Patient-reported outcomes (PROs) from the Phase III IMbrave150 trial of atezolizumab (atezo) + bevacizumab (bev) vs sorafenib (sor) as first-line treatment (tx) for patients (pts) with unresectable hepatocellular carcinoma (HCC).

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Background: Atezo + bev in pts with unresectable HCC who had not received prior systemic therapy has shown statistically significant and clinically meaningful improvement in OS and PFS per independent review facility-assessed RECIST 1.1 vs sor in the Phase III IMbrave150 study (Cheng ESMO Asia 2019). Here, we report PRO data from this trial to show pt perspectives on the overall clinical benefit of atezo + bev. **Methods:** Pts were randomized 2:1 to receive either atezo 1200 mg IV q3w + bev 15 mg/kg IV q3w or sor 400 mg PO BID until loss of clinical benefit or unacceptable toxicity. Pts completed the EORTC QLQ-C30 and EORTC QLQ-HCC18 questionnaires before tx, every 3 wk on tx, and every 3 mo after tx discontinuation or disease progression. A pre-specified secondary endpoint was time to deterioration (TTD; first $\geq$ 10-point decrease from baseline held for 2 consecutive assessments or 1 assessment followed by death within 3 wk) of pt-reported quality of life (QOL), physical functioning, and role functioning. Pre-specified exploratory analyses included TTD of and proportion of pts with a clinically meaningful change ($\geq$ 10 points from baseline) in key pt-reported symptoms. **Results:** Questionnaire completion rates were $\geq$ 92% in both arms from baseline through most of the tx period. Compared with sor, atezo + bev delayed TTD of pt-reported QOL (median TTD, 11.2 vs 3.6 mo; HR, 0.63 [95% CI: 0.46, 0.85]), physical functioning (median TTD, 13.1 vs 4.9 mo; HR, 0.53 [95% CI: 0.39, 0.73]), and role functioning (median TTD, 9.1 vs 3.6 mo; HR, 0.62 [95% CI: 0.46, 0.84]). Atezo + bev also delayed TTD in pt-reported appetite loss, fatigue, pain, and diarrhea vs sor; a lower proportion of pts on atezo + bev experienced clinically meaningful deterioration in each of these symptoms vs sor. **Conclusions:** High-quality PRO results from IMbrave150 showed large and consistent benefits in key aspects of the pt experience with atezo + bev, further supporting its overall clinical benefit in pts with unresectable HCC who have not received prior systemic therapy. Clinical trial information: NCT03434379. Research Sponsor: F. Hoffmann-La Roche, Ltd.

Ramucirumab (RAM) or merestinib (MER) or placebo (PL) plus gemcitabine (GEM) and cisplatin (CIS) as first-line treatment for advanced or metastatic biliary tract cancer (BTC): A randomized, double-blind, phase II study.

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Background: We assessed RAM or MER plus standard of care GEM+CIS as first-line treatment for BTC. **Methods:** Patients (pts) with BTC, ECOG PS 0/1, and measurable disease were randomized 2:1:2:1 to oral MER 80 mg QD, oral PL QD, IV RAM 8 mg/kg days 1 and 8 Q3W or IV PL days 1 and 8 Q3W. Pts also received up to 8 cycles IV GEM 1000 mg/m^2 + CIS 25 mg/m^2 days 1 and 8 Q3W. RAM, MER, or PL could continue until disease progression. Primary endpoint: progression-free survival (PFS). Secondary endpoints: overall survival (OS), objective response rate (ORR), and safety. PFS and hazard ratios (HRs) were compared using stratified log-rank tests and Cox regression models, respectively. NCT02711553. **Results:** 309 pts were randomized to RAM (106), MER (102), or pooled PL (101). More pts in the RAM (54.7%) and MER (49.0%) groups had baseline ECOG PS 1 vs PL (38.6%). Efficacy endpoints are in Table. Fewer pts received post-discontinuation systemic therapy in the RAM group (RAM 37.5%, MER 50.0%, PL 52.0%). The most common grade ≥3 treatment-emergent adverse events were: RAM vs PL: neutropenia (49.0% vs 33.0%), thrombocytopenia (34.6% vs 17.0%), and anemia (26.9% vs 19.0%); MER vs PL: neutropenia (47.1% vs 33.0%), thrombocytopenia (18.6% vs 17.0%), and alanine aminotransferase increased (10.8% vs 5.0%). **Conclusions:** PFS, OS, and ORR were not improved with the addition of RAM or MER to GEM+CIS. Treatment was well tolerated, with safety profiles consistent with known profiles for RAM, MER, and GEM+CIS. Translational studies are ongoing. Clinical trial information: NCT02711553. Research Sponsor: Eli Lilly and Company.

Efficacy endpoints.

	RAM+GEM+CIS (N=106)	MER+GEM+CIS (N=102)	PL+GEM+CIS (N=101)
Median PFS, mo (80% CI)	6.47 (5.65 - 7.13)	6.97 (6.21 - 7.13)	6.64 (5.59 - 6.83)
HR vs PL (80% CI)	1.123 (0.904 - 1.395)	0.920 (0.734 - 1.153)	
P-value vs PL	0.4821	0.6417	
Median OS, mo (95% CI)	10.45 (8.48 - 11.76)	14.03 (11.96 - 16.36)	13.04 (11.40 - 15.31)
HR vs PL (95% CI)	1.336 (0.959 - 1.862)	0.948 (0.669 - 1.342)	
P-value vs PL	0.0870	0.7599	
ORR, n (%; 95% CI)	33 (31.1; 22.3 - 39.9)	20 (19.6; 11.9 - 27.3)	33 (32.7; 23.5 - 41.8)
Odds ratio vs PL (95% CI)	1.0 (0.6 - 1.9)	0.5 (0.2 - 0.9)	
P-value vs PL	0.8779	0.0235	

478 Rapid Abstract Session, Fri, 7:00 AM-7:45 AM and Poster Session (Board #A1), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

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

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Background: The programmed death-1 inhibitor NIVO had durable responses and a manageable safety profile in pts with aHCC in CheckMate 040 (NCT01658878; El-Khoueiry et al. *Lancet* 2017) and is approved in the United States, Canada, Australia, and elsewhere for sorafenib (SOR)-treated pts with aHCC. In another CheckMate 040 cohort, NIVO + IPI combination therapy had durable responses in SOR-treated pts with aHCC, with objective response rates (ORRs) $>$ 30% in each dosing arm (Yau et al. *J Clin Oncol* 2019). CABO is also approved for SOR-treated pts with aHCC; a pivotal phase 3 trial reported median overall survival (OS) of 10.2 mo (Abou-Alfa et al. *N Engl J Med* 2018). This is the first report of efficacy and safety of NIVO + CABO +/- IPI (doublet and triplet) combinations in pts with aHCC. **Methods:** SOR-naive or -experienced pts with aHCC were randomized to 2 arms: [1] NIVO 240 mg Q2W + CABO 40 mg daily or [2] NIVO 3 mg/kg Q2W + IPI 1 mg/kg Q6W + CABO 40 mg daily. Treatment continued until intolerable toxicity or disease progression. Primary endpoints included ORR (investigator assessed using RECIST v1.1) and safety/tolerability. Data cutoff was January 2019. **Results:** 71 pts were randomized to NIVO + CABO (n = 36) or NIVO + IPI + CABO (n = 35). Investigator-assessed ORR was 17% (6 pts with partial response [PR]) in the NIVO + CABO arm and 26% (9 pts with PR) in the NIVO + IPI + CABO arm. Disease control rate was 81% for the NIVO + CABO arm and 83% for the NIVO + IPI + CABO arm; median progression-free survival was 5.5 mo for the NIVO + CABO arm and 6.8 mo for the NIVO + IPI + CABO arm. Median OS was not reached in either arm. Grade 3-4 treatment-related adverse events (TRAEs) were reported in 15 pts (42%) in the NIVO + CABO arm and 25 pts (71%) in the NIVO + IPI + CABO arm and led to discontinuation in 1 (3%) and 7 (20%) pts, respectively. No new safety signals were observed in either arm. Updated data describing the efficacy and safety of the combinations will be shown. **Conclusions:** In pts with aHCC, NIVO + CABO +/- IPI combination therapy led to clinically meaningful responses. Although the triplet had a higher rate of TRAEs observed than the doublet regimen, the majority of AEs were manageable and reversible. Clinical trial information: NCT01658878. Research Sponsor: Bristol-Myers Squibb.

479 Rapid Abstract Session, Fri, 7:00 AM-7:45 AM and Poster Session (Board #A2), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Comprehensive molecular profiling of *IDH1/2* mutant biliary cancers (BC).

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Background: Isocitrate dehydrogenases (IDH) play a key role in energetic metabolism and IDH mutations (mut) promote oncogenesis via epigenetic and genetic changes. Data addressing the molecular contexture of *IDH1/2* mut in BC are lacking. We aimed to characterize the molecular profile of *IDH1/2* mutant (mIDH) GI cancers with a focus on BC. **Methods:** 27954 GI cancer samples collected between August 2000 and July 2019 were included: 2057 BC (1159 ICC, 277 extrahepatic CC, 573 gallbladder, 48 unspecified CC), 13807 colorectal, 4183 gastric/esophageal, 3060 other. Samples were analyzed using NextGen DNA sequencing, in situ hybridization, RNA sequencing and immunohistochemistry (Caris Life Sciences, Phoenix, AZ). Tumor mutational burden (TMB) was calculated based on somatic nonsynonymous missense mut. MMR/MSI status was evaluated by a combination of IHC, Fragment Analysis and NGS. **Results:** mIDH frequency in BC was 10.3% (211/2057), with higher prevalence of *IDH1* mut (8.2%). ICC showed the highest mut prevalence: *IDH1* 13.5%, *IDH2* 4%. Mut rates in other GI cancers types were $<$ 1%, except for HCC (1.9%, 11/582) and small bowel (1.1%, 8/736). When compared to *IDH* wild type (WT), mIDH BC showed lower mut rates in *TP53* (13 vs 43%), *KRAS* (8 vs 19%), *CDKN2A* (1 vs 9%), and *SMAD4* (0 vs 9%), whereas *PBRM1* mut were higher (14 vs 5%) ($P < .001$ for all comparisons). There was a trend towards higher frequency of *ARID1A* and *BAP1* in mIDH BC. HER2 expression and amplification rates were lower in mIDH vs WT BC (0.5 vs 3%, $P = .048$ and 0 vs 6%, $P = .002$). *FGFR2* fusion was detected in 7% of WT vs 2% of mIDH BC. mIDH BC showed a lower TMB (0.7 vs 3.7%, $P = .048$) and a trend for lower MSI rates (0.6 vs 3%, $P = .06$) vs WT BC. Conversely, IDH mut were associated with higher TMB and MSI ($P < .001$) and higher PD-L1 expression in other GI cancers. **Conclusions:** This is the largest and most extensive profiling study to investigate the molecular makeup of mIDH BC and GI tumors. Our data show distinct gene alteration patterns characterizing mIDH BC, involving genes related to chromatin remodeling and DNA repair, and a differential expression of immune related markers compared to other mIDH GI tumors. These findings can contribute to the development of rational combination therapies and to improved patient selection in the future. Research Sponsor: National Cancer Institute grant number P30CA014089, the Gloria Borges WunderGlo Foundation-The Wunder Project, the Dhont Family Foundation, the San Pedro Peninsula Cancer Guild, the Daniel Butler Research Fund, the Call to Cure Research Fund and the Fong.

480 Poster Session (Board #A5), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Immune checkpoint blockade (ICB) response evaluation with MRI/MR elastography (MRE) in surgical and nonsurgical patients with HCC.

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Background: Currently, there is a lack of imaging biomarkers of immunotherapy outcome in hepatocellular carcinoma (HCC). The study aim was to determine if HCC enhancement on MRI and stiffness change measured by magnetic resonance elastography (MRE) can predict immunotherapy response. **Methods:** This was a prospective, Institutional Review Board approved study of 38 patients with HCC treated with immune checkpoint blockade (ICB) therapy. All patients had liver MRI/MRE and HCC biopsy at baseline, and MRI/MRE with biopsy or resection after 6 weeks therapy. HCC stiffness (kPa) was measured on MRE elastograms (liver stiffness maps). HCC enhancement and change in stiffness were compared with treatment response to ICB in 1) non-surgical patients (pembrolizumab), and 2) surgical patients (nivolumab +/- ipilimumab). For non-surgical patients, treatment response was defined as overall survival $>$1 year. For surgical patients, treatment response was defined as $<$50% viable tumor at time of resection. Analysis was performed using descriptive statistics and Spearman correlation; *p-value* $<$0.05 was considered statistically significant. **Results:** Twenty-five patients were evaluable. Median age was 67 years (32, 78). Etiology of liver disease was NASH (n=8), HCV (n=8), HBV (n=2) and unknown (n=7). Treatment response occurred in 11/25 (44%) patients. Median HCC size and change in size were 4.7 cm (1.2, 14.0) and –0.32 cm, respectively. Median baseline HCC stiffness and change in stiffness were 5 kPa (2.2, 12.4) and –0.1 kPa (–2.2, 1.5), respectively. Median change in HCC size for responders and non-responders was –1.2 cm (–4.8, 0.4) and 0 cm (–1.5, 1.1), respectively (p = 0.02). Treatment response was associated with absence of portal venous phase capsular enhancement and increase in HCC stiffness, (p$<$0.001). **Conclusions:** Capsular enhancement and MRE stiffness change may be useful biomarkers of immune cell activated response to ICB therapy. Research Sponsor: None.

481 Poster Session (Board #A6), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Clinical predictors of progression of a hepatic lesion from Li-RADS (LR) 3 to LR5 among patients (pts) at risk of hepatocellular carcinoma (HCC).

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Background: We sought to identify predictors of progression of LR3 lesions (i.e. indeterminate for HCC) to LR5 lesions (i.e. definitely HCC) on follow-up imaging among cirrhotic pts. **Methods:** Imaging reports with LR assignments were identified among pts seen at the University of Washington, 2013-2017. Cirrhotic pts with a LR3 lesion and follow-up scan within 1 year (yr) of LR3 lesion date were included (n = 313). Clinical features were abstracted from chart review. Survival analyses employing interval censoring were performed. Variables as potentially predictive of LR3 progression were identified in univariate analyses, with backwards elimination done ($p < 0.05$) to obtain the final multivariate model. **Results:** 20.4% of LR3 lesions progressed to LR5 within 1 yr; 73% were still LR3, 8% progressed to LR4. The population was predominantly male (61%), Caucasian (71%), older than 55 (63%). The most common cirrhotic etiologies were HCV (46.7%), alcohol (32.6%), and NASH (12.8%), not mutually exclusive. AFP at the time of LR3 scan was low if available (39% with AFP <5, 16% 5-10, 28% unknown). 22.7% had impaired liver function (ALBI grade 3); 19.5% lacked data to calculate ALBI grade. CT scan was the most common exam (56%). Multiple LR3 lesions were seen on 51% of scans. Most LR3 lesions were right sided (75%), < 1 cm (51%); 7% of lesions were > 2cm. Men (HR 2.0, p = 0.02), earlier scan yr (HR 0.47 per yr, $p < 0.0001$), older age (HR 1.42 per 15 yr, p = 0.047), lesion size (HR 1.21 for 2cm+, global p = 0.02) appeared as independent predictors of LR3 to LR5 progression based on the final model. Of 16 variables examined, men were more likely to have chronic HCV, history of alcohol use and less likely to have autoimmune hepatitis. No other differences were seen. In an a priori analysis, risk of male sex (HR 1.99, p = 0.03) persisted despite control for HCV, alcohol, age, race, scan yr, lesion size, and number of lesions. **Conclusions:** Identification of clinical factors associated with LR3 progression may allow for risk modeling tools that may assist in determining imaging frequency and timing of intervention. The increased risk among men vs women is not explained by clinical or radiographic features listed above. Research Sponsor: None.

482 Poster Session (Board #A7), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

The comparisons of the outcomes between surgical resection and proton beam therapy for single primary hepatocellular carcinoma.

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Background: There are many treatment choices for hepatocellular carcinoma (HCC). Proton beam therapy (PBT) is considered a treatment option for HCC. The purpose of this study was to compare surgical resection (SR) and PBT in order to clarify the prognostic factors for operable HCC based on a single institution's database. **Methods:** Patients with single primary nodular HCC $\leq$ 100 mm without vessel invasion on pretreatment imaging were divided into the SR group and PBT group. In the PBT group, the patients with unresectable HCC due to their liver function and/or performance status (PS) were excluded. **Results:** There were 314 and 31 patients who underwent SR and PBT, respectively. The median survival time in the SR group was significantly better than in the PBT group (104.1 vs. 64.6 months, p = 0.008). Regarding the relapse-free survival (RFS), there was no significant difference between the SR and PBT groups (33.8 vs. 14.0 months, p = 0.099). **Conclusions:** In RFS, the PBT group and the SR group were comparable. However, the PBT group was significantly worse than SR group in overall survival. SR may therefore be favorable as an initial treatment for HCC compared to PBT. Clinical trial information: 1856. Research Sponsor: None.

483 Poster Session (Board #A8), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

CheckMate 459: Health-related quality of life (HRQoL) in a randomized, multicenter phase III study of nivolumab (NIVO) versus sorafenib (SOR) as first-line (1L) treatment in patients (pts) with advanced hepatocellular carcinoma (aHCC).

Julien Edeline, Thomas Yau, Joong-Won Park, Masatoshi Kudo, Kwang-Hyub Han, Philippe Mathurin, Philippe Merle, Richard S. Finn, Tobias Müller, Fiona Taylor, Mike Greenwood, Damir Begic, Marina Tschaika, Christine Yip, Emma Pranschke, Kim Cocks, Gwilym Thompson, Steven I Blum, Tami Wisniewski, Bruno Sangro; Medical Oncology, Centre Eugene Marquis, Rennes, France; The University at Hong Kong, Hong Kong, China; Center for Liver Cancer, National Cancer Center Korea, Goyang-Si, South Korea; Kindai University Faculty of Medicine, Osaka, Japan; Severance Hospital, Yonsei University, Seoul, South Korea; Centre Hospitalo-Universitaire Claude Huriez, Service d'Hépatologie, Lille, France; Hepatology Unit, Croix-Rousse Hospital, Lyon, France; Geffen School of Medicine, UCLA Medical Center, Santa Monica, CA; Charité-Universitätsmedizin Berlin, Campus Virchow Klinikum, Berlin, Germany; Adelphi Values, Boston, MA; Adelphi Values, Bollington, United Kingdom; Bristol-Myers Squibb, Princeton, NJ; Bristol-Meyers Squibb, Uxbridge, United Kingdom; Clinica Universidad de Navarra and CIBEREHD, Pamplona, Spain

Background: SOR is approved as 1L therapy for pts with aHCC, but there is still an unmet need to help improve or maintain HRQoL. This phase 3 study compared HRQoL of NIVO vs SOR as 1L therapy in pts with aHCC as an exploratory endpoint. **Methods:** FACT-Hep was administered cycle 1, day 1 and every other cycle. The effect of NIVO vs SOR on HRQoL using FACT-Hep was assessed via repeated measures mixed models (MMRM). Kaplan–Meier curves and Cox proportional-hazards models determined between-treatment differences in time to first and time until definitive deterioration (TTD/TUDD) based on prespecified thresholds for minimally important differences. The GP5 item from FACT-Hep was used to assess the burden associated with treatment side effects. **Results:** 743 pts with aHCC were randomized to NIVO (n = 371) or SOR (n = 372). Median OS was 16.4 mo for NIVO, 14.7 mo for SOR (HR 0.85 [95% CI 0.72–1.02]; *P* = 0.0752). ORR was 15% for NIVO, 7% for SOR (OR 2.41 [95% CI 1.48–3.92]). HRQoL scores were completed at baseline by 94.6% and 92.5% of participants, respectively, and were similar (FACT-Hep total: NIVO 140.7 [SD 21.5] and SOR 140. 6 [SD 19.1]. Questionnaire compliance rates exceeded 70% at most visits. MMRM analyses yielded clinically meaningful and statistically significant least squares means differences favoring NIVO on FACT-Hep total (10.1 [95% CI 7.3–13.0]), physical well-being (PWB; 2.0 [95% CI 1.4–2.6]), and functional well-being (FWB; 2.5 [95% CI 1.7–3.2]) scores. No sub-scales favored sorafenib. TTD was significantly delayed in NIVO for FACT-Hep total (HR 0.62 [95% CI 0.51–0.74]), PWB (HR 0.62 [95% CI 0.52–0.74]), FWB (HR 0.73 [95% CI 0.61–0.88]), and hepatobiliary cancer subscale (HR 0.57 [95% CI 0.48–0.69]). TUDD results were consistent with TTD. A greater proportion of NIVO pts did not experience increased burden of side effects (50%–67.7%) compared with SOR (26.8%–45%) based on the GP5 item. **Conclusions:** These patient-reported findings demonstrate that pts taking NIVO had superior HRQoL and reduced side effect burden, further supporting clinical data showing a treatment benefit for 1L NIVO in aHCC. Clinical trial information: NCT02576509. Research Sponsor: Bristol-Myers Squibb.

484 Poster Session (Board #A9), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Effect of baseline medications on response to immunotherapy in hepatocellular carcinoma.

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Background: Immunotherapy (IO) response rates in advanced hepatocellular carcinoma (HCC) are less than 20%. The microbiome has been shown to mediate IO response in experimental models, and clinical studies have observed that antibiotics, especially prior to IO initiation, are associated with reduced IO response. We reasoned that commonly prescribed antacid medications, such as proton pump inhibitors (PPIs) and histamine receptor antagonists (H2RAs), which are known to influence the microbiome, may also influence IO response. **Methods:** This is a retrospective chart review-based study of 95 patients with advanced HCC treated with IO at a single academic medical center. The primary outcome was overall survival (OS). The secondary outcome was overall response rate (ORR). The primary predictors were antibiotic or antacid exposure in the 60 days prior to IO. A secondary predictor was antibiotic or antacid exposure in the 30 days prior to IO. **Results:** The cohort was predominantly male (84%), was racially diverse (31% White, 23% Black, 23% Asian, 13% Hispanic), and had a median age of 65 years. There were 49 deaths with a median follow up of 0.96 years. The most common underlying liver diseases were HCV (49%), HBV (31%), and NASH (11%). The majority of patients had cirrhosis (80%), with a median Child Pugh score of 6. Within 60 days before IO, 25 patients received antibiotics, 40 received PPIs and 5 received H2RAs. Most patients receiving antibiotics also received a PPI (92%). The median duration of antibiotics was 5 days. Neither antibiotic nor antacid exposure within 60 or 30 days prior to IO was significantly correlated with OS in univariate or multivariate analyses, nor were they correlated with ORR. **Conclusions:** No significant associations between baseline exposure to antibiotics and antibiotics and OS or ORR were identified in this single-institution study. Larger observational studies or mechanistic studies are needed to clarify interactions between medications, the microbiome, and IO response. Research Sponsor: None.

Univariate Cox regression for overall survival.

Variable	Hazard Ratio	P value	Lower .95	Upper .95
Antibiotics, 60d	1.36	0.32	0.74	2.49
PPI, 60d	1.35	0.30	0.77	2.39
H2RA, 60d	0.76	0.71	0.19	3.14
Antacid, 60d	1.24	0.46	0.70	2.18

485 Poster Session (Board #A10), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Potential use of lenvatinib for patients with unresectable hepatocellular carcinoma beyond progression of sorafenib treatment: A real-world evidence and in vitro assessment with protein phosphorylation array.

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Background: No information is available on the efficacy and safety of lenvatinib (LEN) as a second/third-line treatment for unresectable hepatocellular carcinoma (HCC) after sorafenib (SOR) therapy. We evaluated the characteristics and the therapeutic efficacy and safety of LEN as a second- and third-line treatment as well as first- treatment for unresectable HCC patients in clinical settings. Moreover, to rationalize these clinical findings in vitro, we assessed the anti-tumor activity of LEN on SOR-resistant cell line and performed a comprehensive phosphorylated protein array analysis associated with 377 signal transduction pathways using SOR-resistant and parental HCC cells. **Methods:** We retrospectively enrolled 51 unresectable HCC patients. Radiologic responses in 41 patients were evaluated by modified RECIST. Active signal transduction pathways in the cells were identified by protein array analysis, including 1205 proteins. **Results:** The evaluated patients comprised 25 TKI-naive (first- line), 7 intolerant to SOR (second-line), and 9 patients resistant to regorafenib (third-line). The ORRs were 64% in first-line, 42.8% in second-line, and 22.2% in third-line groups (first-line vs. third-line $p < 0.05$). The OS in the first-line was significantly longer than that in third-line group ($p < 0.05$). Patients with better liver functional reserve (Child score, ALBI grade) exhibited higher ORR and longer OS. LEN was well-tolerated in the second/third-line treatment. The IC50 value of LEN against PLC/PRF5-R2 (30 μM) was significantly higher than that against PLC/PRF5 (6.4 μM). LEN significantly inhibited more signal transduction pathways related to FRS2, a crucial FGFR downstream molecule, in PLC/PRF5 than in PLC/PRF5-R2 cells. **Conclusions:** Our study indicates that LEN was active and safe in the second/third-line treatment for unresectable HCC. LEN seems more effective for HCC patients with better hepatic reserve function, or before TKI-resistance is acquired because of the partial cross-resistance to SOR. Research Sponsor: None.

