF1 (n = 4, 1.3%), RAF1 (n = 4, 1.3%), GNAS (n = 3, 1.0%), KIT (n = 3, 1.3%), BRCA2 (n = 2, 0.7%), CCND2 (n = 2, 0.7%), CTNNB1 (n = 2, 0.7%), JAK2 (n = 2, 0.7%), NRAS (n = 2, 0.7%), SMAD4 (n = 2, 0.7%), and TERT (n = 2, 0.7%). Alterations in AKT1, ALK, ATM, BRCA1, CCND1, CDKN2A, FGFR2, MTOR, RHOA, SMO and STK11 were all reported once (n = 1, 0.3%). **Conclusions:** Evaluation of ctDNA is feasible among individuals with NET. Liquid biopsies are not invasive and can provide personalized options for targeted therapies in NET patients.

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4111 **Poster Session (Board #216), Mon, 8:00 AM-11:00 AM**

Analysis of patient diaries in the NETTER-1 Study of 177Lu-DOTATATE versus high-dose octreotide in progressive midgut neuroendocrine tumors.

Jonathan R. Strosberg, Edward M. Wolin, Beth A. Chasen, Matthew H. Kulke, David L Bushnell, Martyn Caplin, Richard P. Baum, Timothy J. Hobday, Andrew Eugene Hendifar, Paola Santoro, Per Broberg, Arnaud Demange, Kjell E. Oberg, Philippe B. Ruszniewski, Laura Ravasi, Eric Krenning; Moffitt Cancer Center, Tampa, FL; University of Kentucky, Lexington, KY; Department of Nuclear Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX; Boston Medical Center, Boston, MA; Veterans Administration Medical Center, Iowa City, IA; Royal Free Hospital, London, United Kingdom; Zentralklinik, Bad Berska, Bad Berska, Germany; Mayo Clinic, Rochester, MN; Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA; Advanced Accelerator Applications, Geneva, Switzerland; Uppsala University Hospital, Uppsala, Sweden; Beaujon Hospital, Clichy, France; Erasmus MC, Rotterdam, Netherlands

Background: The primary statistical analysis for the NETTER-1 trial showed a clinically and statistically significant PFS benefit with ^{177}Lu-DOTATATE vs. high-dose octreotide. ^{177}Lu-DOTATATE treatment was also correlated with a significant delay in time to deterioration in HRQoL. In addition to HRQoL questionnaires, patients were asked to record presence or absence of a range of symptoms in a daily diary. **Methods:** A Mixed Model Repeated Measures (MMRM) was used to analyze the change, compared to baseline, of the occurrence of abdominal Pain, diarrhea and cutaneous flushing as these symptoms were regarded as the most relevant to judge the overall disease status. For each visit (week = 0, 4, 8, etc.) the number of days with symptoms during the previous period was calculated. At baseline, the number of days with symptoms was counted over the previous 6 weeks, whereas the time frame between visits lasted 4 weeks. **Results:** The estimated number of days with symptoms declined significantly more in the ^{177}Lu-dotatate arm compared to the octreotide arm. The difference in change and the confidence intervals for the symptoms abdominal pain, diarrhea and flushing of skin are, respectively: -3.11 [-4.88; -1.34], -3.11 [-5.04; -1.18] and -1.98 [-3.88; -0.08]**. Conclusions:** Analysis of symptom diaries confirms that ^{177}Lu-Dotatate can palliate clinically relevant symptoms when compared to high-dose octreotide.

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4112 **Poster Session (Board #217), Mon, 8:00 AM-11:00 AM**

Efficacy and safety of pembrolizumab in patients with advanced adrenocortical carcinoma.

Nitya Prabhakar Raj, Youyun Zheng, Virginia Kelly, Seth Katz, Joanne F Chou, Richard K. G. Do, Marinela Capanu, Dmitriy Zamarin, Charlotte Eielson Ariyan, Brian R. Untch, Eileen Mary O'Reilly, Anuradha Gopalan, Michael F. Berger, Kelly Olino, Neil Howard Segal, Diane Lauren Reidy; Memorial Sloan Kettering Cancer Center, New York, NY; Memorial Sloan-Kettering Cancer Center, New York, NY; Memorial Sloan Kettering Cancer Center, New York City, NY; Yale School of Medicine, New Haven, CT; Thoracic Oncology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY

Background: Adrenocortical carcinomas (ACC) are rare and aggressive. Treatment options are limited and marked by poor efficacy and substantial toxicity. In this phase II single-center study, the efficacy and safety of pembrolizumab was assessed in patients (pts) with advanced ACC. **Methods:** Enrolled pts were aged ≥18 y with advanced ACC, ECOG ≤ 1, available tumor samples for biomarker analysis. Pts received pembrolizumab 200 mg Q3W for 2 y or until disease progression, intolerable toxicity, physician/patient decision to stop treatment. Imaging was performed every 9 wks. Tumor PD-L1 positivity (modified proportion score ≥ 1% or presence of stromal interface) was evaluated. Primary endpoint was ORR (by RECIST v1.1). Secondary endpoints included DOR, PFS, OS, safety. Somatic and germline next-generation sequencing was performed. **Results:** 39 pts were treated. Median age 62 (range, 19-87), 28% ECOG 0, 72% received ≥ 1 therapy. In available samples to date, 7/31 (23%) PD-L1+. At time of analysis, median follow-up among survivors was 17.8 mo (range, 5.4-34.7). ORR was 23.1% (95% CI, 11.1-39.3); 0 CR, 9PR. Seven pts (17.9%) had SD as best response. Among the 9 PRs, median time to PR was 4.1 mo (range, 1.7-10.5) and median DOR was not reached (95% CI, 4.1-not reached). Three pts achieving PR have completed 2 y of treatment with ongoing response noted. Tumor PD-L1 status is currently available in 6 pts with PR, 2/6 (33%) PD-L1+. Median PFS was 2.1 mo (95% CI, 2.0-10.7). Median OS was 24.9 mo (95% CI, 4.2-not reached); 2-year OS rate was 50% (95% CI, 36-69%). In the 34 tested tumors, germline testing identified 2 PR pts with Lynch syndrome; the remaining 7 PRs were MSS. Median tumor mutation burden for all PRs was 4.1 mutations/megabase (range, 0-31.5). There was no significant relationship between somatic alterations and response to treatment. Grade 3/4 treatment-related AEs occurred in 7/39 (17.9%) pts. Two pts discontinued therapy due to AEs; both pts achieved PRs and continue to respond. All pts with PRs had LFT elevation ≥ grade 2. **Conclusions:** Pembrolizumab demonstrated antitumor activity and was well tolerated in advanced ACC. Durable responses were noted. Complete evaluation of tumor PD-L1 and microsatellite status will be reported at the meeting. Clinical trial information: NCT02673333.

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4113 **Poster Session (Board #218), Mon, 8:00 AM-11:00 AM**

Surgery and peptide receptor radionuclide therapy: An effective multimodal approach for metastatic neuroendocrine tumors.

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Background: Neuroendocrine neoplasia (NEN) of the pancreas (PanNEN) or small bowel (SBNEN) frequently present with metastases at initial diagnosis, undermining the efficacy of surgical treatment. Peptide receptor radionuclide therapy (PRRT) with radiolabelled somatostatin analogues, ^{90}Y-DOTATOC and ^{177}Lu-DOTATATE, has been shown to achieve prolonged progression-free survival (PFS) and overall survival (OS) in a substantial number of non-surgical patients with advanced NEN. Our aim was to prospectively determine the efficacy of a combination of radical loco-regional surgery and 177Lu PRRT in patients with metastasised NEN. **Methods:** A set of inclusion criteria was defined (e.g. PanNEN or SBNEN, G1/G2 NEN, initial tumour diagnosis, treatment naïve patient, stage IV NEN, positivity on 68Ga DOTATATE or DOTATOC PET/CT, eligibility for surgery and PRRT). Patients underwent PRRT within 3 months following surgery. Follow-up included biochemistry and imaging. Outcome measures included 1-, 3-, and 5-year OS and PFS from initial diagnosis. **Results:** Forty-one patients met eligibility criteria and were included. There were 26 males (63.4%) and median age at surgery was 58.8 years (range 32.1-78.3). All patients with SBNEN underwent right hemicolectomy, terminal ileal resection and mesenteric lympadenectomy. In PanNEN patients either Whipple procedure or distal pancreatectomy and peri-pancreatic lymphadenectomy were performed. The median number of PRRT cycles was 4 (range 2-6). Post-treatment mortality was 0%. Surgical morbidity was 12% (all grade 1 according Clavien-Dindo) and transient grade 1 toxicity occurred post PRRT in 40%. There was no grade 3 toxicity. Median follow-up was 5.48 years (range 0.53 – 11.98). Median PFS and OS were 3.33 years and 9.07 years, respectively. Progression-free survival (with 95% CI) was at 1-, 3-, and 5-years 80% (68.7-92.6), 60.9% (45.9-75.9) and 43.3% (27.4-59.3), respectively. Overall survival (with 95% CI) at 1-, 3-, and 5-years was 97.6% (93-100), 97.6% (93-100), and 95% (87-100), respectively. **Conclusions:** Radical loco-regional surgery for primary tumours combined with PRRT provides a novel, highly efficacious approach in metastasised NEN.

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4114 **Poster Session (Board #219), Mon, 8:00 AM-11:00 AM**

Clinical efficacy and toxicity data on phase I study of fosbretabulin in combination with everolimus in neuroendocrine tumors.

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Background: Fosbretabulin, a synthetic, water-soluble, phosphorylated prodrug of the natural product combretastatin A4 (CA4P), initially isolated from the bark of the South African bush willow, Combretum caffrum, is the lead compound in a class of agents termed vascular disrupting agents (VDAs). Everolimus, an mTOR inhibitor, is FDA approved for the management of well-differentiated NETs. A Phase I trial combining fosbretabulin and everolimus to determine the recommended Phase II trial dose (RP2D), safety data and early clinical efficacy in metastatic GEPNET patients was conducted. **Methods:** An investigator-initiated, single center, open-label, phase I study involving GEPNETs incorporated partial order continual reassessment method (PO-CRM) to define the dose escalation. The primary objective was to establish the maximum tolerated dose (MTD) of the combination of everolimus and fosbretabulin in NETs that have progressed after at least one prior regimen for metastatic disease. Secondary objective included identifying the safety profile of the combination using NCI CTCAE4 reporting criteria. Patients received daily oral everolimus (2.5 mg, 5 mg, 7.5 mg, and 10 mg). Fosbretabulin was administered IV 60 mg/m2 either q3 weekly or q weekly based on PO-CRM. Patients were treated for 12 weeks with all combinations. RECIST 1.1 was used to evaluate radiological responses at 3 month. **Results:** Of the 17 patients enrolled, 16 completed the 12-week trial. One patient was not evaluable due to noncompliance. No DLTs were observed at day 21. The highest dose of 10 mg daily oral everolimus in combination with weekly 60mg/m2 IV fosbretabulin is the RP2D. No grade 4 or 5 toxicities were noted. Grade 3 toxicities were seen in 5 patients; abdominal pain and hyperglycemia (not related to study drug), fatigue (possibly related), decreased lymphocyte count and anemia (related). Several patients had delay in treatment due to grade 2 AE's (GI symptoms, rash, thrombocytopenia) and one patient was unable to complete treatment due to pneumonitis. All evaluable patients except one had stable disease at 3 months. One patient showed SD but non target lesion demonstrated PD. One patient had $>$ 30% decrease in tumor size but overall sum of lesions showed SD. A detailed table with all grade toxicities and waterfall plot of RR will be presented at the meeting. **Conclusions:** Ten mg PO daily everolimus plus 60 mg/m2 fosbretabulin IV weekly is the RP2D. Early clinical data suggests clinical activity and stable disease in all but one patient at 3 months. Clinical trial information: NCT0301429.

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4115 **Poster Session (Board #220), Mon, 8:00 AM-11:00 AM**

Antitumor efficacy of concurrent everolimus with hepatic transarterial bland embolization (evero-embo) in patients with metastatic well differentiated neuroendocrine tumor (NET).

Lowell Brian Anthony, Aman Chauhan, Jianrong Wu, Steven J Krohmer, Gaby Gabriel, Val R. Adams, Mark Evers, Susanne M. Arnold, Riham Khouli; University of Kentucky, Lexington, KY; University of Kentucky, Division of Medical Oncology, Lexington, KY; Univ of Kentucky, Lexington, KY; University of Kentucky, lexington, KY; Markey Cancer Center, University of Kentucky, Lexington, KY

Background: Hepatic transarterial embolization (HAE) is an effective loco-regional therapy for neuroendocrine tumor (NET) management. Systemic targeted therapies, such as everolimus and sunitinib, are typically held 2-4 weeks prior to and after procedures. The safety of concurrent use of everolimus with HAE has been previously reported (GI-ASCO). HAE induces anoxic injury while everolimus effects cell growth, proliferation and survival. Combining these two modalities may result in clinical synthetic lethality effectively debulking significant hepatic disease and/or delay progression. Historically bland HAE has a median hepatic PFS of ~9 months. In this study, the clinical efficacy of evero-embo is examined. **Methods:** A review of clinical and radiographic data was conducted for all sequential patients who underwent evero-embo between September 2016 and April 2018 at the University of Kentucky Markey Cancer Center. An independent radiologist performed RECIST measurements. Patients were required to have had systemic everolimus for $\geq$ 1 month prior to embolization in order to be included in this study and be on everolimus immediately post procedure. Patients with at least 12 months post procedure follow up were included for efficacy review. **Results:** A total of 51 HAEs with concurrent systemic everolimus were performed in 34 NET patients. Twenty one of 24 patients were noted to have a partial response. Rest had stable disease. Hepatic progression was not observed. Twenty-one of the 34 patients have had 12 or more months of follow up post procedure (median of 17 months). None of these 21 patients have had hepatic progression. **Conclusions:** Evero-embo results in a partial response rate of 62% and may have significant antitumor activity when compared to bland hepatic artery embolization in NET patients. With a median follow-up of 17 mos, hepatic progression has not occurred in any patient. Additional follow up is necessary to compare the median hepatic PFS of evero-embo to the historical drug-eluting bead HAE PFS.

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4116 **Poster Session (Board #221), Mon, 8:00 AM-11:00 AM**

Immune checkpoint inhibitors (ICIs) in gastrointestinal (GI) cancer: Immune-related adverse events (IRAEs) and efficacy.

Satya Das, Kristen Keon Ciombor, Sigurdis Haraldsdottir, Yoanna S Pumpalova, Ibrahim Halil Sahin, Yu Shyr, Shih-Kai Chu, Emily Pei-Ying Lin, Chih-Yuan Hsu, Laura Williams Goff, Dana Backlund Cardin, Mehmet Asim Bilen, Jordan Berlin, Christina Wu; Vanderbilt University Medical Center, Nashville, TN; Stanford University, Stanford, CA; Stanford University, Palo Alto, CA; 1574, Atlanta, GA; Vanderbilt-Ingram Cancer Center, Nashville, TN; Emory University Winship Cancer Institute, Atlanta, GA; Vanderbilt University, Nashville, TN; Ohio State University Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, Columbus, OH

Background: Despite the therapeutic promise of ICIs for patients (pts) with some advanced malignancies, they are FDA-approved for only a few GI cancer pts. In NSCLC, melanoma and urothelial carcinoma, there is emerging data that pts who experience IRAEs while on ICIs have improved outcomes compared with pts who do not. This association in GI cancer pts has not been reported. **Methods:** We retrospectively analyzed outcomes for metastatic GI cancer pts receiving ICIs for FDA-approved indications (later-line MSI-H tumors, 2nd line hepatocellular carcinoma (HCC), 3rd line PD-L1+ gastric (GA)/gastroesophageal junction (GEJ) adenocarcinoma), at Vanderbilt Ingram Cancer Center, Winship Cancer Institute and Stanford Cancer Institute. Our primary aim was to compare progression-free survival (PFS) and overall survival (OS) between pts who did and did not experience IRAEs. Secondary aims were comparison of these outcomes within pts who experienced IRAEs, by initial IRAE severity (Grade (G)3/G4 vs G1/G2) (CTCAE v5.0), time-to-onset (TTO) ($\leq$ 6 weeks (w) vs $>$ 6 w) and management (steroids vs drug cessation vs observation). PFS and OS were determined by Kaplan-Meier (KM) analysis; KM comparisons were done by the logrank test. **Results:** Between 1/2015-12/2018 61 GI cancer pts with HCC (28), colorectal cancer (27) and GA/GEJ cancer (6) were treated with ICIs; median age was 63 years. The majority (59) received single-agent nivolumab or pembrolizumab while minority (2) received nivolumab and ipilimumab; median time on ICIs was 5.9 months (mos). Twenty-four pts experienced initial IRAEs (6 G3/G4, 18 G1/G2); median TTO was 3.8 mos. Pts who experienced any IRAE had improvements in PFS and OS compared to those who did not (PFS: 32.4 mos (95% confidence interval (CI), 32.4-not reached (NR)) vs 4.8 mos (95% CI, 2.9-8.7), p = 0.0001; OS: 32.4 mos (95% CI, 32.4-NR) vs 8.5 mos (95% CI, 6-NR), p = 0.0036). Among pts who experienced IRAEs, PFS and OS differences between above-specified subgroups did not meet statistical significance. **Conclusions:** GI cancer pts who experienced IRAEs while on ICIs had marked improvements in PFS and OS compared to those who did not, suggesting the predictive potential for IRAEs as a clinical biomarker in this population.

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4117 **Poster Session (Board #222), Mon, 8:00 AM-11:00 AM**

Updated results of a phase IIa study to evaluate the clinical efficacy and safety of erdafitinib in Asian advanced cholangiocarcinoma (CCA) patients with FGFR alterations.

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Background: Patients (pts) with advanced CCA who progressed on or after first line chemotherapy have no approved treatment options. Fibroblast growth factor receptor (FGFR) gene alterations are observed in many tumor types including 14-17% in CCA. Erdafitinib, an orally bioavailable, selective pan-FGFR kinase inhibitor, has shown clinical activity against solid tumors with FGFR alterations. **Methods:** LUC2001 is an open-label, multicenter, Ph2a study in advanced CCA pts with FGFR alterations (FoundationOne), who progressed after $\geq$ 1 prior treatment. The primary endpoint is objective response rate (ORR; RECIST 1.1). The secondary endpoints are disease control rate (DCR), progression free survival (PFS), duration of response (DOR), safety and pharmacokinetics (PK). Disease is evaluated every 8 weeks until disease progression (PD). **Results:** As of 3 Dec 2018, 222 CCA pts were molecularly screened; 34 had FGFR alterations, of whom 14 (8 FGFR2 fusion, 3 FGFR2 mutation, 1 FGFR3 fusion, 2 FGFR3 mutation) were dosed 8 mg once daily with up titration option. Median age was 51.5 years. 13/14 and 12/14 pts had prior platinum or gemcitabine based therapy respectively, 7/14 pts got re-treated with platinum or gemcitabine based therapy, and 9/14 pts had $\geq$2 prior lines of therapy. Median number of treatment cycles was 5.0 (range: 1; 22) and treatment duration was 4.83 (range: 0.5; 20.3) months. In 12 evaluable pts, there were 6 confirmed partial response (PR), 4 stable disease (SD) and 2 PD; ORR (CR+PR) was 6/12 (50.0%), DCR (CR+PR+uCR+uPR+SD) was 10/12 (83.3%); median DOR was 6.83 months (95% CI: 3.65; 12.16); median PFS was 5.59 months (95% CI: 1.87, 13.67). In 10 evaluable FGFR2+ pts, ORR was 6/10 (60.0%); DCR was 10/10(100%); median PFS was 12.35 months (95% CI: 3.15, 19.38). The most common TEAEs ($>$ 30%) were hyperphosphatemia, dry mouth, stomatitis, and dry skin. 9 pts had $\geq$ Grade 3 AEs (8 Grade 3,1 Grade 5), of which 7 drug related. TEAE led to treatment 1 discontinuation, 6 dose reductions and 1 death (not drug related). The results of PK and PK/PD relationship were consistent with other erdafitinib studies in different ethnic background pts. **Conclusions:** Asian advanced CCA pts with FGFR alterations treated with erdafitinib had encouraging efficacy and acceptable safety profile similar to experience in other tumor types and populations. Clinical trial information: NCT02699606.

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4118 **Poster Session (Board #223), Mon, 8:00 AM-11:00 AM**

Efficacy and safety of lanreotide 120 mg in the treatment of clinical symptoms associated with inoperable malignant intestinal obstruction (IMIO): Results from a phase II multicenter study.

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Background: Intestinal obstruction is a severe complication in patients (pts) with digestive or gynecological cancers. For inoperable pts, there is a need to relieve symptoms and limit nasogastric tube (NGT) use. Previous studies have suggested the efficacy of somatostatin analogues in relieving obstruction-related symptoms such as nausea, vomiting and pain. **Methods:** This was a single arm, prospective study (NCT02275338). Pts with IMIO received one deep subcutaneous injection of LAN 120mg at day 0 (D0). Evaluations were performed on D7, 14 and 28. The primary endpoint was the proportion of responders before or at D7. Response was defined as $\leq$2 vomiting episodes/day (for pts without NGT at baseline) or no vomiting recurrence (after NGT removal), during at least 3 consecutive days at any time point between the D0 and D7. In line with the literature, a proportion of 30% responders was used as reference for defining statistical significance. Responders at D28 were offered a second LAN 120 mg injection. **Results:** 52 pts with advanced GI or ovarian malignancies were included in 15 Belgian sites. 17 pts without NGT and 35 with NGT. 21 pts received a second dose of LAN. Median age was 68.0 (59.5; 76.0) years. On D7 the proportion of responders in the ITT population was 24/52 (46.2%), significantly greater than the reference proportion of 30% (one-sided binomial test: $p = 0.006$). Pts without NGT responded better (15/17, 88.2%) than pts with NGT (9/35, 25.7%). Pts without ascites responded better (57.7% *vs* 34.6%). Pts with NGT showed a steady trend for clinical improvement leading to sustainable responses of 45.7% on D14. Median time to response was 9 days for the overall population; 3 days for patients without NGT vs 14 days for patients with NGT ($p < 0.001$). The most frequently reported AEs were GI disorders (in 34 pts). The most common events were diarrhoea and abdominal pain. **Conclusions:** Our study is the first using long acting LAN 120mg in patients with IMIO and suggests an effect in controlling clinical symptoms in pts with and without NGT at baseline. LAN 120 mg safety profile was similar to that reported for the other indications. Clinical trial information: NCT02275338.

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4119 **Poster Session (Board #224), Mon, 8:00 AM-11:00 AM**

Molecular profile of ampulla of vater carcinoma (AVC): A rare tumor type with meaningful molecular alterations.

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Background: AVC is a rare type of cancer with dismal prognosis and limited therapeutic options due to the lack of specific clinical trials. Two histologic subtypes predominate, namely pancreatobiliary and intestinal. A variety of molecular alterations have been described in AVC, but their clinical and therapeutic implications have not been studied in detail. **Methods:** Retrospective cohort study of patients (pts) diagnosed with AVC treated in our institution from 2010 to 2018. We routinely performed Next Generation Sequencing in all AVC tumors. Our main objectives were to describe the molecular profile of AVC and correlate with clinical outcomes. **Results:** Out of 26 pts with AVC, 13 pts were male (50%), median age 65 (range 43-83), 7 pts (27%) had stage IV disease at diagnosis. Histologic type was pancreatobiliary in 18 pts (69%), intestinal in 7 pts (27%) and mixed in one case (4%). We identified KRAS mutations (mut) in 10 pts (7 pancreatobiliary, 2 intestinal, 1 mixed), TP53 mut in 6 pts (4/1/1), PIK3CA mut in 3 pts (3/0/0), ERBB2 mut in 3 pts (2/1/0), CTNNB1 mut in 3 pts (2/1/0). In pancreatobiliary we found single cases with RNF43, BRCA1 and CHEK2 mut; while in intestinal we found single cases with NRAS and BRAF mut. One tumor of intestinal subtype had microsatellite instability (MSI). Three pts were included in phase I clinical trials, 2 of them with trials based on tumor profile (ERBB2 mut with pan-HER inhibitor and MSI with immunotherapy). Median overall survival (OS) was 21 months for pts with stage I, II and III disease (95% CI 12.37-not reached) and 13.2 months for stage IV disease at diagnosis (95% CI 5.73-not reached). In cox models, median OS was not dependent on KRAS or TP53 mutation status, or histological subtypes. **Conclusions:** AVC is a rare type of cancer with two differentiated histological subtypes harboring unique molecular alterations that can be matched to investigational therapies. A broader knowledge of the biology of these tumors is needed to improve patient outcomes.

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4120 **Poster Session (Board #225), Mon, 8:00 AM-11:00 AM**

Paclitaxel/carboplatin with or without cetuximab for treatment of carcinoma with unknown primary (PACET-CUP): Results of a multi-center randomized phase II AIO trial.

Alwin Krämer, Alexander Stein, Gerdt Huebner, Michael Stahl, Stefan Kasper, Albrecht Kretzschmar, Claus-Henning Kohne, Viktor Grünwald, Ralf Hofheinz, Katharina Schütte, Harald Löffler, Carsten Bokemeyer, Gunnar Folprecht, Arbeitsgemeinschaft Internistische Onkologie (AIO) - CUP group; Clinical Cooperation Unit Molecular Hematology/Oncology, German Cancer Research Center (DKFZ) and Dept. of Internal Medicine V, University of Heidelberg, Heidelberg, Germany; University Medical Center Hamburg-Eppendorf, Department of Oncology, Haematology, Stem Cell transplantation and Pneumology, Hamburg, Germany; Oho! Ostholstein-Onkologie, Oldenburg I.H., Germany; Evang. Kliniken Essen-Mitte, Essen, Germany; University Hospital Essen, Essen, Germany; MVZ Mitte, Leipzig, Germany; Universitätsklinik für Innere Medizin – Onkologie und Hämatologie, Oldenburg, Germany; Dept. Hematology, Hemostaseology, Oncology & Stem Cell Transplantation, Hannover Medical School, Hannover, Germany; University Medical Center Mannheim, Tagestherapiezentrum am ITM, Mannheim, Germany; University Hospital Carl Gustav Carus, Dresden, Germany; Marienhospital, Stuttgart, Germany; University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background: Paclitaxel/carboplatin is one of the standard regimens for empiric treatment of patients (pts) with carcinoma with unknown primary (CUP) when a specific therapy is not available. The EGFR antibody cetuximab demonstrated efficacy in several cancer types. **Methods:** Pts with newly diagnosed non-resectable, undifferentiated or adeno-CUP were randomized to 6 cycles paclitaxel 175 mg/m² and carboplatin AUC 5 every three weeks (arm A) or the same chemotherapy plus cetuximab (400 mg/m², then 250 mg/m² weekly; arm B) at 13 German centres. CUP pts belonging to favorable prognosis groups [i.e. women with isolated peritoneal carcinomatosis or axillary lymph node metastases, men with retroperitoneal lymph nodes, pts with specific tumor entities according to histology / immunohistochemistry] were excluded from the trial. The primary endpoint was progression-free survival (PFS), secondary endpoints were response rate (RR) and overall survival (OS). **Results:** Between 03/2010 and 03/2017, 72 pts were randomized to arm A and 78 pts to arm B. The median age was 61 years, 84 pts were male (40 and 44 pts in arm A and B). 58 pts had a performance status (PS) of 0 (24 and 34 pts), 89 pts a PS of 1 (47 and 42 pts in arm A and B), and one patient in arm A had a PS of 2. PFS and OS did not differ between arms. The median PFS was 3.7 [95%CI: 3.0 - 4.4] and 4.6 [95%CI: 2.9 - 6.2] months in arms A and B (HR 0.98 [95%CI: 0.70-1.37]), the median OS 8.1 [95%CI: 6.5 - 9.8] and 7.4 [95%CI: 5.1 - 9.6] months in arms A and B, respectively (HR 1.10 [95%CI: 0.77 - 1.56]). There was a statistically non-significant trend towards a higher RR with cetuximab: 11 pts had a partial response in arm A (15% [95%CI: 7.9 - 26%]), and 17 pts in arm B (22% [95%CI: 13%-33%], p = 0.30). Twenty-five pts in each arm had stable disease, and 36 pts in each arm had progressive disease or were not evaluable for response. **Conclusions:** This study represents one of the largest trials in pts with CUP and demonstrates that randomized trials are feasible in this disorder with high medical need. The outcome of CUP pts in the unfavorable prognosis group was not improved by adding cetuximab to empiric therapy paclitaxel/carboplatin. Clinical trial information: NCT00894569.

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4121 **Poster Session (Board #226), Mon, 8:00 AM-11:00 AM**

H3B-6527 clinical biomarker assay development and characterization of HCC patient samples.

Pavan Kumar, Vicki Rimkunas, Kun Yu, Zhaojie Zhang, Crystal MacKenzie, Joanne Schindler, Peter Smith, Ping Zhu, Anand Selvaraj, Lihua Yu, Subhasree Das, Jaya Julie Joshi; H3 Biomedicine, Inc., Cambridge, MA; H3 Biomedicine, Cambridge, MA; Atlas Venture, Cambridge, MA; H3 Biomedicine Inc., Cambridge, MA

Background: FGFR4/FGF19 signaling axis is a novel therapeutic target in HCC. Multiple covalent FGFR4 inhibitors, including H3B-6527, are under clinical development. Preclinical efficacy studies in mice (including PDX) have shown that FGF19 expression ($FGF19^+$) is a predictive biomarker for FGFR4 inhibitor response. The mechanisms driving FGF19 expression in HCC is largely unknown however, in some cases, focal amplification of ch11q13.3 containing FGF19 gene is thought to drive the FGF19 expression. Consistent with the preclinical observations, clinical studies have also shown that $FGF19^+$is a predictive biomarker for FGFR4 inhibitor response. However, these trials have also reported a large number of $FGF19^+$patients failing to respond to FGFR4 inhibitors necessitating refinement of patient selection strategies. In an attempt to obtain deeper insights into the role of $FGF19^+$as a predictive biomarker and potentially uncover additional biomarkers that will enable improvement in patient selection strategies, we have characterized a set of 258 HCC patient samples **Methods:** Samples were acquired from biobanks and utilized to qualify clinical assays including FGF19 copy number (FISH), mRNA expression (qRT-PCR), FGF19 protein (IHC), and a focused NGS panel for assessing both mutations and copy number. A multiplexed protein and mRNA platform enabled assessment of p-ERK and Ki67 (protein) and Cyp7A1 (mRNA) amongst other exploratory PD biomarkers from two FFPE slides. **Results:** FGF19 positivity rates for IHC and qRT-PCR were 18% (41/225) and 42% (87/209), respectively. The overall correlation was 60%, with 63% (22/235) IHC positive cases also being positive by qRT-PCR. For IHC+/qRT-PCR (-) cases, RNA quality may have impacted assay sensitivity. 4% (9/244) of samples were positive for FGF19 copy number. Among samples with FGF19 copy number gains, 22% (2/9) did not show positive FGF19 expression. **Conclusions:** Based on our data, FGF19 mRNA is a more inclusive selection strategy and offers an approach to further refine thresholds for efficacy as determined in the clinic. Multiplexed protein-mRNA assays were also validated and implemented to enable a more comprehensive clinical biomarker program.

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4122 **Poster Session (Board #227), Mon, 8:00 AM-11:00 AM**

Variation in the surgical management of locally advanced pancreatic cancer.

Bradley Norman Reames, Alex Blair, Robert Wallace Krell, James Padussis, Sarah P. Thayer, Massimo Falconi, Christopher Lee Wolfgang, Matthew J. Weiss, Chandrakanth Are, Jin He; University of Nebraska Medical Center, Omaha, NE; Johns Hopkins University, Baltimore, MD; Memorial Sloan Kettering Cancer Center, New York, NY; Chirurgia, Verona, Italy; Johns Hopkins University School of Medicine, Baltimore, MD

Background: Recent reports suggest patients with locally advanced pancreatic cancer (LAPC) may become candidates for curative resection following neoadjuvant therapy, with encouraging survival outcomes. Yet the optimal management approach for LAPC remains unclear. We sought to investigate surgeon preferences for the management of patients with LAPC. **Methods:** An extensive electronic survey was systematically distributed by email to an international cohort of pancreas surgeons. Data collected included surgeon practice characteristics, preferences for staging and management, and 6 clinical vignettes (with detailed videos of post-neoadjuvant arterial and venous imaging) to assess attitudes regarding eligibility for surgical exploration. **Results:** A total of 150 eligible responses were received from 4 continents. Median duration in practice was 12 years (IQR 6-20) and 75% respondents work in a university setting. Most (84%) are considered high volume, 33% offer a minimally-invasive approach, and 48% offer arterial resection in selected patients. A majority (70%) always recommend neoadjuvant chemotherapy, and 62% prefer FOLFIRINOX. Preferences for duration of neoadjuvant therapy varied widely: 39% prefer ≥2 months, 41% prefer ≥4 months, and 11% prefer 6 months or more. Forty-one percent frequently recommend neoadjuvant radiation, and 51% prefer standard chemoradiotherapy. Age ≥80 years and CA 19-9 of ≥1000 U/mL were commonly considered contraindications to exploration. In 5 clinical vignettes of LAPC, the proportion of respondents that would offer exploration following neoadjuvant varied extensively, from 15% to 54%. In a vignette of oligometastatic pancreatic liver metastases, 32% would offer exploration if a favorable biochemical and imaging response to therapy is observed. **Conclusions:** In an international cohort of high volume pancreas surgeons, there is substantial variation in attitudes regarding staging preferences and surgical management of LAPC. These results underscore the importance of coordinated multi-disciplinary care, and suggest an evolving concept of "resectability." Patients and their oncologists should have a low threshold to consider a second opinion for the surgical management of LAPC, if desired.

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4123 **Poster Session (Board #228), Mon, 8:00 AM-11:00 AM**

Neoadjuvant FOLFIRINOX versus adjuvant gemcitabine in pancreatic cancer.

Adam R Wolfe, Eric David Miller, Laith I. Abushahin, Jordan Cloyd, Adrei Manilchuck, Mary Dillhoff, Dayssy Alexandra Diaz Pardo, Anne M. Noonan, Terence M Williams; Ohio State, Columbus, OH; Ohio State University Wexner Medical Center, Columbus, OH; University of Iowa Hospitals and Clinics, Holden Comprehensive Cancer Center, Iowa City, IA; The Ohio State University, Columbus, OH; Ohio State University Comprehensive Cancer Center, Columbus, OH; The Ohio State University Comprehensive Cancer Center, Arthur G. James Cancer Hospital, Columbus, OH; The Ohio State University Comprehensive Cancer Center, James Cancer Hospital, Solove Research Institute, Columbus, OH

Background: In the metastatic or adjuvant setting for pancreatic cancer, the combination chemotherapy of fluorouracil, leucovorin, irinotecan, and oxaliplatin (FOLFIRINOX) resulted in longer overall survival (OS) compared to gemcitabine therapy. We conducted an institutional study to compare the efficacy of neoadjuvant modified FOLFIRINOX (neo-mFOLFIRINOX) to adjuvant gemcitabine (adj-gem) for pancreatic cancer patients who completed resection. **Methods:** The study retrospectively enrolled patients from 2006 to 2017 from Ohio State University. While patients who received adjuvant gemcitabine were considered to be resectable upfront, patients who received neo-mFOLFIRINOX were either staged as borderline resectable (BR) or un-resectable (UR) by the institutional tumor board group. 111 patients received adj-gem (average cycles, 5.5) and 52 patients received neo-mFOLFIRINOX (average cycles, 3.5). The survival rates were determined by the Kaplan-Meier method and analyzed using Cox regression and log-rank test. **Results:** At a median follow up of 21.3 months, the median OS was 35.4 months in the neo-mFOLFIRINOX group and 21.8 months in the adj-gem group (hazard ratio, 0.56, 95% confidence interval (CI), 0.37-0.84 p = 0.005). The OS rate at 3 years was 46% in the neo-mFOLFIRINOX group and 22% in the adjuvant gemcitabine group (p = 0.001). The median disease free survival (DFS) was 18.6 months in the neo-mFOLFIRINOX group and 12.0 months in the adj-gem group (hazard ratio, 0.63, 95% CI, 0.43-0.93 p = 0.022). The DFS rate at 3 years was 17% in the neo-mFOLFIRINOX group and 11% in the adj-gem group (p = 0.02). On surgical pathological specimen review, the neo-mFOLFIRINOX group had statistically ($p < 0.05$) lower tumor grade, lower rates of perineural invasion and lymphovascular invasion, lower pathological T stage, lower pathological N stage, and lower number of nodes positive compared to the adj-gem group. Frequencies of obtaining R0 resections were higher in the neo-mFOLFIRINOX versus adj-gem groups but not statistically different (51.9% vs 40.4, p = 0.2). The average age and performance status were similar between the two groups. **Conclusions:** At our institution, BR and UR pancreatic cancer patients who received neo-mFOLFIRINOX and completed resection had longer OS, DFS, and more favorable pathological indicators compared to those patients who had upfront surgery and adjuvant gemcitabine. Randomized clinical trials comparing neoadjuvant versus adjuvant FOLFIRINOX are needed to validate these findings.

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4124 **Poster Session (Board #229), Mon, 8:00 AM-11:00 AM**

A phase Ib dose-escalation and cohort-expansion study of safety and activity of the transforming growth factor (TGF) β receptor I kinase inhibitor galunisertib plus the anti-PD-L1 antibody durvalumab in metastatic pancreatic cancer.

Davide Melisi, Antoine Hollebecque, Do-Youn Oh, Emiliano Calvo, Anna M. Varghese, Erkut Hasan Borazanci, Teresa Macarulla Mercade, Francesca Simionato, Joon Oh Park, Johanna C. Bendell, Sandrine J. Faivre, Yumin Zhao, Ivelina Gueorguieva, Michael Man, Shawn Estrem, Karim Adnane Benhadji, Mark Lanasa, Susan C. Guba, Rocio Garcia-Carbonero; University of Verona, Verona, Italy; Gustave Roussy, Villejuif, France; Seoul National University Hospital, Seoul, South Korea; START Madrid, Centro Integral Oncológico Clara Campal, Madrid, Spain; Memorial Sloan Kettering Cancer Center, New York, NY; HonorHealth Research Institute, Scottsdale, AZ; Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; University of Verona, Tonezza Del Cimone, Italy; Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; Sarah Cannon Research Institute/ Tennessee Oncology, Nashville, TN; Service d'Oncologie Médicale, Clichy, France; Eli Lilly and Company, Indianapolis, IN; Eli Lilly and Company, Erl Wood, United Kingdom; Eli Lilly, Indianapolis, IN; Eli Lilly and Company, New York, NY; AstraZeneca, Gaithersburg, MD; Hospital Universitario 12 de Octubre, IIS imas12, UCM, CNIO, CIBERONC, Madrid, Spain

Background: Pancreatic cancer (PC) is characterized by a highly immunosuppressive microenvironment, and immune checkpoint inhibitors as monotherapy have been ineffective to date. TGFβ is commonly viewed as a powerful immunosuppressive cytokine, and inhibition of its signaling reverses this suppression and activates adaptive immune responses. A combination of TGFβ and PD-L1 inhibition may act synergistically to induce immune restoration and to improve antitumor responses. This Phase 1b study (NCT02734160) evaluated the combination of galunisertib plus durvalumab in recurrent or refractory metastatic PC. **Methods:** Eligible patients (pts) were ≥18 years old, had ECOG status ≤1, and had not received treatment with anti-PD-1, anti-PD-L1, or TGFβ R1 kinase inhibitors. The primary objective was to assess the safety and the recommended dose of galunisertib given 14 days on/14 days off in combination with durvalumab 1500 mg every 4 weeks. Four dose levels of galunisertib were tested in the dose escalation portion of the study: 50 mg QD, 50 mg BID, 80 mg BID and 150 mg BID, followed by the cohort expansion portion of the study at the recommended Phase 2 dose (RP2D). Secondary objectives included preliminary assessment of activity by response rate, (RECIST v1.1), median PFS (mPFS), and OS (mOS). **Results:** 42 pts (25F/17M) were treated in the study (median age 56.5 y; 71.4% had received ≥2 prior systemic regimens). There was no dose limiting toxicity and galunisertib 150 mg BID was chosen as the RP2D. In the 32 pts treated at this dose, Grade ≥3 related AEs included AST and GGT elevations (2 pts each), and ALT and alkaline phosphatase elevations, and neutropenia (1 pt each). One partial response and 7/32 stable diseases were observed (disease control rate 25%); mPFS was 1.9 months (95% CI: 1.5, 2.2) and mOS was NR (95% CI: 3.6, NR). Biomarker data will be presented at the meeting. **Conclusions:** The combination of galunisertib plus durvalumab had an acceptable tolerability and safety profile. The activity of this combination in second and third line PC patients warrants further consideration. Clinical trial information: NCT02734160.

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4125 **Poster Session (Board #230), Mon, 8:00 AM-11:00 AM**

PanCO: An open-label, single-arm pilot study of phosphorus-32 (P-32; Oncosil) microparticles in patients with unresectable locally advanced pancreatic adenocarcinoma (LAPC) in combination with FOLFIRINOX or gemcitabine + nab-paclitaxel (GNP) chemotherapies.