486 Poster Session (Board #A11), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

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

Ahmed Omar Kaseb, Dan G. Duda, Hop Sanderson Tran Cao, Yehia I. Abugabal, Luis M. Vence, Asif Rashid, Roberto Pestana, Jorge M. Blando, Shalini Singh, Jean-Nicolas Vauthey, Manal Hassan, Hesham M. Amin, Aliya Qayyum, Yun Shin Chun, Ching-Wei David Tzeng, Divya Sakamuri, Robert A. Wolff, James C. Yao, James Patrick Allison, Padmanee Sharma; The University of Texas MD Anderson Cancer Center, Houston, TX; Massachusetts General Hospital, Boston, MA; Baylor College of Medicine, Houston, TX; University of Texas MD Anderson Cancer Center, Houston, TX; MD Anderson Cancer Center, São Paulo, Brazil; Department of Immunology, The University of Texas MD Anderson Cancer Center, Houston, TX; The University of Texas-MD Anderson Cancer Center, Houston, TX; University of Kentucky, Lexington, KY

Background: In HCC, surgical resection is associated with high recurrence rates, and no effective neoadjuvant or adjuvant therapies currently exist. Immunotherapy using anti-PD-1 antibodies has shown promised but limited increase in survival in advanced disease. To maximize the benefit, we are studying the efficacy and safety of anti-PD-1 (nivolumab) and anti-CTLA-4 (ipilimumab) antibodies against HCC for resectable HCC. **Methods:** This is a randomized phase II trial of nivolumab (Arm A) or nivolumab + ipilimumab (Arm B) as pre-operative treatment for patients with HCC who are eligible for surgical resection. Pts are given nivolumab 240 mg every 2 weeks (wks) for a total of 6 wks. Pt in Arm B are treated concurrently with ipilimumab 1 mg/kg every 6 wks. Surgical resection occurs within 4 wks after last cycle of therapy. Pts continue adjuvant immunotherapy for up to 2 years after resection. The primary objective is the safety/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:** Twenty-six patients were enrolled at the time of this interim analysis, of which 20 have evaluable data. Most pts (55%) were between 60-70yo and male (75%). Four pts were HCV-positive, 6 had HBV and 10 had no hepatitis. 20 patients proceeded with resection as planned, surgery was aborted for 5 patients (1 for frozen abdomen and 2 development of contralateral liver nodule). Three are still receiving preoperative therapy. Pathologic complete response (pCR) was observed in 5/20 evaluable patients – 2 in Arm A and 3 Arm B (25% pCR rate). Five patients in Arm B and 1 in Arm A experienced grade 3 or higher toxicity prior to surgery. No grade 4 or higher toxicity were observed. **Conclusions:** We report a pCR rate of 25% for resectable HCC after preoperative immunotherapy in a randomized phase II pilot trial. Treatment was safe and surgical resection was not delayed. The study is ongoing. These promising results may contribute to a paradigm shift in the perioperative treatment of resectable HCC. Clinical trial information: NCT03510871. Research Sponsor: Bristol-Myers Squibb SPORE.

487 Poster Session (Board #A12), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Economic burden and patterns of care in patients with advanced hepatocellular carcinoma.

Abdalla Aly, Elisabetta Malangone-Monaco, Virginia Noxon, Caroline Henriques, Fernando Benavente, Amy K. Kim; AstraZeneca, Gaithersburg, MD; IBM Watson Health, Cambridge, MA; Johns Hopkins School of Medicine, Baltimore, MD

Background: Hepatocellular carcinoma (HCC) is often diagnosed in advanced stages. While sorafenib has been the standard of care for advanced HCC, treatment guidelines are not clearly defined. We studied real world systemic lines of therapy (LOT) and economic burden in HCC patients. **Methods:** The MarketScan database was used to identify patients newly diagnosed with HCC (ICD-9 155.0, ICD-10 C22.0, C22.8) from 2011-2018 and continuously enrolled for ≥6 months prior and ≥1 month post HCC diagnosis. Patients with prior liver transplantation or metastasis, or other primary cancers, pregnancy, or clinical trial participation at any time were excluded. Systemic LOT were identified and ended due to discontinuation, switch, or end of follow up. Transarterial procedures (chemoembolization [TACE], radioembolization [TARE]) were also reported. **Results:** A total of 1,558 patients (mean age, 62; 78% male; median follow up, 8.8 months) were studied. The first LOT was mostly sorafenib (78%). The median time from HCC diagnosis to start of sorafenib was 43 days. The median duration of therapy on sorafenib was 60 days, with patients ending sorafenib use due to discontinuation (40%) or switching (6%). Only 16% of patients received second LOT, of which 10% were PD-1 inhibitors. Use of TACE and TARE over the follow up period was 15% and 12%, respectively. TACE was more prevalent prior to first LOT (11%) compared to during first LOT (4%) and between first and second LOT (6%). This trend was also observed for TARE (7%, 3%, and 4%, respectively). Patients incurred a mean all-cause total cost of $181,036 and $17,235 per-patient per-month (PPPM), of which $9494 were HCC-specific (Table). **Conclusions:** Most patients received sorafenib as first line in advanced HCC, but only for 2 months. Only 16% of patients receive second line therapy. HCC patients have a high economic burden and there is a need for more effective and safe treatments. Research Sponsor: AstraZeneca.

HCC-Specific PPPM Cost	Mean (SD)
Total	$9,494 ($9,475)
Prescription chemotherapy	$3,071 ($3,244)
Inpatient	$1,937 ($5,070)
Radiology	$996 ($2,724)
Embolization procedure	$811 ($2,698)
Outpatient chemotherapy	$313 ($1,672)
Laboratory	$242 ($453)
Office visits	$184 ($206)
ER	$63 ($387)
Other outpatient service	$1,877 ($3,350)

488 Poster Session (Board #A13), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

IGF-1 Child-Turcotte-Pugh score as a predictor of overall survival to therapy in CTP-A, BCLC stage C patients with advanced hepatocellular carcinoma.

Yehia I. Abugabal, Aliya Qayyum, Manal Hassan, Lianchun Xiao, Dan G. Duda, Rikita Hatia, Sunyoung S. Lee, Robert A. Wolff, Roberto Pestana, Jeffrey Morris, 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; The University of Texas-MD Anderson Cancer Center, Houston, TX; Massachusetts General Hospital, Boston, MA; Roswell Park Comprehensive Cancer Center, Buffalo, NY; MD Anderson Cancer Center, São Paulo, Brazil; Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Child-Turcotte-Pugh (CTP) A is the standard population for active HCC therapy. The IGF-CTP score, comprises levels of type 1 insulin-like growth factor (IGF-1), bilirubin, INR, and albumin, significantly improved the prediction of overall survival (OS) in recently published studies. Our current study aimed to investigate the accuracy of the IGF-CTP score in predicting OS in HCC Child-Pugh A patients (pts) treated with local and/or systemic therapies (tx). The overall hypothesis is that the IGF-CTP score can further distinguish CP-A pts in terms of overall survival, PFS. **Methods:** Between 2014 and 2018, a total of 274 pts with new advanced HCC BCLC stage who had available baseline plasma IGF-1 level were retrospectively enrolled. Clinicopathologic features and treatment history were collected. We calculated IGF-CTP scores, used Kaplan-Meier method and log rank test to estimate and compare time to event outcomes between subgroups of patients. **Results:** 198 pts were CTP Class A, 209 patient underwent systemic tx, 65 underwent local tx [see table]; 161 were re-classified as IGF-CTP-A with a median OS of 16.09 months (95% CI = 13.06 to 23.29 months) ($p < 0.0001$), whereas 37 patients were reclassified as intermediate risk (IGF-CTP-B) and had significantly shorter OS of 10.66 months (95% CI = 5.49 to 26.51) ($p < 0.0001$). **Conclusions:** The results of this study support our biologically-driven hypothesis that IGF-CTP score is predictive of overall survival to therapy in advanced HCC treated with local and/or systemic therapy. Among HCC pts with CTP-A class, some are reclassified as IGF-CP-B/C and were found to have significantly poorer prognosis in terms of shorter OS. Future validation of the predictive ability of our IGF-1 score may lead to adopting it as a stratification tool in clinical trials as well as to predict HCC outcome and guide therapy decision in routine practice. Research Sponsor: U.S. National Institutes of Health.

Therapy	Name	Frequency	Percent
Local therapy	Y90 or TACE	35	12.7%
	Surgery or RFA	30	10.9%
Systemic therapy	Sorafenib alone	136	49.6%
	Sorafenib+ Local	35	12.8%
	Other systemic	38	13.8%
Total		274	100%

489 Poster Session (Board #A14), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Impact of population center (PC) size on access to care in advanced hepatocellular carcinoma (HCC).

Irene S. Yu, Shiru Lucy Liu, Valeriya O. Zaborska, Tyler Raycraft, Janine Marie Davies; BC Cancer, Vancouver, BC, Canada; University of British Columbia, Vancouver, BC, Canada; British Columbia Cancer Agency-Centre for the Southern Interior, Kelowna, BC, Canada

Background: To evaluate access to subspecialists, local therapies, treatment at a specialized HCC center, and survival in advanced HCC patients (pts) based on geographical distribution. **Methods:** Retrospective chart review was performed on HCC pts who received sorafenib in British Columbia from 2008 to 2016. Pts were stratified by Statistics Canada PC size criteria: large urban PC (LUPC), medium urban PC (MUPC), and small urban PC (SUPC). Chi-square tests and Kaplan Meier were used to analyze the groups. **Results:** Of 288 pts, geographical distribution was: LUPC 75%, MUPC 16%, SUPC 8%, and rural 0.3%. Age, gender, and ECOG performance status were similar; a higher proportion of Asians (50 vs 9 vs 4%), Child Pugh A (93 vs 83 vs 83%), and hepatitis B (37 vs 15 vs 4%) was observed in LUPC vs MUPC and SUPC, respectively. SUPC pts were less likely to see a hepatologist (p=0.04, Table); access to other subspecialists was similar. Pts from LUPC were more likely to have transarterial chemoembolization compared to MUPC and SUPC (38 vs 20 vs 21%; p=0.04); receipt of other local therapies was similar. Sixty percent were treated at a specialized HCC center and were more likely to see a hepatologist (83 vs 19%), hepatobiliary surgeon (57 vs 42%), and/or interventional radiologist (32 vs 13%) (all $p<0.01$). Median OS was higher for pts treated at a HCC center (24.7 vs 13.2 mo, $p<0.01$), but similar when stratified by PC size (overall mOS 19.3 mo, p=0.59). **Conclusions:** Geography did not significantly impact access to care or survival, but pts treated at a specialized HCC center have improved survival. Further research is needed to better understand social and clinical factors that influence these findings. Research Sponsor: None.

Access to Specialists/Local Therapies.

	Rural N, %	SUPC N, %	MUPC N, %	LUPC N, %	P value
Hepatology	1 (100)	9 (38)	22 (48)	134 (62)	0.04
Gastroenterology	1 (100)	6 (25)	9 (20)	67 (31)	0.17
Internal Medicine	0 (0)	7 (29)	12 (26)	34 (16)	0.17
Hepatobiliary	1 (100)	13 (54)	20 (44)	112 (52)	0.55
General Surgery	0 (0)	5 (21)	10 (22)	28 (13)	0.36
Interventional Radiology	0 (0)	5 (21)	8 (17)	48 (27)	0.50
Resection	0 (0)	8 (33)	11 (24)	59 (27)	0.78
Ablation	0 (0)	3 (13)	6 (13)	34 (16)	0.92
Alcohol Injection	0 (0)	0 (0)	3 (7)	10 (5)	0.66
TACE	0 (0)	5 (21)	9 (20)	82 (38)	0.04
TARE	0 (0)	1 (4)	0 (0)	11 (5)	0.48

490 Poster Session (Board #A15), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Efficacy and safety of lenvatinib (LEN) in Korean patients (pts) with advanced hepatocellular carcinoma (aHCC): Multicenter retrospective analysis.

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Background: LEN has demonstrated the efficacy and safety in pts with aHCC as first-line treatment in the pivotal REFLECT trial. Further evaluation in real-world setting is necessary to measure the clinical outcomes of LEN in daily practice. **Methods:** This is a multicenter retrospective analysis from 3 Korean referral cancer institutions. Between September 2018 and August 2019, a total of 74 pts received LEN for the management of BCLC B or C aHCC, and 66 pts who had at least one follow-up visit after the start of LEN were included in this analysis. **Results:** Median age was 58 years (range, 19-81), and 46 pts (69.7%) were male. Baseline characteristics were as follows; Child-Pugh class A/B/C in 46 (69.7%)/14 (21.2%)/6 (9.1%), BCLC B/C/D in 1 (1.5%)/63 (95.5%)/2 (3.0%), prior systemic therapy in 25 (37.9%) including 14 (21.2%) with prior immune checkpoint inhibitors (ICIs). LEN was used as first/second/third to fourth lines of therapy in 41 (62.1%)/13 (19.7%)/12 (18.2%) pts, and 27 (40.9%) had extensive disease extent excluded in the REFLECT trial. With a median follow-up duration of 4.8 months (95% CI, 3.4–6.1), the median PFS and OS were 4.6 (95% CI, 3.2-6.0) and 7.5 months (mo) (95% CI, 3.7–11.2), respectively, in overall pts: first-line setting, 4.2 (95% CI, 3.2-5.2) and 6.5 mo (95% CI, 5.0-8.1), respectively; ≥ second-line setting, 6.1 mo (95% CI, 3.6–8.5) and not reached, respectively. In pts with prior ICIs, median PFS was 6.1 mo (95% CI, 1.8-8.4) and median OS was not reached. According to the RECIST v 1.1, response rates and disease control rate were 12.1% and 71.2%, respectively, in overall pts. The most common grade 3-4 toxicities were hyperbilirubinemia (n=9, 13.6%), AST elevation (n=5, 7.6%), diarrhea (n=4, 6.1%) and fatigue (n=4, 6.1%). **Conclusions:** LEN was effective and well tolerated in pts with aHCC in Korean real-life setting. Research Sponsor: None.

491 Poster Session (Board #A16), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Eligibility for second-line therapy in patients with advanced hepatocellular carcinoma (aHCC): A BC Cancer population-based study.

Erica S. Tsang, Janine Marie Davies, Jonathan M. Loree, Howard John Lim, Daniel John Renouf, Sharlene Gill; BC Cancer, Vancouver, BC, Canada; British Columbia Cancer Vancouver, and CCTG Co-chair, Vancouver, BC, Canada; BC Cancer Agency, Vancouver, BC, Canada

Background: Evidence supporting second-line therapies has become available for aHCC, including regorafenib, cabozantinib, ramucirumab, and nivolumab. The optimal second-line treatment regimen is unknown, and there remains limited real-world data about the eligibility of patients for second-line therapies in aHCC. We aimed to characterize the real-world eligibility and use of second-line therapies post sorafenib. **Methods:** We identified all patients with aHCC who received ≥1 cycle of first-line sorafenib between January 1, 2014 and December 31, 2017 across 6 centers in British Columbia (BC), Canada. All patients were required to be Child-Pugh class A for initiation of sorafenib in BC. Baseline characteristics and clinical outcomes were reviewed. Eligibility for second-line therapy was determined using the RESORCE and CELESTIAL study entry criteria. **Results:** Of 144 patients with advanced HCC who received ≥1 cycle of first-line sorafenib, median age was 65.3 years (range 32.2-83.4) and 85% were male. Median duration of sorafenib was 2.6 months. 12 patients (8%) went on to receive second-line treatment. 37 patients (26%) were deemed eligible for second-line systemic therapy. Primary reasons for ineligibility included ECOG ≥2 (58%), and deterioration to Child-Pugh status B (28%). On Cox regression, improved survival was associated with better ECOG and recurrent disease. (Table). Kaplan-Meier analysis demonstrated that eligibility for second-line treatment was associated with improved median overall survival from end of first-line treatment (8.5 vs. 5.1 months; $p<0.01$). **Conclusions:** Only a minority of real-world patients with aHCC were eligible for second-line therapies based on second-line trial criteria. Given the high-rate of attrition, improved first-line treatment options are urgently needed.
Research Sponsor: None.

	Hazard Ratio (95% CI)	p-value
Age	0.51 (0.97-1.01)	0.51
Baseline ECOG	1.81 (1.35-2.42)	**<0.01**
Number of metastatic sites	1.11 (0.88-1.40)	0.39
Child-Pugh score (B vs. A)	1.83 (0.88-3.80)	0.11
Recurrent disease (vs. de novo)	0.42 (0.27-0.64)	**<0.01**

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

Biliary tract cancer (BTC) in the elderly: A real-world tertiary cancer center experience.

Massimiliano Salati, Francesco Caputo, Krisida Cerma, Andrea Spallanzani, Fabio Gelsomino, Chiara Santini, Alessandro Bocconi, Maria Laura Riggi, Gabriele Luppi, Andrea Casadei Gardini, Massimo Dominici; PhD Program in Clinical and Experimental Medicine, University of Modena and Reggio Emilia, Modena, Italy; Department of Oncology and Hematology, University Hospital of Modena, Modena, Italy; Department of Oncology, University of Modena and Reggio Emilia, Modena, Italy; University Hospital of Modena, Modena, Italy; Department of Oncology, University Hospital of Modena, Forli, Italy

Background: Although BTC is mostly a disease of the elderly, only limited data ara available on the optimal management of this patient (pt) population. In fact, older pts are underepresented in clinical trials and results are seldom reported by age group. In this study, we aimed at evaluating pattern of care and treatment outcome in BTC aged ≥ 70 years and comparing them with their younger counterparts. **Methods:** Medical records of BTC followed at the Modena Cancer Centre from 2007 and 2019 were retrospectively reviewed.. Overall survival (OS) was estimated with the Kaplan-Meier curves and compared by log-rank test. Differences between categorical variables were assessed using the chi square test. Univariate and multivariate analyses were performed to assess the impact of covariates on survival. **Results:** A total of 120 BTC patients (49%) ≥ 70 were included in the analysis. 54% (64) were female, 47% (56) had iCCA, 41% (49) GBC, and 12% (15) eCCA. 68% (81) had unresectable locally advanced or metastatic disease. 32% (39) underwent surgical resection, 60% (72) were treated with first-line chemotherapy (1L), while 29% (21) of them went on to receive second-line (2L). No differences in terms of both chance to receive surgery (p=0.59) and survival (p=0.25) were recorded compared to youngers. In the advanced-disease setting, median OS was 8 months and was significantly worse than that of the younger counterparts (p<0.001). Older patients were less likely to receive 1L (p<0.001) and 2L (p<0.001) chemotherapy and doublet regimens (p<0.001). Female gender (p=0.031), ECOG PS 0 (p<0.001), stage III (p<0.001) and NLR>3 (p<0.001) were independently associated with a better prognosis in older BTC receiving 1L, with 1-year OS of 82% (95%CI 68-91, p=0.031). **Conclusions:** In this real-world study, no survival difference was found between older and non-older surgically-treated patients. Contrariwise, elderly BTC were less frequently treated with chemotherapy for advanced disease and their outcome is poorer than youngers. However, clinical and biochemical prognostic have been identified that may assist in selecting older pts more likely to benefit from systemic treatment, both in clinical trials and daily practice. Research Sponsor: None.

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

The impact of skeletal muscle loss for hepatocellular carcinoma treated with lenvatinib.

Mao Okada, Hiroyuki Nakanishi, Masayuki Kurosaki, Kento Inada, Sakura Kirino, Koji Yamashita, Shuhei Sekiguchi, Yuka Hayakawa, Leona Osawa, Wan Wang, Mayu Higuchi, Kenta Takaura, Chiaki Maeyashiki, Shun Kaneko, Nobuharu Tamaki, Yutaka Yasui, Kaoru Tsuchiya, Jun Itakura, Yuka Takahashi, Namiki Izumi; Musashino Red Cross Hospital, Tokyo, Japan; Musaino Red Cross Hospital, Tokyo, Japan; Department of Gastroenterology and Hepatology, Musashino Red Cross Hospital, Musashino, Tokyo, Japan

Background: Many previous reports have shown that skeletal muscle loss (SML) is one of the prognostic factors for hepatocellular carcinoma (HCC) patients treated with sorafenib. However, there are few reports about the impact of SML for the HCC patients treated with lenvatinib. Therefore, we evaluated the relation between SML and overall survival (OS) of HCC patients treated with lenvatinib (LEN). **Methods:** We retrospectively analyzed 50 HCC patients treated with LEN from April 2018 to February 2019. We included 36 patients who continued LEN more than 8 weeks and evaluated CT scans before treatment and after 8 weeks. Skeletal muscle area was measured on axial image at the level of the third lumber vertebra (L3) using sliceOmatic. Skeletal Mass Index (SMI) was calculated by dividing the muscle area (㎠) with square of height (㎡). The definition of myopenia is based on the guideline described by the Japan Society of Hepatology (42㎠/㎡ in men and 38 ㎠/㎡ in women). ΔSMI is a chronological change of SMI for 8 weeks. We calculated decreasing rate of ΔSMI. We evaluated the relation between chronological change of SMI and OS. **Results:** The patients with myopenia at baseline were 12 (33.3 %). The decreasing rate of ΔSMI at 8 weeks was -2.57 % [-5.9, 0.2]. SMI had decreased in 27 patients (75 %) for 8 weeks. There was no significant difference between OS and baseline myopenia (p = 0.2), ALBI grade (p = 0.2), BCLC stage (p = 0.5), up to 7 in or out (p = 0.35), previous TKI treatment (p = 0.15), metastasis (p = 0.91), or vascular invasion (p = 0.12). However, the patients who had decreased SMI had significantly poor prognosis (p = 0.028). In backgrounds, there was no significant difference between patients with or without decreasing of ΔSMI, such as baseline myopenia (p = 0.7), ALBI grade (p = 0.4), BCLC stage (p = 1.0), Child Pugh score (p = 0.8), age (p = 0.6), sex (p = 0.3), up to7 in or out (p = 1.0), previous TKI treatment (p = 0.3), and relative dose intensity at 4 weeks (p = 0.9). **Conclusions:** There was no significant correlation between baseline myopenia and OS. However, chronological decreasing of SMI for 8 weeks was a prognostic factor of HCC patients treated with LEN. Therefore, monitoring and preventing of decreasing of skeletal muscle mass may be important. Research Sponsor: None.

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

Clinical outcome associated with neoadjuvant chemoradiation and orthotopic liver transplantation versus definitive chemoradiation in 49 patients with unresectable, hilar, or extrahepatic cholangiocarcinoma.

Brady S. Laughlin, Molly M. Petersen, Jonathan Ben Ashman, William G. Rule, Mitesh J. Borad, Bashar A. Aqel, Mohamad Bassam Sonbol, Tanios S. Bekaii-Saab, Daniel H. Ahn, Nathan Y. Yu, Todd DeWees, Terence Tai Weng Sio; Mayo Clinic Arizona, Phoenix, AZ; Mayo Clinic, Rochester, MN; Mayo Clinic, Scottsdale, AZ; Mayo Clinic, Phoenix, AZ; Mayo Clinic Cancer Center, Scottsdale, AZ; Ohio State University Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, Columbus, OH; Washington University in St. Louis, St. Louis, MO

Background: Our aim was to compare survival between patients receiving neoadjuvant chemoradiation and orthotopic liver transplantation (OLT group) versus definitive chemoradiation (CRT group) for extrahepatic or hilar cholangiocarcinoma. **Methods:** 49 patients (20 in OLT group vs. 29 in CRT group) with unresectable hilar/extrahepatic cholangiocarcinoma were treated at Mayo Clinic Arizona between Feb. 1998–Sep. 2019. Treatment included external beam radiation therapy (median 4500cGy) and boost (median 900cGy) with either continuous 5-flurouracil (dose range 180–225 mg/m2) or capecitabine (dose range 825–1000 mg/m2 BID) prior to or without OLT. Radiation boosts were delivered with EBRT or bile duct brachytherapy. Patients were between 27.9–84.3 years (median 64.3) at diagnosis. 18 patients had previous diagnosis of PSC. **Results:** Between Feb. 1998–Sep. 2019, 31(63%) of 49 patients died by the end of follow-up. Of patients treated with neoadjuvant therapy and OLT, 7(35%) of 20 patients died. 24(86%) of 28 patients treated with definitive therapy died. The OLT cohort were younger (mean age 56.5 vs. 69.0 years), more likely to have PSC and UC (65% vs. 17%), and had a lower CA 19-9 (median 43 vs. 535)($P < 0.003$). From the end date of radiation, median overall survival was 76.8 months vs. 15.6 months for the OLT and CRT groups, respectively. Survival rates at 3 and 5 years were 78% and 69% in the OLT group compared to 19% and 6% in the CRT group (HR 7.73; 3.04-19.65:($P < 0.0001$)). Progression-free survival (89% vs. 30% at 3 years), and distant metastasis-free survival (88% vs. 66% at 3 years) favored OLT versus CRT alone (HR 5.74;1.12-29.34:($P < 0.02$)). Univariate analysis demonstrated that the method of treatment (OLT vs. CRT) was the only variable associated with better clinical outcomes. **Conclusions:** In patients with unresectable extrahepatic/hilar cholangiocarcinoma, survival was higher in those who underwent chemoradiation and OLT. Patients who received definitive chemoradiation in the absence of OLT were expected to have worse overall, progression-free, and metastasis-free survival. Research Sponsor: None.

495 Poster Session (Board #A20), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Variations in surgical treatment of stage I gallbladder carcinoma impacts survival.

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Background: Variations in surgical care for stage I gallbladder carcinoma (GBC) may be associated with inferior outcomes. The aim of this study was to identify the variations in surgical treatment of GBC. **Methods:** All patients diagnosed with stage I GBC by AJCC 8 criteria from 2004-2013 were identified in the NCDB. Surgical treatment was categorized as cholecystectomy (C), cholecystectomy with lymph node dissection (C+LND), or radical cholecystectomy (RC). Independent predictors of improved overall survival (OS) and extent of surgery were identified by multinomial regression analyses. **Results:** Of 1756 patients with stage I GBC, 26% were T1a, 56% T1b, and 18.5% T1NOS. The majority were White non-Hispanic (61.8%) and female (68.5%), with 55.1% > 70 years of age. Two-thirds of T1a tumors were treated with more aggressive surgery (28% C+LND, 4.2% RC), which did not differ by age. However, only 44.4% of patients with T1b tumors had more aggressive surgery, which was significantly less likely in patients > 70 years, even after controlling for other factors (C+LND (OR:0.60; CI:0.44-0.81), RC (OR:0.52; CI:0.29-0.91)). Five-year OS was 54.34% for T1a and 43.05% for T1b (p = 0.02). After controlling for other factors, both C+LND (HR:0.46, CI:0.26-0.81) and RC (HR:0.31, CI:0.16-0.62) significantly improved 5-year OS for T1b tumors, whereas RC also improved 5-year OS for all patients > 70 years old (p = 0.04). **Conclusions:** A majority of patients with T1b GBC had less than adequate surgery by the current AJCC staging, which significantly decreased survival in all patients. This was especially evident in older patients who were also the least likely to receive more aggressive surgery. Research Sponsor: None.

496 Poster Session (Board #A21), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

The adherence to The American Association for The Study of Liver Disease (AASLD) guidelines in treating patients with hepatocellular carcinoma: Institutional experience.