Paul J. Ross, Daniel Croagh, Morteza Aghmesheh, Adnan Nagrial, Nam Nguyen, Mehrdad Nikfarjam, Harpreet Singh Wasan, Thankamma V. Ajithkumar, Chinenye Iwuji, Alain Hendlisz, Thomas Maher, Anna Kraszewski, Marion Harris; Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom; Monash Health, Clayton, Australia; Illawarra Cancer Care Centre, Wollongong, NSW, Australia; Crown Princess Mary Cancer Centre, Westmead Hospital, Sydney, Australia; Royal Adelaide Hospital, Adelaide, SA, Australia; Austin Health, Melbourne, VIC, Australia; Imperial College Healthcare NHS Trust, London, United Kingdom; Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom; Oncology Department, Leicester, United Kingdom; Medical Oncology Department, Institut Jules Bordet - Université Libre de Bruxelles (ULB), Brussels, Belgium; OncoSil Medical Ltd, London, United Kingdom; OncoSil Medical Ltd, Sydney, NSW, Australia; Monash Medical Centre, Melbourne, Australia

Background: LAPC is associated with a poor prognosis. Current standard treatment is limited to chemotherapy or chemo-radiotherapy. P-32 Microparticles is a brachytherapy device that implants a predetermined dose of P-32 into pancreatic tumours via endoscopic ultrasound (EUS) guidance. This reports the initial results of a pilot study in combination with chemotherapy. **Methods:** Eligible patients were permitted to receive either GNP or FOLFIRINOX. P-32 was implanted at week 4 or 5. The dose of P-32 was calculated from tumour volume to deliver an absorbed dose of 100 Gy. Diffusion pattern of the P-32 suspension was assessed by EUS and bremsstrahlung SPECT/CT imaging. Safety data was graded using CTCAE v4.0 criteria. Response was assessed according to RECIST 1.1 with CT scans every 8 weeks and FDG-PET scans at baseline and week 12. **Results:** 50 patients were enrolled (Intent-to-Treat population (ITT)) of which 42 were implanted with the device (Per Protocol population (PP)). 10 received FOLFIRINOX and 40 GNP. Median age was 65, 28 were male and all had a PS 0/1. 1070 adverse events (ITT) were reported; 153 (80% of patients) were $\geq$ Grade 3. The most common AEs of $\geq$ Grade 3 were haematological (39, 46%) and gastrointestinal disorders (30, 34%). No serious device- or radiation-related toxicities have been reported. PP Local Disease Control Rate at Week 16 was 90%; 95% CI: 77-97% and at Week 24 was 71%; 95% CI: 55-84%. Overall Response Rate (ORR) was 31%; 95% CI: 18-47%. Median change in tumour volume from Baseline to Week 16 and to Week 24 was -38% (range +89% to -90%) and -27.5% (range +139% to -79%). Ten (24%) patients underwent surgical resection following repeat staging. Eight patients had R0 margin. **Conclusions:** The use of EUS-guided implantation of P-32 is feasible, with an acceptable safety profile in combination with first-line chemotherapy for LAPC patients. Encouraging OR and DCR are observed. Further follow-up to inform results of local progression free survival and progression free survival is warranted. Acknowledgement: Nab-paclitaxel was supported by Specialised Therapeutics Australia Pty Ltd. Clinical trial information: NCT03003078.

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4126 **Poster Session (Board #231), Mon, 8:00 AM-11:00 AM**

The effect of neoadjuvant chemotherapy with gemcitabine and S-1 for resectable pancreatic cancer (randomized phase II/III trial; Prep-02/JSAP-05).

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Background: Despite recent progress of adjuvant chemotherapy for resected pancreatic ductal adenocarcinoma (PDAC), its survival remains limited. We conducted a randomized controlled trial to compare neoadjuvant chemotherapy (NAC) with upfront surgery (UP-S) for patients with resectable PDAC. **Methods:** Patients with resectable PDAC, all confirmed cytologically or histologically were enrolled. Patients received 2 cycles of gemcitabine and S-1 regimen (GS) followed by surgery (NAC) or UP-S after randomization (1:1). Patients in both arms received adjuvant chemotherapy using S-1 for 6 months after surgical resection. The primary endpoint was overall survival (OS); secondary endpoints included adverse events, resection rate, recurrence-free survival, residual tumor status, nodal metastases, and tumor marker kinetics. **Results:** A total 362 patients were randomly assigned to NAC-GS (n=182) or UP-S (n=180) for 3 years (2013-16). The median OS was 36.7 months in NAC-GS and 26.6 months in UP-S; HR 0.72 (p=0.015, stratified log-rank test) at 2.5 year after final enrollment. Crude resection rate for NAC and UP-S were 77%, 72% respectively. There was no operative mortality in both groups. Although G3/4 adverse events were observed frequently (73%) during NAC, no significant difference for both groups was observed for perioperative outcomes including blood loss, operation time, R0 resection rate and postoperative morbidity. Significant decrease of pathological nodal metastases in NAC was noted compared to those in UP-S by pathological evaluation for resected patients($p<0.01$). Although significant decrease of viable tumor cells was observed in primary tumor after NAC compared to UP-S ($p<0.01$), Evans IIb or more was found in only 14 % of resected patients in NAC. Hepatic recurrence after surgery was significantly reduced in NAC (30.0%) compared to UP-S (47.5%) in observed period. **Conclusions:** The strategy of NAC showed significant longer survival compared to that of UP-S with acceptable feasibility. The effect of NAC might imply the control of subdiagnostic liver metastases before surgery for resectable PDAC. Clinical trial information: UMIN000009634.

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4127 **Poster Session (Board #232), Mon, 8:00 AM-11:00 AM**

Final results of JASPAC05: Phase II trial of neoadjuvant S-1 and concurrent radiotherapy followed by surgery in borderline resectable pancreatic cancer.

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Background: Borderline resectable pancreatic cancer (BRPC) is frequently associated with positive surgical margins and a poor prognosis when treated with upfront surgery. This study was designed to assess whether neoadjuvant chemoradiotherapy (CRT) with S-1 increases the R0 resection rate. **Methods:** This was a multicenter, single-arm, phase II study. Patients with BRPC received S-1 (40 mg/m^2 bid) and concurrent radiotherapy (50.4 Gy in 28 fractions) before surgery if they fulfilled any of the following: (1) bilateral impingement of the superior mesenteric vein or portal vein; and (2) tumor contact $\leq 180°$ with the superior mesenteric artery, common hepatic artery, or celiac axis. The primary endpoint was the R0 resection rate in BRPC confirmed by central review. Secondary endpoints were overall survival (OS), progression-free survival (PFS), response rate (RECISTv1.1), pathological response rate, surgical morbidity (Clavien–Dindo classification), and toxicity (CTCAEv4.0). At least 40 patients were required, with one-sided $\alpha = 0.05$ and $\beta = 0.05$, with an expected and threshold value for the primary endpoint of 30% and 10%. **Results:** Fifty-two patients were eligible, of whom 41 had BRPC by central review. CRT was completed in 50 (96%) patients and was well tolerated. The rate of grade 3/4 toxicity with CRT was 43%. The R0 resection rate was 52% (95% CI, 37.6%–66.0%) in 52 eligible patients and 63% (95% CI, 46.9%–77.9%) in 41 patients with BRPC. The radiological response rate was 5.8%, while destruction of $> 50\%$ of tumor cells was shown microscopically in 32% of patients. Postoperative grade III/IV adverse events were observed in 7.5% of operated patients. Among the 52 eligible patients, the 2-year OS rate, median OS, and median PFS were 51%, 25.8 mo, and 6.7 mo. Of the 41 patients with BRPC, the 2-year OS rate, median OS, and median PFS were 58%, 30.8 mo, and 10.4 mo. **Conclusions:** S-1 and concurrent radiotherapy appear to be feasible and effective at increasing the R0 resection rate with encouraging survival rates in BRPC. A phase II/III trial evaluating this treatment is ongoing. Clinical trial information: NCT02459652.

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4128 **Poster Session (Board #233), Mon, 8:00 AM-11:00 AM**

NEONAX trial: Neoadjuvant plus adjuvant or only adjuvant nab-paclitaxel plus gemcitabine for resectable pancreatic cancer, a phase II study of the AIO pancreatic cancer group (AIO-PAK-0313)—Safety interim analysis.

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Background: Survival in pancreatic cancer (PDAC) is still poor even after curatively intended resection. Perioperative treatment approaches improve outcome in various tumor entities. Data on perioperative treatment in resectable PDAC are limited and there is a debate whether neoadjuvant treatment might impair subsequent surgery by adding perioperative morbidity or mortality. **Methods:** NEONAX is a randomized phase II study (planned 166 patients) of perioperative gemcitabine/nab-paclitaxel (Arm A: 2 pre- and 4 post-operative cycles, Arm B: 6 cycles adjuvant) for patients with primarily resectable PDAC. Primary objective is DFS at 18 months after randomization. Secondary objectives are 3-year OS-rate and DFS-rate, progression during neoadjuvant therapy, R0/R1 resection rate and QoL. **Results:** NEONAX was initiated in March 2015 in 26 centers for PDAC surgery in Germany. The data represent the safety interim analysis (IA) of the first 48 patients. 25 patients were randomized to Arm A and 23 to Arm B. Patients' median age was 65.3 years (56.3% males, 43.8% females, 85.4% ECOG 0). Out of 25 patients in Arm A 20 patients (80%) underwent surgery, compared to 21 of 23 patients (91.3%) in Arm B with upfront surgery. Reasons for no resection were intraoperatively determined small liver metastases (2 cases, Arm A), withdrawal of informed consent (2 cases in each arm) and 1 patient with uncontrolled cholestasis (arm A). Postoperative complications occurred in 45% of arm A and 42.8% of arm B. (pancreatic fistula: 15% in arm A and 9.5% in arm B, infections: 10% in arm A and 9.5% in arm B) All resected patients were alive 60 days after surgery. At least 1 adverse event (AE) NCI-CTCAE $\geq$ grade 3 occurred in 60% of the perioperative and 39.1% of adjuvant treatment arm. Most common AEs were neutropenia (16.7%), fatigue (10.4%) and infections (10.4%). **Conclusions:** There was an increase in NCI-CTCAE $\geq$ grade 3 events in the perioperative arm, but this was manageable and did not result in increased peri- or postoperative mortality. 8% of patients in the perioperative arm did not get resected due metastases detectable during surgery, but not on preoperative imaging immediately prior to surgery. Therefore, it cannot be determined whether these metastases were preexistent or developed during neoadjuvant treatment. In conclusion, the first interim analysis of the NEONAX trial shows that this protocol can be safely applied to patients with resectable PDAC in a perioperative setting. Clinical trial information: NCT02047513.

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4129 **Poster Session (Board #234), Mon, 8:00 AM-11:00 AM**

Metformin use and pancreatic cancer survival in U.S. veterans with diabetes mellitus: Are there racial differences?

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Background: Experimental and observational studies suggest that metformin holds promise in improving survival among pancreatic cancer patients. However, findings from prior observational studies have been questioned because most did not control for immortal time bias, which can overestimate the survival benefit of a drug. In addition, previous studies did not present data on African American patients. Thus, it is unknown if any survival advantage from metformin extends to African Americans. To address these limitations, we analyzed data from the U.S. Veterans Health Administration (VHA). **Methods:** A population-based retrospective cohort study of 3,811 (N = 773 are African Americans) pancreatic cancer patients with pre-existing diabetes mellitus diagnosed within the VHA between October 1, 1998 and December 30, 2010, and followed until December 2014. We calculated hazard ratios (HR) and 95% confidence intervals (CI) using both the time-varying Cox proportional hazards regression model, which controls for immortal time bias, and conventional Cox model. Analyses were adjusted for confounders. We also stratified analyses by race. Further, we performed analyses among patients who were metformin naïve (N = 1158) at the time of pancreatic cancer diagnosis (most representative of patients enrolled in clinical trials). **Results:** Median survival was 4.5 months among metformin users versus 3.7 months among non-users. Metformin use was not associated with pancreatic cancer survival in analysis using the time-varying Cox model: HR = 1.05 (95% CI 0.92-1.14, P-value = 0.28). Results were identical among non-Hispanic Whites and African Americans. In analysis using conventional Cox model, metformin use was associated with an artificial survival benefit: HR = 0.89 (95% CI 0.83-0.98, P-value = 0.01). Among patients who were metformin naïve at the time of pancreatic cancer diagnosis, metformin use was associated with improved survival in analysis using the time-varying Cox model: HR = 0.77 (95% CI 0.61-0.98, P-value = 0.03). The HRs were 0.78 (95% CI 0.61-0.99, P-value = 0.04) among non-Hispanic Whites and 1.20 (95% CI 0.75-1.93, P-value = 0.45) among African American patients. **Conclusions:** We observed no associations between metformin use and pancreatic cancer survival. Nevertheless, we noted improved survival (limited to non-Hispanic White patients) among patients who were metformin naïve at the time of pancreatic cancer diagnosis, which requires conformation in other studies.

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4130 **Poster Session (Board #235), Mon, 8:00 AM-11:00 AM**

Relacorilant (RELA) with nab-paclitaxel (NP): Safety and activity in patients with pancreatic ductal adenocarcinoma (PDAC) and ovarian cancer (OvCA).

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Background: Glucocorticoid receptor (GR) pathway activation has been linked with chemotherapy resistance (CTR). RELA (formerly CORT125134, Corcept Therapeutics), a potent selective GR modulator, in combination with paclitaxel reduced CTR and enhanced activity against tumor growth in preclinical models of solid tumors. **Methods:** Patients (pts) with advanced solid tumors, $\leq$3 prior lines of cytotoxic therapy, ECOG status 0-1, and adequate marrow function received RELA (100, 150, or 200mg) + NP (60, 80, or 100mg/m^2). Once daily RELA was given either continuously (CON) or intermittently (INT) (day before, of, and after NP). NP was dosed weekly for 3 of 4 weeks (wks) of a 28-day cycle. Prior NP therapy was allowed. **Results:** 72 pts have been enrolled [mean age 60 (range 18-81), mean number of prior therapies 3, prior taxane (TXN) treatment 54/72 (75%)]. 61 pts received $\geq$1 dose of RELA. Grade $\geq$3 AE $\geq$10% for CON: neutropenia (6/43, 14%); INT: neutropenia (6/18, 33%), anemia (2/18, 11%), and mucosal inflammation (2/18, 11%). Prophylactic G-CSF became mandatory in later cohorts. Recommended Phase 2 Dose: RELA 100mg-CON/150mg-INT + NP 80mg/m^2 (exposures similar to NP 100mg/m^2 due to CYP3A4 inhibition by RELA). Disease control (DC) $>$ 24 wks was noted in 5/27 (19%) PDAC pts: 3 PR, 2 SD (27-50 wks). 3 pts achieved benefit despite progression on prior TXN with time to progression (TTP) 1.9-3.6x longer than prior TXN. 4/13 (31%) OvCA pts had DC $>$ 24 wks: 1 CR, 1 PR, 2 SD (33-54+ wks). 1 pt had TTP 4.4x longer than prior TXN. 3 additional PRs were observed: acinar pancreatic cancer, TTP 31 wks (4.4x prior TXN); vulvar SCC HPV+, TTP 55 wks (3.9x prior TXN); cholangiocarcinoma, DC 29+ wks. Expression of GR-regulated genes involved in inflammation, apoptosis, and CTR distinguished pts with DC from pts without DC, providing proof of mechanism. **Conclusions:** RELA+NP resulted in durable disease control in pts with metastatic PDAC, OvCA, and other solid tumors, including those that have progressed on prior TXN. TTP was often several-fold longer than previously achieved on TXN therapy. Toxicities are manageable with prophylaxis for neutropenia. Further evaluation in OvCA NCT03776812, PDAC, and others are planned. Clinical trial information: NCT02762981.

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4131 **Poster Session (Board #236), Mon, 8:00 AM-11:00 AM**

Elevated pretreatment serum IL-8 and PD-L1 and overall survival in a phase III randomized advanced pancreatic cancer clinical trial.

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Background: We previously reported the prognostic and predictive utility of pretreatment serum PD-L1 in the CCTG MA.31 serum bank (SABCS 2018, abstr PD3-10). IL-8 (CXCL8) is a pro-inflammatory cytokine that binds to CXCR1 and CXCR2 and promotes tumor immune escape and progression. High serum IL-8 levels are associated with poor prognosis in many cancers, and have recently been reported to predict for reduced OS to nivolumab in lung cancer and melanoma (ASCO 2018, abstr #3025). In this study, we retrospectively evaluated combined pretreatment serum IL-8 and PD-L1 on overall survival (OS) from a phase III randomized pancreatic cancer trial of first-line therapy (octreotide + 5-FU vs. 5-FU) that had reported no significant OS difference between treatment arms. **Methods:** This study had 147 patients with serum available for this retrospective biomarker analysis from an advanced pancreatic cancer phase III clinical trial.TheELLA immunoassay platform (ProteinSimple, San Jose, CA) was utilized to quantitate serum levels of IL-8 and PD-L1. Kaplan-Meier life table analysis was used to correlate serum biomarkers with overall survival (OS). **Results:** In univariate analysis, pretreatment serum IL-8 was a significant biomarker as a continuous variable (HR = 1.004; p = 0.012) and trended significant at the median cutpoint (HR = 1.379; p = 0.098) for OS, however serum PD-L1 was not significant at any cutpoint. When serum PD-L1 and IL-8 levels were analyzed as combined biomarkers (median cutpoints), the serum IL-8 high / PD-L1 high cohort had a significantly shorter OS vs the serum IL-8 low / PD-L1 low cohort (HR = 1.816; p = 0.017). **Conclusions:** In this phase III randomized clinical trial in advanced pancreatic cancer, pretreatment serum IL-8 was a significant biomarker for OS, but serum PD-L1 was not. Higher combined pretreatment serum levels of PD-L1 and IL-8 (both biomarkers high vs. both low) were prognostic for reduced OS in this phase III pancreatic cancer trial. Further study of circulating IL-8 and PD-L1 is warranted in pancreatic cancer for evaluation of targeted and investigational therapies, including the immune checkpoint inhibitors and anti-IL8 therapy.

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4132 **Poster Session (Board #237), Mon, 8:00 AM-11:00 AM**

Homologous recombination deficiency (HRD): A biomarker for first-line (1L) platinum in advanced pancreatic ductal adenocarcinoma (PDAC).

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Background: HRD is an emerging biomarker for platinum therapy in PDAC. The clinical implications regarding differences in outcome between germline and somatic HRD in advanced PDAC treated with 1L platinum is unexplored. **Methods:** We evaluated overall survival (OS) for advanced PDAC (stage III/IV) based on their pathogenic germline (gHRD) and somatic HRD (sHRD) using integrated genomic profiling from MSK-IMPACT and 1L platinum use. HRD defined by pathogenic alterations from the following genes: *BRCA1/2, PALB2, ARID1A/B/2, ATR, ATRX, ATM, BAP1, RAD50/51C/D, BRIP1, NBN, CHECK1/2, FANCA/C, CDK12, and MRE11*. **Results:** Advanced PDAC patients (n=461) treated at MSK enrolled in a prospective database, were evaluated. Median follow-up was 27.6 months (95% CI, 24.6-30.6). Both germline and somatic profilings were available for n=350 (76%) but only somatic profiling was available for n=111 (24%). We identified n=52 patients with gHRD (11.3%), n=42 patients with sHRD (9.1%), and 48 patients with somatic VUS for HRD genes. From all 461 patients, the OS was not different between 1L non-platinum vs. 1L platinum groups (19 M vs. 19.3 M), regardleess of their HRD status. (Table) The OS was superior for gHRD vs. non-gHRD (28.7 M vs. 18.2 M), regardless of 1L treatment choice. However, similar significant OS superiority was neither observed in sHRD vs. non-sHRD, nor in VUS sHRD vs. non-VUS sHRD. In a subgroup analysis of 1L platinum treated patients, the OS was superior in gHRD vs. non-gHRD (NR vs. 17.9 M); however, there was no OS difference between sHRD and non-sHRD. **Conclusions:** In advanced PDAC patients, only gHRD predicted better overall survival for first-line platinum chemotherapy. These findings emphasize the importance of germline mutation testing of HRD in PDAC. Biomarker validation and functional definition of HRD such as loss of heterozygosity analysis is underway.

	All treatments (461)			1L non-platinum (184)			1L platinum (277)		
(N)	OS (M)	HR	p-value	OS (M)	HR	p-value	OS (M)	HR	p-value
All pts (461)	19.0	-	-	19.0	-	-	19.3	0.95	0.676
No gHRD (409)	18.2	0.54	0.003	18.8	0.74	0.419	17.9	0.47	0.004
HRD (52)	27.7			24.3			NR		
No sHRD (419)	18.3	0.92	0.670	18.2	0.68	0.252	18.3	1.12	0.666
sHRD (42)	21.5			23.8			20.6		

Overall survivals for different HRD groups and 1L treatment groups.

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4133 **Poster Session (Board #238), Mon, 8:00 AM-11:00 AM**

Association of *BRCA*-mutant pancreatic cancer with high tumor mutational burden (TMB) and higher PD-L1 expression.

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Background: In the U.S. 56,000 Americans are expected to be diagnosed with pancreatic cancer in 2019. Prognosis in pancreatic cancer is poor. Therefore, new treatment strategies are urgently needed to improve survival. *BRCA1* and *BRCA2* mutations have been described to be the most common genetic mutations involved in familial pancreatic cancer. The optimal treatment regimen to use in *BRCA*-mutant pancreatic cancer has still to be established. Moreover, no data are available on association of *BRCA* mutation with immune-associated markerssuch as tumor mutational burden (TMB), microsatellite instability (MSI) or PD-L1 expression. **Methods:** Tumor samples of 2824 patients with pancreatic ductal adenocarcinoma were analyzed for BRCA mutation by NGS and for other genes (MiSeq on 47 genes, NextSeq on 592 genes) at Caris Life Sciences, Phoenix, AZ. TMB was calculated based on somatic nonsynonymous missense mutations, and MSI was evaluated by NGS of known MSI loci. PD-L1 expression was evaluated using immunohistochemistry. **Results:** In 4.4% (N = 124) of all pancreatic adenocarcinoma samples *BRCA* mutations were detected. *BRCA2* mutations were more common: 3.1% (N = 89) vs 1.1% *BRCA1* mutations (N = 35). *BRCA* mutations were associated with younger age (*BRCA1*: 61 yrs for mutated vs. 64 for wild-type, $p = 0.07$; *BRCA2*: 61 yrs vs. 64, $p = 0.002$; both: $p < 0.001$). *BRCA* mutations were associated with higher MSI-H frequency (4.8% vs. 1.2%, $p = 0.002$), elevated PD-L1 expression (22% vs. 11%, $p < 0.001$) and higher TMB (mean 8.7 mut/MB vs. 6.5, $p < 0.001$); the differences remain significant in MSS tumors ($p < 0.05$). *BRCA*-mutant pancreatic carcinomas showed a significantly lower mutation frequencies in *TP53* (59% vs 73%, $p = 0.001$), *CKDN2A* (13% vs 25%, $p = 0.006$), but higher frequencies in *APC* (6.5% vs 2.2%), *KMT2A* (1.9% vs 0.2%), *AMER1* (1.9 vs 0.5%) and *SETD2* (3.7% vs 0.4%) mutations ($p < 0.05$ for all comparisons). **Conclusions:** *BRCA* mutations are found in a significant subgroup of pancreatic ductal adenocarcinoma and these carcinomas are associated with an immunogenic tumor profile. These data suggest evaluating PARP inhibitors in combination with immunotherapy in patients with *BRCA*-mutant pancreatic adenocarcinoma especially in tumors that are MSS.

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4134 **Poster Session (Board #239), Mon, 8:00 AM-11:00 AM**

Hereditary cancer genetic testing among patients with pancreatic cancer.

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Background: Pancreatic cancer (PC) is typically diagnosed at a late, untreatable stage, with a 5-year survival rate of only ~8%. Genetic testing for individuals with PC may aid in therapy decisions, as those with a germline or somatic pathogenic variant (PV) in a DNA-repair gene may benefit from PARP inhibitors. In addition, germline genetic testing for unaffected family members can identify high risk individuals who may be appropriate for surveillance studies. We assessed the results of hereditary cancer genetic testing among individuals with a personal history of PC and evaluated several possible risk factors. **Methods:** Individuals with PC who had germline testing for 25-29 cancer-susceptibility genes between September 2013 and November 2018 were included in this analysis (N = 1,676). Clinical characteristics were obtained from provider-completed test request forms and included personal cancer history (PHx), family cancer history (FHx), and age at diagnosis. **Results:** Overall, 12.6% (212/1676) of patients with PC carried a PV, most commonly in *BRCA2* (3.8%), *ATM* (2.7%), and *PALB2* (1.2%). PVs were more common in men and for individuals who had a PHx of additional cancer(s) (see Table). Age at PC diagnosis did not impact the positive PV rate. The PV positive rate was elevated among individuals with PC and at least two relatives with PC (15.1%) and for individuals with a FHx of cancer at an early age (14.2%). The PV positive rate remained > 10% regardless of nearly all other FHx characteristics evaluated, including the absence of any FHx (see Table). **Conclusions:** In this cohort, a substantial proportion of individuals with a PHx of PC carried PVs, regardless of age at diagnosis and personal and family cancer history.

Risk Factor	Total	Positive PV Rate
Cohort	1676	12.6%
Gender		
Men	542	15.3%
Women	1134	11.4%
PHx Cancer		
PC Only	958	11.3%
PC + Other Cancer(s)	718	14.5%
Age at PC diagnosis		
≤50 years	265	12.8%
> 50 years	1278	13.1%
FHx of PC		
Any FHx of PC	544	12.7%
≥2 relatives with PC	126	15.1%
1 relative with PC	418	12.0%
No FHx of PC	1132	12.6%
FHx of Any Cancer		
FHx of Other Cancer(s)	1500	12.8%
≥2 relatives with Other Cancer(s)	1184	13.9%
1 relative with Other Cancer(s)	316	8.5%
No FHx	97	10.3%
Age at Diagnosis for FHx		
Any Cancer Diagnosed ≤50	815	14.2%
Any Cancer Diagnosed > 50	651	10.8%

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4135 **Poster Session (Board #240), Mon, 8:00 AM-11:00 AM**

Clinical and immune responses using anti-CD3 x anti-EGFR bispecific antibody armed T cells (BATs) for locally advanced or metastatic pancreatic cancer.

Lawrence G. Lum, Tri Minh Le, Minsig Choi, Archana Thakur, Matthew Reilley, Paul Raymond Kunk, Abhinav Deol, Karen K. Ballen, Tamila L. Kindwall-Keller, Dana Schalk, Ewa Kubicka, Manley Huang, Philip Agop Philip, Hussein Aoun, Gregory Dyson, Qin Liu, Anthony Frank Shields; University of Virginia, Charlottesville, VA; Stony Brook University, Stony Brook, NY; The University of Texas MD Anderson Cancer Center, Houston, TX; Blood and Marrow Transplant Program, Wayne State University/ Karmanos Cancer Institute, Detroit, MI; Massachusetts General Hospital, Boston, MA; Univ of Virginia, Crozet, VA; Karmanos Cancer Institute, Detroit, MI; Barbara Ann Karmanos Cancer Institute, Wayne State University School of Medicine, Detroit, MI; Department of Statistics, Wayne State University, Detroit, MI; Wistar Institute, Philadelphia, PA; Karmanos Cancer Institute, Wayne State University, Detroit, MI

Background: Conventional chemotherapy (chemo) for locally advanced pancreatic cancer (LAPC) and metastatic pancreatic cancer (MPC) has dismal responses and poor survival rates. Arming activated T cells (ATC) with anti-CD3 x anti-EGFR bispecific antibody (BATs) makes every ATC into an EGFR-specific cytotoxic T cell that secretes cytokines, proliferates, and kills tumor. **Methods:** We report on 5 phase I (P1) and 15 phase II (P2) patients. In our phase I study, BATs were used to treat LAPC or MPC patients at Karmanos Cancer Institute (NCT0140874) in a dose escalation involving 3 weekly infusions of 1, 2, and 4 x 10^{10} BATs/infusion, followed by a booster infusion at 3 months (mos) for a total of up to 8 x 10^{10} BATs. No dose limiting toxicities were observed in the outpatient infusions. Fifteen patients treated on a phase II (NCT02620865) at KCI and (NCT03269526) at University of Virginia received biweekly infusions of 10^{10} BATs/infusion over 4 weeks for a total of 8 x 10^{10} EGFR BATs. **Results:** Four patients had stable disease (SD) for 6.1, 6.5, 5.3, and 36 mos. Two patients had complete responses (CR) when chemo was restarted after BATs. The median overall survival (OS) for 17 evaluable patients (3 of 4 infusions in the P1 and all 8 infusions in the P2) was 31 mos, and the median OS for all 20 patients (3 in the P2 who did not complete 8 infusions) is 14.5 mos (95% CI, 7.5-45.2 mos). Patient IT20104 had an apparent "pseudoprogression" after 3 BATs infusions, but achieved a CR after restarting capcitabine and is alive off therapy at 54 mos (24 mos after stopping capecitabine). Immune evaluations on the P1 patients show specific cytotoxicity to MiaPaCa-2 by peripheral blood mononuclear cells (PBMC) increased from 21% to 31% 2 weeks after the 3rd infusion, and IFN-γ EliSpots increased from < 20 to 1000 IFN-γ EliSpots/10^6 PBMC ($p < 0.03$). Patient IT 20121 (SD for 36 mos) increased IFN-γ EliSpots from 250 to 3200/10^6 PBMC after 8 infusions. Innate cytotoxicity responses in the P1 patients increased significantly after infusions ($p < 0.04$). Levels of IP-10 increased significantly ($p < 0.04$), and levels of IL-8 decreased but not significantly ($p < 0.07$). **Conclusions:** Infusions of BATs are safe and induce endogenous adaptive anti-tumor responses. Targeting PC with BATs may stabilize disease, leading to improved OS, as well as evidence that BATs infusions can induce anti-tumor activity and immunosensitize tumors to subsequent chemo. Clinical trial information: NCT014084,NCT03269526,NCT02620865.

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4136 **Poster Session (Board #241), Mon, 8:00 AM-11:00 AM**

Methylated circulating tumor DNA (Met-DNA) as an independent prognostic factor in metastatic pancreatic adenocarcinoma (mPAC) patients.

Daniel Pietrasz, Shufang Wang-Renault, Laetitia Dahan, Julien Taieb, Karine Le Malicot, Yves Rinaldi, Solene Doat, Jean-Marc Phelip, Valerie Taly, Jean-Baptiste Bachet, Pierre Laurent-Puig; Paul Brousse Hospital, Villejuif, France; Paris Descartes University, Paris, France; La Timone University Hospital, Marseille, France; Hôpital Européen Georges-Pompidou, Sorbonne Paris Cite/Paris Descartes University, Paris, France; FFCD and INSERM U1231, Dijon, France; Hôpital Européen, Marseille, France; University Hospital Pitie Salpetriere APHP, Paris, France; Universite Jean Monnet, Saint-Etiennes, France; Pitié-Salpêtrière Hospital, Paris, France

Background: Circulating tumor DNA has emerged as prognostic biomarker in oncology. Many different genes can be mutated within a tumor, complicating procedures, even with highly sensitive next-generation sequencing (NGS). DNA methylation in promotor of specific genes is an early key epigenetic change during oncogenesis. Specific methylated genes could be a potential relevant cancer biomarker that may substitute for NGS panels. The aim of this study was to assess the prognostic value of Met-DNA in mPAC. **Methods:** Prognostic value of Met-DNA was assessed in a prospective cohort (PLAPAN) of mPAC (training cohort), correlated with NGS, then in two prospective independent validation cohorts from two randomized phase II trials (PRODIGE 35 and 37). Plasma samples were collected before chemotherapy on EDTA-coated tubes. Met-DNA was quantified using two specific markers of pancreatic DNA methylation by digital droplet PCR and correlated with prospectively registered patient (pts) characteristics and oncologic outcomes (progression free survival (PFS) and overall survival (OS)). **Results:** 330 patients (pts) were enrolled. 60% (n = 58) of the 96 pts of the training cohort had at least one Met-DNA marker. The correlation with NGS assessment was R = 0.93 (Pearson; $p < 0.001$). 59.5% (n = 100/168) and 59% (n = 39/66) of pts had detectable Met-DNA in the 2 validation cohorts. In the training cohort, Met-DNA was correlated with poor OS (HR = 1.82; 95%CI 1.07-2.42; p = 0.026). In validation cohorts, Met-DNA was a prognostic factor of PFS (HR = 1.62; 95%CI 1.17-2.25, p = 004) and OS (HR = 1.79; 95%CI 1.28-2.49, $p < 0.001$) in PRODIGE 35, as in PRODIGE 37: PFS HR = 1.79 (95%CI 1.07-2.99; p = 0.026) and OS HR = 2.08 (95%CI [1.18-3.68], p = 0.01), respectively. In multivariate analysis adjusted on gender, age, CA19-9 > 40UI.mL, treatment arm, number of metastatic sites and stratified on center, Met-DNA was independently associated with poor OS in both trials: HR = 1.81 (95%CI 1.10-2.98; p = 0.02) and HR = 3.62 (95%CI: 1.32-9.93; p = 0.01). **Conclusions:** This study demonstrates that Met-DNA is a strong independent prognostic factor in mPAC. These results argue for patient's stratification on ctDNA status for further randomized trials. Clinical trial information: NCT02827201 and NCT02352337.

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4137 **Poster Session (Board #242), Mon, 8:00 AM-11:00 AM**

SWOG S1505: Initial findings on eligibility and neoadjuvant chemotherapy experience with mFOLFIRINOX versus gemcitabine/nab-paclitaxel for resectable pancreatic adenocarcinoma.

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Background: Clinical outcomes after curative therapy of resectable pancreatic ductal adenocarcinoma (PDA) remain suboptimal. For early control of systemic disease with aggressive perioperative chemotherapy (CTx), we conducted a prospective trial in the National Clinical Trials Network (NCTN) setting. **Methods:** S1505 was a randomized phase II trial of periop (12 weeks pre-, 12 weeks post-op) CTx with either mFOLFIRINOX (5-fluorouracil, irinotecan, oxaliplatin – without bolus 5-FU and leucovorin; Arm 1), or gemcitabine/nab-paclitaxel (Arm 2). Eligibility required adult patients with ECOG PS 0 or 1, confirmed tissue diagnosis of PDA, and resectable disease: no involvement of the celiac, common hepatic, or superior mesenteric arteries (and, if present, variants); $< 180°$ interface between tumor and vessel wall, of the portal or superior mesenteric veins; patent portal vein/splenic vein confluence; no metastases. Primary outcome is 2-year overall survival (OS), using a "pick the winner" design; for 100 eligible patients, accrual up to 150 patients was planned, to account for cases deemed ineligible at central radiology review. **Results:** From 2015 to 2018, 147 patients were enrolled; 74 to Arm 1; 73 to Arm 2. At central radiology review, 42/147 (29%) were ineligible; of these, 15 (36%) had venous involvement $\geq 180°$, 22 (52%) had arterial involvement, 28 (67%) had distant disease. One patient had distal cholangiocarcinoma (ineligible); one withdrew consent after randomization. Eligible patients (n = 103) had median age 64 years; males 58%; whites 89%; PS 0 64%. Of 103, 99 (96%) started and 86 (83%) completed preop CTx. There was one death due to sepsis and 61 additional patients experienced grade 3/4 toxicities. To date, 76 of 99 (77%) patients went to surgery and 72 (73%) underwent resection. **Conclusions:** This is the first-ever NCTN study of periop CTx for resectable PDA. Accrual was brisk, establishing feasibility. Ineligible cases after central radiology review highlight quality control and physician education imperatives for neoadjuvant PDA trials. Preop CTx safety and resection rates are encouraging. Follow up for OS is ongoing. Clinical trial information: NCT02562716.

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4138 **Poster Session (Board #243), Mon, 8:00 AM-11:00 AM**

Improved overall survival (OS) for advanced pancreatic cancer (PDAC) patients (pts) enrolled in the Know Your Tumor (KYT) program whose tumors harbored highly actionable molecular alterations and who received molecularly-matched therapies (tx).

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Background: Initial results from the KYT program demonstrated that 27% of PDACs harbor highly actionable molecular alterations (herein labelled "actionable biomarkers"), defined as biomarkers that predict for a high response rate to appropriately targeted tx, *in any cancer type*. Within this cohort, the median progression-free survival on molecularly-matched tx was 2 months longer than unmatched tx. Here, we present OS data emphasizing the 125 pts with "actionable biomarkers" who did or did not receive molecularly-matched tx. **Methods:** PanCAN and Perthera have coordinated tumor molecular profiling through commercial labs (NGS/IHC panels) for PDAC pts since 2014. Results are reviewed by a molecular tumor board, and tx options are prioritized based on the actionable biomarkers, in the context of the pt's tx history. Pts are followed longitudinally to track physician tx choices and survival outcomes. Cox regression was used to assess differences in OS (measured from date of diagnosis until death). **Results:** Of 1053 pts who received a Perthera Report, 25% had "actionable biomarkers". OS analyses across 454 pts with adequate tx history are shown in the Table below. Notably, pts with "actionable biomarkers" who received a molecularly-matched tx had a significantly increased OS compared to those with "actionable biomarkers" but who did not receive molecularly-matched tx. Subgroup analyses related to tx history and specific molecular pathways that warrant further investigation will be discussed. **Conclusions:** When the ~25% of PDAC pts whose tumors harbored "actionable biomarkers" received molecularly-matched tx, they had a better OS. These findings support the need to test all pts with PDAC, and just as importantly, to maximize access to molecularly-matched tx for appropriate pts, to achieve the best pt outcomes.

Cohort	# Patients	mOS (years)	p-value (HR [95% CI])
"Actionable biomarkers", Matched Tx	25	2.58	--
***vs.* "Actionable biomarkers", Unmatched Tx**	100	1.51	0.00700 (0.46 [0.26-0.81])
***vs.* No "actionable biomarkers"**	329	1.42	0.00125 (0.42 [0.25-0.71])

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4140 **Poster Session (Board #245), Mon, 8:00 AM-11:00 AM**

BIONADEGE: Genomic profiling of small bowel adenocarcinoma from the NADEGE prospective cohort.

Thomas Aparicio, Magali Svrcek, Julie Henriques, Pauline Afchain, Astrid Lièvre, David Tougeron, Johan Gagniere, Eric Terrebonne, Guillaume Piessen, Jean-Louis Legoux, Cedric Lecaille, Marc Pocard, Jean-Marc Gornet, Aziz Zaanan, Sandrine Lavau-Denès, Thierry Lecomte, Mourad Benallaoua, Sabine Helfen, Dewi Vernerey, Pierre Laurent-Puig; Department of Gastroenterology, Saint Louis Hospital, Paris, France; AP-HP, Hôpital Saint-Antoine, Paris, France; Methodology and Quality of Life Unit, Department of Oncology University Hospital, Besançon, France; Saint Antoine Hospital, Paris, France; CHU Pontchaillou, Rennes, France; Poitiers University Hospital, Poitiers, France; CHU Estaing, Clermont Ferrand, France; Pôle Appareil Digestif, Endocrinologie et Nutrition CHU de Bordeaux, Bordeaux, France; Department of Surgical Oncology, University Hospital of Lille, Lille, France; Centre Hospitalier Régional Universitaire, Orléans, France; Department of Gastroenterology, Polyclinique Nord Aquitaine, Bordeaux, France; Hopital Lariboisiere AP-HP, Service de Chirurgie Digestie et Cancérologie, Paris, France; Department of Hepato-Gastroenterology, Saint-Louis Hospital, Paris, France; Hopital Européen Georges Pompidou, Paris, France; Unité de Recherche Clinique, Hôpital Dupuytren, Limoges, France; Hôpital Trousseau, Tours, France; Hôpital Avicenne, Bobigny, France; AP-HP, Hôpital Avicenne, Bobigny, France; Methodology and Quality of Life in Oncology Unit, Besançon University Hospital, Besançon, France; Paris Descartes University, Paris, France

Background: Small bowel adenocarcinoma (SBA) is a rare tumour. Large genomic analyses with prognostic assessments are lacking. **Methods:** BIONADEGE is an ancillary study of the NADEGE cohort that enrolled 347 patients (pts) with SBA from 2009 to 2012. Next generation sequencing investigates the presence of 740 hot spot somatic mutations in 46 genes involved in carcinogenesis. The MSI (MicroSatellite Instable) status was assessed using 5 microsatellites. The MMR (MisMatch Repair) status was assessed by immunochemistry (4 antibodies). **Results:** A total of 196 tumour samples were collected and 125 pts had conclusive results for mutation analysis. The clinical and tumours characteristics were comparable in the NADEGE and BIONADEGE cohort except for metastatic stage at diagnostic underrepresented in the BIONADEGE cohort (17.7%) due to missing tumour sample. A predisposing disease was reported in 25 (20.0%) cases (among them 14 Lynch syndromes and 7 Crohn diseases). The number of mutation observed was 0 in 9.6% pts, only 1 in 32.0%, 2 in 26.4% and $\geq$3 in 32.0%. The most frequent genomic alteration were *KRAS* (44.0%), *TP53* (38.4%), *PIK3CA* (20.0%), *APC* (18.4%), *SMAD4* (14.4%) and *ERBB2* (7.2%). Altogether, a genomic alteration was observed in 90.3% of tumour. *KRAS* mutation were more frequent in synchronous metastatic tumour than in localized tumour (72.7% vs 38.2%, p = 0.003). There was no significant difference of mutation rate according to primary location for the most frequently altered gene. With caution to small sample, *IDH1* mutation is more frequent and *APC* mutation never seen in Crohn disease. The rate of dMMR tumor was 38.6% in localized tumour and 0% in synchronous metastatic tumour. After a median follow-up of 55 months (95%CI [44-63]), M0 stage, pN0, pT1-2 were associate with better survival in univariate analysis. No significant prognostic value of genomic alteration was associated with OS. dMMR status was associate with a better prognosis for OS in pts with MMR status determined by immunohistochemistry (HR = 0.55 [0.29-1.01], p = 0.055). **Conclusions:** A high frequency of targetable alteration is observed in SBA. There is several specificities according to predisposing disease. No association between genomic alteration and prognostic was observed except a trend for a better prognosis associate with dMMR.