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Background: The American Association for the Study of Liver Disease (AASLD) guidelines outline an algorithm regarding the treatment modality of choice for patients with hepatocellular carcinoma (HCC) based on Barcelona Clinic Liver Cancer (BCLC) stage. The AASLD guidelines have several limitations and the adherence rate has been reported to be low. The adherence to AASLD guidelines in treating patients with HCC was explored in this study. **Methods:** Between 2017 and 2019, 106 patients with HCC were identified. In our cohort, 70 patients (66%) were discussed in the multidisciplinary tumor board (MDTB) and their first-line treatment modality was selected based on consensus recommendations from the MDTB team members. The adherence rate of MDTB recommendations to AASLD guidelines was calculated. **Results:** Median age was 65 (range 42-90). Males represented 84% while females represented 16%. Caucasians, African Americans and Asians represented 69%, 30% and 1% respectively. BCLC stage 0, A, B, C and D represented 7%, 32%, 23%, 27% and 11% respectively. First-line treatment modality of choice recommended by MDTB is summarized in Table. The overall adherence rate of MDTB recommendations to AASLD guidelines is 60%. For BCLC stage 0, A, B, C and D, the adherence rate was 60%, 86%, 44%,58% and 25% respectively. **Conclusions:** Our MDTB recommendations adherence rate to AASLD guidelines was 60%. The reported low adherence rate to the guidelines suggest that AASLD guidelines would benefit from further refinement and periodic update. Research Sponsor: None.

BCLC stage	Number of Patients	Surgical resection	Ablation	TACE / Yttrium-90	SBRT	OLT	Systemic therapy	BSC
Stage 0	5		3	1/1				
Stage A	22	2	2	8/7			3	
Stage B	16	1	2	4/3	2		4	
Stage C	19		2	4/5	1	1	6	
Stage D	8			1	2		3	2

Treatment modalities for patients with HCC. TACE: transarterial chemoembolization; SBRT: stereotactic body radiotherapy; OLT: orthotopic liver transplant; BSC: best supportive care.

497 Poster Session (Board #A22), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Survival by line of therapy of older patients with advanced biliary tract cancer (BTC).

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Background: Overall survival (OS) in advanced or metastatic BTC has not been adequately described outside the clinical trial setting. Further, real-world descriptions of OS by line of therapy, including in patients who do not receive systemic chemotherapy, are not widely available. In this study, we used data from a recent cohort of US patients available in the SEER-Medicare linked database to examine OS from diagnosis of advanced or metastatic BTC as well as from initiation of first- and second-line treatment. **Methods:** Patients with advanced or metastatic BTC diagnosed between 2010 and 2013 were identified in SEER-Medicare, with follow-up through 2014. Demographic and clinical characteristics were analyzed. The Kaplan-Meier estimator was used to describe OS from diagnosis among all patients, OS from diagnosis among patients who did not receive systemic treatment, and OS by line of treatment, from date of treatment initiation. The Cox proportional hazards model was used to identify demographic and clinical factors associated with survival. **Results:** Of the 1,461 eligible patients aged ≥66 years, 39% had gallbladder, 22% had intrahepatic, 22% had extrahepatic, and 9% had ampulla of Vater cancer. More than two-thirds of patients had stage IV disease, and 38% of patients (n = 558) received systemic chemotherapy. Systemic treatment patients were somewhat younger, more likely to be white, have stage IV cancer and less likely to have mobility limitations (24% vs. 38%) than patients who did not receive systemic treatment. Among all patients, unadjusted median OS from diagnosis was 5.6 months (95% CI 5.0-6.1). Among patients who were not treated, unadjusted median survival was 3.3 months (n = 903; 95% CI 2.8-4.0) from diagnosis. When OS was evaluated by line of treatment, median OS was 8.2 months (n = 558; 95% CI 7.6-9.0) from first-line initiation and 5.6 months (n = 220; 95% CI 4.6-6.5) from second-line initiation. **Conclusions:** Among newly diagnosed, older US patients, less than half receive systemic treatment for their advanced BTC, and outcomes among both treated and untreated patients remain poor. There is an immediate need for better therapies to treat patients with advanced BTC. Research Sponsor: Merck KGaA, Darmstadt, Germany and GlaxoSmithKline.

498 **Poster Session (Board #B1), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

Primary liver angiosarcoma and factors associated with improved outcomes: An analysis of the National Cancer Database.

Prantesh Jain, Gino Cioffi, Nirav Patil, Aman Opneja, Asrar Alahmadi, David Lawrence Bajor, Joel N. Saltzman, Patrick J. Getty, John Brian Ammori, Aashish D. Bhatt, David B. Mansur, Richard T. Lee, Ankit Mangla; Department of Hospital Medicine, Cleveland Clinic, OH, Cleveland, OH; Department of Population and Quantitative Health Sciences, Case Western Reserve University School of Medicine, Cleveland, OH; University Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, OH; University Hospitals Seidman Cancer Center, Cleveland, OH; University Hospitals Seidman Cancer Center, Case Comprehensive Cancer Center, Case Western Reserve University, Cleveland, OH; Case Western Reserve University, School of Medicine, Cleveland, OH; Univ Hosp Case Medcl Ctr, Cleveland, OH; Univ Hosps Seidman Cancer Ctr, Cleveland, OH; The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Primary liver angiosarcoma (LAS) is a rare and aggressive tumor of the liver. In this analysis of the national cancer database (NCDB) we sought the risk of mortality and factors associated with survival amongst patient diagnosed with LAS. **Methods:** Patients diagnosed with hepatocellular carcinoma (HCC) or LAS from 2004 – 2014 were identified in the NCDB. The Kaplan-Meier method with the log-rank test was used to calculate survival for HCC and LAS patients. Additional analyses were performed on the cohort with LAS to assess the impact of surgery, chemotherapy, radiation therapy (RT) and facility type on overall survival (OS). Multivariable analyses using cox proportional methods, adjusted for age, sex, Charlson/Deyo score, race, ethnicity, insurance status, facility location and type, surgery status, and chemotherapy status were performed to obtain adjusted hazard ratio (aHR). **Results:** Total of 118,066 patients with HCC and 346 patients with LAS were identified in the database. Median survival for HCC patients was 11.9 months (95% CI: 11.7-12.2) and 2.0 months for LAS patients (95% CI: 1.8 – 2.4). Risk of mortality was higher for patients with LAS compared to those with HCC (aHR (95% CI): 2.23 (1.97 - 2.53), $p < .0001$). Among the LAS patients, those who received surgery had a median survival of 8.6 months (95% CI: 5.6 - 17.3), and 1.8 months for those who did not (95% CI: 1.48 - 1.94). Risk of mortality was lower in patients who received surgery compared to those who did not (aHR (95% CI): 0.23 (0.15 - 0.37), $p < .0001$). Patients treated at and academic center had a higher median survival (3.3 months, 95% CI: 2.2 - 4.1) then those treated at a non-academic center (1.5 months, 95% CI: 1.2 - 1.8). Though, there was no significant difference in OS (aHR (95% CI): 0.48 (0.21 - 1.10), $p = 0.082$). A very small number of patients received chemotherapy or RT to conduct a meaningful analysis. **Conclusions:** Patients diagnosed with primary LAS have a worse OS compared to those with HCC. Amongst patients with primary LAS, surgical resection is associated with best survival outcomes. Treatment at an academic center is associated with better median survival, although OS did not reach statistical significance in our analysis. Research Sponsor: None.

499 Poster Session (Board #B2), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Real-world experience of regorafenib in patients with hepatocellular carcinoma: A multicenter United Kingdom study.

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Background: Regorafenib was the first treatment to demonstrate a survival benefit in patients with HCC after progression on sorafenib. The RESORCE trial found that regorafenib improved overall survival with acceptable toxicity, in patients with disease progression on sorafenib who tolerated ≥400mg sorafenib daily and had Child-Pugh A liver function. **Methods:** We performed a multicentre, retrospective, observational study of patients with HCC receiving regorafenib in the UK, following its availability in April 2018. **Results:** Data on a total of 104 patients were included from April 2018–August 2019, and 80.8% were male. Age was collected in 85 patients, with a median of 68 years (range 22–86). 23.5% had NAFLD, 21.2% had ALD, 12.9% had HBV, and 3.5% had HCV. Prior management included sorafenib (100%), TACE (30.8%), resection (12.9%). Duration of sorafenib treatment was evaluable in 99/104 patients, and reported a median of 8.7 months (range 1.8–76.6). Duration of regorafenib treatment was evaluable in 92/104 patients, and reported a median of 3.9 months (range 0.0–15.7). Following treatment with regorafenib, 6 patients (5.8%) achieved partial response, 37 (35.6%) achieved stable disease and 45 (43.3%) had progressive disease as the best response. 15 (14.4%) were not assessed and 1 (1.1%) had mixed response. Survival data is immature with 62/101 (61.4%) patients alive at the time of census with median survival currently 6.5 months. Fatigue was the most frequent AE, with 69/88 patients (85.2%) for all grades. 12/88 patients (14.8%) had Grade 3 fatigue. Other significant AEs include hand-foot syndrome (6/85 patients [7.3%] had Grade 3) and diarrhoea (4/83 patients [4.9%] had Grade 3). **Conclusions:** The population in our real-world experience of regorafenib for HCC had a similar duration of prior sorafenib to those in the RESORCE trial. However, there was different balance of aetiologies with a lower proportion of patients with HBV and HCV. The rate of partial response is similar to the RESORCE trial with fewer patients achieving stable disease. The incidence of fatigue was higher, but the incidence of hand-foot syndrome and diarrhoea were lower. Further expansion and follow-up of this population is warranted. Research Sponsor: Bayer Pharmaceutical/Biotech Company.

500 Poster Session (Board #B3), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Insurance status and cholangiocarcinoma: A NCDB analysis.

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Background: There is an increasing rise of cholangiocarcinoma though the cause is unclear. Cholangiocarcinoma is more often than not incurable at diagnosis and associated with a high mortality rate. Our goal was to compare survival of patients with differing insurance types diagnosed with cholangiocarcinoma identified in the National Cancer Database (NCDB). **Methods:** We identified 5,638 patients with cholangiocarcinoma in the NCDB diagnosed between 2004-2014. Patients included were categorized as having no insurance, private insurance, Medicaid, or Medicare were included. Between-insurance survival differences were estimated by the Kaplan-Meier method and associated log-rank tests; Tukey-Kramer adjusted $p < .05$ indicated statistical significance. **Results:** Statistically significant survival differences were indicated between all insurance groups (all adjusted $p < 0.05$), such that privately insured patients had the highest median survival. The discrepancy in survival between uninsured and privately insured patients was the largest (6.5 months vs 13.1 months, respectively). Medicaid patients on average had a survival of 7.5 months, while Medicare patients had a median survival of 7.8 months. 2.8% of uninsured patients presented with stage I cholangiocarcinoma, whereas 34% of privately insured patients presented with stage I cholangiocarcinoma. More Medicare patients were treated at community cancer programs compared to privately insured patients (56.7% vs 30.7%, respectively). Likewise, more Medicare patients were treated at academic/research programs compared to those with private insurance, Medicaid, or those who were uninsured (44.7% vs 38.7% vs 7.2% vs 3.7%, respectively). **Conclusions:** Our study shows the discrepancies in survival between patients with differing insurance statuses. Of all insurances, those privately insured had the largest median survival. Research Sponsor: None.

Median survival and percentage surviving.

	Median Survival in Months	Patients Alive at 6 Months (%)	Patients Alive at 12 Months (%)	Patients Alive at 24 Months (%)
Uninsured	6.5	51.4	34.8	19.2
Privately Insured	13.1	67.7	52.4	31.6
Medicaid	7.5	54.2	41.1	25.0
Medicare	7.8	55.1	40.2	24.0

501 Poster Session (Board #B4), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Role of hepatologists in management of hepatocellular carcinoma in the new era of transplant oncology.

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Background: There have been global efforts to manage hepatobiliary malignancies such as hepatocellular carcinoma (HCC) in a multidisciplinary setting under the concept of transplant oncology. We published preliminary data of hepatology-directed treatment of HCC (Ann Hepatol 2019). However, the actual role of hepatologists in this setting is not well defined. **Methods:** We evaluated 107 patients with newly diagnosed HCC, undergoing locoregional therapy (LRT) as a first therapy (microwave ablation, TACE, TARE or SBRT) in our institution between 1/2017 to 2/2019 and being followed until 8/2019. Patients were divided into three groups based on referral pathways: outside referral directly to oncologists (O-group, n=24), internal referral from hepatologists to oncologists (H/O-group, n=62) and hepatologist directed HCC treatment (H-group, n=21). The hepatologist performed all microwave ablations in H-group; rest of the LRTs were performed by either interventional radiology or radiation oncology. **Results:** The baseline gender, etiology of liver disease, MELD score, Child-Pugh score, BCLC stage, CLIP score, AFP and proportion of patients within Milan criteria were similar between 3 groups (p=n.s.). However, O-group included older patients (median 70 vs 63/62 y.o., $p<0.01$), and had larger HCC size (median diameter 41 vs 26/28mm, $p<0.01$). In H-group, there were more cases discussed in multidisciplinary tumor boards (77% vs 46%, p=0.012) and referrals for liver transplantation (71% versus 50%, p=0.046). Time between the diagnosis and the first procedure was shorter in H-group than others (median 53 vs 69 days, p=0.048). The rate of complete response/partial response per mRECIST criteria was highest in H-group (91 vs 66%, p=0.024). The 2-year cumulative survival was comparable among three groups (70, 74 and 76% in O-group, H/O-group and H-group, respectively, p=0.4). **Conclusions:** Hepatologists are often the first point of contact and can play a key (and even more direct) role in subsequent management of HCC. To further accomplish the concept of multidisciplinary approach and transplant oncology, primary/secondary care institutions might be a potential target for intervention for outreach. Research Sponsor: None.

502 Poster Session (Board #B5), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Association of socioeconomic disparities with underutilization of palliative care in patients with metastatic foregut cancer.

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Background: Metastatic foregut cancers (MFC) are frequently associated with debilitating symptoms that have significant negative impact on patients' quality of life. Palliative care (PC) is effective in mitigating disease-, psychosocial-, and treatment-related effects. However, PC remains heavily underutilized. The aim of our study was to characterize the rate of PC utilization in MFC and determine the impact of various clinicopathologic and socioeconomic factors associated with the receipt of PC. **Methods:** We conducted a retrospective review of 277,957 National Cancer Database patients diagnosed with MFC between 2004-2013. Chi-squared tests were used to analyze differences between groups. Logistic regression was performed to assess the impact of factors on the likelihood of receiving PC. **Results:** PC utilization increased among all groups over time (12.3% 2004-2006 vs. 14.7% 2007-2010 vs. 16.4% 2011-2013 for all cancers). Female sex, Medicaid, median income $<$ $46,000/year, higher education level, higher Charlson/Deyo Score, and pancreatic or biliary cancers were associated with increased likelihood of PC interventions. Additionally, patients treated at an academic center or integrated network cancer program were more likely to receive PC than patients treated in the community setting. When receipt of PC was stratified by race, Hispanics were significantly less likely to have undergone palliative interventions compared to non-Hispanic Whites (OR 0.70, 95% CI 0.66-0.73). Patients with Medicare or private insurance were less likely to receive PC than uninsured patients (OR 0.92, 95% CI 0.87-0.97 and 0.81, 95% CI 0.77-0.89, respectively). **Conclusions:** Differences in palliative care receipt rates exist with regards to racial/ethnic and socioeconomic factors such as insurance status, median household income, and education level. Patients receiving care in the community setting were also less likely to receive palliative care than those treated at academic or integrated network cancer program centers. Further studies are needed to delineate why these disparities exist with regards to palliative care utilization. Research Sponsor: None.

503 Poster Session (Board #B6), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Sociodemographic characteristics as predictors of outcomes in hepatocellular carcinoma: A retrospective cohort study.

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Background: It has been established that race, insurance status, and socioeconomic class play an important role in predicting health care outcomes. However, the impact of these factors has yet to be investigated in the setting of hepatocellular carcinoma (HCC). **Methods:** We designed a retrospective cohort study utilizing data from the SEER program (2007-2015) to identify patients with resectable HCC (N = 28518). Exposures of interest were race (Asian [AS], Black [BL], Native American/Alaska Native [NA/AN], or White [WH]), insurance status (Medicare/Private Insurance [ME/PI], Medicaid [MAID], or No Insurance [NI]), and median household income. Endpoints included: (1) likelihood of surgical recommendation and (2) overall survival. Multinomial logistic regression for relative risk ratio (RRR) and Cox models were used to identify pertinent associations. **Results:** Race, insurance status, and socioeconomic class had statistically significant effects on the likelihood of surgical recommendation and overall survival. AS were more likely to receive a recommendation for hepatic resection (RRR = 1.60; 95% CI: 1.42 – 1.80; Reference Race: BL) and exhibited prolonged overall survival (HR = 0.77; 95% CI: 0.73 – 0.82) as compared to members of other ethnic groups; there was no difference in these endpoints between BL, NA/AN, or WH individuals. Patients who had ME/PI were more likely than those with MAID or NI to receive a surgical recommendation. ME/PI was also associated with superior overall survival. Individuals with a household income in the highest quintile were less likely to receive a surgical recommendation than those in the lower quintiles, but nevertheless demonstrated prolonged survival. **Conclusions:** Race, insurance status, and socioeconomic class have measurable effects on HCC management and outcomes. The underlying causes of these disparities warrant further investigation. Research Sponsor: None.

Race, insurance status, and overall survival.

Variable	Hazard Ratio	P Value
Race	1.00	--
Black	0.77	< 0.001
Asian	0.97	0.149
White	0.88	0.068
Native American/Alaska Native		
Insurance Status	1.00	--
Medicare/Private	1.30	< 0.001
Medicaid	1.17	< 0.001
No Insurance		

504 Poster Session (Board #B7), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Impact of facility type, insurance status, and income on use of single agent chemotherapy (SACT) for advanced hepatocellular carcinoma (AHCC): Analysis of National Cancer Database (NCDB).

Richard T. Lee, Gino Cioffi, Aman Opneja, Asrar Alahmadi, Nirav Patil, Nelroy Jones, David Lawrence Bajor, Joel N. Saltzman, Amr Mohamed, Ankit Mangla, Jill Barnholtz-Sloan; The University of Texas MD Anderson Cancer Center, Houston, TX; Department of Population and Quantitative Health Sciences, Case Western Reserve University School of Medicine, Cleveland, OH; University Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, OH; University Hospitals Seidman Cancer Center, Cleveland, OH; University Hospitals, Cleveland, OH; University Hospitals Seidman Cancer Center, Case Comprehensive Cancer Center, Case Western Reserve University, Cleveland, OH; University Hospitals-Seidman Cancer Center, Cleveland, OH; Case Comprehensive Cancer Center and Department of Population and Quantitative Health Sciences, Case Western Reserve University School of Medicine, Cleveland, OH

Background: This study analyzes the pattern of use of SACT in the treatment and survival of AHCC before and after sorafenib was FDA approved in late 2007. **Methods:** Adult patients diagnosed with HCC and treated with only chemotherapy (CT) from 2004 – 2014 were identified in NCDB database. Patients were analyzed during 3 time frames: 2004–2006 (pre-sorafenib (PS), 2007–2011 (early sorafenib (ES) and 2012–2014 (late sorafenib (LS)). Cox proportional hazards models and Kaplan-Meier method were used for analyses. **Results:** The NCDB contained 31,107 patients with HCC diagnosed from 2004–2014 and treated with CT alone. Patients were generally men (77.3%), >50 years of age (92.5%), and with a variety of T-stages - T1 (31.0%), T2 (23.9%), T3 (28.3%), and T4 (16.9%). The use of SACT was only 6.2% in the PS period, increased to 15.5% in the ES period, and to 22.3% in the LS period ($p<0.0001$). During this later period, the highest proportion of SACT is among academic and integrated network facilities (23.4%) as compared to community facilities (16.4%, $p<0.0001$). The MS of patients with AHCC treated only with CT has improved significantly over the study periods from 10 months (m) (95% CI: 9.5-10.6) to 12.5m (12.0-12.9) to 16m (15.6-16.4, $p< 0.001$). Significant differences in MS were found between facility types in all time frames (Table). Multivariate analysis indicates worse outcomes for patients treated at community cancer programs (HR 1.66, 1.53-1.79) as compared to academic programs as well as for no insurance (HR 1.13, 1.05-1.22) and estimated household income of <$63,000 (HR 1.09, 1.05-1.13). **Conclusions:** Despite an overall improvement in survival for AHCC patients treated with only CT, significant differences in the utilization of SACT and survival exist by facility type, insurance status, and income. Research Sponsor: None.

MS of HCC patients treated with SACT.

	Year of cancer diagnosis		
Facility Type	**2004-2006**	**2007-2010**	**2011-2014**
Academic/Integrated Network Cancer	11.9 (11.0-12.5)	15.6 (15.0-16.3)	19.9 (19.2-20.5)
Community Cancer	6.4 (5.1-8.6)	6.0 (5.4-6.7)	8.1 (7.5-9.6)
Comprehensive Community Cancer	7.9 (7.1-8.8)	8.7 (8.3-9.4)	11.3 (10.6-12)

505 Poster Session (Board #B8), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Early nutritional risk assessment by NRS 2002 to predict survival in patients with advanced biliary tract cancer.

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Background: Biliary tract cancer (BTC) has heterogenous disease with dismal prognosis. We investigated the predictors of overall survival (OS) among Korean patients with advanced BTC according to their baseline nutritional risks estimated by Nutritional Risk Screening (NRS) 2002 score. **Methods:** From September 2006 to July 2017, we retrospectively reviewed the data of 601 patients with BTC. Data on demographic and clinical parameters were collected from electronic medical records, and overall survival (OS) and progression-free survival (PFS) was estimated using the Kaplan–Meier method. Stepwise Cox regression analysis was used to determine the factors associated with survival. Patients with a NRS 2002 score $\leq$2 were classified as "no-risk; " those with a score of 3 were classified as "moderate-risk; " and those with a score of $\geq$4 were classified as "high-risk." **Results:** Following nutritional screening at baseline, 333 patients (55%) were classified as the "no risk" group; 109 patients (18%), as the "moderate risk" group; and 159 patients (27%) as the "high risk" group. Survival analysis showed significant differences in the median OS according to the NRS 2002 groups: "no risk" group: 12.6 months (95% CI: 11.5–13.7); "moderate risk" group: 6.1 months (95% CI: 4.3–8.0); and "high risk" group: 3.9 months (95% CI: 3.2 – 4.6) ($p<0.001$). On the Cox's regression analysis, NRS 2002 score came out as the most independent factor for OS (for "moderate-risk" HR 1.610, 95% CI 1.288-2.027, $p<0.001$; for "high-risk", HR 2.121, 95% CI 1.728-2.612, $p<0.001$), compared with other prognostic factors including liver metastasis, peritoneal seeding, white blood cell count, platelet count, neutrophil-to-lymphocyte ratio, cholesterol, CEA, and CA19-9. **Conclusions:** Our study demonstrated OS of advanced BTC was strongly related to their baseline nutritional status assessed by NRS 2002. Constitutional nutritional assessment can help to improve patient prognosis through proactive and individualized nutritional intervention. Baseline nutritional status should be integrated for implementing prognostic scoring system, which can provide more sophisticated risk stratification of patients with metastatic BTC. Research Sponsor: None.

506 Poster Session (Board #B9), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Determination of quality of care for patients with hepatocellular carcinoma in Nova Scotia.

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Background: Hepatocellular carcinoma (HCC) is the most common primary malignancy found in the liver. Little is known about the outcomes of HCC patients in the province of Nova Scotia (NS). There is suggestion that closer proximity to tertiary cancer center provides better outcomes for HCC patients. We postulate that cancer care for HCC patients differs based on a patient's accessibility to an academic cancer care center. **Methods:** A retrospective chart review of HCC patients diagnosed from 2015 to 2017, looking at referrals patterns, treatments and wait time was undertaken. Patients who live within the urban area of Halifax, NS (N = 97), where the academic cancer center is, was compared to patients who live outside Halifax (rural, N = 70). **Results:** 167 patients were identified with a diagnosis of HCC, which included 139 males and 28 females with median age of 68 years old at HCC diagnosis. During that period, only 35.3% of patients diagnosed with HCC had a tissue diagnosis and 67.7% had a baseline AFP (16% had an AFP $>$ 400). Just over 76% were diagnosed based on clinical features. Surgical intervention occurred in 15.6% and local treatments including radiation and TACE occurred in 35.3% of patients .Referral rate to Medical Oncology (MO) was 37.7%, of which 34.1% of patients had seen a MO at the time of data cut off (09-15-2019). 22 patients were eligible for systemic therapy but only 14 patients received systemic treatment (sorafenib n = 14). **Conclusions:** Initial data suggests patients who live in Halifax appear to have better outcomes than those outside. Further analysis is required to identify what differs between the urban and rural centers accounting for the seen difference in survival. Research Sponsor: None.

	Urban (N = 97) N(%)	Rural (N = 70) N(%)	Total (N = 167) N(%)	p-value
Age > 65	56 (57.7)	54 (77.1)	110 (65.9)	**0.013**
ECOG ≥2	11 (11.3)	4 (5.7)	15 (9.0)	0.277
Surgical Treatments	16 (16.5)	10 (14.3)	26 (15.6)	0.830
Local Treatments	41 (42.3)	18 (25.7)	59 (35.3)	**0.033**
Medical Oncology Consult	36 (37.1)	21 (30.0)	57 (34.1)	0.409
Time from Diagnosis to Surgical assessment (days)	63.65	59.98	62.21	0.796
Time from Diagnosis to MO assessment (days)	82.07	225.66	164.74	**0.012**
Received 1L systemic treatment	8 (8.2)	6 (8.6)	14 (8.4)	1.000
1 yr OS	50 (51.5)	19 (27.1)	69 (41.3)	**0.002**

507 **Poster Session (Board #B10), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

Comparison of the frequency of adverse events requiring interventions determined by telephone follow up in hepatocellular carcinoma patients treated with sorafenib and lenvatinib.