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TPS4141 **Poster Session (Board #246a), Mon, 8:00 AM-11:00 AM**

TENERGY: Multicenter phase II study of atezolizumab monotherapy following definitive chemoradiotherapy with 5-FU plus cisplatin in patients with locally advanced esophageal squamous cell carcinoma.

Hideaki Bando, Daisuke Kotani, Takahiro Tsushima, Hiroki Hara, Shigenori Kadowaki, Ken Kato, Keisho Chin, Kensei Yamaguchi, Shun-ichiro Kageyama, Hidehiro Hojo, Masashi Wakabayashi, Miki Fukutani, Yosuke Togashi, Nozomu Fuse, Hiroyoshi Nishikawa, Takashi Kojima; Aichi Cancer Center Hospital, Nagoya, Japan; National Cancer Center Hospital East, Kashiwa, Japan; Division of Gastrointestinal Oncology, Shizuoka Cancer Center, Shizuoka, Japan; Saitama Cancer Center, Saitama, Japan; Department of Gastrointestinal Medical Oncology, National Cancer Center Hospital, Tokyo, Japan; Department of Gastroenterology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; Division of Radiation Oncology and Particle Therapy, National Cancer Center Hospital East, Kashiwa, Japan; Clinical Research Support Office, National Cancer Center Hospital East, Kashiwa, Japan; Division of Cancer Immunology, National Cancer Center, Kashiwa, Japan; National Cancer Center, Kashiwa, Japan

Background: The standard treatment for patients with unresectable locally advanced esophageal squamous cell carcinoma (ESCC) is definitive chemoradiotherapy (CRT) using 5-FU plus cisplatin. However, complete response (CR) rates are only 11% to 25%, and median overall survival (OS) is 9 to 10 months. The improved therapeutic efficacy of combining immunotherapy with radiation has been gaining interest. Our basic research suggested that sequential treatment with anti-PD-L1 agents soon after completion of CRT is the best combination. Twelve months of anti-PD-L1 antibody following platinum-based CRT significantly improved progression-free survival (PFS) and OS in patients with locally advanced non-small cell lung cancer (Antonia SJ, et al. N Engl J Med. 2018). Based on this background information, we have planned a phase II clinical trial to evaluate the safety and efficacy of atezolizumab monotherapy following definitive CRT in patients with locally advanced ESCC. **Methods:** The main inclusion criteria are unresectable locally advanced ESCC without distant metastasis, completion of treatment with 60 Gy of radiation plus two concomitant cycles of chemotherapy (cisplatin 70 mg/m^2 on day 1 and 5-FU 700 mg/m^2 on days 1–4, every 28 days), and adequate organ function. Within 4 weeks after CRT, patients will be registered in the study and started on 1200 mg of atezolizumab every three weeks until 12 months or disease progression. The primary endpoint is the CR rate by the investigator's assessment. Overall response rate, PFS, OS, treatment-related adverse events, and CR rate by central assessment are secondary endpoints. A total of 50 patients will be enrolled, including 40 with primary locally advanced ESCC and 10 with postoperative loco regionally recurrent ESCC. As an exploratory biomarker study, biopsies from the primary site and blood collections will be performed at 3 time points (before CRT, after CRT, and four weeks after the start of atezolizumab). We will analyze the phenotype of immune-competent cells, neoantigens, tumor mutation burden, PD-L1 status, and Human Leukocyte Antigen haplotyping. Clinical trial information: UMIN000034373.

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TPS4142 **Poster Session (Board #246b), Mon, 8:00 AM-11:00 AM**

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

Salah-Eddin Al-Batran, Claudia Pauligk, Ralf Hofheinz, Sylvie Lorenzen, Andreas Wicki, Alexander Rheinhard Siebenhuener, Michael Schenk, Manfred Welslau, Vera Heuer, Eray Goekkurt, Harald Schmalenberg, Peter C. Thuss-Patience, Lisa Waberer, Jonathan Talbot, Thorsten Oliver Goetze, Nils Homann; Institute of Clinical Research (IKF) at Krankenhaus Nordwest, UCT-University Cancer Center, Frankfurt, Germany; University Cancer Center Frankfurt, Institut für Klinisch-Onkologische Forschung and IKF Klinische Krebsforschung GmbH am Krankenhaus Nordwest, Frankfurt, Germany; University Medical Center Mannheim, Tagestherapiezentrum am ITM, Mannheim, Germany; Third Department of Internal Medicine (Hematology/Medical Oncology), Klinikum rechts der Isar, Technische Universitat Munchen, Munich, Germany; Universitätsspital Basel, Basel, Switzerland; Klinik für Medizinische Onkologie und Hämatologie, UniversitätsSpital Zürich, Zurich, Switzerland; Hospital Barmherzige Brüder Regensburg, Regensburg, Germany; Klinikum Aschaffenburg, Medizinische Klinik II, Aschaffenburg, Germany; MVZ St. Anna Hospital, Herne, Germany; Hämatologisch-Onkologische Praxis Eppendorf (HOPE), Facharztzentrum Eppendorf, Hamburg, Germany; Krankenhaus Dresden-Friedrichstadt, IV. Medizinische Klinik, Dresden, Germany; Charité–University Medicine Berlin, Department of Haematology, Oncology and Tumorimmunology, Berlin, Germany; IKF GmbH am Krankenhaus Nordwest, Frankfurt, Germany; F. Hoffmann-La Roche Ltd., Basel, Switzerland; MED. Klinik II, Klinikum Wolfsburg, Wolfsburg, Germany

Background: Perioperative FLOT chemotherapy has become a standard of care for locally advanced, resectable gastric cancer and adenocarcinoma of the GEJ. However, patient outcomes are still unsatisfactory and 5-year survival in T3-4 or nodal positive disease is still around 50%. Targeting the PD-1/PD-L1 pathway has proven active in different cancers, including esophagogastric cancer, and was associated with response rates in the 10-15% range in unselected, heavily pre-treated gastric cancer patients. Atezolizumab is a PD-L1 inhibitor with established efficacy and tolerability profiles. This study evaluates atezolizumab in the perioperative treatment of locally advanced, potentially resectable gastric or GEJ adenocarcinoma in combination with FLOT. **Methods:** This is a large, multinational, prospective, multicenter, randomized, investigator-initiated, open label phase II trial. Patients with locally advanced, potentially resectable adenocarcinoma of the stomach and GEJ ($\geq$cT2 and/or N-positive) without distant metastases are enrolled. Eligibility status is centrally evaluated. Patients are randomized 1:1 to 4 pre-operative 2-week cycles (8 weeks) of FLOT (Docetaxel 50 mg/m^2; Oxaliplatin 85 mg/m^2; Leucovorin 200 mg/m^2; 5-FU 2600 mg/m^2) 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) as assessed by the Kaplan-Meier-Method. The statistical design is based on a target HR of 0.68, a power of 0.8, and a significance level of $p< 0.05$ (1-sided log rank test). A total of 295 patients will be randomized. Main secondary endpoints are rates of centrally assessed pathological regression (rates of complete and nearly complete pathological regression), overall survival, R0 resection, and safety. Recruitment started in Sept 2018; by February 2019, a total of 27 patients have been randomized. Clinical trial information: NCT03421288.

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TPS4143 **Poster Session (Board #247a), Mon, 8:00 AM-11:00 AM**

CA224-060: A randomized, open label, phase II trial of relatlimab (anti-LAG-3) and nivolumab with chemotherapy versus nivolumab with chemotherapy as first-line treatment in patients with gastric or gastroesophageal junction adenocarcinoma.

Kynan Feeney, Ronan Kelly, Lara Rachel Lipton, Joseph Chao, Mirelis Acosta-Rivera, Dennis Earle, Ming Lei, Georgia Kollia, Niall C. Tebbutt; St. John of God Hospital, Murdoch, Notre Dame University, Fremantle and Edith Cowan University, Joondalup, WA, Australia; Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; Royal Melbourne Hospital, Victoria, Australia; City of Hope Comprehensive Cancer Center, Duarte, CA; Fundación de Investigación Oncology Trials, San Juan, PR; Bristol-Myers Squibb, Princeton, NJ; Austin Health, Heidelberg, VIC, Australia

Background: Blockade of the immune checkpoint receptor programmed death-1 (PD-1) has shown clinical benefit in multiple tumor types. Nivolumab (anti–PD-1) has demonstrated a survival advantage versus (vs) placebo in patients (pts) with advanced gastric cancer (GC) or gastroesophageal junction cancer (GEJC) (Kang YK et al. *Lancet* 2017;390:2461–71). Lymphocyte activation gene 3 (LAG-3) is an immune checkpoint molecule that negatively regulates effector T-cell function and is a marker of T-cell exhaustion. Preliminary data in melanoma suggest that combining nivolumab with relatlimab (anti–LAG-3) could improve efficacy without substantially increasing toxicity vs nivolumab especially, but not exclusively, in LAG-3-expressing pts (Ascierto PA et al. *Ann Oncol* 2017;28(S5):LBA18). Furthermore, LAG-3 expression was as high as 33% in an analysis of solid tumors including GC (Edwards R et al. *J Immunother Cancer* 2017;5(S3):P510). Study CA224-060 will assess the clinical efficacy and safety of relatlimab and nivolumab with chemotherapy for first-line treatment of GC or GEJC. **Methods:** This is a randomized, open-label, multicenter, phase 2 study of relatlimab and nivolumab with oxaliplatin-based chemotherapy vs nivolumab with oxaliplatin-based chemotherapy. Approximately 250 adult pts with untreated, locally advanced, unresectable or metastatic GC or GEJC will be enrolled. To be randomized, pts must have tumor tissue for analysis of biomarkers, LAG-3 status, and PD-L1 combined positive score. Key exclusion criteria include HER2-positive status, untreated CNS metastases, or significant cardiovascular disease. The primary endpoint is objective response rate (ORR) using RECIST v.1.1 by blinded independent central review in LAG-3-expressing pts. Other endpoints include investigator-assessed ORR, ORR in LAG-3-negative pts, duration of response, overall survival, progression-free survival, and safety and tolerability. Efficacy signals in biomarker subgroups will be explored. Currently, 26 sites are activated with 15 randomized pts. Clinical trial information: NCT03662659.

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TPS4144 **Poster Session (Board #247b), Mon, 8:00 AM-11:00 AM**

Modified FOLFOX versus modified FOLFOX plus nivolumab and ipilimumab in patients with previously untreated advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction: Moonlight, a randomized phase 2 trial of the German Gastric Group of the AIO.

Salah-Eddin Al-Batran, Claudia Pauligk, Thorsten Oliver Goetze, Jorge Riera-Knorrenschild, Eray Goekkurt, Stefan Angermeier, Frank Kullmann, Peter C. Thuss-Patience, Nils Homann, Thomas Jens Ettrich, Sabine Junge, Ralf Hofheinz, Sylvie Lorenzen; Institute of Clinical Research (IKF) at Krankenhaus Nordwest, UCT-University Cancer Center, Frankfurt, Germany; University Cancer Center Frankfurt, Institut für Klinisch-Onkologische Forschung and IKF Klinische Krebsforschung GmbH am Krankenhaus Nordwest, Frankfurt, Germany; Universitatsklinikum, Giessen Und Marburg, Germany; Hämatologisch-Onkologische Praxis Eppendorf (HOPE), Facharztzentrum Eppendorf, Hamburg, Germany; Klinikum Ludwigsburg, Medizinische Klinik I, Ludwigsburg, Germany; Department of Internal Medicine I, Academic Teaching Hospital Weiden, Weiden, Germany; Charité–University Medicine Berlin, Department of Haematology, Oncology and Tumorimmunology, Berlin, Germany; MED. Klinik II, Klinikum Wolfsburg, Wolfsburg, Germany; Ulm University Hospital, Ulm, Germany; IKF Klinische Krebsforschung GmbH at Krankenhaus Nordwest, Frankfurt, Germany; University Medical Center Mannheim, Tagestherapiezentrum am ITM, Mannheim, Germany; Third Department of Internal Medicine (Hematology/Medical Oncology), Klinikum rechts der Isar, Technische Universitat Munchen, Munich, Germany

Background: The majority of patients (pts) with gastroesophageal cancer present with inoperable or metastatic disease and there is a strong need for efficient and tolerable first-line (1L) treatment. Oxaliplatin-based regimens like FOLFOX have become one standard of care. However, median survival is still below 12 months. Results from trials using nivolumab plus ipilimumab treatment of subjects with advanced/metastatic GC and GEJ cancers demonstrated clinical activity, in pts whose tumors did or did not express PD-L1; in addition, nivolumab alone and in combination with ipilimumab demonstrated clinical benefits in various other tumor types. Based on this clinical experience, the AIO-STO-0417 trial (Moonlight) has been designed to evaluate the combination of chemotherapy with two checkpoint inhibitors in first-line therapy of pts with gastroesophageal adenocarcinoma. **Methods:** This is a prospective, multicenter, randomized, investigator-initiated phase II trial. Pts with Her2-negative, inoperable, advanced or metastatic gastric or esophagogastric junction cancer will be randomized 1:1 to 1L treatment with FOLFOX (Oxaliplatin 85 mg/m^2; Leucovorin 400 mg/m^2; 5FU 400 mg/m^2 on d1 of each treatment cycle and 5FU 1200 mg/m^2 continuous infusion over 24 hrs d1 and d2) every 2 weeks plus Nivolumab 240 mg every 2 weeks and Ipilimumab 1mg/kg every 6 weeks (Arm A) or FOLFOX alone (Arm B). Primary endpoint of the trial is progression-free survival based on the ITT population. Main secondary endpoints are overall survival, objective response rate, Safety and Quality of life (EORTC QLQ-C30). 118 pts (59 per arm) will be enrolled to provide 80% power for detecting an average HR of 0.68 using the log rank test at a one-sided type I error of 10%. At the date of submission, (Feb 2019), 28 of planned 118 pts are randomized. Clinical trial information: NCT03647969.

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TPS4145 **Poster Session (Board #248a), Mon, 8:00 AM-11:00 AM**

Phase II study of a telomerase-specific oncolytic adenovirus (OBP-301, Telomelysin) in combination with pembrolizumab in gastric and gastroesophageal junction adenocarcinoma.

Uqba Khan, Talia Biran, Allyson J. Ocean, Elizabeta C. Popa, Joseph T. Ruggiero, Doru Paul, Chelsea Garcia, David Carr-Locke, Reem Sharaiha, Yasuo Urata, Manish A. Shah; Weill Cornell Medical College, New York, NY; Oncolys Biopharma, Fort Lee, NJ; Weill Cornell Medicine, New York-Presbyterian Hospital, New York, NY; Oncolys BioPharma Inc., Tokyo, Japan

Background: Although checkpoint inhibitors (CPIs) can produce durable responses in gastric cancer patients (pts) in the 3rd line setting, the response rate is only 10-15%. Therefore, there is a huge unmet need to enhance the response rate of CPIs to provide benefit to wide range of pts. A novel concept in immuno-oncology is the use of cancer specific oncolytic viral therapy. In addition to the specific killing of the tumor by the virus, these agents can induce an immunogenic cell death in the tumor to augment the immune activation driven by PD-1 inhibition. OBP-301 is an oncolytic adenovirus genetically modified to be able to selectively replicate in cancer cells by introducing human telomerase reverse transcriptase (hTERT) promoter. Results of a phase I study of OBP-301 in solid tumor pts demonstrated the safety and efficacy of intra-tumoral injection of OBP-301. A pre-clinical study of the combination of OBP-301 with anti-PD-1 antibody has also shown significant synergistic activity as well. Based on these encouraging pre-clinical and clinical data, we designed a phase II clinical trial to examine the safety and efficacy of combination of pembrolizumab and OBP-301 in the treatment of PD-L1 positive metastatic gastric/GEJ adenocarcinoma. **Methods:** This is a multicenter, non-randomized phase II trial of OBP-301 with pembrolizumab in metastatic gastric/GEJ adenocarcinoma that has progressed on at least 2 lines of prior therapy. Eligibility criteria include PD-L1 positive tumors as defined by a combined positive score, performance status $\leq$1, and good end organ function. The primary endpoints are to examine objective response rate and safety of OBP-301 with pembrolizumab. The secondary endpoints are to examine disease control rate, duration of response, overall survival and progression free survival. Correlative studies are planned to identify biomarkers for response to combination therapy by using multiparameter flowcytometry, single-cell transcriptional profiling and immunohistochemistry. All eligible pts will receive $1x10^{12}$Viral Particles/mL of OBP-301 administered every 2 weeks for total of 4 injections, injected directly into tumor via upper endoscopy. Every pt will also receive pembrolizumab 200 mg IV every 3 weeks for 2 years or until progression. Pts will be enrolled in a Simon two stage design, with 18 pts in the first stage. If 3 or more pts respond to the combination therapy, the study will move forward to stage 2, with 19 more pts enrolled. The study is currently enrolling pts.

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TPS4146 **Poster Session (Board #248b), Mon, 8:00 AM-11:00 AM**

KEYNOTE-811 pembrolizumab plus trastuzumab and chemotherapy for HER2+ metastatic gastric or gastroesophageal junction cancer (mG/GEJC): A double-blind, randomized, placebo-controlled phase 3 study.

Yelena Yuriy Janjigian, Yung-Jue Bang, Charles S. Fuchs, Shukui Qin, Taroh Satoh, Kohei Shitara, Josep Tabernero, Eric Van Cutsem, Z. Alexander Cao, Xinqun Chen, S. Peter Kang, Chie-Schin Shih, Hyun Cheol Chung; Memorial Sloan Kettering Cancer Center, New York, NY; Seoul National University College of Medicine, Seoul, South Korea; Yale Cancer Center, New Haven, CT; Cancer Center of People's Liberation Army, Nanjing, China; Osaka University, Osaka, Japan; National Cancer Center Hospital, Kashiwa, Japan; Vall d'Hebron University Hospital and Institute of Oncology, Universitat Autonoma de Barcelona, Barcelona, Spain; University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium; Merck & Co., Inc., Kenilworth, NJ; Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea

Background: Combination therapy with the anti-HER2 antibody trastuzumab with fluoropyrimidine and platinum is the current standard for patients with HER2+ mG/GEJc. We hypothesize that combination anti–PD-1 and anti-HER2 therapy will result in T-cell activation, augment ADCC, and potentiate antitumor immune response in HER2+ patients. This phase 2 study in HER2+ mG/GEJc demonstrated the safety and preliminary efficacy of trastuzumab/pembrolizumab/chemotherapy; the overall response rate was 87%, and the disease control rate was 100% Janjigian YY, ASCO GI 2019). KEYNOTE 811, a global, multicenter, randomized, placebo-controlled, phase 3 study, is underway. **Methods:** Key eligibility criteria are age $\geq$18 years; previously untreated unresectable or metastatic HER2+ (centrally confirmed IHC 3+ or IHC 2+/ISH $>$2.0) G/GEJ adenocarcinoma; life expectancy $>$6 months with RECIST v1.1 measurable disease; adequate organ function and performance status. Patients will be randomly assigned 1:1 to receive chemotherapy with pembrolizumab 200 mg IV flat dose or placebo with trastuzumab 6 mg/kg (after 8 mg/kg load) Q3W up to 2 years or until intolerable toxicity or disease progression. Investigator choice chemotherapy will include day 1 cisplatin 80 mg/m^2 IV and /5-fluorouracil 800 mg/m^2/day IV (days 1-5) or oxaliplatin 130 mg/m^2 IV and capecitabine 1000 mg/m^2 BID days 1-14 (Q3W). Primary end points are progression-free survival and overall survival. Secondary end points are objective response rate, duration of response, and safety and tolerability. Adverse events are graded per NCI CTCAE v4.0 and will be monitored for 30 or 90 days after treatment. Patients will be followed up for survival. Planned enrollment is approximately 692 patients. Clinical trial information: NCT03615326.

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TPS4147 **Poster Session (Board #249a), Mon, 8:00 AM-11:00 AM**

A single-arm, open phase II clinical trial of anti-programmed death-1 antibody SHR-1210 combined with nimotuzumab as second-line treatment of advanced esophageal squamous cell carcinoma.

Feng Wang, Xiangrui Meng, Qingxia Fan; Department of Oncology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; Department of Oncology, The First AffIliated Hospital of Zhengzhou University, Zhengzhou, China

Background: Approximately 40% of patients (pts) with esophageal cancer are diagnosed with advanced unresectable or metastatic disease; the 5-year survival rate for advanced disease is 5%. No standard therapy is available in China for Advanced Esophageal Squamous Cell Carcinoma(ESCC) patients progressed after first-line chemotherapy.Inhibition of programmed cell death protein-1 (PD-1) has demonstrated promising antitumor activity and manageable safety in pts with advanced unresectable or metastatic ESCC. SHR-1210, a humanized IgG4 monoclonal antibody, has high affinity and specificity for PD-1 molecule. SHR-1210 was generally well tolerated and had preliminary antitumor effects in pts with solid tumors, including ESCC. Nimotuzumab, a humanized anti-epidermal growth factor receptor monoclonal antibody h-R3, has been shown to be effective and safe in the treatment of head and neck cancer,non-small cell lung cancer (NSCLC) and esophageal Cancer in several phase II studies.The purpose of this study is to observe and evaluate the efficacy and safety of anti-PD-1 antibody SHR-1210 combined with nimotuzumab as second-line therapy in patients with advanced ESCC. **Methods:** Patients, age 18-75, with measurable tumor lesion, failed in or progression after 1st line chemotherapy, were enrolled in this study.Patients received SHR-1210 200 mg once every 2 weeks (Q2W) combined nimotuzumab 200 mg weekly until disease progression, death or unacceptable toxicity.Assessments included response by RECIST v1.1 every 6 wks and safety (physical examination, vital signs, ECOG PS, laboratory tests).The primary endpoint is the objective response rate (ORR),and the secondary end points include the diseases control rate (DCR),duration of response (DOR),progression-free survival (PFS),and overall survival(OS). Additionally, we try to identify biomarker to predict efficacy of SHR-1210 and Nimotuzumab with target capture sequencing and gene expression profile as exploratory endpoints. Clinical trial information: NCT03766178.

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TPS4148 **Poster Session (Board #249b), Mon, 8:00 AM-11:00 AM**

RAP: A phase II trial with ramucirumab, avelumab, and paclitaxel as second line treatment in gastro-esophageal adenocarcinoma of the arbeitsgemeinschaft internistische onkologie (AIO).

Anica Högner, Kirstin Breithaupt, Alexander Stein, Axel Hinke, Mario Lorenz, Salah-Eddin Al-Batran, Peter C. Thuss-Patience; Charité–University Medicine Berlin, Department of Haematology, Oncology and Tumorimmunology, Berlin, Germany; University Medical Center Hamburg-Eppendorf, Department of Oncology, Haematology, Stem Cell transplantation and Pneumology, Hamburg, Germany; CCRC, Düsseldorf, Germany; Institute of Clinical Research (IKF) at Krankenhaus Nordwest, UCT-University Cancer Center, Frankfurt, Germany

Background: Combination of ramucirumab and paclitaxel resembles the standard treatment option in second line therapy with improvement of response rate and overall survival (REGARD, RAINBOW). Response rates to PD-1/L1 blockade in gastro-esophageal cancer patients rank within 10–20%, whereby PD-1/L1 blockade is reported to impressively extend survival rates in responders. Trials investigating either the synergistic effect of anti-angiogenesis and anti-PD-L1 or chemotherapy combined with anti-PD-L1 are promising. Based on these data we hypothesize benefit from combining immunotherapy by checkpoint inhibition with VEGF-directed treatment and chemotherapy induced increase of immunogenicity of tumor cells. This study investigates the incorporation of PD-L1 blockade by avelumab in the second line setting by combination with the actual best second-line chemotherapy regimen in metastatic gastric cancer patients (paclitaxel+ramucirumab). **Methods:** The RAP trial (AIO-STO-0218, registered at ClinicalTrials.gov) is a single arm multicenter phase II trial. A total of 59 patients with metastatic or locally advanced gastric or gastro-esophageal junction adenocarcinoma, ECOG 0–1, who progressed after having received first-line therapy with platinum and fluoropyrimidine doublet with or without anthracycline, docetaxel or trastuzumab within the last six months will receive avelumab and ramucirumab on day 1, 15 and paclitaxel on day 1, 8 and 15 of a 28-day cycle until disease progression (RECIST v1.1), intolerable toxicity, withdrawal of consent or at a maximum treatment of 1 year. The primary endpoint is the overall survival rate (OSR) at 6 months. Sample size calculation is based on a Simon 2-stage design with a one-sided alpha error of 10% and a power of 80%, an expected OSR at 6 months of $\geq$ 65% and a 0 hypothesis $\leq$ 50%. Secondary endpoints include OS, OSR at 12 months, PFS, safety and tolerability, duration of response. Ethics commission approved the study protocol in January 2019. Updated patient accrual will be presented. Clinical trial information: AIO-STO-0218.

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TPS4149 **Poster Session (Board #250a), Mon, 8:00 AM-11:00 AM**

A phase II study of TAS-102 in combination with ramucirumab in advanced, refractory gastric or gastroesophageal junction (GEJ) adenocarcinoma.

Rutika Mehta, Richard D. Kim, Neal Shah, Estrella M. Carballido, Youngchul Kim, Iman Imanirad, Dae Won Kim; Roswell Park Cancer Institute, Buffalo, NY; H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; H. Lee Moffitt Cancer Center, Tampa, FL; Mayo Clinic, Scottsdale, AZ; H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; Tallahassee Memor Hosp, Tallahassee, FL; The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Patients with advanced gastric cancer experience a 5 year survival rate $<10\%$ even with multimodality therapy representing a clear unmet need for improved treatment. In advanced gastric and gastroesophageal junction (GEJ) adenocarcinoma, ramucirumab (a monoclonal antibody against VEGFR2) has demonstrated clinical activity and has been approved as second line therapy in combination with paclitaxel with a response rate of 28% and absolute overall survival benefit of 8 weeks when compared to placebo. However, there are many patients that cannot tolerate paclitaxel due to prior exposure to oxaliplatin causing neuropathy. Therefore, novel combinations with ramucirumab, is highly desirable. TAS-102 is an oral cytotoxic agent with two active components; trifluridine (TFD) which inhibits tumor cell growth by being incorporated into DNA during DNA synthesis and tipiracil (TPI) which inhibits the metabolism of TFD, thereby prolonging its ability to exert effect. TPI also inhibits platelet derived endothelial cell growth factor which plays a key role with VEGF in tumor angiogenesis. The combination of a cytotoxic agent with an antiangiogenic agent has demonstrated a significant anticancer activity in multiple cancers. In a recent Phase III study, TAS-102 significantly prolonged overall survival as compared to best supportive care in patients with GEJ and gastric cancers that had received at least 2 prior lines of treatment. We hypothesize that a combination of TAS-102 and ramucirumab might increase efficacy without causing unmanageable toxicity. **Methods:** This is a single institutional phase II single arm two-stage design trial using the combination of TAS-102 and ramucirumab in advanced, refractory gastric or GEJ adenocarcinoma. Eligible patients include those with histologically confirmed gastric or GEJ adenocarcinoma that have received at least 1 prior line of treatment with performance status 0 or 1 and preserved organ function. Ramucirumab will be administered 8mg/kg every 2 weeks and TAS-102 at doses of 35 mg/m^2 twice daily. Each cycle length will be 28 days. The primary endpoint is 6 month OS and secondary endpoints are safety, objective response rate and PFS. Fifteen patients will be enrolled in the first stage. If ≥ 7 of the 15 are alive at 6 months, an additional 10 patients will be enrolled in the second phase. Enrollment is currently ongoing. Clinical trial information: NCT03686488.

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TPS4150 **Poster Session (Board #250b), Mon, 8:00 AM-11:00 AM**

Ramucirumab and irinotecan in patients with previously treated gastroesophageal adenocarcinoma.

Haeseong Park, Nikolaos Trikalinos, Aravind Sanjeevaiah, Katrina Pedersen, Nusayba Ali Bagegni, Andrew B. Nixon, Jesse Huffman, Benjamin R. Tan, Rama Suresh, Kian-Huat Lim, Manik A. Amin, Andrea Wang-Gillam, A. Craig Lockhart; Washington University School of Medicine, St. Louis, MO; The University of Texas Southwestern Medical Center, Dallas, TX; Duke University Medical Center, Durham, NC; University of Miami Sylvester Comprehensive Cancer Center, Miami, FL

Background: Ramucirumab is used for treatment of metastatic gastroesophageal adenocarcinoma after disease progression on first-line chemotherapy. Superior survival outcome is expected when combined with paclitaxel. However, many patients suffer from neuropathy after oxaliplatin-containing first-line chemotherapy and are unable to tolerate paclitaxel. Irinotecan has shown survival benefit as a single agent or in combination with other agents, but has not been used in combination with ramucirumab for treatment with gastroesophageal cancer. We hypothesize that this combination regimen of irinotecan plus ramucirumab administered as second-line treatment will be well-tolerated with improved outcomes similar to paclitaxel plus ramucirumab in patients with advanced gastroesophageal cancer. Circulating levels of angiogenic factors are correlatives of particular interest in this study. **Methods:** This is a multi-institutional, single-arm phase II clinical trial of ramucirumab and irinotecan. Primary objective of the study is to determine the progression-free survival in patients treated with this combination after disease progression on first-line chemotherapy. Secondary objectives are to determine other indices of efficacy including overall survival, time to progression, objective response rate, and clinical benefit rate; and to evaluate toxicity and tolerability. Patients with confirmed diagnosis of gastroesophageal adenocarcinoma with measurable disease are included. Patients are required of have disease progression during or within 4 months of first line chemotherapy. Key exclusion criteria include squamous histology; prior irinotecan or ramucirumab use; active brain metastases; or other contraindications to ramucirumab including recent history of gastrointestinal bleeding or perforation, thromboembolic event, and uncontrolled hypertension. Patients receive ramucirumab 8mg/kg with irinotecan 180mg/m^2 IV every 14 days. We plan to enroll 40 patients which will provide 85% power at a 0.05 significance level to detect a median progression free survival time of 4 months compared to historic control of 2.5 months. 25% of patient accrual is complete as of February 2019. Clinical trial information: NCT03141034.

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TPS4151 **Poster Session (Board #251a), Mon, 8:00 AM-11:00 AM**

Assessment of ramucirumab plus paclitaxel as switch maintenance versus continuation of first-line chemotherapy in patients (pts) with advanced HER2-negative gastric or gastroesophageal junction cancers: The ARMANI phase III trial.

Federica Morano, Monica Niger, Salvatore Corallo, Sara Lonardi, Stefano Tamberi, Samantha Di Donato, Elisa Giommoni, Francesco Giuliani, Giovanni Luca Frassineti, Gianluca Tomasello, Ferdinando De Vita, Giovanni Gerardo Cardellino, Graziella Pinotti, Maria Pia Brizzi, Lorenza Rimassa, Mario Scartozzi, Rossana Berardi, Filippo G. De Braud, Filippo Pietrantonio, Maria Di Bartolomeo; Medical Oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Istituto Oncologico Veneto-IRCCS, Padova, Italy; Degli Infermi Hospital, Oncology Unit, Faenza, Italy; Medical Oncology Department Nuovo Ospedale-Santo Stefano Instituto Toscano Tumori, Prato, Italy; Azienda Ospedaliero Universitaria Careggi, Firenze, Italy; NCI, Bari, Italy; Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Medical Oncology Unit, Meldola (FO), Italy; ASST di Cremona – Ospedale di Cremona, Cremona, Italy; Medical Oncology, Second University of Naples, Naples, Italy; University Hospital, Udine, Italy; Department of Oncology, ASST Sette Laghi, Varese, Italy; AOU San Luigi Gonzaga, Orbassano, Italy; Medical Oncology and Hematology Unit, Humanitas Cancer Center, Humanitas Clinical and Research Center, IRCCS, Rozzano, Italy; Medical Oncology Department, University Hospital, University of Cagliari, Cagliari, Italy; University Hospital and Polytechnic University Ancona, Marche, Italy; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; Medical Oncology Department, Fondazione IRCSS - Istituto Nazionale dei Tumori, Milan, Italy; Fondazione IRCCS-Istituto Nazionale dei Tumori, Milan, Italy

Background: Platinum/fluoropyrimidine regimens are the backbone of first-line therapy for advanced gastric cancer (AGC). The optimal duration of first-line therapy is still unknown and its continuation until disease progression represents the standard. However this strategy is often associated with cumulative toxicity and rapid development of drug resistance. Moreover, only 40% of AGC pts are eligible for second-line treatment. This study aims at assessing whether switch maintenance to ramucirumab plus paclitaxel will extend the progression-free survival (PFS) of subjects with HER-2 negative AGC who have not progressed after a first-line with a platinum/fluoropyrimidine regimen. The hypothesis is that the early administration of an active, non-cross resistant regimen may delay disease progression and, consequently, improve pts' quality of life. This strategy may also rescue all those subjects that become ineligible for a second-line therapy due to the rapid clinical deterioration. **Methods:** This is a randomized, open-label, multicenter, phase III trial. Eligibility criteria are: unresectable/metastatic HER-2 negative AGC or gastroesophageal junction (GEJ) cancer; ECOG PS 0-1; measurable and/or evaluable disease by RECIST v1.1; no progression after 3 months of therapy with either FOLFOX4, mFOLFOX6 or XELOX . The primary endpoint is to compare PFS of pts in ARM A (continuation of the same first-line therapy with oxaliplatin/fluoropyrimidine) versus ARM B (switch maintenance to ramucirumab and placlitaxel). Secondary endpoints are: overall survival, time-to-treatment failure, overall response rate, duration of response, percentage of pts receiving a second-line therapy per treatment arm, safety and quality of life. Exploratory analyses to identify primary resistance and prognosis biomarkers are planned, including Next-Generation Sequencing (NGS) on archival tumor tissues. The ARMANI study is sponsored by the Fondazione IRCCS Istituto Nazionale dei Tumori and it is ongoing at 29 Italian centers with a planned population of 280 pts. Clinical trial information: NCT02934464.

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TPS4152 **Poster Session (Board #251b), Mon, 8:00 AM-11:00 AM**

Lenvatinib (len) plus pembrolizumab (pembro) for the first-line treatment of patients (pts) with advanced hepatocellular carcinoma (HCC): Phase 3 LEAP-002 study.

Josep M Llovet, Masatoshi Kudo, Ann-Lii Cheng, Richard S. Finn, Peter R. Galle, Shuichi Kaneko, Tim Meyer, Shukui Qin, Corina E. Dutcus, Erluo Chen, Leonid Dubrovsky, Andrew X. Zhu; Icahn School of Medicine at Mount Sinai, New York, NY; Kindai University School of Medicine, Osakasayama, Japan; National Taiwan University Hospital Cancer Center, Taipei, Taiwan; David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA; University of Mainz Medical Center, Mainz, Germany; Kanazawa University Hospital, Kanazawa, Japan; University College London Cancer Institute, London, United Kingdom; People's Liberation Army 81 Hospital, Nanjing, China; Eisai Inc., Woodcliff Lake, NJ; Merck & Co., Inc., Kenilworth, NJ; Massachusetts General Hospital, Boston, MA

Background: Len, an inhibitor of VEGF receptors 1-3, FGF receptors 1-4, PDGF receptor α, RET, and KIT, is approved for first-line treatment of unresectable HCC (uHCC) based on the open-label phase 3 REFLECT study in which len showed noninferior overall survival (OS) and significantly improved objective response rate (ORR), progression-free survival (PFS), and time-to-progression (TTP) vs sorafenib. In the phase 2 KEYNOTE-224 study of pembro (a PD-1 inhibitor) as second-line treatment of advanced HCC, pembro showed meaningful clinical efficacy in pts previously treated with sorafenib, with median PFS 4.9 mo, median OS 12.9 mo, and a manageable safety profile. In results from the phase 1b KEYNOTE-524 trial, len+pembro was well-tolerated, with promising antitumor activity in pts with uHCC. LEAP-002 is a phase 3 study to evaluate the safety and efficacy of len+pembro vs len+placebo as first-line therapy for advanced HCC. **Methods:** Eligible pts are $\geq$18 y and have HCC confirmed by radiology, histology, or cytology; ECOG PS 0/1; BCLC stage C or stage B disease not amenable to locoregional therapy or curative treatment approach; CP class A liver score within 7 days before study; and $\geq$1 measurable lesion by RECIST v1.1. Pts with past or ongoing HCV infection and those with controlled HBV are eligible. 750 pts will be randomized 1:1 to receive len 12 mg (body weight [BW] $\geq$60 kg) or 8 mg (BW $<$60 kg) orally once daily plus pembro 200 mg or placebo IV Q3W. Pembro and len will be administered until disease progression or unacceptable toxicity, with a maximum 35 cycles for pembro. Stratification will be by geographic region (Asia vs Japan and Western regions); macroscopic portal vein invasion or extrahepatic spread or both (yes or no); alpha fetoprotein $\leq$400 ng/mL vs $>$400 ng/mL; and ECOG PS 0/1. Primary end points are PFS per RECIST v1.1 by blinded independent central review (BICR) and OS. Secondary end points are ORR, duration of response, disease control rate, and TTP per RECIST v1.1 by BICR, efficacy per modified RECIST, pharmacokinetics, and safety. Imaging assessments will be performed Q9W on study. AEs will be graded per CTCAE v4.0 and monitored up to 90 days after last dose. Clinical trial information: NCT03713593.

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TPS4153 **Poster Session (Board #252a), Mon, 8:00 AM-11:00 AM**

A multicenter phase II trial of rucaparib in combination with nivolumab as maintenance therapy for patients with advanced biliary tract cancer.

Vaibhav Sahai, Nguyen H. Tran, Kent A. Griffith, Mark Zalupski; University of Michigan, Ann Arbor, MI

Background: Patients (pts) with advanced biliary tract cancers (BTC) have a poor prognosis with a median overall survival (OS) less than 12 months. Using whole exome NGS, 26 (49%) pts in a 53 pt cohort had either DNA damage repair (DDR) pathway mutations (somatic and/or germline, n = 18), or isocitrate dehydrogenase 1 (IDH1) mutations (n = 8), and may have potentially benefited from PARP inhibition. Further, disruption of the mutated DDR pathways with a PARP inhibitor may result in increased mutational burden and neoantigens leading to immunogenicity, thus providing the rationale for combination with a PD-1 antibody. This phase 2 trial is designed to investigate the role of a PARP inhibitor in combination with a PD-1 antibody in pts with advanced BTC. **Methods:** Key eligibility criteria include histologically confirmed advanced, unresectable biliary adenocarcinoma (intra- or extra-hepatic, and gallbladder) without progression after 4-6 months of 1st line platinum-based systemic chemotherapy, measurable disease per RECIST v1.1, ECOG PS 0-1, Child-Pugh A or B7, and absence of autoimmune disease or chronic steroid use. Primary objective is to evaluate progression-free survival (PFS) rate at 4 months. Secondary objectives include evaluation of objective response rate per immune related (ir) RECIST criteria, median PFS and OS, and safety in this patient population. Exploratory objectives include identification of predictive biomarkers of response and mechanisms of resistance through serial biopsies and blood collection (pre, on and post therapy), including sequential whole exome/transcriptomic analysis with immune cell subset analysis. Treatment includes rucaparib 600 mg PO BID on days 1-28 with nivolumab 240 mg on days 1, 15 Q4 weeks. In absence of disease progression, pts may continue therapy up to 2 years. Accrual goal is 32 evaluable pts. Using a null hypothesis value of a 63% PFS rate at 4 months, and an 85% alternative hypothesis, this ongoing study has 80% power, with a one-sided alpha of 0.05 to identify treatment efficacy in the study arm. Clinical trial information: NCT03639935.

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TPS4154 **Poster Session (Board #252b), Mon, 8:00 AM-11:00 AM**

A multi-center phase Ib/II study of nal-irinotecan, 5-fluouracil and leucovorin in combination with nivolumab as second-line therapy for patients with advanced unresectable biliary tract cancer.