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Background: The REFLECT trial demonstrated that lenvatinib is non-inferior to sorafenib for first-line treatment of unresectable hepatocellular carcinoma (uHCC). However, no comparison of the frequency of adverse events (AEs) requiring interventions has been reported yet between uHCC patients receiving sorafenib and those receiving lenvatinib. At the National Cancer Center Hospital East, Japan, pharmacists conduct telephone follow-up (TF) during the first month after the start of treatment with sorafenib or lenvatinib in uHCC patients, for the purpose of detecting and treating AEs early. The aim of this study was to reveal the frequency of AEs requiring interventions between patients receiving sorafenib and those receiving lenvatinib, based on TF. **Methods:** The characteristics, AEs and contents of intervention by TF of 56 uHCC patients who had been started on treatment with sorafenib and lenvatinib were reviewed retrospectively. The study subjects were 33 patients initiated on sorafenib treatment and monitored by TF from March 2017 to March 2018 (Group S) and 23 patients initiated on lenvatinib treatment and monitored by TF from March 2018 to March 2019 (Group L). **Results:** The total numbers of TFs in Group S and Group L were 91 and 48, respectively. The rate of AEs requiring interventions was significantly higher in Group S as compared to Group L (Group S, 17.6% (16/91); Group L, 4.2% (2/48); p = 0.032). The frequencies of the interventions, including use of supportive treatments (A), withdrawal of sorafenib or lenvatinib (B), and medical examination (C), differed between the two groups (A/B/C: Group S, 8/5/3 times vs. Group L, 2/0/0 times). The most frequently observed AE that necessitated intervention in Group S was the hand-foot syndrome (HFS) (75.0%, 12/16). **Conclusions:** The frequency of interventions for AEs appears to be higher in uHCC patients receiving sorafenib than in those receiving lenvatinib. Although a great number of patients taking sorafenib had symptomatic AEs, such as HFS, early detection of the symptoms through TF contributed to prevention of treatment withdrawal on account of AEs. Research Sponsor: None.

508 Poster Session (Board #B11), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Hepatic adverse events during treatment with immune checkpoint inhibitors (ICI) in cancer patients: A territory-wide patient cohort study.

Stephen Lam Chan, Terry Cheuk-Fung Yip, Vincent Wai-Sun Wong, Anthony W.H. Chan, Cathy Ka Kiu Tong, Yee Kit Tse, Becky Wing-Yan Yuen, Hester Wing-Sum Luk, Grace Chung-Yan Lui, Henry L.Y. Chan, Tony S. K. Mok, Grace Lai-Hung Wong; Department of Clinical Oncology, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, China; Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Shatin, China; Department of Anatomical and Cellular Pathology, The Chinese University of Hong Kong, Shatin, China; Department of Statistics, The Chinese University of Hong Kong, Shatin, China; Department of Clinical Oncology The Chinese University of Hong Kong, Hong Kong, China

Background: Hepatic adverse events (AEs) are commonly encountered during ICI treatment in cancer. We evaluated the incidence and impact of hepatic AEs in a territory-wide cohort of 1509 patients who received ICI for cancer treatment. **Methods:** This is a territory-wide retrospective observational cohort study in Hong Kong. We identified patients through the regional hospital database (CDARS), based on the drug record of ICIs from 1 Jan 2014 to 31 Oct 2018. Serial liver functions before, during and at 3-month after ICI, were retrieved. Hepatic AEs were graded according to CTCAE 4.0. **Results:** The mean age was 60 years and 65.4% were male with the commonest malignancies being lung cancer (37.0%), liver cancer (17.0%) and gastrointestinal (GI) cancer (8.4%). Grade 1-2 and grade 3-4 hepatic AE occurred 39.8% and 23.3% of patients, respectively, during or within 3 months after ICI. During ICI, 39.5% developed grade 1-2 and 13.0% had grade 3-4 hepatic AE. The most common manifestations of hepatic AE occurred as elevation of ALT/AST (grade 1-2: 38.7%; grade 3-4: 10.3%). The median time of duration from ICI 1st dose to hepatic $\geq$ Grade 3 AE was 54 days (IQR: 22-124). Patients with liver cancer were more likely to develop hepatic AE (grade 1-2: 37.4%; grade 3-4: 55.5%). In all patients and cancer subgroup, patients with grade 3-4 hepatic AE had worse OS than grade 1-2 hepatic AE (Table). **Conclusions:** Hepatic AE occurs in more than half of the patients receiving ICI, with over 20% being grade 3-4 AE. Regardless of tumor types, development of hepatic AE during ICI is associated with poor prognosis. Research Sponsor: None.

12-month overall survival rate.

Patients	Without hepatic AE	With hepatic AE	*P* value*	Grade 1-2 hepatic AE	Grade 3-4 hepatic AE	*P* value#
All	48.9% (42.3%-55.1%)	32.7% (29.5%-36.0%)	<0.001	38.9% (34.8%-42.9%)	18.5% (14.1%-23.5%)	<0.001
Lung cancer	45.3% (35.7%-54.4%)	32.4% (26.9%-38.0%)	0.003	36.4% (30.2%-42.6%)	9.9% (3.2%-21.0%)	<0.001
Liver cancer	79.3% (47.8%-92.9%)	36.5% (29.2%-43.8%)	0.005	55.6% (44.3%-65.6%)	18.3% (10.9%-27.2%)	<0.001
GI cancer	24.2% (6.8%-47.3%)	22.7% (14.9%-31.4%)	0.927	28.8% (18.3%-40.2%)	11.3% (3.6%-24.0%)	0.009

509 Poster Session (Board #B12), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM and Poster Walks, Fri, 4:45 PM-5:30 PM

Celecoxib versus parecoxib versus oxycodone in pain control for transcatheter chemoembolization in patients with hepatocellular carcinoma.

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Background: Abdominal pain is one of the most common side effects of transarterial chemoembolization (TACE) in patients with unresectable hepatocellular carcinoma. Previous studies reported that perioperative controlled-release oxycodone (CRO) intake or administration of parecoxib resulted in adequate pain control after TACE. However, there are currently no studies comparing opioids with nonsteroidal anti-inflammatory drugs (NSAIDs) in controlling postoperative pain. Therefore, we conducted a clinical trial to compare the analgesic effect and safety among celecoxib (oral COX-2 inhibitor), parecoxib (injectable COX-2 inhibitor), and CRO (oral opioids) in patients undergoing TACE. **Methods:** The study was a prospective, randomized, paralleled trial in which 213 patients were enrolled between September 2016 and March 2019. Patients were randomly assigned at the ratio of 1:1:1 to receive celecoxib, parecoxib or CRO 1 h before TACE (T0) and once every 12 h for 2 days after TACE. Pain level, morphine consumption and adverse events were evaluated and compared among the three regimens. **Results:** Highest incidence of pain occurred within the first 12 hours (T12) after TACE. Analysis of pain control showed no significant difference among the mean highest pain scores, percentage distribution of pain categories and mean morphine consumption in the three groups at T0, T12, T24, T36, and T48. At T24, 11 patients (15.7%) in oxycodone group had fever, which was higher than parecoxib regimen (1 patient [1.5%], P = 0.003). At T36, 13 patients (18.6%) in oxycodone regimen had fever, which was higher than celecoxib regimen (2 patients [2.9%], P = 0.003) and parecoxib regimen (1 patient [1.5%], $P < 0.001$). At T48, 11 patients (15.7%) in oxycodone regimen had fever, which was higher than celecoxib regimen (2 patients [2.9%], P = 0.010) and parecoxib regimen (0 patients, P = 0.001). **Conclusions:** The results suggested that patients obtained celecoxib, parecoxib or CRO once every 12 hours can have the same level of analgesic effect during each time period of TACE. However, body temperature balance in oxycodone regimen was significantly worse than celecoxib regimen and parecoxib regimen. Clinical trial information: NCT03059238. Research Sponsor: Sun Yat-sen University Clinical Research 5010 Program.

510 Poster Session (Board #B13), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Early experiences with triple immunochemotherapy in young adults with high-risk fibrolamellar carcinoma.

Claire O'Grady, Ariel Gliksberg, Paul Kent; Rush University Medical Center, Chicago, IL

Background: Fibrolamellar Carcinoma (FLC) is a rare liver cancer affecting young adults without underlying liver disease. Surgery is the only proven therapy, and recurrence is common. There are no proven systemic treatments, especially for high-risk FLC (unresectable, relapse, progression, metastatic). Research suggests that immunotherapy may work. We share our experience using systemic "triple immunochemotherapy" (TT): 2 week cycles of 7 days continuous infusion 5FU or oral capecitabine, interferon alpha-2b on days 1,3,5,7 or PEG-Interferon and nivolumab on day 1. **Methods:** Data from all patients who received TT from 5/2018 to 9/2019 was reviewed to assess tolerability, survival and toxicity. **Results:** 14 patients were treated with TT of which 10 (8F,2M with a median age of 20) were evaluable. They received a median of 13 cycles (6-31). At time of analysis, the median progression free survival was 6 months, 22% longer than prior to TT, with 80% of patients (8) stable or improving, 1 progression, and 1 who died 2 months after initiating TT. For the 4 patients who achieved surgical remission, none have relapsed (PFS 9 months). Overall objective response (CR+PR) and tumor control rate (CR+PR+SD) were 60% and 80%, respectively. There were no withdrawals from treatment due to side effects, though 2 had dose adjustments. All experienced mild adverse effects, most commonly fever and headache, but only 2 patients had grade 3 toxicity. **Conclusions:** Our early results of TT for high-risk FLC are promising, with good tolerability and treatment response, particularly in patients who have achieved surgical CR. Further longitudinal data is needed to confirm outcomes, especially in patients still early in their treatment. Research Sponsor: None.

Patient #	Clinical Status at start of TT	Type of TT	Cycles of TT	RECIST Response	# of Previous Relapses	Shortest Time to Relapse Prior to TT (months)	PFS after TT (months)	TT Status	# of Grade 3+ AEs
1	CR	A	6	SD	1	12	4	0	0
2	PD	N + A	19	CR	2	1	10	0	0
3	PD	N	18	PR	2	5	8	0	0
4	PD	N	12	SD	4	2	6	0	0
5	PD	N	7	SD	4	9	5	0	2
6	SD	N	14	PR	0	n/a	8	DC	1
7	SD	N + A	31	CR	1	5	16	0	0
8	SD	A	14	CR	0	n/a	6	0	0
9	SD	A	6	death	0	n/a	2	DC	0
10	SD	A	8	PR	0	n/a	4	0	0

CR = Clinical Remission, SD = Stable Disease, PD = Progressive disease, PR = Partial Response, N = Neo-adjuvant, A = Adjuvant 0 = Ongoing, DC = Discontinued.

511 **Poster Session (Board #B14), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

Effect of neoadjuvant immunotherapy and targeted therapies on surgical resection in patients with solid tumors: A systematic review and meta-analysis.

Pablo Emilio Serrano Aybar, Sameer Parpia, Leyo Ruo, Kasia Tywonek, Sandra Lee, Connor O'Neill, Noor Faisal, Ali Alfayyadh, Marylrose Gundayao, Brandon M. Meyers; McMaster University, Department of Surgery, Division of General Surgery, Hamilton, ON, Canada; Ontario Clinical Oncology Group, Hamilton, ON, Canada; Western University, London, ON, Canada; Royal College of Surgeons in Ireland, Dublin, Ireland; Juravinski Cancer Centre, Hamilton, ON, Canada

Background: Neoadjuvant immunotherapy with anti-programmed cell death protein-1 (PD-1) or anti-programmed cell death ligand-1 (PD-L1) and tyrosine kinase inhibitor (TKI) therapy is currently being used to treat certain solid tumours prior to surgery. Neoadjuvant therapy may cause delays to resection potentially losing a window of opportunity. We explored the pooled proportion of patients with solid tumours receiving neoadjuvant therapy who completed planned surgical resection. **Methods:** Medline, CENTRAL and Embase databases were searched for single arm or randomized controlled trials studying neoadjuvant PD-1/PD-L1 immunotherapy or TKI therapy. Random-effects model was used to estimate the pooled proportion of patients undergoing planned resection, and weights were estimated using inverse variance method. Statistical heterogeneity was calculated using the I^2 and chi-squared test. **Results:** From 368 relevant articles, eleven studies with a total of 382 patients receiving neoadjuvant PD-1 immunotherapy (n = 234) or neoadjuvant TKI therapy (n = 148) were analyzed. The types of tumours included hepatocellular carcinoma (1 study), renal cell carcinoma (8 studies), bladder carcinoma (1 study) or non-small cell lung cancer (1 study). The pooled proportion of patients who completed planned surgery after neoadjuvant therapy was 95% (95% CI 0.92 to 0.99). The overall partial response rate prior to surgery was 12% (95% CI 0.07 to 0.16) in the PD-1 therapy group and 46% (95% CI -0.12 to 1.03) in the TKI group. The pooled serious adverse events rate was 17% (95% CI 0.02 to 0.32) in the PD-1 therapy group and 29% (95% CI -0.10 to 0.68) in the TKI group. For all patients receiving neoadjuvant therapy, the pooled median overall survival was 23.41 months (95% CI 16.21 to 30.62) and median progression free survival was 7.46 months (95% CI 4.41 to 10.51). **Conclusions:** Neoadjuvant PD-1 or TKI therapy prior to surgery for solid tumours is safe, does not delay surgical resection and can result in a partial radiological response prior to surgery. Research Sponsor: None.

512 Poster Session (Board #B15), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

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

Aiwu Ruth He, Thomas Yau, Chiun Hsu, Yoon-Koo Kang, Tae-You Kim, Armando Santoro, Bruno Sangro, Ignacio Melero, Masatoshi Kudo, Ming-Mo Hou, Ana Matilla, Francesco Tovoli, Jennifer J. Knox, Bassel F. El-Rayes, Mirelis Acosta-Rivera, Jaclyn Neely, Yun Shen, Marina Tschaika, Anthony B. El-Khoueiry; Georgetown University Hospital, Washington, DC; The University at Hong Kong, Hong Kong, China; National Taiwan University Hospital, Taipei, Taiwan; Asan Medical Center, University of Ulsan, Seoul, South Korea; Seoul National University, Seoul, South Korea; Istituto Clinico Humanitas, Rozzano, Italy; Clinica Universidad de Navarra and CIBEREHD, Pamplona, Spain; Universidad de Navarra, Pamplona, Spain; Kindai University Faculty of Medicine, Osaka, Japan; Chang Gung Memorial Hospital, Taipei, Taiwan; Servicio de Digestivo, Hospital General Universitario Gregorio Marañón y CIBEREHD, Madrid, Spain; Department of Medical & Surgical Sciences, University of Bologna, Bologna, Italy; Princess Margaret Cancer Centre, Toronto, ON, Canada; Emory University Winship Center, Atlanata, GA; Fundación de Investigación, San Juan, PR; Bristol-Myers Squibb, Princeton, NJ; USC Norris Comprehensive Cancer Center, Los Angeles, CA

Background: NIVO monotherapy is approved in the United States and other countries for pts with HCC treated with sorafenib (SOR) based on CheckMate 040 (NCT01658878) results, which reported 14% objective response rate (ORR) and 16-month median overall survival (mOS; El-Khoueiry et al. *Lancet* 2017). Primary efficacy and safety of NIVO + IPI in pts with aHCC previously treated with SOR were presented recently (Yau et al. *J Clin Oncol* 2019). Here, we will present subgroup analyses from this study. **Methods:** Pts were randomized to 3 arms: [A] NIVO 1 mg/kg + IPI 3 mg/kg Q3W (4 doses) or [B] NIVO 3 mg/kg + IPI 1 mg/kg Q3W (4 doses), each followed by NIVO 240 mg Q2W, or [C] NIVO 3 mg/kg Q2W + IPI 1 mg/kg Q6W. Treatment continued until intolerable toxicity or disease progression. Primary endpoints included safety/tolerability, ORR, and duration of response (DOR; investigator assessment per RECIST v1.1). Key secondary endpoints included disease control rate (DCR), OS, and progression-free survival (blinded independent central review [BICR] per RECIST v1.1); key exploratory endpoints included ORR (BICR per RECIST v1.1). Data cutoff was January 2019. **Results:** A total of 148 pts were randomized. Minimum OS follow-up from last pt randomization date to data cutoff was 28 months. At baseline, 34% of all pts had vascular invasion; 82% had extrahepatic spread; and 91% had Barcelona Clinic Liver Cancer stage C; 84% discontinued SOR because of disease progression and 14% because of toxicity. For all treated pts, ORR was 31% (7 had complete response), with median DOR of 17 months; DCR was 49%; the 30-month OS rate was 37%. NIVO + IPI was well tolerated; 38% of pts had grade 3–4 treatment-related adverse events (TRAEs; most common any grade: pruritus and rash; most common grade 3–4: aspartate aminotransferase increase and lipase increase); 5% had grade 3–4 TRAEs leading to discontinuation. Subgroup analyses based on duration of prior SOR therapy and other pt characteristics will be presented. **Conclusions:** NIVO + IPI led to clinically meaningful benefits, with a manageable safety profile in pts previously treated with SOR. NIVO + IPI may provide a new treatment option for these pts. Clinical trial information: NCT01658878. Research Sponsor: Bristol-Myers Squibb.

513 Poster Session (Board #B16), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

A phase Ib study of lenvatinib (LEN) plus nivolumab (NIV) in patients (pts) with unresectable hepatocellular carcinoma (uHCC): Study 117.

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Background: LEN, a multikinase inhibitor of VEGFR 1–3, FGFR 1–4, PDGFRα, RET, and KIT with immunomodulatory activity, is approved in multiple countries for first-line treatment of uHCC. NIV is an anti-PD-1 monoclonal antibody approved in multiple countries as a second-line treatment for HCC. We report early results from a phase 1b trial of LEN + NIV in pts with uHCC. **Methods:** In this open-label study, pts with uHCC, BCLC stage B (not eligible for transarterial chemoembolization) or C, Child-Pugh class A, and ECOG PS $\leq$ 1 received LEN (bodyweight $\geq$ 60 kg: 12 mg/day; $<$ 60 kg: 8 mg/day) PO QD and 240 mg NIV IV Q2W. The primary endpoint was tolerability and safety of the combination. Objective response rate (ORR; mRECIST by investigator) was a secondary endpoint. Tolerability was evaluated by assessing dose-limiting toxicities (DLTs) during the first cycle in pts for whom no other appropriate therapy was available (Part 1). Once tolerability was confirmed, additional pts with no prior systemic therapy for uHCC were enrolled (Part 2). **Results:** At data cutoff (May 17, 2019), 30 pts had received LEN + NIV (Part 1: n=6; Part 2: n=24). Pts had BCLC stage B (n=17) or C (n=13) and Child-Pugh scores of 5 (n=23) or 6 (n=7). 4 pts in Part 1 (66.7%) had received prior anticancer medications (3 pts had 1; 1 pt had $\geq$3). No DLTs were reported in Part 1. TEAEs leading to discontinuation of LEN were reported in 2 (6.7%) pts; 4 (13.3%) pts had TEAEs leading to discontinuation of NIV. TEAEs occurred in all 30 pts; the most common were palmar-plantar erythrodysesthesia (56.7%) and dysphonia (53.3%). Adverse events were manageable. Efficacy outcomes are reported (Table). **Conclusions:** LEN + NIV was well tolerated with encouraging anti-tumor activity in pts with uHCC. Clinical trial information: NCT03418922. Research Sponsor: Eisai Inc., Woodcliff Lake, NJ, USA and Ono Pharmaceutical Co., Ltd.

Efficacy summary.

	LEN + NIV (N=30) mRECIST by Investigator		
Parameter, n (%)	**Part 1 (n=6)**	**Part 2 (n=24)**	**Overall (N=30)**
Best Overall Response[a], n (%)			
Complete response (CR)	0	4 (16.7)	4 (13.3)
Partial response (PR)	4 (66.7)	15 (62.5)	19 (63.3)
Stable disease	2 (33.3)	4 (16.7)	6 (20.0)
Progressive disease	0	1 (4.2)	1 (3.3)
Not evaluable	0	0	0
ORR[b], n (%)	4 (66.7)	19 (79.2)	23 (76.7)
95% CI	(22.3–95.7)	(57.8–92.9)	(57.7–90.1)

[a]Confirmation not required.

[b]ORR = Proportion of CR + PR.

514 Poster Session (Board #B17), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Effect of postoperative apatinib treatment after resection of hepatocellular carcinoma with portal vein invasion: A phase II study.

Hui-Chuan Sun, Xiao-Dong Zhu, Jian Zhou, Qiang Gao, Ying-Hong Shi, Zhen-Bing Ding, Cheng Huang, Shuang-Jian Qiu, Ning Ren, Guo-Ming Shi, Jian Sun, Qing-Hai Ye, Xiao-Wu Huang, Xin-Rong Yang, Jia Fan; Liver Cancer Institute and Zhongshan Hospital, Fudan University, Shanghai, China

Background: Adjuvant therapy for hepatocellular carcinoma (HCC) is an unmet need. Apatinib, a VEGFR2 inhibitor, showed antitumor activity and tolerable toxicity for advanced HCC in a phase 2 study. We were aiming to explore the safety and efficacy of apatinib in adjuvant settings after resection of HCC with portal vein tumor thrombosis (PVTT). **Methods:** This is a single-center single-arm phase 2 study. The key inclusion criteria were: (1) pathologically confirmed HCC; (2) underwent liver resection with curative intention within 4-6 wk before recruitment; (3) PVTT assessed by preoperative imaging or intraoperative findings. Eligible pts received apatinib at 500 mg/day for a maximum of 12 mo until unacceptable toxicity or tumor recurrence. The primary outcome was recurrence-free survival (RFS) defined as the interval between surgery and the diagnosis of tumor recurrence or death from any causes whichever comes first. The secondary outcome is overall survival (OS) and treatment safety. **Results:** From Aug 17, 2017 to Dec 18, 2018, 49 pts were screened, and 30 pts were recruited. PVTT were classified as Vp1 (n = 7), Vp2 (n = 11), and Vp3 (n = 12) according to the LCSGJ classification. As the data cutoff on Aug 22, 2019, 4 pts are still on treatment. The median follow-up was 14.3 mo (IQR 12.3-19.3). Median duration of treatment was 4.8 mo (IQR 2.0–8.8). 20 recurrence and 2 death occurred including one death without recurrence. The mRFS was 7.6 mo (95% CI, 3.7-11.5), and the 1-year RFS rate was 36.1%. The mOS was not reached, and 1-year OS rate was 93.3% (standard error, 4.6%). Treatment-related adverse events occurred in 29 pts (96.7%). Grade 3 or 4 adverse events were reported in 14 pts (46.7%) (Table). Dose modification due to adverse events was recorded in 23 pts (76.7%). **Conclusions:** Apatinib is tolerant in most pts after resection for HCC with PVTT. A controlled study is warranted to prove its efficacy on tumor recurrence. Clinical trial information: NCT03261791. Research Sponsor: Hengrui Medicine Inc.

Grade 3 or 4 adverse events	n
Platelet count decrease	5
Neutrophil count decrease	4
Proteinuria	3
Hypertension	3
ALT increased	1
AST increased	1
Diarrhea	1
Upper GI hemorrhage	1
Hoarseness	1
Palmar-plantar erythrodysesthesia syndrome	1

515 Poster Session (Board #B18), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Clinical and genomic factors associated with outcome following ablative radiotherapy for oligometastatic and oligoprogressive liver tumors.

Danielle Sara Bitterman, Andrzej Niemierko, Emily E. Van Seventer, Daniel W. Kim, Motaz Qadan, Lawrence Scott Blaszkowsky, Jeffrey William Clark, Andrew X. Zhu, Lipika Goyal, Florence Keane, Christine Elissa Eyler, Aparna Raj Parikh, Ryan Bruce Corcoran, Jennifer Yon-Li Wo, Theodore S. Hong; Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA; Massachusetts General Hospital, Boston, MA; Department of Surgical Oncology, Massachusetts General Hospital, Boston, MA; Hematology/Oncology, Massachusetts General Hospital, Boston, MA

Background: There is increasing use of ablative radiotherapy (RT) for oligometastatic and/or oligoprogressive cancer, but the population who may benefit from this more aggressive treatment remains poorly defined. We aimed to identify factors associated with improved outcomes following ablative RT for oligometastatic/oligoprogressive liver tumors. **Methods:** We retrospectively analyzed 106 patients who had tumor genomic profiling and received a 5, 6, or 15-fraction course of ablative RT for liver metastases from 2008-2019. The interval off systemic therapy post-RT was calculated for patients who did not continue treatment through RT. Overall survival (OS) was estimated using the Kaplan-Meier method. The association between clinical and genomic variables and OS were assessed using uni- and multivariable Cox regression. **Results:** Median follow-up was 12.6 months. Median age was 61.3 years and 57% were male. The most common primary site was colorectum (42%), followed by pancreas (25%) and non-small cell lung cancer (10%). 42% had colorectal adenocarcinoma, 46% had other adenocarcinoma, and 12% had other histology. A BRAF/RAS family mutation (KRAS, NRAS, and/or BRAF) was present in 41%, 69% had >1 metastasis, and 38% had extra-hepatic disease. Median biological effective dose ($\alpha/\beta = 10$) (BED) was 92 Gy. The RT field encompassed all liver metastases in 91%, and 11% received radiosensitizing chemotherapy. Median time off systemic agents was 5 months. Patients with 1 vs >1 metastasis had a longer interval off systemic therapy (9 vs 4 months, $p = 0.026$). Median OS was 12.6 months. The table shows the multivariable Cox model for OS. **Conclusions:** Presence of a BRAF/RAS family mutation, extra-hepatic metastases, exclusion of liver metastases from RT fields, lower BED, and concurrent radiosensitizing chemotherapy were associated with worse OS. This may inform patient selection and RT delivery for aggressive local therapy for liver metastases. Research Sponsor: None.

Covariable	HR	95% CI
BRAF/RAS family mutation present	1.8	1.1-2.7
Extra-hepatic metastases present	1.6	1.0-2.4
BED ≥ 92 Gy	0.7	0.4-1.0
RT field encompassed all liver metastases	0.4	0.3-0.9
Radiosensitizing chemotherapy given	2.7	1.4-5.2

516 Poster Session (Board #B19), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Major impact of personalized dosimetry using 90Y loaded glass microspheres SIRT in HCC: Final overall survival analysis of a multicenter randomized phase II study (DOSISPHERE-01).