Vaibhav Sahai, Tyler Howard Buckley, Kent A. Griffith, Mark Zalupski; University of Michigan, Ann Arbor, MI

Background: Patients (pts) with advanced biliary tract cancers (BTC) have poor prognosis despite systemic chemotherapy, and treatment beyond first-line platinum doublet remains investigational. The immunomodulatory properties of conventional cytotoxic therapy, particularly in regard to the upregulation of PD-L1 expression rendering tumor cells more sensitive to T cell-mediated lysis and neoantigen production, rapid emergence of chemotherapy resistance, and known modest efficacy of single agent PD-1 antibody in BTC provide a rationale for combining chemotherapy and immunotherapy. This multi-center, phase Ib/II, single-arm study is designed to investigate the role of nal-irinotecan, 5-FU and leucovorin in combination with nivolumab as second-line therapy in pts with advanced BTC. **Methods:** Key eligibility criteria include histologically confirmed advanced, unresectable biliary carcinoma (intra- or extra-hepatic and gallbladder) with progression or intolerance of first-line systemic therapy (excluding irinotecan and PD-1/PD-L1 antibody), measurable disease per RECIST v1.1, ECOG PS 0-1, Child Pugh A or B7, and absence of autoimmune disease or chronic steroid use. Primary objective of the phase Ib portion is to determine the recommended phase 2 dose, and of the phase II portion is to evaluate the median progression-free survival. Secondary objectives include evaluation of objective response rate per immune related (ir)RECIST, median OS and safety in this patient population. Exploratory objectives include identification of biomarker predictors of response and mechanisms of resistance through serial biopsies and blood collection (pre, on and post therapy), including sequential whole exome/transcriptomic analysis and immune cell subset analysis (tissue and blood). Therapy includes nal-irinotecan 70 mg/m^2, leucovorin 200 (dose level -1) or 400 mg/m^2 (dose level 0), 5-fluouracil 2400 mg/m^2 IV over 46 hours, and nivolumab 240 mg on day 1 every 2 weeks for 6 months. In the absence of disease progression, pts may continue therapy for up to 2 years. Accrual goal is 30 evaluable pts. Using a null hypothesis value of median PFS of 2.9 months, and an alternative hypothesis of 5.0 months, this ongoing study has $>$ 80% power, with a two-sided alpha of 0.05 to identify treatment efficacy of study arm. Clinical trial information: NCT03785873.

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TPS4155 **Poster Session (Board #253a), Mon, 8:00 AM-11:00 AM**

Infigratinib versus gemcitabine plus cisplatin multicenter, open-label, randomized, phase 3 study in patients with advanced cholangiocarcinoma with FGFR2 gene fusions/translocations: The PROOF trial.

Milind M. Javle, Ivan Borbath, Stephen John Clarke, Erika Hitre, Christophe Louvet, Teresa Macarulla Mercade, Do-Youn Oh, Jennifer L. Spratlin, Juan W. Valle, Karl Heinz Weiss, Craig Berman, Michael Howland, Yining Ye, Terry Cho, Susan Moran, Ghassan K. Abou-Alfa; MD Anderson Cancer Center, Houston, TX; Cliniques Universitaires St Luc Bruxelles, Bruxelles, Belgium; University of Sydney, Sydney, Australia; National Institute of Oncology, Budapest, Hungary; Institut Mutualiste Montsouris, Paris, France; Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; Seoul National University Hospital, Seoul, South Korea; Alberta Health Services, Edmonton, AB, Canada; University of Manchester/The Christie, Manchester, United Kingdom; University Hospital Heidelberg, Heidelberg, Germany; QED Therapeutics Inc, San Francisco, CA; Memorial Sloan Kettering Cancer Center, New York, NY

Background: Cholangiocarcinoma is the most common biliary tract malignancy with approximately 5,000–10,000 new cases annually in the USA. The fibroblast growth factor receptor (FGFR) family plays an important role in cholangiocarcinoma, with *FGFR2* gene fusions detected in about 15% of patients with cholangiocarcinoma. Infigratinib is an ATP-competitive, FGFR1–3-selective oral tyrosine kinase inhibitor. First-line treatment with chemotherapy offers only modest benefit and more effective treatment options are needed. Based on preliminary response data of infigratinib in relapsed/refractory cholangiocarcinoma with *FGFR2* fusions/translocations (Phase 2 Study CBJG398X2204), the PROOF trial is evaluating infigratinib versus gemcitabine + cisplatin in front-line patients with advanced cholangiocarcinoma with *FGFR2* gene fusions/translocations. **Methods:** Patients with advanced/metastatic or inoperable cholangiocarcinoma are randomized 1:1 to oral infigratinib once daily for 21 days of a 28-day treatment cycle versus IV gemcitabine (1000 mg/m^2) + cisplatin (25 mg/m^2) on days 1 and 8 of a 21-day cycle. Treatment will continue until confirmed progressive disease by central review, intolerance, withdrawal of informed consent, or death. After 8 cycles of gemcitabine + cisplatin, patients can continue treatment if the investigator considers that they are deriving continued benefit. Patients on the gemcitabine + cisplatin arm who progress can cross-over to infigratinib. The primary endpoint is progression-free survival (PFS, per RECIST v1.1 central review). Secondary endpoints include overall survival, PFS (investigator determined), overall response rate, disease control rate, duration of response, and safety. Quality of life, PK and exploratory genetic alterations/biomarkers will also be measured. Current status: The study was initiated in February 2019 with planned enrollment of 350 patients with confirmed *FGFR2* gene fusions/translocations. Clinical trial information: NCT03773302.

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TPS4156 **Poster Session (Board #253b), Mon, 8:00 AM-11:00 AM**

NUC-1031 in combination with cisplatin for first-line treatment of advanced biliary tract cancer.

Jennifer J. Knox, Mairead Geraldine McNamara, Daniel H. Palmer, T.R. Jeffry Evans, David Goldstein, John A. Bridgewater, Juan W. Valle; Princess Margaret Cancer Centre, Toronto, ON, Canada; University of Liverpool, Liverpool, United Kingdom; University of Glasgow, Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom; Prince of Wales Hospital, University of New South Wales, Cancer Survivors Centre, Randwick, Australia; University College London Cancer Institute, London, United Kingdom; University of Manchester/The Christie, Manchester, United Kingdom

Background: Cisplatin and gemcitabine (CisGem) is the global standard of care for 1st-line treatment of patients (pts) with advanced biliary tract cancer (BTC). No agents have regulatory approval for this disease. CisGem achieves an objective response rate (ORR) of 26% and median overall survival (OS) of 11.7 months (ABC-02). Key cancer resistance mechanisms limit gemcitabine efficacy. NUC-1031, a phosphoramidate transformation of gemcitabine, is designed to overcome resistance mechanisms associated with poor gemcitabine response. Promising signs of efficacy have been observed with single agent in a phase I study in solid tumors (Blagden et al 2018) and in the phase Ib ABC-08 study of NUC-1031 + cisplatin 25 mg /m^2 d1, d8 q 21 days for the 1st-line treatment of advanced BTC. 14 pts have been enrolled across 2 cohorts (NUC-1031: 625 mg/m^2 and 725 mg/m^2). In 11 pts evaluable for response ORR was 64% (1 CR, 6 PRs) and DCR was 73%. PFS/OS data is maturing. The combination was very well-tolerated with no unexpected adverse events or dose-limiting toxicities. The RP2D in combination with cisplatin is 725 mg/ m^2. Safety, coupled with encouraging efficacy signal has led to initiation of a global Phase III development program. **Methods:** A Phase III, open-label, randomized head-to-head study of NUC-1031 + cisplatin versus CisGem for the 1st-line treatment of advanced BTC will include pts ≥18 years with histologically- or cytologically-proven BTC (including cholangiocarcinoma, gallbladder, or ampullary cancer), that is not resectable and who have had no prior systemic chemotherapy for locally advanced/metastatic disease. A total of 828 pts will be randomized (1:1) to either 725 mg/m^2 NUC-1031 + 25 mg/m^2 cisplatin or 1000 mg/m^2 gemcitabine + 25 mg/m^2 cisplatin, administered on Days 1 and 8 of a 21-day cycle, respectively. Primary objectives are OS and ORR. Secondary objectives include further measurements of efficacy, safety, pharmacokinetics, and patient-reported quality of life. The study will be conducted at approximately 120 sites across North America, Europe and Asia Pacific countries. Clinical trial information: NCT02351765.

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TPS4157 **Poster Session (Board #254a), Mon, 8:00 AM-11:00 AM**

Phase 3 (COSMIC-312) study of cabozantinib (C) in combination with atezolizumab (A) versus sorafenib (S) in patients (pts) with advanced hepatocellular carcinoma (aHCC) who have not received previous systemic anticancer therapy.

Robin Kate Kelley, Ann-Lii Cheng, Fadi S. Braiteh, Joong-Won Park, Fawzi Benzaghou, Steven Milwee, Anne Borgman, Anthony B. El-Khoueiry, Zeid K Kayali, Andrew X. Zhu, Lorenza Rimassa; UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA; National Taiwan University College of Medicine, Taipei, Taiwan; Medical Oncology, Comprehensive Cancer Centers of Nevada, Las Vegas, NV; National Cancer Center Korea, Goyang-Si, South Korea; IPSEN, Paris, France; Exelixis, Inc., South San Francisco, CA; Exelixis, Alameda, CA; Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA; Riverside Community Hospital, Rialto, CA; Massachusetts General Hospital Cancer Center, Harvard Medical Center, Boston, MA; Medical Oncology and Hematology Unit, Humanitas Cancer Center, Humanitas Clinical and Research Center, IRCCS, Rozzano, Italy

Background: C inhibits tyrosine kinases involved in tumor growth, angiogenesis, and immune regulation, including MET, VEGFR, and TAM kinases (Tyro3, AXL, MER). C is approved for treatment of aHCC after prior S based on improved overall survival (OS) vs placebo in the phase 3 CELESTIAL trial (Abou-Alfa NEJM 2018). Standard of care for first-line treatment of aHCC is tyrosine kinase inhibition with S or lenvatinib, and phase 3 trials of immune checkpoint inhibitors (ICIs) in first- and second- line aHCC are ongoing. C may promote an immune-permissive tumor environment, which could enhance response to ICIs. C is being evaluated in combination with the anti-PD-L1 antibody A in multiple tumor types including HCC in a phase 1 study; and dose, preliminary clinical activity, and safety have been established in aRCC (Agarwal Ann Oncol 2018). A in combination with bevacizumab, an anti-VEGF antibody, has shown preliminary clinical activity in first-line aHCC (Pishvaian Ann Oncol 2018). Here, we present the study design of a phase 3 trial of C+A vs S in pts with aHCC who have not received prior systemic therapy. **Methods:** This international, randomized, open-label phase 3 trial (NCT03755791) is evaluating the efficacy and safety of C+A vs S as first-line treatment for aHCC. Eligibility criteria include age $\geq$18 years, BCLC stage B or C, Child-Pugh A, ECOG PS 0 or 1, and measurable disease per RECIST 1.1. Patients are randomized 6:3:1 to an experimental arm of C (40 mg qd) + A (1200 mg infusion q3w), a control arm of S (400 mg bid), and an exploratory arm of C monotherapy (60 mg qd). 640 pts are planned at ~200 sites globally. Randomization is stratified by disease etiology (HBV [with or without HCV], HCV [without HBV], or other), region (Asia, other), and the presence of extrahepatic disease and/or macrovascular invasion (yes, no). OS and progression-free survival are coprimary endpoints and objective response rate is a secondary endpoint. Additional endpoints include safety, pharmacokinetics, and correlation of biomarker analyses with clinical outcomes. Enrollment in COSMIC-312 is ongoing. Clinical trial information: NCT03755791.

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TPS4158 **Poster Session (Board #254b), Mon, 8:00 AM-11:00 AM**

NET-02: A multi-center, randomised, phase II trial of liposomal irinotecan (nal-IRI) and 5-fluorouracil (5-FU)/folinic acid or docetaxel as second-line therapy in patients (pts) with progressive poorly differentiated extra-pulmonary neuroendocrine carcinoma (PD-EP-NEC).

Mairead Geraldine McNamara, Jayne Swain, Zoe Craig, Jonathan Wadsley, Nicholas Reed, Olusola Olusesan Faluyi, Angela Lamarca, Richard Hubner, Wasat Mansoor, Debashis Sarker, Helen C Howard, David A. Cairns, Tim Meyer, Juan W. Valle; Institute of Cancer Sciences, University of Manchester, Medical Oncology Department, The Christie NHS Foundation Trust, Manchester, United Kingdom; University of Leeds, Leeds, United Kingdom; Weston Park Hospital, Sheffield, United Kingdom; Beatson Oncology Centre, Glasgow, United Kingdom; Clatterbridge Cancer Centre, Bebington, Wirral, United Kingdom; Department of Medical Oncology, The Christie NHS Foundation Trust / Institute of Cancer Sciences, University of Manchester, Manchester, United Kingdom; Christie NHS Foundation Trust, Manchester, United Kingdom; Christie NHS, Manchester, United Kingdom; King's College Hospital, Institute of Liver Studies, London, United Kingdom; Clinical Trials Research Unit, University of Leeds, Leeds, United Kingdom; Clinical Trials Research Unit, Leeds Institute of Clinical Trials Research, University of Leeds, Leeds, United Kingdom; University College London Cancer Institute, London, United Kingdom; Institute of Cancer Studies, University of Manchester, The Christie Hospital, Manchester, United Kingdom

Background: The prognosis for pts with PD-EP-NEC is poor. First-line treatment for advanced disease is etoposide/platinum-based chemotherapy, analogous to that of high grade lung NEC, with no standard second-line treatment, and is an area of unmet need. **Methods:** This is a multi-centre, randomised, phase II trial of nal-IRI; 80mg/m^2 intravenously (IV) over 90 mins, prior to 5-FU; 2400 mg/m^2 infusion over 46 hrs and folinic acid, Q14 days, or docetaxel; 75mg/m^2 IV over 60 mins, Q21 days, as second-line therapy in pts with progressive PD-EP-NEC (Ki-67 $>$ 20%), with the overall aim of selecting a treatment for continuation to a phase III trial. The standard arm is that used in high-grade lung NEC, of which docetaxel is a second-line therapy option (NCCN guidelines) and combination regimens such as Irinotecan/5-FU are a second-line therapy option currently used without trial evidence for this subset of pts. Pts must have had prior treatment with first-line platinum-based chemotherapy, have documented disease progression and have an ECOG performance status of $\leq$2. This study plans to recruit 102 pts from 16 UK centres (over 37 mths). Primary endpoint is 6-mth progression-free survival (PFS) rate; trial is designed to have an 80% chance of demonstrating that the one-sided 95% confidence interval of the 6 mth PFS rate excludes 15%, if the true rate is at least 30%, where 30% is the required level of efficacy, and a rate of $<$ 15% would give grounds for rejection. If both treatment arms exceed the required level of efficacy to warrant further evaluation in a phase III trial, treatment with the higher PFS rate at 6 mths will be selected. Secondary endpoints include overall survival, objective response rate, toxicity, quality of life, serum neuron-specific enolase. Exploratory endpoints include quantification of circulating tumour cells (CTCs), circulating tumour deoxyribonucleic acid (ctDNA) and molecular profiling of CTCs, ctDNA and tumour tissue, and generation of CTC-derived xenografts. This trial is open and has enrolled 6 pts at time of submission. Clinical trial information: 10996604.

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TPS4159 **Poster Session (Board #255a), Mon, 8:00 AM-11:00 AM**

Phase 2 trial of Lu-177-DOTATATE in inoperable pheochromocytoma/paraganglioma.

Frank Lin, Jaydira Del Rivero, Jorge A. Carrasquillo, Abhishek Jha, Melissa K Gonzales, Liza Lindenberg, Baris Turkbey, Emily Lin, Esther Mena, Corina Millo, Clara Chen, Peter Herscovitch, Peter L. Choyke, Karel Pacak; National Institutes of Health, National Cancer Institute, Bethesda, MD; National Cancer Institute, Bethesda, MD; Memorial Sloan-Kettering Cancer Center, New York, NY; National Institutes of Health, Bethesda, MD; Molecular Imaging Program, National Cancer Institute at the National Institutes of Health, Bethesda, MD; Molecular Imaging Program, Center for Cancer Research, National Cancer Institute at the National Institutes of Health, Bethesda, MD; PET Department at National Institutes of Health, Bethesda, MD; Department of Nuclear Medicine, Clinical Center, National Institutes of Health, Bethesda, MD; PET Department, Clinical Center, National Institutes of Health, Bethesda, MD; National Cancer Institute at the National Institutes of Health, Bethesda, MD; Section on Medical Neuroendocrinology, Eunice Kennedy Shriver National Institute of Child Health and Human Services, Bethesda, MD

Background: Pheochromocytoma/paraganglioma (PHEO/PGL) is a rare malignancy that arises from chromaffin cells of typically the adrenal medulla but can also be of extra-adrenal origin. These tumors produce excessive catecholamines such as epinephrine and norepinephrine which causes labile hypertension, tachycardia, and flushing. Lu-177-DOTATATE (Lu-177-dodecanetetraacetic acid-tyrosine-3-octreotate) is a radiolabeled somatostatin analog that is FDA approved for somatostatin receptor-positive neuroendocrine tumors. It is being being investigated in PHEO/PGL, which over-express somatostatin receptors. Amino acid solutions containing lysine/arginine (L/A) are routinely co-administered with Lu-177-DOTATATE for renal radioprotection, although solutions containing other amino acids are also used. **Methods:** This is a prospective, single center, open label Phase 2 study evaluating the efficacy of Lu-177-DOTATATE in PHEO/PGL. Ninety patients will be enrolled, divided into two cohorts of 45 patients each (*SDHx* mutation vs. apparent sporadic). Lu-177-DOTATATE is given at a fixed dose of 200 mCi with a co-administration of L/A amino acid solution q8 weeks for 4 cycles. The primary endpoint is the progression-free-survival (PFS) rate at 6 months. Secondary endpoints include response rate, overall survival, time to progression, quality of life measures, and examination of potential biomarkers such as biochemical profiles, Ga-68-DOTATATE PET, and F-18-FDG PET scans. Eligibility criteria include inoperable disease (including non-metastatic), histological confirmation of PHEO/PGL, evidence of disease progression by RECIST 1.1, ECOG performance status of 1 or better, and a positive Ga-68-DOTATATE PET scan. Exclusion criteria include prior treatment with systemic radionuclide therapy such as I-131-MIBG, brain parenchymal metastases, and standard organ dysfunction limitations. Interim analysis using a Simon two-stage optimal design will be performed separately for each cohort after enrollment of 18 patients. First patient accrual to this ongoing study was in the Fall of 2017, and as of February 2019, fourteen patients have been accrued. Preliminary results will be reported at the completion of stage 1 for each cohort. Clinical trial information: NCT03206060.

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TPS4160 **Poster Session (Board #255b), Mon, 8:00 AM-11:00 AM**

A randomized noncomparative phase II study of maintenance therapy with multiepitope vaccine Tedopi (OSE2101) ± nivolumab or FOLFIRI after induction chemotherapy (CT) with FOLFIRINOX in patients (Pts) with advanced pancreatic ductal adenocarcinoma (aPDAC) (TEDOPaM–PRODIGE 63 GERCOR D17-01 study).

Cindy Neuzillet, Vincent Hautefeuille, Aurélien Lambert, Marie-Line Garcia-Larnicol, Dewi Vernerey; Medical Oncology Department, Curie Institute, Versailles Saint-Quentin University, Saint Cloud, France; Amiens University Hospital, Amiens, France; Institut de Cancérologie de Lorraine, Nancy, France; GERCOR, Paris, France; Bourgogne Franche-Comté University, INSERM, Etablissement Français du Sang Bourgogne Franche-Comté, UMR1098, Interactions Hôte-Greffon-Tumeur/ Ingénierie Cellulaire et Génique, Besançon, France

Background: FOLFIRINOX (5-fluorouracil [5FU], folinic acid [FA], irinotecan [Iri], and oxaliplatin [Ox]) is a standard 1st-line treatment in fit Pts with aPDAC. Anti-PD-1/PD-L1 as single agents have failed in PDAC so far and new combination immunotherapies are needed. Tedopi (OSE2101) is a multiple neoepitope vaccine restricted to HLA-A2 positive Pts, targeting 5 tumor-associated antigens (CEA, HER2, MAGE2, MAGE3, TP53) that are frequently expressed in PDAC. This study aims to assess the efficacy and safety of Tedopi alone and in combination with anti-PD-1 nivolumab, or FOLFIRI as maintenance therapy in Pts with aPDAC after FOLFIRINOX induction CT. **Methods:** TEDOPaM - PRODIGE 63 is a 3-arm, Fleming 2-stage, open-label, randomized, non-comparative phase II study. 156 Pts with locally advanced or metastatic, pathologically proven PDAC; ECOG performance status 0-1; HLA-A2 genotype; controlled disease (objective response or stable disease) after 8 cycles of (modified) FOLFIRINOX; and adequate organ functions, are randomized (1:1:1, stratified on center, tumor stage, and best response to FOLFIRINOX) into 3 arms: Clinical trial information: NCT03806309. In Arms B and C, FOLFIRI is reintroduced at disease progression or unacceptable toxicity. Primary endpoint: overall survival rate at M12. Secondary endpoints: progression-free survival (CT-scan Q8W), duration of disease control, safety, objective response rate, RECIST v1.1/iRECIST comparison, HRQoL (EORTC QLQ-C30), Q-TWiST. An interim analysis is planned after inclusion of 20 Pts in each arm. Translational research will be performed on tumor tissue (initial FFPE biopsy and optional re-biopsy at inclusion): RNAseq (cancer and stroma), mutation burden, MMR status, immune infiltrates; and in blood (before and on-treatment): cytokine panel, PBMC phenotyping, vaccine-antigen specific T-cells, TCR repertoire, and extracellular vesicles, to explore biomarkers and pharmacodynamics effects of Tedopi ± nivolumab. Enrollment (12th Feb 2019): 1. ClinicalTrials Registration: NCT03806309.