Etienne Garin, Lambros Tzelikas, Boris Guiu, Julia Chalaye, Julien Edeline, Thierry De Baere, Vania Tacher, Corentin Robert, Eric Assenat, Marie Terroir-Cassou-Mounat, Hélène Regnault, Xavier Palard, Sophie Laffont, Boris Campillo-Gimenez, Yann Rolland; Cancer Institute Eugène Marquis, Rennes, France; Medical Imaging, Gustave Roussy, Villejuif, France; University Hospital, Radiology Department, Montpellier, France; CHU Henri Mondor, Créteil, France; Medical Oncology, Centre Eugene Marquis, Rennes, France; Institut Gustave Roussy, Villejuif, France; CHU Montpellier, Montpellier, France; Gustave Roussy, Villejuif, France; Centre Eugene-Marquis, Rennes, France; Centre Eugène-Marquis, Rennes, France

Background: 90Y loaded microsphere SIRT (radioembolization) is a treatment option in advanced HCC. However, no personalized dosimetric endpoints are currently used. The goal of this study was to compare the efficacy of 90Y loaded glass microsphere SIRT in HCC using a standard versus a personalized dosimetric approach. **Methods:** DOSISPHERE-01 was a multicenter, randomized phase 2 trial in unresectable HCC patients with at least one tumor ≥7cm. Treatment arm was randomly assigned (1:1) to standard dosimetry arm (SDA), with a goal to deliver 120±20Gy to the treated volume or to personalized dosimetry arm (PDA) with a goal to deliver at least 205Gy to the index lesion. The primary endpoint was the response rate (RR) of the index lesion according to EASL criteria. Secondary endpoints included dose response evaluation, safety and overall survival (OS). **Results:** Sixty HCC patients were randomized (PDA 31, SDA 29, intent to treat population-ITTP-), and 56 treated (28 in each arm). RR was significantly increased in the PDA versus the SDA, in the ITTP, respectively 64.5% versus 31% (p=0.0095) as in the safety population -SP- (treatment effectively received, personalized 35, standard 21), respectively 74.3% versus 14.3% (p<0.0001). Median OS was significantly increased in the PDA versus the SDA, in the ITTP, respectively 26.7m (CI 95%:11.7-NR) versus 10.6m (CI 95%:6-16.8), p=0.0096, HR=0.421 (95%CI:0.215-0.826), p=0.0119, as in the SP, respectively 26.7m (CI 95%:11.7- NR) versus 9.5m (CI 95%:4.8-14.9), p=0.0015, HR=0.342 (95%CI:0.171-0.683), p=0.0023. Median OS was 26.7m (CI 95%:13.5-NR) versus 6.0m (CI 95%:3.8-14.9) for the patients who received a tumor dose ≥205 Gy or <205 Gy respectively, p=0.0106, HR=0.336 (95%CI:0.154-0.735), p=0.0063. Treatment-related clinically relevant hepatic ≥grade 3 AEs were observed in 5.7% and 14.2% of the patients of the PDA and SDA arms, respectively, (p=ns). **Conclusions:** MAA SPECT/CT based personalized dosimetry is safe and dramatically increased RR and OS of HCC patients. These results question the interpretation of all phase 3 trials of SIRT designed without personalized dosimetry in HCC. Clinical trial information: 2015-A00894-45. Research Sponsor: BTG UK LtD.

517 Poster Session (Board #B20), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Sex difference in patients with biliary tract cancer receiving chemotherapy: Post hoc analysis of ABC-01, -02, -03, -04, BILCAP.

Eiichiro Suzuki, John A. Bridgewater, Juan W. Valle, John Neil Primrose, Anna Dorothea Wagner, Andre Lopes, Richard Fox; Department of Gastroenterology, Graduate School of Medicine, Chiba University, Chiba, Japan; University College London Cancer Institute, London, United Kingdom; The Christie NHS Foundation Trust, Manchester, United Kingdom; University of Southampton, Southampton, United Kingdom; Lausanne University Hospital, Lausanne, Switzerland; Cancer Research UK and UCL Cancer Trials Centre, London, United Kingdom; University of Birmingham, Birmingham, United Kingdom

Background: The relationship between toxicity from chemotherapy and clinical outcome in biliary tract cancer (BTC) is uncertain. Aim: This post hoc analysis evaluated differences by sex in the frequency of adverse events (AEs) and overall survival (OS) and its impact on progression-free survival (PFS)/recurrence-free survival (RFS) for BTC patients. **Methods:** Individual patient data were retrieved from ABC -01, -02, -03, -04, and BILCAP study. AEs were graded according to National Cancer Institute's Common Toxicity Criteria v 4.02 and odds ratios along with 95%CI and p-values derived from logistic regression were used to assess the effect of sex on the risk of AEs. Time to event outcomes were evaluated using Cox regression and plotted using Kaplan-Meier plots. All statistical tests were two-sided. **Results:** Overall 994 patients-data were examined: 86 in ABC-01, 324 in-02, 124 in -03, 13 in -04 and 447 in BILCAP. A total of 484 (49%) were males (M) and 510 (51%) were females (F). 770 patients were evaluable for AEs because a total of 224 patients in BILCAP study belonged to the observation group. Urinary tract infection (M, 1.6%; F, 5.5%), nausea (M, 50.7%; F, 69.9%), vomiting (M, 29.1%; F, 46.1%), alopecia (M, 11.3%; F, 27.3%), are dominant in F, hyperbilirubinaemia (M, 36.7%; F, 29.1%) and thrombocytopenia (M, 43.1%; F, 34.3%) and hiccups (M, 2.4%; F, 0.5%) are dominant in M at any grade. Vomiting (M, 3.5%; F, 7.0%) and fatigue (M, 4.0%; F, 8.5%) are higher in F than in M for grade 3-5. The median OS (M, 16.2 months (Mo); F, 17.5 Mo), PFS (M, 6.4 Mo; F, 6.5 Mo) and RFS (M, 20.8 Mo; F 19.4 Mo) were similar. Amongst the subgroup of patients with gallbladder, F achieved longer OS (M, 11.5 Mo; F 13.3 Mo, 0.73 (95%CI: 0.54,0.99), p = 0.041) and RFS than M (M, 20.8 Mo; median PFS for F not reached, HR:0.52 (95%CI: 0.27,1.02), p = 0.057). **Conclusions:** Females with BTC have tended to have more AEs, especially grade 3+. Although no difference was observed in OS, PFS, and RFS between males and females for the overall cohort of patients, females with gallbladder cancer had an improved OS and RFS compared with males. These findings suggest, in BTC, sex may play a role when designing clinical trials as well as in making treatment decisions. Research Sponsor: None.

518 Poster Session (Board #B21), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Updated efficacy and safety of KEYNOTE-224: A phase II study of pembrolizumab (pembro) in patients with advanced hepatocellular carcinoma (HCC).

Masatoshi Kudo, Richard S. Finn, Julien Edeline, Stéphane Cattan, Sadahisa Ogasawara, Daniel H. Palmer, Chris Verslype, Vittorina Zagonel, Laetitia Fartoux, Arndt Vogel, Debashis Sarker, Gontran Verset, Stephen Lam Chan, Jennifer J. Knox, Bruno Daniele, Ellen B Gurary, Abby B. Siegel, Lokesh Jain, Ann-Lii Cheng, Andrew X. Zhu, for the KEYNOTE-224 Investigators; Kindai University Faculty of Medicine, Osaka, Japan; University of California Los Angeles, Los Angeles, CA; Medical Oncology, Centre Eugene Marquis, Rennes, France; Centre Hospitalier Universitaire, Lille, France; Chiba University Graduate School of Medicine, Chiba, Japan; University of Liverpool, Liverpool, United Kingdom; University Hospitals Leuven, Leuven, Belgium; Medical Oncology Unit 1, Department of Oncology, Istituto Oncologico Veneto IOV IRCCS, Padova, Italy; Hopital de la Pitie Salpetriere, Paris, France; Hannover Medical School, Hannover, Germany; King's College Hospital, Institute of Liver Studies, London, United Kingdom; ULB-Hopital Erasme, Brussels, Belgium; State Key Laboratory in Oncology of South China, The Chinese University of Hong Kong, Shatin, China; Princess Margaret Cancer Centre and University of Toronto, Toronto, ON, Canada; Azienda Ospedaliera G. Rummo, Benevento, Italy; Merck & Co., Inc., Kenilworth, NJ; National Taiwan University Hospital and National Taiwan University Cancer Center, Taipei, Taiwan; Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA

Background: Pembro received accelerated approval in pts with advanced HCC in the second-line setting based on results of the KEYNOTE-224 trial. Results of a 2 y follow-up analysis of the efficacy and safety in this trial are presented here. **Methods:** Eligible pts had histologically confirmed HCC, radiographic progression on/intolerance to sorafenib and disease not amenable to curative treatment, Child Pugh A, ECOG PS 0-1 and BCLC stage C or B. Pts received pembro 200 mg IV Q3W for 2 y or until disease progression, unacceptable toxicity, consent withdrawal or investigator decision. Response was assessed every 9 wk. Primary endpoint was ORR (RECIST v1.1, central review). Secondary endpoints were DOR, DCR, PFS, OS and safety. **Results:** Efficacy and safety were assessed in 104 pts. The median time from randomization to data cutoff (Jun 05, 2019) was 31.2 mo (27.5-35.5 mo). Pt characteristics were: median age 68 y (43-87), 21.2% HBV+, 25% HCV+, 94.2% Child Pugh A, 79.8% had PD on sorafenib, 17.3% had MVI and 64.4% had extrahepatic disease. ORR was 18.3% (95% CI 11.4-27.1) and was similar across subgroups. Median DOR was 21.0 mo (3.1-28+ mo); 77% had responses lasting ≥12 mo (Kaplan Meier). Best overall responses were 4 (3.8%) CRs, 15 (14.4%) PRs, 45 (43.3%) SDs and 34 (32.7%) PDs; DCR was 61.5%. The median PFS (95% CI) was 4.9 mo (3.5-6.7) and OS was 13.2 mo (9.7-15.3). PFS 24 mo rate was 11.3% and OS 24 mo rate was 30.8%. ORR was shown to be a predictor of longer OS by landmark analysis. Treatment-related AEs occurred in 76 (73.1%) pts; the most common AEs were fatigue, increased aspartate aminotransferase, pruritus and diarrhea observed in ≥10% pts. Grade ≥3 treatment related AEs occurred in 27 (26.0%) pts. Immune-mediated hepatitis occurred in 3 (2.9%) pts; no cases of HBV/HCV flare were identified. **Conclusions:** At 2 y follow-up, pembro continued to provide durable anti-tumor activity and prolonged survival (30.8% OS, 24 mo rate), further supporting its use in previously treated pts with advanced HCC. With longer follow-up, increases in ORR (18.3% vs 17.0%), DOR ≥12 mo (77.0% vs 61.4%) and CR rates (3.8% vs 1%) were seen. The safety profile was similar to the primary analysis. Clinical trial information: NCT02702414. Research Sponsor: Merck & Co., Inc., Kenilworth, NJ, USA.

519 Poster Session (Board #B22), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Real-world treatment patterns and survival in patients (pts) with hepatocellular carcinoma in the United States.

Michael Morse, Anne-Marie Meyer, Marcus Lawrance, Marta Pereira, Shivani K. Mhatre, Vincent Gaillard, Farshid Dayyani; Duke University Medical Center, Durham, NC; F. Hoffmann-La Roche, Ltd., Basel, Switzerland; Roche Products Limited, Welwyn Garden City, Hertfordshire, United Kingdom; Genentech, Inc., South San Francisco, CA; UCI Hematology and Oncology, Orange, CA

Background: Outcomes in pts with hepatocellular carcinoma (HCC) vary by epidemiology, degree of hepatic dysfunction and tx. We analyzed the relationship between tx patterns and outcomes to help characterize emerging clinical data in the context of contemporary disease management. **Methods:** Retrospective observational study of the Flatiron Health de-identified electronic health record–derived database to analyze the relationship between first recorded tx (1tx) and overall survival (OS) in pts diagnosed with HCC (any stage) Jan 2011 to Nov 2018. Tx categories included transplant, resection/SBRT/RFA, TACE/TARE/TAE, tyrosine kinase inhibitor (TKI), cancer immunotherapy (CIT), and others. Descriptive statistics were used to summarize tx distribution and pt characteristics; Kaplan-Meier method was used to estimate OS by tx category. **Results:** A total of 2134 pts with HCC were categorized by 1tx: transplant (n = 35), resection/SBRT/RFA (n = 408), TACE/TARE/TAE (n = 830), TKI (n = 751), and CIT (n = 20). Pt demographics were generally similar across txs (Table). Overall, pts with HCC had a median OS of 16.6 mo; varying from 71.5 mo in pts receiving transplant to 5.0 mo in pts treated with TKI. **Conclusions:** Pts receiving systemic tx for HCC have poor prognoses in clinical practice. Despite the limitations of data availability, this study showed a substantial unmet need for more effective HCC tx options. Research Sponsor: F. Hoffmann-La Roche, Ltd.

	All Treatments N = 2134	Transplant n = 35	Resection/ SBRT/RFA n = 408	TACE/TARE/TAE n = 830	TKI n = 751	CIT n = 20
Age, mean (SD), y	66.1 (9.5)	59.3 (6.8)	65.9 (10.2)	66.0 (9.1)	66.5 (9.3)	67.0 (7.5)
Male, n (%)	1654 (78)	27 (77)	285 (70)	655 (79)	601 (80)	16 (80)
Community practice, n (%)	1654 (78)	8 (23)	292 (72)	574 (69)	698 (93)	17 (85)
Diagnosis year ≥2017, n (%)	623 (29)	7 (20)	108 (26)	242 (29)	217 (29)	18 (90)
Hepatitis C, n (%)	966 (45)	23 (66)	171 (42)	407 (49)	322 (43)	8 (40)
Hypoalbuminemia (< 3.5 g/dL), n (%)[a]	548 (43)	14 (67)	38 (23)	178 (40)	295 (52)	9 (47)
Abnormal bilirubin (< 0.3 or > 1.2 mg/dL), n (%)[a]	482 (35)	26 (96)	47 (23)	145 (29)	229 (41)	9 (47)
Median OS (95% CI), mo	16.6 (15.1, 19.2)	71.5 (55.9, NE)	47.0 (38.7, 58.3)	25.4 (23.1, 28.9)	5.0 (4.5, 6.1)	6.7 (1.1, NE)

[a]% of pts with known lab values (≈60% of total N, varies by lab).

520 Poster Session (Board #C1), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Subsequent anticancer procedures following first-line lenvatinib (LEN): A post hoc analysis from the phase III REFLECT study in unresectable hepatocellular carcinoma (uHCC).

Angel Alsina, Masatoshi Kudo, Arndt Vogel, Ann-Lii Cheng, Won Young Tak, Baek-Yeol Ryoo, T.R. Jeffry Evans, Carlos Lopéz Lopéz, Bruno Daniele, Jean-Frédéric Blanc, Min Ren, Rae Lynn Baldwin, Namiki Izumi, Shukui Qin, Richard S. Finn; Tampa General Hospital, Tampa, FL; Kindai University Faculty of Medicine, Osaka, Japan; Hannover Medical School, Hannover, Germany; National Taiwan University Hospital and National Taiwan University Cancer Center, Taipei, Taiwan; Kyungpook National University Hospital, Daegu, South Korea; Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; University of Glasgow, Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom; Marqués de Valdecilla University Hospital, Santander, Spain; Azienda Ospedaliera G. Rummo, Benevento, Italy; Hospital Saint-André, Bourdeaux, France; Eisai Inc., Woodcliff Lake, NJ; Musashino Red Cross Hospital, Tokyo, Japan; Nanjing Bayi Hospital, Nanjing, China; Geffen School of Medicine, UCLA Medical Center, Santa Monica, CA

Background: The availability of newer therapeutic options has shifted the treatment paradigm for uHCC, evoking questions regarding the sequencing of anticancer therapies. REFLECT was a phase 3 study comparing the efficacy and safety of LEN versus sorafenib (SOR) in first-line treatment of patients (pts) who have uHCC. In this post hoc analysis, we investigated overall survival (OS) during the follow-up survival period between treatment arms for pts who did and did not receive subsequent anticancer procedures and for responders to first-line LEN who received subsequent anticancer procedures. **Methods:** Pts in REFLECT were randomized 1:1 to LEN or SOR. The follow-up period commenced at the first visit after stopping study medications. Pts were followed-up every 12 weeks until data cutoff (Nov 13, 2016) or death. OS was estimated using the Kaplan–Meier method and presented with a 95% confidence interval (CI). Pts receiving subsequent radiotherapy were excluded from the OS analysis. **Results:** Of the 954 pts enrolled in REFLECT, 122/478 (26%) LEN- and 130/476 (27%) SOR-treated pts received subsequent anticancer procedures, with the most common being transarterial chemotherapy embolization (LEN n = 69 [14.4%]; SOR n = 81 [17.0%]) and hepatic intra-arterial chemotherapy (LEN n = 23 [4.8%]; SOR n = 25 [5.3%]). Eastern Cooperative Oncology Group performance status scores and laboratory assessments, including liver function, were comparable between arms at first-line treatment discontinuation. Of the pts who received subsequent anticancer procedures, those randomized to first-line LEN (n = 99) had a longer median OS (23.0 vs 19.6 months, respectively; hazard ratio [HR]: 0.71; 95% CI: 0.51–1.01) than those randomized to first-line SOR (n = 112). Responders to first-line LEN who received subsequent anticancer procedures (n = 45) had a median OS of 27.2 months (95% CI: 20.7–29.8). There were too few SOR responders (n = 10) who received subsequent anticancer procedures to evaluate OS. **Conclusions:** Pts randomized to first-line LEN who received subsequent anticancer procedures had longer OS compared with the similar sequence for pts taking first-line SOR. Clinical trial information: NCT01761266. Research Sponsor: This study was sponsored by Eisai Inc., Woodcliff Lake, NJ, USA, and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Inc., Kenilworth, NJ, USA.

521 **Poster Session (Board #C2), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

Optimal timing of radiotherapy for incomplete transarterial chemoembolization in BCLC stage B hepatocellular carcinoma.

Hwa Kyung Byun, Nalee Kim, Jinsil Seong; Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; Yonsei University College of Medicine, Seoul, South Korea

Background: Numerous studies have reported on the efficacy of radiotherapy (RT) after incomplete transarterial chemoembolization (TACE). However, the optimal timing of RT remains unclear. This study investigated the optimal time of initiating RT for incomplete TACE in patients with BCLC stage B hepatocellular carcinoma (BCLC-B HCC). **Methods:** Between 2001 and 2016, 116 lesions in 104 patients with BCLC-B HCC were treated with RT after TACE. The time interval between the last session of TACE and initiation of RT was obtained from medical records and analyzed retrospectively. The optimal cut-off time-interval that maximized the difference in local failure-free rate (LFFR) was determined using maximally selected rank statistics. **Results:** The median duration between TACE and RT was 26 (range: 2–165) days. Median number of TACE treatments on the target lesion before RT was 2; median tumor size was 7 cm. At a median follow-up of 18 (range: 3–160) months, the median overall survival was 18 months. The probability of local control increased as the time interval between TACE and RT decreased. The optimal cut-off value of the time interval was 5 weeks. With the cut-off of 5 weeks, 65 and 39 patients were classified into early and late RT groups, respectively. The early RT group had significantly poorer Child-Pugh class and higher alpha-fetoprotein levels. Most characteristics including tumor size (7 cm vs. 6 cm; P = .144) were not significantly different between the groups. One-year LFFR was significantly higher in the early RT group (94.6% vs. 70.8%; P = .005). On multivariate analysis, early RT was an independent predictor of favorable LFFR (hazard ratio: 3.82, 95% confidence interval: 1.64–8.88, P = .002). **Conclusions:** The optimal time for the administration of RT for incomplete TACE is within 5 weeks following TACE. Early administration of RT within 5 weeks after TACE was associated with better local control. Research Sponsor: None.

522 Poster Session (Board #C3), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Initial lenvatinib therapy with no prior TACE in patients with intermediate-stage hepatocellular carcinoma beyond up-to-seven criteria and Child-Pugh A liver function: A proof-of-concept study.

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Background: Intermediate-stage HCC is a heterogenous population with subgroups of patients that do not benefit from TACE. Hence, we conducted a matched cohort study to compare the efficacy of lenvatinib to TACE in intermediate-stage HCC patients with large or multinodular tumours exceeding the up-to-7 criteria. **Methods:** This study first identified 642 consecutive patients with HCC initially treated with lenvatinib or conventional TACE (cTACE) between January 2006 and December 2018. Of these patients, 176 who received lenvatinib or cTACE as an initial treatment and met the eligibility criteria [unresectable, beyond the up-to-7 criteria, without prior TACE/systemic therapy, no vascular invasion, no extrahepatic spread and Child-Pugh A liver function] were selected. Propensity score matching was used to adjust for patients' demographics. **Results:** After propensity-score matching, outcome of 30 patients prospectively treated with lenvatinib (14 in clinical trials [1 Phase II and 13 Phase III REFLECT trial], 1 in early access program and 15 in real world setting) and 60 patients treated with cTACE as the initial treatment was compared. The lenvatinib group showed a higher objective response rate (73.3% vs. 33.3%; $p < 0.001$) and longer median progression-free survival than the cTACE group (16.0 vs. 3.0 months; $p < 0.001$). Median overall survival was also significantly longer in the lenvatinib group than in the cTACE group (37.9 vs. 21.3 months; hazard ratio: 0.48, $p < 0.01$). The change of ALBI score from baseline to the end of treatment were -2.61 to -2.61 for 30 patients in lenvatinib group ($p = 0.254$) and -2.66 to -2.09 in cTACE group ($p < 0.01$), respectively. **Conclusions:** In patients with large or multinodular intermediate-stage HCC exceeding the up-to-7 criteria with Child-Pugh A liver function, who usually do not benefit from TACE, lenvatinib is associated with better outcome than TACE. In particular, leventinib is associated with preservation of hepatic function during treatment while TACE is associated with deterioration of hepatic function. Research Sponsor: None.

523 Poster Session (Board #C4), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Analysis of OX40 agonist antibody (PF-04518600) in patients with hepatocellular carcinoma.

Anthony B. El-Khoueiry, Jean-Philippe Spano, ERIC ANGEVIN, Toshihiko Doi, Andrea J. Bullock, William Proctor Harris, Omid Hamid, Paul Gougis, Alison Forgie, Wenjing Yang, Ken Liao, Ruifeng Li, Carrie T. Taylor, Jeffrey Chou, Ferry Eskens; University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA; Pitié-Salpêtrière Hospital, Sorbonne University, Cancer University Institute, Paris, France; Drug Development Department (DITEP), Institut Gustave Roussy, Villejuif, France; National Cancer Center Hospital East, Chiba, Japan; Beth Israel Deaconess Medical Center, Boston, MA; University of Washington School of Medicine, Seattle, WA; The Angeles Clinic and Research Institute, Los Angeles, CA; Groupe Hospitalier Pitié-Salpêtrière Oncologie Medicale, Paris, France; Pfizer Inc., San Francisco, CA; Pfizer Inc., San Diego, CA; Pfizer Inc., Cambridge, MA; Pfizer Inc., New York, NY; Erasmus MC Cancer Institute, Rotterdam, Netherlands

Background: PF-04518600 (PF-8600) is a humanized agonist IgG2 monoclonal antibody to the tumor necrosis factor superfamily receptor OX40. PF-8600 was given to patients (pts) with advanced/metastatic hepatocellular carcinoma (HCC) in dose expansion of a phase 1 study (NCT02315066). Safety and tolerability were primary endpoints and exploratory endpoints included biomarker analyses. **Methods:** Pts received either 30 mg (Arm 1) or 250 mg (Arm 2) of PF-8600 intravenously Q2W. Pts had pathologic diagnosis of advanced HCC, a Child-Pugh score of A or B7, and had ≤2 prior lines of therapy, or if treatment naïve, had declined standard of care. Radiological tumor assessments were conducted Q8W. Biopsy samples collected at baseline and wk 6 were analyzed by immunohistochemistry and RNA sequencing for pharmacodynamic (PD) analyses. Whole blood samples were collected longitudinally for DNA extraction for high-throughput sequencing of the T cell receptor β-chain. **Results:** Arm 1 enrolled 16 pts (mean age 65.6 yrs; range 54-81 yrs; prior PD-1/PD-L1: 5 pts) and Arm 2 enrolled 19 pts (mean age 61.7 yrs; range 26-79 yrs; prior PD-1/PD-L1: 3 pts). All grade treatment related adverse events (TRAEs) occurred in 69% of pts in Arm 1 and 58% of pts in Arm 2. The rate of ≥Grade 3 TRAEs was 31% and 16% in Arms 1 and 2, respectively. For both arms combined, the most common (≥10%) TRAEs were rashes and pruritus. In Arm 1, 8 pts (50%) and in Arm 2, 10 pts (53%) achieved stable disease (SD), with a mean duration of 18.4 (range: 14.0-30.3 wks) and 17.4 wks (range: 8.0-31.9 wks), respectively. PD effects were more evident in Arm 1 than Arm 2, including increased OX40 tumor expression and positive changes in gene signatures, reflecting an active anti-tumor immune response. **Conclusions:** PF-8600 was generally well tolerated and provided meaningful disease control. While safety and efficacy were not significantly different between the 2 doses, there were potential differences in the PD data. The safety and relative durability of SD in HCC pts may provide a rationale for exploration of combination therapy in this pt population. Clinical trial information: NCT02315066. Research Sponsor: Pfizer Inc.

524 Poster Session (Board #C5), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Baseline liver function and outcomes in the phase III REFLECT study in patients with unresectable hepatocellular carcinoma (uHCC).

Arndt Vogel, Catherine Frenette, Max W. Sung, Bruno Daniele, Ari David Baron, Stephen Lam Chan, Jean-Frédéric Blanc, Toshiyuki Tamai, Min Ren, Howard John Lim, Daniel H. Palmer, Yuko Takami, Masatoshi Kudo; Hannover Medical School, Hannover, Germany; Scripps Green Hospital, San Diego, CA; Tisch Cancer Institute at Mount Sinai, New York, NY; Azienda Ospedaliera G. Rummo, Benevento, Italy; Sutter Health/California Pacific Medical Center Research Institute, San Francisco, CA; The Chinese University of Hong Kong, Shatin, China; University of Bordeaux, Bordeaux, France; Eisai Co., Ltd., Tokyo, Japan; Eisai Inc., Woodcliff Lake, NJ; British Columbia Cancer Agency, Vancouver, BC, Canada; University of Liverpool, Liverpool, United Kingdom; National Hospital Organization Kyushu Medical Center, Fukuoka, Japan; Kindai University School of Medicine, Osakasayama, Japan

Background: Lenvatinib (LEN) is approved for first-line treatment of uHCC. Baseline (BL) liver function (Child-Pugh score [CPS] and albumin-bilirubin grade [ALBI]) was prognostic in uHCC patients (pts) who received sorafenib (SOR) but has not been assessed with LEN in uHCC. Here, we report post hoc analysis of BL liver function and efficacy/safety outcomes from the phase 3 REFLECT study. **Methods:** Overall survival (OS), progression-free survival (PFS), objective response rate (ORR), and safety were stratified by BL ALBI or CPS. OS and PFS were estimated by Kaplan–Meier method. Independent radiologic review utilized mRECIST criteria for ORR. Safety was assessed using NCI-CTCAE, version 4.0. **Results:** Liver function measured by ALBI and CPS seemed to be prognostic for OS and ORR. Median OS was longer in ALBI grade 1 (ALBI-1) vs grade 2 (ALBI-2) pts or for CPS-5 vs CPS-6 on either treatment arm and was longer for LEN vs SOR. ORR was higher in pts with better ALBI or CPS and for LEN vs SOR. Rates of treatment-emergent adverse events grade ≥3 were lower with better BL liver function (ALBI-1 vs ALBI-2: 70% vs 86%; CPS-5 vs CPS-6: 72% vs 86%). Study-drug withdrawal, dose reduction, and dose interruption occurred more often in pts with worse BL liver function. **Conclusions:** This post hoc analysis suggests ALBI (by OS, PFS and ORR) and CPS (by ORR) may be prognostic in uHCC pts and that BL liver function may be linked with efficacy/safety outcomes. This analysis also found that LEN provided benefit vs SOR for uHCC, regardless of BL liver function. The benefit of LEN may be underestimated, as more ALBI-2 pts and fewer ALBI-1 pts received LEN vs SOR. Clinical trial information: NCT01761266. Research Sponsor: This study was sponsored by Eisai Inc., Woodcliff Lake, NJ, USA, and Merck Sharp & Dohme Corp., a subsidiary of Merck & Co. Inc., Kenilworth, NJ, USA.

Parameter	ALBI-1 LEN n=318	ALBI-1 SOR n=340	HR/OR (95% CI)	ALBI-2 LEN n=158	ALBI-2 SOR n=134	HR/OR (95% CI)	CPS-5 LEN n=368	CPS-5 SOR n=357	HR/OR (95% CI)	CPS-6 LEN n=107	CPS-6 SOR n=114	HR/OR (95% CI)
Median OS, months[a]	17.4	14.6	0.85 (0.70–1.02)	8.6	7.7	0.95 (0.73–1.25)	15.3	14.2	0.91 (0.77–1.09)	9.4	7.9	0.91 (0.67–1.24)
Median PFS, months[a]	7.4	3.6	0.57 (0.47–0.70)	5.5	3.5	0.76 (0.56–1.03)	7.3	3.7	0.63 (0.53–0.76)	7.4	3.5	0.65 (0.45–0.94)
ORR, %[b]	45.0	13.8	5.48 (3.70–8.10)	32.3	9.0	5.37 (2.61–11.06)	42.9	14.0	4.88 (3.37–7.08)	33.6	7.9	5.25 (2.32–11.85)

[a]Hazard ratio (HR); [b]Odds ratio (OR)

525 Poster Session (Board #C6), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Nivolumab (NIVO) and drug eluting bead transarterial chemoembolization (deb-TACE): Preliminary results from a phase I study of patients (pts) with liver limited hepatocellular carcinoma (HCC).

James J. Harding, Hooman Yarmohammadi, Kim Anna Reiss, Joanne F. Chou, Marinela Capanu, Richard K. G. Do, Danny Khalil, Imane H. El Dika, Joseph Daniel Giardina, Taha Merghoub, William R. Jarnagin, Gregory Nadolski, Joseph Patrick Erinjeri, Michael C. Soulen, Benjamin R. Tan, Ghassan K. Abou-Alfa; Memorial Sloan Kettering Cancer Center, New York, NY; University of Pennsylvania Abramson Cancer Center, Philadelphia, PA; Memorial Sloan Kettering Cancer Center, New York City, NY; Washington University, St. Louis, MO; University of Pennsylvania, Philadelphia, PA; Washington University School of Medicine, St. Louis, MO

Background: Regional therapies in HCC impact the immune microenvironment and may augment the effects of immune checkpoint inhibitors. **Methods:** This is a multicenter phase 1 study of NIVO and deb-TACE in unresectable HCC pts (BCLC Stage B) and Child Pugh A cirrhosis (NCT03143270). The primary objective is to assess safety. Secondary objectives include response rate by RECIST v1.1, progression-free and overall survival by Kaplan-Meier methodology, and blood/tumor immune correlates. A 3 + 3 design sequentially evaluates 3 cohorts of differing schedules of NIVO relative to deb-TACE. Deb-TACE (75mg of doxorubicin) is administered on Day 0. NIVO is dosed at 240mg IV every 14 days for 1 year (Cohort 1: NIVO begins day +14 after deb-TACE; Cohort 2, interrupted NIVO dosing begins at Day -28 but is held on the Day 0 then restarted on Day +14; Cohort 3, continuous NIVO dosing begins on Day -28 without interruption). **Results:** As of July 2019, 9 pts have been treated [median 65 years (range: 54-76), male (89%), viral (44%;1 HBV, 3 HCV), non-viral (56%;2 EtOH, 1 NASH, 2 unknown), prior resection (44%), prior regional therapy (44%), 3 pts in each cohort]. No cases of treatment related liver failure, dose-limiting toxicity, or Grade 5 adverse events (AEs) were observed. Grade $\geq$3 AEs possibly related to nivolumab, deb-TACE, or both included: transaminase elevation (1 pt: day 1 post TACE resolved in 7 days without treatment; 2 pts: $\geq$30 days post TACE resolved with steroids between 20-41 days), post-embolization syndrome (1 pt: resolved in 5 days), asymptomatic lipase increase (1 pt: resolved in 14 days), post-procedural groin hematoma (1 pt: resolved in 2 days). All 9 pts were evaluable for efficacy: 2 (22%) confirmed PR and 7 (78%) SD. 4/9 pts remain on study with SD or better—2 pts continue $>$ 18 months post embolization with durable PRs. 12 months OS rate was 71%. Ongoing correlates will be presented at a separate meeting. **Conclusions:** Nivolumab given at various times relative to deb-TACE appears safe and tolerable. Cohort 3 continues to accrue to provide a better estimate of safety and antitumor activity of the combination. Clinical trial information: NCT03143270. Research Sponsor: Bristol Myer Squibb.

526 Poster Session (Board #C7), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Phase III study of pembrolizumab (pembro) versus best supportive care (BSC) for second-line therapy in advanced hepatocellular carcinoma (aHCC): KEYNOTE-240 Asian subgroup.

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Background: Pembro received accelerated approval for second-line therapy in aHCC based on KEYNOTE-224 (phase 2). KEYNOTE-240 (NCT02702401) is a randomized, phase 3 study of pembro v BSC in previously treated aHCC. We report outcomes for the Asian subgroup. **Methods:** Pts with a radiographic/pathologic HCC diagnosis, radiographic progression with/intolerance to sorafenib, Child-Pugh A disease, and ECOG PS 0/1 were randomized 2:1 to pembro (200 mg) + BSC or PBO + BSC Q3W ($\leq$35 cycles or until confirmed PD/unacceptable toxicity). Pts were stratified by geographic region (Asia without Japan; non-Asia with Japan), AFP, and macrovascular invasion. Response was assessed Q6W (RECIST v1.1, central review). Primary end points: OS, PFS; secondary end points: ORR, DOR, safety. Data cutoff: Jan 2, 2019. **Results:** 413 pts were randomized (overall cohort: n = 278 pembro, n = 135 PBO; Asian subgroup [Hong Kong, Japan, Philippines, S Korea, Taiwan, Thailand]: n = 107, n = 50). HBV+ status and BCLC stage C were higher in Asian subgroup (HBV+: 51% v 24.5% overall; stage C: 86.6% v 79.4%). Median follow-up: pembro (21.3 mo overall; 23.5 mo); PBO (21.5 mo overall; 23.0 mo). Pembro improved OS v PBO (median OS [95% CI]: 13.9 [11.6-16.0] v 10.6 [8.3-13.5] mo; HR: 0.781; 95% CI, 0.611-0.998; P = 0.0238) and PFS (HR: 0.718; 0.570-0.904; P = 0.0022) for overall cohort and Asian subgroup (median OS: 13.8 [10.1-16.9] v 8.3 [6.3-11.8] mo; HR: 0.548; 0.374-0.804; P = 0.0009; PFS: HR: 0.475; 0.324-0.696; $P < 0.0001$). Differences did not meet prespecified significance level for overall cohort. ORR in overall cohort was 18.3% (14.0-23.4) for pembro; 4.4% (1.6-9.4; P = 0.00007) for PBO; in Asian subgroup, 20.6% (13.4-29.5) and 2.0% (0.1-10.6; P = 0.00135). Safety was consistent with that previously reported in pembro studies. No HBV/HCV flares were identified. **Conclusions:** Pembro reduced risk for death by 22% in overall cohort and 45% in Asian subgroup and improved PFS v PBO. Safety was comparable to that of pembro monotherapy. Results are consistent with KEYNOTE-224 and magnitude of OS benefit was enhanced in Asian subgroup, supporting a favorable risk-benefit balance for second-line pembro in HCC. Clinical trial information: NCT02702401. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

527 Poster Session (Board #C8), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Postoperative adjuvant transarterial infusion chemotherapy with FOLFOX could improve outcomes of hepatocellular carcinoma patients with microvascular invasion: A preliminary report of a phase III, randomized, controlled clinical trial.

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Background: Microvascular invasion (MVI) is a risk factor for recurrence after hepatectomy for hepatocellular carcinoma (HCC) patients. This study aimed to investigate to efficacy and safety of postoperative adjuvant transarterial infusion chemotherapy (TAI) with FOLFOX regimen for HCC patients with MVI. **Methods:** In this prospective, phase III, randomized, open-labeled, controlled clinical trial, HCC patients with histologically confirmed MVI were randomly assigned (1:1) after hepatectomy to receive either 1-2 cycles adjuvant TAI (AT group) or follow-up without any adjuvant treatment (FU group). The primary endpoint was disease-free survival (DFS), the secondary endpoints are overall survival (OS) and safety. **Results:** Between June, 2016 and April 2019, 127 patients were randomly assigned to AT group (n=63) or FU group (n=64). Clinicopathological characteristics were balanced between the two groups. The 6-, 12-, and 18-month OS rates for AT group were 100.0%, 97.7%, and 97.7%, and were 94.5%, 89.6%, and 78.5% for FU group, respectively. The 6-, 12-, and 18-month DFS rates for AT group were 84.7%, 61.8%, and 58.7%, and were 62.9%, 48.1%, and 38.6% for FU group, respectively. The OS and DFS were significantly better in AT group than in FU group (p=0.037 and 0.023, respectively). No patients in AT group experienced grade 3 or more severe adverse events (AEs). **Conclusions:** Adjuvant TAI after hepatectomy may bring survival benefits of OS and DFS for HCC patients with MVI. Clinical trial information: NCT03192618. Research Sponsor: None.

528 Poster Session (Board #C9), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

RECIST v1.1 and irRECIST outcomes in advanced HCC treated with pembrolizumab (pembro).

Julien Edeline, Mark Karwal, Andrew X. Zhu, Richard S. Finn, Stéphane Cattan, Sadahisa Ogasawara, Chris Verslype, Vincenzo Dadduzio, Laetitia Fartoux, Arndt Vogel, Olivier Rosmorduc, Gontran Verset, Stephen Lam Chan, Jennifer J. Knox, Bruno Daniele, Ann-Lii Cheng, Gregory V. Goldmacher, Erin Jensen, Abby B. Siegel, Masatoshi Kudo; Centre Eugène Marquis, Rennes, France; University of Iowa, Iowa City, IA; Harvard Medical School, Boston, MA; University of California Los Angeles, Los Angeles, CA; Hôpital Claude Huriez, Centre Hospitalier Régional Universitaire de Lille, Lille, France; Graduate School of Medicine, Chiba University, Chiba, Japan; University Hospital Gasthuisberg, Leuven, Belgium; Istituto Oncologico Veneto-Istituto di Ricovero e Cura a Carattere Scientifico (IOV-IRCCS), Padua, Italy; Hôpital Universitaire Pitié-Salpêtrièe, Paris, France; Medizinische Hochschule, Hannover, Germany; Assistance Publique-Hôpitaux de Paris, Pitié-Salpêtrière Hospital, Paris, France; Hôpital Erasme, Brussels, Belgium; State Key Laboratory of Translational Oncology, The Chinese University of Hong Kong, Shatin, China; Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada; Ospedale del Mare, Naples, Italy; National Taiwan University Hospital, Taipei, Taiwan; Merck & Co., Inc., Kenilworth, NJ; Kindai University, Osaka, Japan

Background: IO can cause pseudoprogression (PP): apparent tumor growth followed by stability or favorable response. We assess PP in aHCC treated with pembro (KEYNOTE-224 [ph 2], NCT02702414; KEYNOTE-240 [ph 3], NCT02702401). **Methods:** aHCC pts with PD on/intolerance to sorafenib received pembro 200 mg IV Q3W until unacceptable toxicity, study withdrawal, 2 y of therapy, or RECIST v1.1 PD; if pt clinically stable at PD, physician could continue therapy and repeat scans to confirm PD per irRECIST. PP=RECIST v1.1 PD then irRECIST response other than PD. Data cutoff: Jan 02, 2019 (KEYNOTE-240); Feb 13, 2018 (KEYNOTE-224). **Results:** 245/382 pembro-treated pts had RECIST v1.1 PD: 138 irRECIST repeat scan; 105 PD; 33 (8.6%; 33/382) outcomes other than PD. Of 33 PP, 29 had SD, 3 PR, 1 CR (irRECIST; 29 had this at first irRECIST scan; 4 [2 SD, 2 PR] at subsequent scan). For initial RECIST v1.1 PD, 16/33 PP had PD at first postbaseline scan (pembro cycles 2-4); 17/33 PP had PD at pembro cycles 4-18. Median (range) time to RECIST v1.1 PD in the 33 PP was 80 (37-378) days. OS shown in Table. KEYNOTE-240 had 135 PBO-treated pts: 8 (5.9%) PP; small samples bar meaningful interpretation. **Conclusions:** PP in aHCC, per irRECIST, has a similar incidence to other cancers (eg, melanoma) and does not seem to correlate with OS. Data may help physicians assess when to continue pembro after PD. Clinical trial information: NCT02702414, NCT02702401. Research Sponsor: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

OS, pembro-treated pts[a].

	RECIST v1.1 PD, excluding PP (n=212)[b]	RECIST v1.1 PD and ≥1 irRECIST scan with PP (n=33)	RECIST v1.1 PD and ≥1 irRECIST scan, no PP (n=105)	RECIST v1.1 PD, no irRECIST follow-up (n=107)
Deaths, n (%)	141 (66.5)	25 (75.8)	73 (69.5)	68 (63.6)
Median OS, mo (95% CI)[c]	13.4 (10.0-15.7)	15.5 (10.4-20.4)	14.5 (12.3-16.8)	10.0 (7.8-16.2)
3-mo, %	92.9 (88.5-95.7)	100.0 (100.0-100.0)	98.1 (92.6-99.5)	87.9 (80.0-92.8)
6-mo, %	75.5 (69.1-80.7)	90.9 (74.4-97.0)	85.7 (77.4-91.1)	65.4 (55.6-73.6)
9-mo, %	64.5 (57.7-70.6)	78.8 (60.6-89.3)	71.4 (61.8-79.1)	57.8 (47.9-66.5)
12-mo, %	53.1 (46.2-59.6)	54.5 (36.3-69.6)	62.9 (52.9-71.3)	43.6 (34.1-52.8)
15-mo, %	45.1 (38.3-51.7)	54.5 (36.3-69.6)	48.6 (38.6-57.8)	41.6 (32.2-50.8)

[a]Pts received no other treatments.

[b]Pts with no irRECIST scan (n=107) + ≥1 irRECIST scan but no CR, PR, SD (n=105).

[c]Product-limit K-M method for censored data.

529 Poster Session (Board #C10), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM and Poster Walks, Fri, 4:45 PM-5:30 PM

Cisplatin plus irinotecan versus cisplatin plus gemcitabine in the treatment of advanced or metastatic gallbladder or biliary tract cancer: Results of a randomized phase II trial (NCT01859728)– the Gambit trial.

Lucas Vieira dos Santos, Gustavo Sanches Faria Pinto, Mauricio Wagner Souto Ferraz, Arinilda Bragagnoli, Florinda Santos, Sarah Haddad, Ana Barros, Isadora Clarissa Cordeiro Dias, Joao Paulo SN Lima, Kathia C Abdalla; Beneficencia Portuguesa de São Paulo, São Paulo, Brazil; Barretos Cancer Hospital, Barretos, Brazil; Barretos Cancer Center, Barretos, Brazil; Hospital de Câncer de Barretos, Barretos, Brazil; AC Camargo Cancer Center, São Paulo, Brazil; Fundação Faculdade de Medicina de Sâo José do Rio Preto, São José Do Rio Preto, Brazil

Background: The combination of gemcitabine-cisplatin (GC) is the current standard of care chemotherapy for metastatic/unresectable biliary tract cancer (BTC). However, the prognosis remains poor. This randomized trial aimed to evaluate the efficacy and safety of irinotecan plus cisplatin (IP) versus GC in advanced or metastatic BTC. **Methods:** Patients with biopsy-proven, chemo-naïve, unresectable or metastatic BTC, ECOG 0-2, measurable disease per RECIST 1.1, adequate organ function and written informed consent were stratified by ECOG (0 or 1 vs 2) and distant metastases and randomized to receive irinotecan 65 mg/m^2 IV D1 and D8 plus cisplatin 60 mg/m^2 D1 repeated every 3 weeks (IP) or gemcitabine 1000 mg/m^2 IV D1 and D8 plus cisplatin 25 mg/m^2 IV D1 and D8 repeated every 3 weeks, until disease progression or unacceptable toxicity. The primary endpoint was overall response rate (ORR). Results: Between January 2013 and April 2018, 47 pts were randomized (1:1) to receive IP (N = 24) or GC (N = 23). Overall, groups were well balanced according to prognostic factors. The ORR was 35% (complete response 5%, partial response 30%) and 31.8% in IP and GC arms, respectively. Median progression-free survival were 5.3 vs 7.8 months (HR = 1.165, 95%CI 0.628-2.161, p = 0.628) and median overall survival were 11.9 and 9.8 months (HR = 0.859, 95%CI 0.431 – 1.710, p = 0.665) for IP and GC, respectively. Adverse events were not statistically different between arms, and results were consistent with previous experiences with these regimens. No therapy-related death were reported. Conclusions: Irinotecan-cisplatin combination is active in BTC, with similar ORR, PFS and OS when compared to gemcitabine-cisplatin. Irinotecan-cisplatin were well tolerated, and adverse events were manageable. Irinotecan-cisplatin could be considered as an alternative to gemcitabine-cisplatin. Clinical trial information: NCT01859728. Research Sponsor: Barretos Cancer Hospital.

531 Poster Session (Board #C12), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Impact of baseline and concomitant corticosteroid therapy on the outcomes of hepatocellular carcinoma treated with immune checkpoint inhibitor therapy.

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Background: The impact of corticosteroid treatment (CT) on the efficacy of immune checkpoint inhibitors (ICI) in hepatocellular carcinoma (HCC) is undefined. We evaluated whether CT administered at baseline (bCT) or concurrently to ICI (cCT) influences clinical outcomes of HCC patients treated with ICI. **Methods:** This retrospective, multi-center observational study was conducted across 9 tertiary academic referral centers collected 341 HCC patients who received ICI across 3 continents between January 1, 2016 and April 1, 2019. Outcome measures included overall (OS) and progression-free survival (PFS) calculated from time of ICI commencement and overall response rates (ORR) defined by Response Evaluation Criteria in Solid Tumors (v1.1) on 6-8 weekly periodic restaging. **Results:** Of 331 eligible patients, 254 (76%) had BCLC-C stage HCC and received mostly PD(L)-1 ICI monotherapy (n=250, 85%). Median OS was 12.1 months (95%CI 9.2-15.0 months) and median PFS was 8.1 months (95%CI 6.3-10 months). In total 81 patients (24%) received >10 mg prednisone equivalent daily either as bCT (n=15, 4%) or cCT (n=66, 20%). Indications for CT included procedure/prophylaxis (n=37, 45%), management of irAE (n=31, 37%), cancer-related symptoms (n=5, 2%) or comorbidities (n=8, 3%). Neither overall CT, bCT nor cCT predicted for worse OS, PFS nor ORR in uni- and multi-variable analyses ($p>0.05$). CT for cancer-related indications predicted for shorter PFS (2.4 vs. 11.3 months, p=0.01), OS (4.5 vs. 12.8 months, p=0.05) and reduced ORR (p=0.03) compared to cancer-unrelated indications. **Conclusions:** This is the first study to demonstrate that neither bCT nor cCT appear to influence response and OS following ICI in HCC. Worse survival and ORR in CT recipients for cancer-related indications appears driven by the poor prognosis associated with symptomatic HCC. Research Sponsor: None.

532 Poster Session (Board #C13), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Respiratory-gated magnetic resonance image guided radiation therapy for hepatocellular carcinoma: A pilot study.

Hyun-Cheol Kang, Jin Ho Kim, Eui Kyu Chie; Department of Radiation Oncology, Seoul National University Hospital, Seoul, South Korea; Seoul National University College of Medicine, Seoul, South Korea

Background: Hypofractionated RT has shown encouraging results in hepatocellular carcinoma (HCC) patients. However, HCC adjacent to the gastrointestnal (GI) tract should be carefully treated using the high-precision irradiation technique due to risk of radiation damage. We evaluated the feasibility of a respiratory-gated magnetic resonance image guided radiation therapy (RgMRg-RT) for hepatocellular carcinoma (HCC). **Methods:** Thirty-three patients with HCC underwent RgMRg-RT in our hospital from 2015 to February 2019, including patients with Child-Pugh A/B7 cirrhosis and unresectable tumors near the gastrointestinal tract. The median radiation dose was 50 Gy (range, 25–60) and median fraction number was 5 (range, 4–15). Gating was performed based on real-time magnetic resonance image without an external surrogate. **Results:** The median follow-up period was 11.7 months (range, 3.6–37.9 months). The rates of local control of the target tumor at 6 months and 1 year were 90.2 and 86.9%, respectively. The overall survival rates at 6 months, 1, and 2 years were 84.3, 76.3, and 61%, respectively. The median distances from gross tumor to the esophagus, stomach, duodenum and colon were 6.1 (range, 1.9-14.3), 6.4 (0-13.4), 3.8 (0-13.5) and 4cm (0.3-13), respectively. A total of 15 tumors (45.5%) were located within 2 cm of the gastrointestinal tract and 9 tumors (27.3%) within 1cm. Grades 3 treatment-related bleeding was observed in one patient and one patient had radiation-induced liver disease. **Conclusions:** Hypofractionated RgMRg-RT was a safe and potentially ablative therapy for HCC. RgMRg-RT is a good alternative treatment for patients with HCCs that are unsuitable for surgical resection or local ablative therapy. Research Sponsor: None.

533 Poster Session (Board #C14), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Immunotherapy versus biologics as second-line therapy in advanced hepatocellular carcinoma (HCC).

Mohammed Al-Jumayli, Hannah Hildebrand, Saqib Abbasi, Anup Kasi, Anwaar Saeed; Kansas University Cancer Center, Kansas, KS; University of Kansas Medical Center, Kansas City, KS; Kansas University Cancer Center, Westwood,, KS; University of Kansas Cancer Center, Westwood, KS

Background: Sorafenib or lenvatinib are the current frontline options for advanced HCC. Multiple biologic agents including multi-Tyrosine Kinase Inhibitors (TKI) cabozantinib & regorafenib have been recently approved for the previously treated population. Immunotherapy (IO) agent Nivolumab have also been approved in the same setting. Due to lack of prospective head to head comparison, there is no standardized way for alternating those agents beyond frontline. **Methods:** We performed a retrospective review of KU cancer registry. Patients with advanced HCC were divided into 2 groups based on the 2nd line systemic regimen (IO vs non-IO). Kaplan–Meier and Cox proportional hazards models were utilized to evaluate progression free survival (PFS) and overall survival (OS). **Results:** Between 2016-2019, 98 patients were identified, 41 received IO, while 57 received biologics. All patients had sorafinib as 1st line therapy. Most patients have ECOG 0-1 and Child-Pugh class A or B. 55% had hepatitis C, 6% hepatitis B and 27 % have history of alcohol misuse. Almost 50% of patients have received prior liver directed therapy. Comparing IO vs non-IO groups, median PFS was 3.9 months vs 3 months and median OS was 10 months vs 10 months. There was no statistically significant difference in PFS & OS but there was a delay separation in the survival curve favoring IO. Similar outcome was seen in a sub-group analysis of the hepatitis C patients. **Conclusions:** This retrospective comparative review of current 2nd line regimens is one of the first & largest studies reported. In this study population, IO was not superior to multi-TKI as a 2nd line regimen. The late survival curve separation favoring IO might suggest a delay IO effect in a subgroup of patients. Future studies should define specific biomarkers that could predict response and allow treatment to be optimized depending on patient and tumor characteristics. Furthermore, combining IO plus multi-TKI might be a promising next step in development. A number of ongoing trials are testing this strategy including our CAMILLA trial of Cabozantinib plus Durvalumab, currently enrolling patients at the University of Kansas Cancer Center NCT03539822. Research Sponsor: None.

534 Poster Session (Board #C15), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Objective response (OR) by mRECIST to predict overall survival (OS) in patients with hepatocellular carcinoma (HCC) treated with sorafenib in the SILIUS trial.