Arm A (reference): FOLFIRI (n = 52)	**IV; FA 400 mg/m², Iri 180 mg/m², 5FU bolus 400 mg/m² + continuous 2400 mg/m²/46h**
Arm B (experimental): Tedopi (n = 52)	Subcutaneous injection on D1 Q3W for 6 doses then Q8W until month 12 [M12] then Q12W up to M24
Arm C (experimental): Tedopi + nivolumab (n = 52)	Tedopi + nivolumab 360 mg IV on D1 Q3W for 6 infusions then 480 mg Q4W up to M24

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TPS4161 **Poster Session (Board #256a), Mon, 8:00 AM-11:00 AM**

A randomized phase II trial of niraparib plus either nivolumab or ipilimumab in patients with advanced pancreatic cancer whose cancer has not progressed on platinum-based therapy.

Kim Anna Reiss, Rosemarie Mick, Mark H. O'Hara, Ursina R. Teitelbaum, Thomas Benjamin Karasic, Charles John Schneider, Peter J. O'Dwyer, Danielle Karlson, Stacy Cowden, Mary Jane Fuhrer, Erica L. Carpenter, Austin A Pantel, Mehran Makvandi, David A. Mankoff, Katharine Nathanson, Kara Noelle Maxwell, Gregory Lawrence Beatty, Susan M. Domchek; University of Pennsylvania Abramson Cancer Center, Philadelphia, PA; University of Pennsylvania, Philadelphia, PA; University of Pennsylvania Perelman School of Medicine, Philadelphia, PA; University of Pennsylvania Abramson Cancer Center, Division of Medical Oncology, Philadelphia, PA; University of Pennsylvania Hospital, Philadelphia, PA; Hospital of the University of Pennsylvania, Philadelphia, PA

Background: The treatment paradigm for advanced pancreatic ductal adenocarcinoma (PDAC) typically involves ongoing chemotherapy until either disease progression or clinical deterioration. A subset of patients with advanced PDAC have exceptional responses to platinum-based chemotherapy. We hypothesized that durable platinum sensitivity in patients with advanced PDAC might be indicative of a DNA repair deficiency, and that these patients may respond to a combination of niraparib, a PARP inhibitor, plus immune checkpoint blockade. **Methods:** We have enrolled 25 of 84 planned patients on study NCT 03404960. Eligibility criteria include inoperable PDAC and stability on platinum-based chemotherapy for $\geq$16 weeks without evidence of progressive disease. Patients who have progressed on platinum-based treatment or who have received prior therapy with PARP inhibitors are excluded. Patients are randomized to receive oral niraparib 200mg PO daily plus nivolumab 240mg IV every two weeks in continuous 28 day cycles or oral niraparib 200mg PO daily plus ipilimumab 3mg/kg IV every three weeks for four doses in continuous 21 day cycles. The primary endpoint is progression-free survival at 6 months. Secondary endpoints include response rate, duration of response and overall survival. Paired biopsies are obtained, as well as serial blood collections for circulating tumor cells (CTCs), circulating tumor DNA (ctDNA) and peripheral blood mononuclear cells (PBMCs). Correlative assays will include germline whole exome sequencing and analyses of serially collected PBMCs, CTCs and ctDNA to identify genomic and immunologic innate and adaptive resistance mechanisms. Clinical trial information: NCT 03404960.

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TPS4162 **Poster Session (Board #256b), Mon, 8:00 AM-11:00 AM**

Improving cascade genetic testing for families with inherited pancreatic cancer (PDAC) risk: The genetic education, risk assessment and testing (GENERATE) study.

Matthew B. Yurgelun, C. Sloane Furniss, Barbara Kenner, Alison Klein, Catherine C. Lafferty, Andrew M. Lowy, Florencia McAllister, Maureen E Mork, Scott H. Nelson, Alison Robertson, Jill E. Stopfer, Meghan Underhill, Allyson J. Ocean, Lisa Madlensky, Gloria M. Petersen, Judy Ellen Garber, Scott Michael Lippman, Michael Goggins, Anirban Maitra, Sapna Syngal; Dana-Farber Cancer Institute, Boston, MA; Kenner Family Research Fund, New York, NY; The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD; UCSD Moores Cancer Center, La Jolla, CA; The University of Texas MD Anderson Cancer Center, Houston, TX; Mayo Clinic, Rochester, MN; Center for Cancer Genetics and Prevention, Dana-Farber Cancer Institute, Boston, MA; Weill Cornell Medical College, New York, NY; University of California, San Diego, La Jolla, CA; Johns Hopkins University, Baltimore, MD; University of Texas MD Anderson Cancer Center, Houston, TX

Background: 4-10% of PDAC patients harbor pathogenic germline variants in cancer susceptibility genes, including *APC*, *ATM*, *BRCA1*, *BRCA2*, *CDKN2A*, *EPCAM*, *MLH1*, *MSH2*, *MSH6*, *PALB2*, *PMS2*, *STK11*, and *TP53*. For families with such pathogenic variants, the greatest potential impact of germline testing is to identify relatives with the same pathogenic variant (cascade testing), thereby providing the opportunity for early detection and cancer interception of PDAC and other associated malignancies. Numerous factors limit cascade testing in real-world practice, including family dynamics, widespread geographic distribution of relatives, access to genetic services, and misconceptions about the importance of germline testing, such that the preventive benefits of cascade testing are often not fully realized. The primary aim of this study is to analyze two alternative strategies for cascade testing in families with inherited PDAC susceptibility. **Methods:** 1000 individuals (from approximately 200 families) with a confirmed pathogenic germline variant in any of the above genes in a $1^{st}/2^{nd}$ degree relative and a $1^{st}/2^{nd}$ degree relative with PDAC will be remotely enrolled through the study website (www.generatestudy.org) and randomized between two different methods of cascade testing (individuals with prior genetic testing will be ineligible): Arm 1 will undergo pre-test genetic education with a pre-recorded video and live interactive session with a genetic counselor via a web-based telemedicine platform (Doxy.me), followed by germline testing through Color Genomics; Arm 2 will undergo germline testing through Color Genomics without dedicated pre-test genetic education. Color Genomics will disclose results to study personnel and directly to participants in both arms. Participants in both arms will have the option of pursuing additional telephone-based genetic counseling through Color Genomics. The primary outcome will be uptake of cascade testing. Secondary outcomes will include participant self-reported genetic knowledge, cancer worry, distress, decisional preparedness, familial communication, and screening uptake, which will be measured via longitudinal surveys. Enrollment will begin February, 2019. Clinical trial information: NCT03762590.

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TPS4163 **Poster Session (Board #257a), Mon, 8:00 AM-11:00 AM**

Phase II multi-institutional study of nivolumab (Nivo), cabiralizumab (Cabira), and stereotactic body radiotherapy (SBRT) for locally advanced unresectable pancreatic cancer (LAUPC).

Deirdre Jill Cohen, Benjamin Medina, Kevin Lee Du, Andrew L. Coveler, Gulam Abbas Manji, Paul Eliezer Oberstein, Serena K Perna, George Miller; Laura and Isaac Perlmutter Cancer Center, NYU Langone Health, New York, NY; NYU Langone Medical Center, New York, NY; Seattle Cancer Care Alliance/University of Washington, Seattle, WA; Columbia University Medical Center and New York-Presbyterian Hospital, New York, NY; Bristol-Myers Squibb, Princeton, NJ

Background: Treatment of LAUPC most commonly involves chemotherapy +/- RT. Patients(pts) who can be downstaged and undergo R0 resection have significant improvement in overall survival, but conventional chemoRT converts $<$ 10% of patients with LAUPC. If the effects of RT can be augmented then higher R0 resection rates may be achieved and improve survival. In pre-clinical models, RT leads to increased expression of M-CSF from pancreatic tumor cells and marked immune suppression within the tumor microenvironment via expansion of tumor associated macrophages (TAMs). Concurrent blockade of M-CSF with RT reduces TAM infiltration, prevents the generation of tumor promoting T cell populations, and increases the therapeutic effect of RT. RT also induces up-regulation of PD-L1 in TAMs, another mode of immune suppression that can account for RT resistance in LAUPC. (Seifert et al. 2016). These data suggest the efficacy of RT in LAUPC is limited by its promotion of innate and adaptive immune suppression. CSF1R blockade with Cabira combined with PD-1 blockade with Nivo may enhance the efficacy of SBRT by reprogramming the TAM compartment in tumors, thereby preventing an immune suppressive phenotype and augmenting T-cell mediated anti-tumor response.
Methods: Single arm phase II study designed to evaluate safety, tolerability, and surgical resection rate in LAUPC pts treated with concurrent Nivo, Cabira, and SBRT. Exploratory endpoints include immune changes within blood and tissue following treatment and correlation with clinical endpoints. Key eligibility: completion of 2- 6 months standard induction chemotherapy, normal organ and marrow function, pre- and on-treatment biopsy, and PS $\leq$ 1. Following initial biopsy and placement of fiducials, Cabira 4mg/kg and Nivo 240mg are given D1 of every 14 day cycle. SBRT 6.6 Gy x 5 consecutive fractions starts D8. After 2 cycles, repeat biopsy and imaging is performed. Treatment with Cabira and Nivo continues every 2 weeks and imaging is done every 8 weeks, at which time pt is assessed for surgical resection. If pt is downstaged, treatment is discontinued and pt proceeds to surgery. Preliminary 6 pt safety cohort is monitored for unacceptable toxicities. If $<$ 3 unacceptable toxicities in the first 6 subjects enrolled, then plan for expansion phase with 14 more pts. As of abstract submission, 3 pts have been enrolled. Clinical trial information: NCT03599362.

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TPS4164 **Poster Session (Board #257b), Mon, 8:00 AM-11:00 AM**

Adaptive Dose Escalation Trial of Stereotactic Body Radiation Therapy (SBRT) in combination with GC4419 in pancreatic cancer.

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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 5-7 Gy/fraction x 5 are constrained by nearby organ tolerance and offer only palliation without improving survival. Safe dose escalation is necessary to improve SBRT efficacy. GC4419, a superoxide dismutase mimetic, selectively converts superoxide (O2 • -) to hydrogen peroxide (H2O2) and oxygen. O2 • -initiates normal tissue damage due to RT. GC4419 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, ASCO 2018). GC4419 improved the survival of mice receiving 8.5 Gy x 5 to the upper abdomen. Cancer cells are less tolerant to elevated H2O2, and more tolerant to elevated O2 • -, than normal cells, and GC4419 demonstrated mechanism-dependent synergy with high dose-fraction RT in a human tumor xenograft with inducible expression of catalase (Sishc, AACR 2018). Thus, adding GC4419 to SBRT may increase both the efficacy and the safety of the latter. **Methods:** 48 patients with localized, unresectable PC without frank duodenal invasion, who have received 3+ cycles of induction chemotherapy, are to be randomized 1:1 to placebo or GC4419, 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 SBRT dose escalation in each arm based on a dual endpoint (Gr 3-4 GI toxicity or death ;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 GC4419 or placebo. Exploratory endpoints include change in tumor radiographic resectability, correlative studies (ctDNA, exosomal DNA, tumor exome/transcriptome sequencing, immune profiling). Supported by Galera Therapeutics, Inc. Clinical trial information: NCT03340974.

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TPS4165 **Poster Session (Board #258a), Mon, 8:00 AM-11:00 AM**

A phase I/II study of GSK3145095 alone and in combination with anticancer agents including pembrolizumab in adults with selected solid tumors.

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Background: The immunosuppressive myeloid infiltrate characteristic of the tumor microenvironment in pancreatic cancer represents a major therapeutic barrier in this disease. Modulation of this infiltrate may increase sensitivity to immune checkpoint blockade in this and other tumors with a similar phenotype. The receptor interacting protein 1 (RIP1) is a serine/threonine kinase that becomes active upon homeostatic disruptions. Bound to RIP3 and mixed lineage kinase domain-like protein (MLKL), RIP1 kinase activity drives necroptosis. However, RIP1 also signals in response to inflammatory stimuli independently of its association with RIP3. A correlation between increased RIP1 protein expression and a worse prognosis has been reported in a variety of solid tumors. Furthermore, in an unbiased screen RIP1 was identified as a top gene contributing to resistance to immunotherapy (Manguso 2017). In murine models, RIP1 kinase activity has been reported to drive pancreatic oncogenesis. Inhibition of RIP1 in the pancreatic TME leads to the replacement of tumor-permissive myeloid infiltrates with innate cells promoting an anti-tumor response by the adaptive immune system (Seifert 2016; Wang 2018) and synergized with anti-PD-1 treatment. These data suggest that the small molecule RIP1 inhibitor GSK3145095 may have therapeutic potential in multiple tumor types. **Methods:** This is a four-part phase 1/2 study designed to evaluate the safety, PK, PD, and preliminary activity of GSK3145095 given orally to participants with selected advanced or recurrent solid tumors. Part 1 will be conducted in approximately 30 adults with pancreatic cancer with escalating doses of GSK3145095. Part 2 will combine escalating doses of GSK3145095 with 200 mg pembrolizumab and may be conducted in a broader population of selected solid tumors. Part 3 represents a cohort expansion of Part 2. Part 4 may investigate the combination of additional anticancer agent(s) with one or more doses of GSK3145095 identified as safe in Part 1. References: Manguso RT. Nature. 2017;547(7664):413-418. Seifert L. Nature. 2016;532(7598):245-249. Wang W. Cancer Cell 2018; 34: 757-774. Clinical trial information: NCT03681951.

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TPS4166 **Poster Session (Board #258b), Mon, 8:00 AM-11:00 AM**

PRIMUS-002: A multicentre, open-label, phase II study examining FOLFOX and *nab*-paclitaxel (FA) and *nab*-paclitaxel and gemcitabine (AG) as neoadjuvant therapy for (borderline) resectable pancreatic cancer (PC), focusing on biomarker and liquid biopsy development.

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Background: There is increasing evidence suggesting benefit from a neoadjuvant approach to PC. However, the optimal regimen is unclear and will likely require a precision medicine approach, where patient and tumor attributes define therapy. Platinum-containing regimens have shown survival benefit for PC, with occasional exceptional responders, but biomarkers (BM) of response are not well defined and treatment decisions are often based on patient performance status (PS) and co-morbidity. Tumors with defects in *BRCA1/2*and other Fanconi Anemia genes show defective DNA damage response (DDR), conferring potential selective sensitivity to DNA-damaging agents (e.g. platinum) and newer targeted agents. We have shown that DDR deficiency (DDRd) is present in up to 20% of PC. This study aims to exploit DDRd as a therapeutic vulnerability, with integrated analysis to define candidate BM for FA and AG response. **Methods:** PRIMUS-002 will enroll patients registered on the Precision-Panc Master Protocol who are molecularly profiled using the Precision-Panc Clinical Cancer Genome including a novel DDRd assay, and the transcriptome with longitudinal sampling (pre-, during, and post-treatment). Patients receive either FA (*nab*-paclitaxel 150mg/m^{2}IV,oxaliplatin 85mg/m^2, folinic acid 350mg flat dose, fluorouracil infusion 2400mg/m^{2}continuous IV infusion), orAG (*nab*-paclitaxel 125mg/m^2, gemcitabine 1000 mg/m^2) for 3 months,based on patient age and PS.Following initial safety analysis, chemoradiation may be introduced. The primary endpoint is disease progression (DP) during neoadjuvant therapy. The study is designed to detect a 20% difference in DP between the BM+ve (10%) and BM –ve (30%) in patients treated with FA (90% power, 5% 1-sided level of statistical significance)., Exploratory translational endpoints include surrogate therapeutic response assessment using CA19.9, PET-CT SUV, DWI-MRI and ctDNA. Current Enrolment: 2 patients enrolled to date: 1 to receive FA and 1 to AG treatment. Clinical trial information: ISRCTN34129115.

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TPS4167 **Poster Session (Board #259a), Mon, 8:00 AM-11:00 AM**

A randomized, phase II clinical trial of preoperative stereotactic body radiation therapy versus conventionally fractionated chemoradiation for resectable, borderline-resectable, or locally advanced type a pancreatic adenocarcinoma.

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Background: There is growing consensus for the use of neoadjuvant therapy in patients with potentially operable pancreatic adenocarcinoma (PC). However, there is not consensus on the type and duration of chemotherapy or radiation therapy (RT) dose. Stereotactic body radiation therapy (SBRT) has gained popularity despite the absence of prospective data for its use in the preoperative setting. Furthermore, SBRT preoperatively has not been standardized. At present, there exists no randomized data comparing preoperative SBRT with conventionally fractionated concurrent chemo-RT. We designed this trial to examine differences between pre-op RT dose and fractionation schedules. **Methods:** This study is a prospective, randomized, two-arm, phase II clinical trial. Eligible patients must have cytologically confirmed PC and be deemed suitable for surgical resection with resectable, borderline resectable, or locally advanced type A disease, based on cross-sectional imaging. Before randomization patients are stratified by clinical node positivity, neoadjuvant chemotherapy, and stage of disease. Patients are then randomized to either 50.4 Gy over 28 fractions with concurrent weekly Gemcitabine vs SBRT to a total dose of 25-35 Gy over 5 fractions. The primary endpoint of the study is pathologic node positivity. We hypothesize that patients treated with neoadjuvant chemotherapy followed by conventionally fractionated chemo-RT will have a lower rate of pathologic node positivity as compared to those patients treated with neoadjuvant chemotherapy followed by SBRT. Secondary endpoints include patient reported quality of life, local recurrence, primary tumor pathologic response, margin status, surgical complications, MR based treatment response, and overall survival. We anticipate a node positivity rate of 37% when using preoperative chemotherapy followed by SBRT. We hypothesize that treatment with chemotherapy followed by conventionally fractionated chemo-RT will reduce the rate of node positivity to 17%. Using a one-sided Type I error rate of 0.1, approximately 88 total patients (44 per arm) provide an 80% power to detect the hypothesized difference in pathologic node positivity between the two arms. To address patient dropout, an additional 14 patients (about 15%) will be enrolled for a total target accrual of 102 patients. The trial opened in November 2018 and 8 of the planned 102 patients have been enrolled. Clinical trial information: NCT03704662.

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TPS4168 **Poster Session (Board #259b), Mon, 8:00 AM-11:00 AM**

Niraparib in metastatic pancreatic cancer after previous chemotherapy (NIRA-PANC): A phase 2 trial.

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Background: Attempts to improve therapy for patients with pancreatic adenocarcinoma with traditional chemotherapy have largely failed to meaningfully improve survival. Therefore, there is a critical need for identification of specific molecular changes that define prognosis and potentially guide therapy decisions. Defective DNA damage response pathways in pancreatic cancer represent a targeted opportunity for treatment. PARP inhibitors exert activity in tumor cells that may not be effectively able to repair initially single-stranded and cumulatively double-stranded DNA breaks and can have a heightened susceptibility in tumor cells over normal tissue. This concept is referred to as synthetic lethality. Niraparib is an orally available, potent, highly selective PARP-1 and -2 inhibitor. We are studying the efficacy of Niraparib in pancreatic cancer patients that harbor DNA repair defects. **Methods:** This study is funded by a research grant from TESARO. Pre-screening of patients to find biomarker positive patients is funded by KU Cancer Center. This is a phase II open label single arm trial in metastatic pancreatic cancer patients with germline or somatic mutations, either already known, or tested after consent to pre-screening tumor tissue analysis in BRCA1/2, PALB2, ATM, NBN, ATR, BRIP1, IDH1/2, RAD51, RAD51B/C/D, RAD54L, CDK12, BARD1, FAM175A, BAP1, CHEK1/2, GEN1, MRE11A, XRCC2, SHFM1, FANCD2, FANCA, FANCC, FANCG, RPA1, ARID1A. Patients are being treated with Niraparib 300mg or 200mg by mouth daily for 28 days (1 cycle = 28 days) (200mg dose is for participants whose baseline weight is $<$ 77 kg [169.756 lbs] or baseline platelet count is $<$ 150,000 μL). The primary objective is to assess antitumor efficacy of niraparib using Objective Response Rate per RECIST 1.1. Secondary objectives include PFS, OS, DCR, DOR, and safety. Eligible patients received $>$ 1 line of therapy, no prior PARP inhibitor(s), have measurable disease, and ECOG PS 0-1. Accrual target enrollment of 18 patients over a period of 24 months with a study duration of 30 months. Correlative studies include assessment of pharmacokinetics, circulating tumor cells and storing samples for future research. The trial is currently enrolling. Clinical trial information: NCT03553004.

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