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Background: In SILIUS (NCT01214343) trial, combination of sorafenib and hepatic arterial infusion chemotherapy did not significantly improve OS in patients with advanced HCC compared with sorafenib alone (Kudo M, et al. Lancet Gastroenterol Hepatol 2018). In this study, we explored the relationship between OR and OS in the sorafenib group in the SILIUS trial. **Methods:** Association between OR and OS in patients treated with sorafenib (n = 103) were analyzed. The median OS of responders was compared with that of non-responders by using Mantel-Byar test to exclude guarantee-time bias. Landmark analyses were performed, as sensitivity analyses, and the effect on OS was evaluated by Cox regression analysis with OR as a time-dependent covariate, with other prognostic factors. **Results:** OS of responders (n = 18) was significantly better than that of non-responders (n = 78) ($p < 0.0001$), where median OS was 27.2 (95% CI, 16.0–not reached) months for responders and 8.9 (95% CI, 6.5–12.6) months for non-responders. HRs from landmark analyses at 4, 6, and 8 months were 0.45 (p = 0.0330), 0.37 (p = 0.0053), and 0.36 (p = 0.0083), respectively. OR by sorafenib was an independent predictor of OS based on unstratified Cox regression analyses. **Conclusions:** In the SILIUS trial, OR achieved by sorafenib per mRECIST is an independent predictor for OS in patients with HCC. Research Sponsor: None.

Multivariable analysis of factors associated with OS.

	Multivariable analysis	
Parameter	**HR (95% CI)**	**p value**
Response (CR+PR vs. SD+PD)	0.38 (0.18–0.84)	0.0164
Age (≥65 vs. <65)		
Sex (male vs. female)		
PS (1 vs. 0)	1.88 (0.91–3.88)	0.0880
Vp (Vp1–4 vs. Vp0)		
Extrahepatic spread (yes vs. no)		
HBV (yes vs. no)	1.39 (0.71–2.72)	0.3381
HCV (yes vs. no)	0.86 (0.50–1.49)	0.5989
Albumin (≥3.6 vs. <3.6 mg/dL)		
Bilirubin (≥0.8 vs. <0.8 mg/dL)	1.35 (0.80–2.26)	0.2608
ALBI grade (grade 2 vs. grade 1)		
AFP (≥400 vs. <400 ng/mL)	1.70 (1.02–2.83)	0.0406
DCP (≥2,050 vs. <2,050 mAU/mL)		

535 Poster Session (Board #C16), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM and Poster Walks, Fri, 4:45 PM-5:30 PM

SHR-1210 combined with GEMOX as first-line treatment in patients with advanced biliary tract cancer.

Xiaofeng Chen, Xiaofeng Wu, Hao Wu, Qianwen Shao, Feipeng Zhu, Xiaofeng Qian, Fengjiao Zhao, Weidong Mao, Jing Sun, Jian Wang, Gaohua Han, Changxian Li, Poshita kumari Seesaha, Quanren Wang, Huajun Li, Yang Shao, Yanhong Gu, Xiangcheng Li, Yongqian Shu; The First Affiliated Hospital of Nanjing Medical University, Nanjing, China; Jiangyin People's Hospital, Jiangyin, China; Taizhou People's Hospital Affiliated to Nantong University, Taizhou, China; Jiangsu Hengrui Medicine Co., Ltd., Lianyungang, China; Nanjing Geneseeq Technology Inc., School of Public Health, Nanjing Medical University, Nanjing, China

Background: This study aimed to evaluate the efficacy and safety of SHR-1210 (a humanized anti-programmed cell death receptor 1 antibody) plus gemcitabine and oxaliplatin (GEMOX) as first line treatment in patients (pts) with biliary tract cancer (BTC). **Methods:** This was a single-arm, single-center, exploratory trial, which included advanced BTC pts. 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 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. The primary endpoint was the 6-month progression free survival (PFS) rate. **Results:** From February 2018 to April 2019, 37 eligible pts were enrolled. The median age was 64 (range 41-74) years, male/female was 70.3/29.7%, and bile duct cancer/gallbladder cancer was 59.5/40.5%. All 37 pts were included in the safety analysis. The overall AE incidence rate was 97.3%. The incidence of grade ≥3 AEs was 73.0%, which mainly included increased GGT (gammaglutamyltransferase, 18.9%), hypokalemia (18.9%), and fatigue (16.2%). Particularly, the incidence of fever is 73.0%, in which 2 pts experienced grade 3/4 fever. Among 36 evaluable pts, 19 pts got partial response (PR, 52.8%), 14 pts stable disease (SD, 38.9%), and 3 pts progressive disease (PD, 8.3%) at best. The primary endpoint 6-month PFS rate was 50.0% (95% CI 32.4-65.4), which indicated that the primary endpoint of the study was reached, and mPFS was 6.2 months (95% CI 4.2-7.1). The 12-month overall survival (OS) rate was 50.5% (95% CI 30.6-67.4), and mOS was 12.1 months (95% CI 8.0-NA). **Conclusions:** This study has reached the predefined primary endpoint with a high response rate. Predictive biomarker analysis was reported in another abstract. Further study is needed to validate the efficacy of this combination. Clinical trial information: NCT03486678. Research Sponsor: None.

536 Poster Session (Board #C17), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Biomarker exploration for SHR-1210 plus GEMOX as first-line treatment in advanced biliary tract cancer.

Xiaofeng Chen, Hao Wu, Xiaofeng Wu, Qianwen Shao, Feipeng Zhu, Xiaofeng Qian, Fengjiao Zhao, Weidong Mao, Jing Sun, Jian Wang, Gaohua Han, Huajun Li, Dongqin Zhu, Liuqing Zhu, Changxian Li, Poshita kumari Seesaha, Yang Shao, Yanhong Gu, Xiangcheng Li, Yongqian Shu; The First Affiliated Hospital of Nanjing Medical University, Nanjing, China; Jiangyin People's Hospital, Jiangyin, China; Taizhou People's Hospital Affiliated to Nantong University, Taizhou, China; Jiangsu Hengrui Medicine Co., Ltd., Lianyungang, China; Nanjing Geneseeq Technology Inc., Nanjing, China; Nanjing Geneseeq Technology Inc., School of Public Health, Nanjing Medical University, Nanjing, China

Background: We conducted a trial to evaluate the efficacy and safety of SHR-1210 (a humanized anti-programmed cell death receptor 1 antibody) plus gemcitabine and oxaliplatin (GEMOX) as in untreated patients (pts) with biliary tract cancer (BTC) (NCT03486678). This study is to explore the predictive biomarkers for efficacy. **Methods:** Baseline lymphocyte count and lactate dehydrogenase (LDH) level were obtained from routine tests. Gene mutation and tumor mutation burden (TMB) from baseline tissue and blood samples were tested by the next generation sequencing (NGS) with a 425-gene panel. The expressions of PD-L1 and markers for lymphocyte, natural killer cells, and macrophages in baseline tumor tissue samples were analyzed by immunohistochemistry (IHC). **Results:** The median progression free survival (PFS) and overall survival (OS) in this trial was 6.2m and 12.1m, respectively. Firstly, pts with normal LDH level ($\leq$271 U/L) had a tendency for longer PFS (6.2m vs 5.0m, p = 0.053) and significantly longer OS (p = 12.6m vs 6.8m, $p < 0.001$) than those with elevated LDH ($>$ 271 U/L). Low baseline lymphocyte count ($\leq 1.1\times10^9$/L) was related to worse OS (12.6m vs 6.9m, $p < 0.001$) and PFS (6.2m vs 3.9m, p = 0.021). Secondly, baseline tissue and ctDNA gene mutations were detected in 33 and 30 pts, respectively. Tissue analysis showed that pts with STK11 (p = 0.0254), CTNNB1 ($p < 0.001$) and SMARCA4 (p = 0.0181) wild type showed significantly longer PFS than those with mutations. Pts with ARID1A gene wild type showed a tendency for longer PFS (p = 0.0634) and significantly longer OS (p = 0.0149). Gene mutations from baseline ctDNA revealed that pts with wild type SMARCA4, CTNNB1, STK11, and NF1 had longer PFS than those with mutations. Lastly, IHC meant that PD-L1 positivity may be related to longer PFS (TPS $>$ 1%, p = 0.08; IPS $>$ 1%, p = 0.05). Besides, pts with CD68+ HLA-DR+ macrophages $>$ 0.01%, CD68+ HLA-DR- macrophages$>$2.5%, and CD56bright$>$1.7% and CD56dim $>$ 0.05 also got PFS benefits (all $p < 0.05$). TMB (cutoff = 7 muts/mbp) was not associated with PFS. **Conclusions:** Despite limited sample size, biomarkers from routine blood test, gene mutation and immune microenvironment can be helpful to stratify pts who are sensitive to immunotherapy in advanced BTC. Clinical trial information: NCT03486678. Research Sponsor: None.

537 Poster Session (Board #C18), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Treatment of hepatocellular carcinoma and liver metastases with hafnium oxide nanoparticles activated by SBRT: A phase I/II trial.

Nicolas Jaksic, Marc Pracht, Yann Rolland, Thierry De Baere, Jerome Durand-Labrunie, France Nguyen, Jean-Pierre Bronowicki, Veronique Vendrely, Antonio Sa Cunha, Valérie Croisé-Laurent, Emmanuel Rio, Samuel Le Sourd, Patricia Said, Sebastian Freund, Edwina Baskin-Bey, Pierre Gustin, Christophe Perret, Didier Peiffert, Eric Deutsch, Enrique Chajon; Centre Eugène Marquis, Rennes Cedex, Rennes, France; Oncodermatology Unit, Eugene Marquis Center CHU-CLCC, Rennes, France; Centre Eugène-Marquis, Rennes, France; Institut Gustave Roussy, Villejuif, France; Hôpital de Brabois Adultes, Vandœuvre-Lès-Nancy, France; CHU Bordeaux, Bordeaux, France; Centre Hépato-Biliaire, AP-HP, Hôpital Paul Brousse, Villejuif, France; Institut de Cancérologie de Lorraine, Nancy, France; ICO-Site René Gauducheau, Saint-Herblain, France; Nanobiotix, Paris, France; Nanobiotix, Cambridge, MA; Institut de Cancérologie de l'Ouest, Nantes, France; Centre Eugène Marquis, Rennes, France

Background: Treatment of unresectable liver cancer or liver metastases (mets) by stereotactic body radiotherapy is well tolerated but limited by the need to preserve liver function. Increasing energy deposition in the tumor while at the same time maintaining the dose in healthy tissue remains a major challenge in radiation oncology that could be achieved by NBTXR3 (hafnium oxide nanoparticles) when activated by radiotherapy (RT). NBTXR3 augments energy dose deposit within tumor cells, increasing tumor cell death compared to RT alone, while sparing healthy tissues. Patients (pts) with hepatocellular carcinoma (HCC) or liver metastasis (mets) may benefit from the mode of action of NBTXR3. A phase I/II clinical trial has been conducted to evaluate NBTXR3 activated by SBRT in these pts [NCT02721056]. **Methods:** The Phase I used a 3+3 dose escalation scheme with 5 NBTXR3 dose levels: 10, 15, 22, 33, and 42% of baseline tumor volume. NBTXR3 was administered by intratumoral injection (ITI) followed by SBRT (45 Gy / 3 fractions / 5 to 7 days or 50 Gy / 5 fractions / 15 days). Primary endpoints were identification of the recommended Phase II Dose and early DLTs. Secondary endpoints included safety profile, liver function evaluated by Child-Pugh score (CPS), AST to Platelet Ratio Index (APRI), and early efficacy by response rate (mRECIST/RECIST 1.1). **Results:** The dose escalation levels of 10, 15, 22 and 33% are completed (n = 17): 6 pts at 10% (2 SBRT doses tested due to organ constraints), 4 pts each at 15% and 22% (due to fiducial displacement and ITI shift) and 3 pts at 33%. No early DLT was observed and only one SAE (bile duct stenosis) related to NBTXR3 and RT occurred. CPS and APRI did not show clinically meaningful changes post-treatment and CT-scan showed no leakage of NBTXR3 into surrounding tissues. Best response for HCC (n = 8) were 5CR, 3PR and for mets (n = 6) the results were: 3 PR, 3SD. **Conclusions:** ITI of NBTXR3 is feasible, demonstrated a very good safety and tolerability profile up to the 33% dose level. Recruitment needs to be finalized at the 42% dose level. Based on early efficacy results NBTXR3 has the potential to address an unmet medical need in pts with unresectable primary or metastatic liver cancer. Clinical trial information: NCT02721056. Research Sponsor: Nanobiotix, S.A.

538 Poster Session (Board #C19), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Expansion part of phase I study of E7090 in patients with cholangiocarcinoma harboring FGFR2 gene fusion and with gastric cancer harboring FGFR2 gene amplification or FGFR2 protein high expression.

Chigusa Morizane, Makoto Ueno, Tatsuya Ioka, Masahiro Tajika, Masafumi Ikeda, Kensei Yamaguchi, Hiroki Hara, Hiroshi Yabusaki, Atsushi Miyamoto, Satoru Iwasa, Manabu Muto, Tsutomu Takashima, Keiko Minashi, Yoshito Komatsu, Tomohiro Nishina, Takako Eguchi Nakajima, Takatoshi Sahara, Setsuo Funasaka, Masakazu Yashiro, Junji Furuse; National Cancer Center Hospital, Tokyo, Japan; Kanagawa Cancer Center, Yokohama, Japan; Osaka International Cancer Institute, Osaka, Japan; Department of Endoscopy, Aichi Cancer Center Hospital, Nagoya, Japan; National Cancer Center Hospital East, Kashiwa, Japan; Department of Gastroenterology, The Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; Department of Gastroenterology, Saitama Cancer Center, Saitama, Japan; Niigata Cancer Center Hospital, Niigata, Japan; Department of Surgery, National Hospital Organization Osaka National Hospital, Osaka, Japan; Department of Experimental Therapeutics, National Cancer Center Hospital, Tokyo, Japan; Department of Clinical Oncology, Kyoto University Hospital, Kyoto, Japan; Osaka City University Graduate School of Medicine, Osaka, Japan; Clinical Trial Promotion Department, Chiba Cancer Center, Chiba, Japan; Hokkaido University Hospital, Sapporo, Japan; National Hospital Organization Shikoku Cancer Center, Matsuyama, Japan; Department of Clinical Oncology, St. Marianna University School of Medicine, Kawasaki, Japan; Eisai Co., Ltd, Tokyo, Japan; Kyorin University, Tokyo, Japan

Background: E7090 is a selective tyrosine kinase inhibitor against FGFR1-3. This first-in-human phase I study has been conducted in Japan and consists of 2 parts. Based on the toxic, pharmacokinetic, and pharmacodynamic profiles in Part 1, dose escalation study, the recommended dose was determined to be 140 mg QD for Part 2, an expansion study part restricted to patients with tumors harboring FGFR gene alterations. Here we provide the interim analysis results of Part 2. **Methods:** In Part 2, patients with cholangiocarcinoma harboring FGFR2 gene fusion (CCA cohort) and gastric cancer harboring FGFR2 gene amplification or FGFR2 protein high expression (GC cohort) were enrolled. Patients received oral dosing of E7090 until disease progression or unacceptable toxicity. Safety was assessed using CTCAE version 4.03. Tumor response was evaluated by site investigators using RECIST 1.1. **Results:** As of 31 March 2019, 16 patients including 6 patients in CCA cohort and 10 patients in GC cohort received E7090 in Part2. Median age was 63 years, 25% were female, ECOG PS of 0 and 1 were 50% respectively. 5 patients (83%) in CCA cohort and 1 patient (10%) in GC cohort achieved partial response as the best overall response. The disease control rates were 100% in CCA cohort and 30% in GC cohort, respectively. Median progression-free survivals were 8.3 months in CCA cohort and 2.8 months in GC cohort at the cut-off date. 2 patients with CCA remain on treatment. The most common treatment-related TEAEs occurring in 30% or more of patients in Part 2 were hyperphosphatemia (100%), palmar–plantar erythrodysesthesia syndrome (56%), paronychia (50%), dysgeusia (38%), stomatitis (31%), diarrhea (31%), increased AST (31%) and blood creatinine increased (31%). Grade≥3 treatment-related TEAEs were reported in 2 out of 16 patients (13%); they were increased AST, lipase increased and retinopathy. **Conclusions:** This study indicated that E7090 has a manageable safety profile in Part 2 and the promising clinical activity in CCA patients with FGFR2 gene fusion. Research Sponsor: Eisai co., Ltd.

539 Poster Session (Board #C20), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Pharmacokinetics/pharmacodynamics (PK/PD) of ivosidenib in patients with mutant *IDH1* advanced cholangiocarcinoma from the phase III ClarIDHy study.

Bin Fan, Ghassan K. Abou-Alfa, Andrew X. Zhu, Shuchi Sumant Pandya, Hongxia Jia, Feng Yin, Liewen Jiang, Camelia Gliser, Hua Yang; Agios Pharmaceuticals, Inc., Cambridge, MA; Memorial Sloan Kettering Cancer Center & Weill Cornell Medical College, New York, NY; Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA

Background: Mutations in isocitrate dehydrogenase 1 (m*IDH1*) occur in up to 20% of intrahepatic cholangiocarcinomas (CC), leading to accumulation of 2-hydroxyglutarate (2-HG) and epigenetic dysregulation, promoting oncogenesis. Ivosidenib (IVO; AG-120), a first in-class, oral, targeted inhibitor of the mIDH1 enzyme, showed improved progression-free survival and a positive trend in overall survival versus placebo (PBO) in ClarIDHy, a global, phase 3, multicenter, double-blind study (Abou-Alfa et al. ESMO 2019 LBA10_PR; NCT02989857). **Methods:** Patients (pts) with unresectable or metastatic m*IDH1* CC were randomized 2:1 to IVO (500 mg once daily in continuous 28-day cycles) or matched PBO, stratified by number of prior systemic therapies (1 or 2). Crossover from PBO to IVO was permitted at radiographic progressive disease. Blood samples for PK/PD analyses, a secondary endpoint, were collected predose, 0.5, 2, and 4 h postdose on day (D) 1 of cycles (C) 1–2, predose and 2 h postdose on D15 of C1–2, and predose on D1 from C3 onwards. Plasma IVO and 2-HG were measured using validated or qualified LC-MS/MS methods. **Results:** As of 31Jan2019, 185 pts were randomized to IVO (n = 124) or PBO (n = 61); 35 pts crossed over to IVO. PK/PD analysis was available from 156 pts receiving IVO. IVO was absorbed rapidly following single and multiple oral doses; exposure, as measured by C_{max} and AUC, was higher at C2D1 than after a single dose, with low accumulation. Plasma IVO reached steady state within C1 of daily dosing. In pts receiving IVO, baseline mean plasma 2-HG concentration was reduced from 1108 ng/mL to 97.7 ng/mL at C2D1, close to levels in healthy subjects (72.6±21.8 ng/mL). 2-HG inhibition was robust and persistent up to Cycle 19. An average 2-HG inhibition of 75.0% (up to 97.3%) was observed at steady-state after multiple IVO administrations. No plasma 2-HG decreases were seen with PBO. Analyses of plasma 2-HG levels and association with clinical outcomes will be presented. **Conclusions:** In pts with advanced m*IDH1* CC, oral IVO 500 mg once-daily demonstrated good exposure, and maintained the inhibition of 2-HG to levels observed in healthy subjects, whereas 2-HG remained elevated with PBO. Clinical trial information: NCT02989857. Research Sponsor: Agios Pharmaceuticals, Inc.

540 Poster Session (Board #D1), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Role of para-aortic lymph node sampling for patients with potentially resectable biliary cancer.

Hiromichi Ito, Yoshihiro Ono, Takafumi Sato, Yosuke Inoue, Yu Takahashi; Japanese Foundation for Cancer Research, Tokyo, Japan

Background: While paraaortic lymph node (PALN) metastasis has been known as poor prognostic indicator for patients with biliary cancer and is regarded as distant metastasis in AJCC staging system. However, preoperative diagnosis of PALN metastasis by current imaging studies is not accurate and the incidence of PALN metastasis among patients with potentially resectable biliary cancer and its impact on their long-term outcomes remain unclear. **Methods:** The patients who underwent exploratory laparotomy with PALN sampling for potentially resectable biliary cancer at our institution from 2006 through 2018 were included. All patients were appropriately staged preoperatively with CT/MRI and patients with suspected PALN metastasis preoperatively were not considered resectable disease, and thus, such patients were not included. The incidence of PALN metastasis and long-term outcomes (recurrence-free and overall survivals [RFS, OS]) for patients with/without PALN metastasis were compared. **Results:** Total 383 patients with three types of biliary cancers (164 perihilar cholangiocarcinoma [PHCC], 115 distal cholangiocarcinoma [DCC] and 104 gallbladder cancer [GBCA]) were included. The median age was 71 years and 65% were man. Majority of them (362 patients [95%]) completed planned resection and 9 patients (2%) died of post-operative complications. PALN metastasis was confirmed on 33 patients (9%) among the entire cohort; the yield of positive PALN sampling was the highest in the patients with GBCA (14%), followed by 9% in those with PHCC and 4% in those with DCC. Among 33 patients with positive PALN, 20 underwent tumor resection. Median RFS and OS following resection for the patients with PALN metastasis were 11 months and 22 months, respectively, compared to 46 months and 56 months for those without, respectively ($p< 0.001$ for both RFS and OS). There were no survivors beyond 5-years among those with PALN metastasis. **Conclusions:** The yield of routine intra-operative PALN sampling is not small even among patients with potentially resectable biliary cancer and positive PALN indicates poor long-term outcomes. This procedure can provide the opportunity to avoid morbid operation for patients who unlikely benefits. Research Sponsor: None.

541 Poster Session (Board #D2), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Irreversible electroporation of the bile duct in swine: A pilot study.

Sang Hyun Kim, Jae Min Lee, Kang Won Lee, Sang Hoon Kim, Se Hyun Jang, Han Jo Jeon, Seong Ji Choi, Hyuk Soon Choi, Eun Sun Kim, Bora Keum, Yoon Tae Jeen, Hoon Jai Chun, Hong Sik Lee, Chang Duck Kim, Department of Gastroenterology, Korea University Anam Hospital; Department of Gastroenterology, Korea University Anam Hospital, Seoul, South Korea; Korea University College of Medicine, Seoul, South Korea; Korea University Anam Hospital, Seoul, South Korea

Background: Irreversible electroporation (IRE) is a relatively new ablative method. However, the application of IRE ablation has not been attempted for the treatment of biliary disease. Minimally invasive approach using endoscopic retrograde cholangio-pancreatography (ERCP) can be a novel therapeutic modality for IRE ablation. In this study, we investigated the feasibility and effect of endoscopic IRE for biliary tract in animal model. **Methods:** A new catheter electrode was developed for endoscopic IRE ablation of biliary tract. The electrode for IRE ablation has two band-shaped electrodes on catheter tip. We performed ERCP and endoscopic IRE ablations on normal common bile duct in 6 Yorkshire pigs. Experimental parameters of IRE were 500V/cm, 1000V/cm and 2000V/cm (under 50 pulses, 100 μs length). Animals were sacrificed after 24 hours and ablated bile duct were collected. H & E stain, immunohistochemistry and western blot were performed. **Results:** Well-demarcated focal color changes were observed on the mucosa of the common bile duct under all experimental parameters. After IRE ablation, bile duct epithelium was disappeared around ablated area and it showed fibrotic change in H&E stain. Depth of change after IRE was different between each experimental parameters. Apoptotic change of bile duct was localized around mucosa in 500V. Diffuse transmural fibrosis of bile duct was shown after IRE ablation with 2000V. TUNEL immunohistochemistry showed the cell death of bile duct mucosa and submucosa along the electrode. Within 24 hours, no complication was observed in pigs after endoscopic IRE ablation. **Conclusions:** Endoscopic IRE ablation using ERCP was successfully performed on common bile duct by using catheter-shaped electrode. It can be a potential therapeutic option as minimally invasive ablation for treatment of biliary tumors. Research Sponsor: None.

542 Poster Session (Board #D3), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Regorafenib in patients with unresectable hepatocellular carcinoma (uHCC) in routine clinical practice: Interim analysis of the prospective, observational REFINE trial.

Ho Yeong Lim, Philippe Merle, Richard S. Finn, Catherine Frenette, Gianluca Masi, Masafumi Ikeda, Hong Zebger-Gong, Sabine Fiala-Buskies, Kirhan Ozgurdal, Masatoshi Kudo, Shukui Qin; Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; Groupement Hospitalier Lyon Nord, Hepatology Unit, Lyon, France; David Geffen School of Medicine at UCLA, Los Angeles, CA; Scripps Green Hospital, La Jolla, CA; Azienda Ospedaliero-Universitaria Pisana, Pisa, Italy; National Cancer Center Hospital East, Kashiwa, Japan; Bayer AG, Berlin, Germany; Bayer AG, Wuppertal, Germany; Bayer, Basel, Switzerland; Kindai University Faculty of Medicine, Osaka, Japan; Chinese People's Liberation Army Cancer Center of Nanjing Bayi Hospital, Nanjing, China

Background: Regorafenib significantly improved overall survival (OS) versus placebo in patients (pts) with uHCC who progressed on prior sorafenib therapy in the phase 3 RESORCE trial. The multicenter, international REFINE trial was designed to evaluate the safety and effectiveness of regorafenib in uHCC in the real-world setting. **Methods:** This prospective, observational trial aims to recruit 1000 pts with uHCC for whom a decision to treat with regorafenib has been made by the treating physician prior to enrollment according to the local health authority approved label. The primary endpoint is the incidence of treatment-emergent adverse events (TEAEs) and dose modifications due to TEAEs (NCI-CTCAE v4.03). Secondary endpoints are OS, progression-free survival, time to progression, best overall tumor response, and duration of treatment. Tumor response and progression are assessed per investigator according to local standard. An interim analysis includes the first 500 pts observed for ≥4 months. We report baseline characteristics, starting dose, and treatment duration for the interim analysis. **Results:** Of 498 pts evaluable for analysis, median age was 67 years (range: 22–91) and 84% were male. 59% were from Asia. Proportions of pts with ECOG performance status 0–1/≥2 were 82%/5% (missing 13%); 67% and 11% of pts had Child–Pugh A and B liver function, respectively (missing/not evaluable 21%). 60% of pts had metastases and 33% had vascular invasion. HCC etiology included hepatitis B 37%, alcohol use 26%, hepatitis C 23%, and NASH 7%. Baseline alpha-fetoprotein levels were < 400/≥400 ng/mL in 44%/26% of pts (missing 31%). The initial regorafenib dose was 160 mg/day (d) in 58% of pts, 120 mg/d in 13%, and 80 mg/d in 28% (8 pts initiated at 40 mg/d). The mean (SD) initial daily dose was 131 mg/d (37). Median duration of treatment was 3.7 months (IQR: 1.9–8.5). **Conclusions:** In this interim analysis of the observational REFINE study, some differences were observed in the characteristics of pts treated with regorafenib from the phase 3 RESORCE trial, reflecting less stringent inclusion criteria in a real-world study. Efficacy and safety analyses are ongoing. Clinical trial information: NCT03289273. Research Sponsor: Bayer.

543 Poster Session (Board #D4), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Capecitabine and cisplatin as a second-line chemotherapy for patients with advanced biliary tract cancer.

Kabsoo Shin, In Seok Lee, Tae Ho Hong, Joori Kim, Myung Ah Lee; The Catholic University of Korea, Seoul St. Mary's Hospital, Seoul, South Korea; Catholic University of Korea, Seoul, South Korea; Department of Surgery, Seoul St. Mary's Hospital, Seoul, South Korea; Seoul St Mary's Hospital, Seoul, South Korea; Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, South Korea

Background: Few data are available on second-line chemotherapy for patients with advanced biliary tract cancer. We retrospectively analyzed the efficacy and safety of capecitabine and cisplatin combination as second-line chemotherapy for advanced biliary tract cancer. **Methods:** Between Mar, 2014 and Dec, 2018, advanced BTC patients who received second-line capecitabine and cisplatin after the failure of the gemcitabine-platinum combination were analyzed. Progression-free survival (PFS) and overall survival (OS) were estimated with the Kaplan-Meier method. Cox models were used for multivariate analyses. **Results:** Of total 40 patients, male: female was 24(60%) to 16(40%), and the median age was 68 years old (range: 45-77) . As primary tumor site, 8(20%) was intrahepatic, 16(40%) was extrahepatic and 16(40%) was gallbladder. Initially metastatic disease was 22(55%), and recurrent disease after curative surgery was 17(42.5%) and locally advanced unresectable disease was 1(2.5%). 30(75%) patients had ECOG performance status of 0-1. The mean number of the chemotherapy cycles was 3.3 $\pm$ 2.0. Objective response rates and stable disease were 12.5% and 25%, respectively. Median PFS and median OS from the beginning of the capcitabine and cisplatin combination were 2.8 and 7.0 months, respectively. Grade 3-4 adverse event were neutropenia (n = 7, 17.5%), anemia(n = 3, 7.5%), hand-foot syndrome (n = 3, 7.5%), nausea and vomiting(n = 2, 5%), peripheral neuropathy (n = 2, 5%) and mucositis(n = 1, 2.5%). And there was no treatment related death. **Conclusions:** This study showed the possible survival benefit of capecitabine and cisplatin combination as second-line chemotherapy for advanced biliary tract cancer. Research Sponsor: None.

544 Poster Session (Board #D5), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Pattern of progression in advanced HCC treated with ramucirumab/placebo: Results from two randomized phase III trials (REACH/REACH-2).

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Background: REACH (NCT01140347) and REACH-2 (NCT02435433) studied ramucirumab (RAM) in pts with advanced hepatocellular carcinoma (HCC) following sorafenib; REACH-2 enrolled pts with baseline alpha-fetoprotein (AFP) ≥400 ng/mL, and met its primary endpoint of overall survival (OS) for RAM vs placebo. This post-hoc analysis examined radiological progression patterns (RPP) incidence every 6 weeks per RECIST v1.1, and if RPP were related to OS and post-progression survival (PPS). **Methods:** Pts with advanced HCC, Child-Pugh A, and ECOG PS 0-1 with prior sorafenib were randomized (REACH 1:1; REACH-2 2:1) to receive RAM 8 mg/kg or placebo Q2W. Among pts with ≥1 RPP (new extrahepatic lesion [NEH], new intrahepatic lesion [NIH], extrahepatic growth [EHG], or intrahepatic growth [IHG]), results were analyzed by trial and for pooled individual patient data of REACH-2 and REACH (AFP ≥400 ng/mL). Cox models evaluated treatment effect of RPP on OS, and prognostic implications of RPP on OS (adjusting baseline ECOG PS, AFP, macrovascular invasion, arm) and on PPS (adjusting ECOG PS, AFP at progression). **Results:** RPP incidence in the pooled population was: NEH 39%; NIH 24%; EHG 39%; IHG 37%. When examining NEH vs other RPP, PPS was worse among those with NEH in REACH (HR 2.33, 95% CI 1.51, 3.60), REACH-2 (HR 1.49, 95% CI 0.72, 3.08), and the pooled data (HR 1.75, 95% CI 1.12, 2.74). Use of post-discontinuation therapy may have influenced results. OS was also significantly reduced in those with NEH across studies (Table). RAM provided OS benefit in the pooled population, including pts with NEH (HR 0.56, 95% CI 0.39, 0.80). **Conclusions:** Acknowledging limitations of post-randomization RPP analysis, the emergence of NEH on RAM or placebo may be an independent poor prognostic factor for PPS. The impact of RAM on OS was consistent across all RPP subgroups. Clinical trial information: NCT01140347 and NCT02435433. Research Sponsor: Eli Lilly and Company.

Multivariate Cox models (HR [95% CI]) of OS by RPP.

RPP Pattern vs All Others	REACH N=414	REACH-2 N=211	Pooled (AFP ≥400 ng/mL) N=398
NEH	**1.84 (1.24, 2.73)**	**1.94 (1.05, 3.60)**	**1.89 (1.27, 2.83)**
NIH	1.10 (0.73, 1.66)	1.55 (0.67, 3.58)	1.24 (0.76, 2.02)
EHG	1.08 (0.75, 1.55)	1.31 (0.71, 2.43)	1.12 (0.75, 1.67)
IHG	1.08 (0.75, 1.57)	1.68 (0.95, 2.97)	1.48 (1.01, 2.16)

545 Poster Session (Board #D6), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Comparative efficacy of second-line treatments for advanced hepatocellular carcinoma: A network meta-analysis.

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Background: Hepatocellular carcinoma (HCC) is the most common primary liver malignancy, and is often advanced at the time of diagnosis. This study conducted a network meta-analysis (NMA) to assess the comparative efficacy of second-line (2L) immunotherapy and tyrosine kinase inhibitors (TKIs) without biomarker selection for advanced HCC (aHCC), including nivolumab (NIVO) + ipilimumab (IPI), cabozantinib (CABO), regorafenib (REG), and placebo (PBO). **Methods:** Randomized trials for CABO and REG (CELESTIAL and RESORCE) were identified through a literature review and included in the NMA. NIVO (1mg/kg) + IPI (3mg/kg) (from CHECKMATE-040) was linked into the evidence network through a matching-adjusted indirect comparison (MAIC) vs. the PBO arm of the CELESTIAL trial. The CELESTIAL trial was chosen due to the similar study design and patient population as the CHECKMATE-040 trial. Clinically relevant characteristics were matched, which included age, sex, Barcelona clinic liver cancer stage, Eastern Cooperative Oncology Group status, α-fetoprotein level, and prior treatments. The NMA included CELESTIAL, RESORCE, and the MAIC results. Investigator-assessed ORR and hazard ratio (HR) of overall survival (OS) were compared in the NMA. **Results:** After matching the baseline characteristics in the MAIC, the ORR of NIVO+IPI was 30.4% and the HR vs. PBO was 0.35. In the NMA, NIVO+IPI had significantly higher ORR (31.2%) compared to TKIs and PBO (REG: 4.8%; CABO: 4.2%; PBO: 1.0%, differences are presented in Table). In addition, NIVO+IPI was associated with significantly prolonged OS vs. TKIs and PBO (HR: NIVO+IPI vs. REG: 0.56; NIVO+IPI vs. CABO: 0.46; NIVO+IPI vs. PBO: 0.35). **Conclusions:** The NMA showed that NIVO+IPI was associated with significantly higher ORR and prolonged OS compared to TKIs as 2L treatments for aHCC. Research Sponsor: Bristol-Myers Squibb.

NMA results.

	NIVO+IPI vs. others (95% credible interval)	
	Difference in ORR (%)	HR of OS
REG	26.4 (14.3, 40.1) *	0.56 (0.32, 0.97) *
CABO	26.9 (15.2, 40.4) *	0.46 (0.27, 0.79) *
PBO	30.1 (18.6, 43.5) *	0.35 (0.21, 0.58) *

* p-value$<$0.05

546 Poster Session (Board #D7), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Hepatic and hematological toxicity associated with selective internal radiation therapy (SIRT): A meta-analysis of randomized clinical trials.

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Background: For advanced hepatocellular cancers (HCCs) and colorectal cancers (CRCs) with liver metastasis, the impact of selective internal radiation therapy(SIRT) with yttrium-90 on survival outcomes is not established. A meta-analysis of randomized clinical trials (RCT) was performed to determine the relative risk (RR) of hepatic and hematological toxicities with the use of SIRT, compared to therapies not including SIRT. For patients with advanced HCC or CRC, we assessed the RR of high grade (grades 3 and 4) hyperbilirubinemia, fatigue, leucopenia, thrombocytopenia and elevated liver enzymes (AST and ALT) with use of SIRT. **Methods:** Citations from PubMed/Medline, clinical trials.gov, package inserts, and abstracts from major conferences were reviewed to include RCTs comparing arms with or without SIRT. Potential publication bias was assessed using the Egger test for funnel plot asymmetry. There was no publication bias and the trials were of high quality per Jadad scoring. Patients in control arms received trans-arterial chemo-embolization (TACE) or sorafenib for HCC or FOLFOX for CRC. The proportion and 95% confidence intervals (CIs) for patients with adverse events were derived for each arm of each study and used to calculate the RR. For the meta-analysis, both the fixed-effects model and the random-effects model were considered; the method proposed by DerSimonian and Laird was used to estimate the random-effects model. **Results:** The RR of grade 3/4 leucopenia was consistently high across high with the use of SIRT across all the studies (RR 2.05, 95% CI (1.22-3.42), p-value 0.027). The risk of hepatic dysfunction and fatigue was higher with SIRT but not statistically significant. **Conclusions:** Since SIRT is associated with increased risk of high-grade leukopenia, caution is advised in selecting patients with HCC's with underlying decompensated cirrhosis or with CRCs and on cytotoxic therapy. Proper selection of patients would reduce toxicities from SIRT alone or SIRT in combination with systemic chemotherapy. Research Sponsor: None.

547 Poster Session (Board #D8), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

A pilot study of durvalumab/tremelimumab (durva/treme) and radiation (XRT) for metastatic biliary tract cancer (mBTC): Preliminary safety and efficacy.

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Background: Metastatic biliary tract cancer (mBTC) is a lethal malignancy with median 5 year OS of less than 10%. Immunotherapy, particularly single agent anti-PD-1/PD-L1, has limited efficacy in mBTC with ORR~9-15%. Recently presented data shows responses in metastatic MSS pancreatic or colon cancer with combination anti-PD-1/CTLA-4 and radiation (XRT) to produce systemic response (abscopal effect) (Parikh A, GI ASCO 2019, ASCO 2019.). We evaluate safety and efficacy of dual PD-1/CTLA-4 inhibition with XRT in MSS mBTC. **Methods:** 15 of a planned 15 mBTC patients were enrolled. Eligible pts had histologically-confirmed mBTC, ECOG-PS 0/1, and must have progressed on at least one line of previous therapy or refused standard therapy. Safety cohort of 6 pts of durva 1500 mg/treme 75 mg q4w was enrolled. If $>$ 2 DLTs, patients were enrolled subsequently to dose level -1 (durva 1125 mg/ treme 75 mg q4w). 3 fractions of 8 Gy of radiation at C2D1 every other day to a single metastatic site. Durva/treme continued for 4 cycles, followed by 4 cycles of maintenance durva until progressive disease, discontinuation or withdrawal. Endpoints include disease control rate (DCR (SD+PR+CR)), PFS and OS and safety. Radiological evaluations were done q2 mo. **Results:** 15 mBTC pts enrolled and evaluable from May 2018 to March 2019. Median age 63 years (range 48-75), 47% male. DLTs occurred in 3 patients during the safety run-in. One patient experienced DLT at dose level -1 and subsequent expansion. 3 patients did NOT reach radiation therapy. DCR was 27% with a 13% PR and 7% CR. Of those who reached radiation, DCR was 33% with a 17% PR and 8% CR. At time of analysis, median PFS was 54 days for ITT mBTC. Duration of response for 4 patients with DCR was 26, 52, 122, 254+ days. Treatment-related adverse events were reported in 12/15 patients (80%). Grade $\geq$3 toxicities were seen in 9/15 pts (60%) with lymphopenia (5 grade 3) and elevated LFTs (2 grade 4 and 4 grade 2) being the main adverse events. All patients with disease control were not MSI. **Conclusions:** Combination of durva/treme XRT is feasible and shows preliminary activity in metastatic BTC. An expansion cohort is being planned to confirm activity. Clinical trial information: NCT03482102. Research Sponsor: Astra Zeneca.

548 **Poster Session (Board #D9), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

The efficacy and safety of lenvatinib in patients with intermediate-stage hepatocellular carcinoma: A nationwide multicenter study in Japan.

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Background: Lenvatinib (LEN) has been used in patients with unresectable hepatocellular carcinoma (u-HCC) since Mar 2018 in Japan. We conducted a nationwide multicenter study and especially focused on the efficacy and safety in the patients with intermediate-stage u-HCC. **Methods:** A total of 240 patients received LEN from March 2018 at 15 sites in Japan was enrolled. Tumour assessments in accordance with modified RECIST were done using dynamic CT or MRI within 4-8 weeks and every 6-8 weeks thereafter. **Results:** In this study, 88 of 240 (36.7%) patients were BCLC stage B. Among them 76 (86.3%) patients received TACE before LEN and the median number of TACE was 2 (1-10). Only 4 patients were TKI experienced and other 84 (95.5%) patients received LEN as a 1st line therapy. The median pretreatment ALBI score was -2.35 and 75 (85.2%) patients were Child-Pugh A. In this cohort, 73 (83.0%) patients were beyond up-to-seven criteria and the median pretreatment AFP was 38.2 (2-12870) ng/mL. The median observation time was 8.5 months and 16 patients died. The median progression free survival was 8.7 months, and the median overall survival (OS) was not reached. Objective response rate (ORR) and disease control rate (DCR) were 48.5% and 80.3%. AFP decrease ($>$ 20%) after 1 month was observed in 52 (59.0%) patients. Child-Pugh B patients (n = 13) had significantly shorter OS than Child-Pugh A (p = 0.02) and median OS in Child-Pugh B patients was 8.8 months. The patients received $>$ 6 times TACE before LEN had significantly shorter OS than patients received $\leq$ 6 times TACE (p = 0.02). Additional TACE was performed in 8 patients and The median time of restarting LEN was 19 days. The median ALBI score before additional TACE, Day 1 after TACE and Day 28 after TACE were -2.38, -2.07, and -2.36.There was no severe adverse event associated with additional TACE. The median duration of LEN in patients treated with LEN and additional TACE was 8.5 months. **Conclusions:** The ORR and DCR of LEN in Child-Pugh A patients with intermediate-stage HCC were 46.6% and 79.3%. The therapeutic strategies for intermediate-stage HCC should be discussed based on the liver function, tumor states, and treatment course about TACE. Research Sponsor: None.

549 Poster Session (Board #D10), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Ramucirumab for patients with intermediate-stage hepatocellular carcinoma (HCC) and elevated alpha fetoprotein (AFP): Pooled results from two phase III studies (REACH and REACH-2).

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Background: Intermediate-stage HCC, as defined as Barcelona Clinic Liver Cancer (BCLC) Stage B, is a heterogeneous disease in terms of liver function and tumor load. REACH (NCT01140347) and REACH-2 (NCT02435433) investigated ramucirumab (RAM) in patients (pts) with HCC after prior sorafenib (SOR), with REACH-2 enrolling only pts with baseline AFP ≥400 ng/mL. An exploratory analysis of outcomes by BCLC stage was performed. **Methods:** All pts had HCC (BCLC stage C or B disease refractory/not amenable to locoregional therapy), Child-Pugh A, ECOG PS 0-1, and prior SOR. Pts were randomized to RAM 8 mg/kg or Placebo (P) Q2W. A pooled meta-analysis of independent pt data (stratified by study) from REACH-2 and REACH (AFP ≥400 mg/mL) was performed. Prognosis of BCLC staging in overall survival (OS) was evaluated by multivariate Cox PH model (adjusted for baseline AFP and treatment (trt) arm); Trt effects in BCLC stage B and C by Cox PH model; median OS/PFS were estimated by Kaplan-Meier method. Objective response rate (ORR) per RECIST v1.1, disease control rate (DCR), and adverse events (AEs) were also reported by BCLC. Liver function was assessed at baseline and prior to each trt with the Albumin-Bilirubin (ALBI) linear predictor. **Results:** Baseline characteristics were generally balanced between trt arms in each BCLC stage. BCLC staging trended as an independent prognosis factor for OS [B v C; HR = 0.756 (0.546, 1.046)]. A consistent trt benefit for RAM v P was observed across staging (Table). Grade ≥3 AEs were consistent with observations from both individual studies; hypertension was the most frequent grade ≥3 AE. No difference in liver function, as measured by ALBI, was observed between trt arms in either BCLC stage. **Conclusions:** Acknowledging limitations of sample size, RAM provided a survival benefit irrespective of BCLC stage. RAM was well tolerated and did not alter liver function compared to P. Clinical trial information: NCT01140347, NCT02435433. Research Sponsor: None Eli Lilly and Company.

BCLC	B	C
Pooled Population (RAM v P)	N = 52 (RAM 30, P 22)	N = 490 (RAM 286, P 204)
OS median, mo	13.7 v 8.2	7.7 v 4.8
HR (95% CI)	0.43 (0.23, 0.83)	0.72 (0.59, 0.89)
PFS median, mo	4.2 v 2.8	2.8 v 1.5
HR (95% CI)	0.33 (0.17, 0.64)	0.60 (0.49, 074)
ORR, %	17 v 5	4 v 1
DCR, %	80 v 59	54 v 35

550 Poster Session (Board #D11), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Hyperprogressive disease during PD-1 blockade in patients with advanced hepatocellular carcinoma.

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Background: Immune checkpoint blockade with PD-1 inhibitors has shown promising clinical efficacy in patients with hepatocellular carcinoma (HCC). However, emerging evidences show that PD-1 blockade can sometimes lead to a flare-up of tumor growth with rapid clinical deterioration (hyperprogressive disease, HPD). This study aimed to evaluate the incidence and pattern of HPD in a multicenter, real-world cohort of East Asian patients with advanced HCC treated with PD-1 blockade. **Methods:** We enrolled 148 advanced HCC patients treated with nivolumab between March 2016 and December 2018 in Korea. Clinicopathologic variables, tumor growth dynamic, and treatment outcomes were comprehensively analyzed. Progressive disease was assessed using tumor growth kinetics (TGK), tumor growth rate (TGR), and time to treatment failure (TTF), and patient with HPD were defined as those who met the criteria of progressive disease by both TGK and TGR. **Results:** In this large cohort of HCC patients, the median age was 60 years and the majority were male (85%) and HBV-infected (72%). The objective response rate was 17.6% including two complete responders (1.4%). Ongoing responses were seen in 46% of responders at data cut-off. The incidence of HPD after PD-1 blockade was 23%. HCC patients with HPD had dismal prognosis with worse progression-free survival (PFS) and overall survival (OS) (HR, 1.947; 95% CI, 1.226-3.093 and HR, 1.839; 95% CI, 1.108-3.055, respectively) than progressive disease without HPD. Among various baseline clinicopatholgic parameters, elevated neutrophil-to-lymphocyte ratio (NLR) was only significantly associated with HPD. The optimal cut-off value of NLR for HPD prediction was 3.74 determined by ROC curves, and NLR $>$ 3.74 was associated with worse PFS and OS. **Conclusions:** The real-world efficacy of PD-1 blockade in HCC patients was consistent with previous studies. However, there was also a corresponding risk of HPD as well as a clinical benefit. Therefore, careful patient selection using immunologic biomarkers, such as NLR, could enhance the therapeutic benefit of PD-1 blockade in clinical trials and real-world practice of HCC.

551 Poster Session (Board #D12), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

In vitro and in vivo efficacy and safety of tumor treating fields (TTFields) and sorafenib combination in hepatocellular carcinoma.

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Background: Hepatocellular carcinoma (HCC) is a leading global cause of cancer-related mortality. Sorafenib (oral multikinase inhibitor) is approved in patients with advanced HCC, yet survival benefit is limited. Tumor Treating Fields (TTFields) are an effective, anti-neoplastic treatment modality delivered via noninvasive, low intensity (1-3 V/cm), intermediate frequency (100-500 kHz), alternating electric fields. The study aim was to explore *in vitro* and *in vivo* effects of TTFields alone and combined with sorafenib for HCC treatment. **Methods:** HCC (HepG2 and Huh-7D12) cells were TTFields treated with at frequencies of 100-400 kHz for 72 hr using the inovitro system. Efficacy of TTFields and sorafenib combined treatment was tested at optimal frequency with various sorafenib concentrations. Cell counts, apoptosis induction, and clonogenic potential were determined. Healthy rats were used to assess safety of TTFields applied to the abdomen. N1S1 HCC cells were injected into the left hepatic lobe of Sprague Dawley rat; after 1 week, TTFields (1.2 V/cm) and sorafenib (10 mg/kg) were applied for 6 days. Tumor growth was evaluated using MRI. **Results:** The optimal TTFields frequency was 150 kHz in HepG2 and Huh-7D12 HCC cells. TTFields 150 kHz treatment (1.0 - 1.7 V/cm, 72 hr) led to cell count reductions (53-55%) and further decreases in clonogenic potential (65-69%). TTFields and sorafenib combination treatment led to a significant reduction in cell count (2-way ANOVA, $P < 0.05$) vs either treatment alone. Also, tumor growth was significantly reduced in the combined treatment group vs the control group (student t test, $P < 0.01$). Tumor volume (fold increase) in the combination treatment group (1.6) was significantly lower vs control (5.9, $P < 0.0001$), TTFields alone (3.3, $P < 0.01$), and sorafenib alone (2.3, $P < 0.05$) groups. Safety studies did not reveal any TTFields related adverse events with delivery to the rat abdomen. **Conclusions:** *In vitro* and *in vivo* data demonstrated efficacy and safety of TTFields in HCC; and improved efficacy in combination with sorafenib. A phase 2 study (HEPANOVA; NCT03606590) will explore the clinical potential of TTFields 150 kHz plus sorafenib. Research Sponsor: Novocure.

552 Poster Session (Board #D13), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Role of precision medicine for patients with advanced biliary tract cancers.

Antoine Hollebecque, Oumrou Nabi, Michel Ducreux, Valerie Boige, Jean-Yves Scoazec, Etienne Rouleau, Alice Boileve, Cristina Smolenschi, Loic Verlingue, Margarida Matias, Pascal Burtin, Caroline Prieux-Klotz, Christophe Massard, David Malka; Gustave Roussy Cancer Campus, Villejuif, France; Gustave Roussy, Villejuif, France; Digestive Oncology, Gustave Roussy, Villejuif, France; Department of Biopathology, Gustave Roussy Cancer Campus, Villejuif, France; Institut Gustave Roussy, Villejuif, France; Gustave Roussy, Université Paris-Saclay, Villejuif, France; Drug Development Unit, Institut Gustave Roussy Cancer Centre, Villejuif, France; Gustave Roussy, Université Paris-Saclay, Département de Médecine Oncologique, Villejuif, France

Background: Biliary tract cancers (BTC) are rare and heterogeneous cancers with poor prognosis. Several actionable genomic targets have been described in BTC but data on the efficacy of targeted therapies remain limited. The main objectives of this retrospective study was to evaluate the frequency of actionable genomic alterations among BTC and the impact of targeted therapy. **Methods:** We performed a retrospective analysis on BTC patients seen at Gustave Roussy (IGR) from Dec 2011 to Jul 2019. All clinical and genomic reports were reviewed. **Results:** The study population included 212 patients with the main following characteristics: median age 61 years, female 51%, intrahepatic cholangiocarcinoma 57%, median of 2 previous lines. Of 212 BTC patients, 170 patients had a genomic profile based on archival tissue or a new tumor biopsy (IGR panel n = 120; Foundation One panel n = 92). 124 patients (73%) had at least one genomic alteration and 68 (40%) patients had genomic alteration considered as actionable. The most common actionable targets were FGFR2 rearrangement/mutation (n = 24, 35.3%), HER2/3 mutations (n = 9, 13.2%) and IDH1/2 mutations (n = 7, 10.3%). Of those 68 patients, 58 received the matched targeted therapy: FGFR inhibitor n = 24, HER2/3 inhibitors n = 9, Akt/PIK3CA/mTOR inhibitors n = 7, IDH1 inhibitor n = 6. In the treated population, the objective response rate was 36.2% and the disease control rate 85.1%. Progression-free survival (PFS) was 6.2 months compared to 2.8 months (p = 0.02) for patients who did not received targeted treatment. Overall survival (OS) was 17.7 months compared to 11.0 months (p = 0.03) for patients who did not received targeted treatment. **Conclusions:** Actionable genomic targets are frequent among BTC. Profiling-directed therapies resulted in a 36% response rate, a 85% tumor control rate and a 6.2 months PFS which compare favorably to second-line chemotherapy. A randomized trial is required to confirm the benefit of precision medicine in BTC. Research Sponsor: None.

553 Poster Session (Board #D14), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

The impact of inflammatory biomarkers, BMI, and sarcopenia on survival in advanced hepatocellular carcinoma treated with immunotherapy.

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Background: Sarcopenia and inflammation are independently associated with worse survival in cancer patients. This study aims to determine the impact of inflammatory biomarkers, BMI and sarcopenia on survival in advanced hepatocellular carcinoma (HCC) patients treated with immunotherapy. **Methods:** We performed a retrospective review of advanced HCC patients treated with immunotherapy-based therapies at Winship Cancer Institute between 2015 and 2019. Baseline computed tomography and magnetic resonance imaging scans were collected at mid-L3 level, assessed for skeletal muscle density using SliceOmatic (TomoVision, version 5.0) and converted to skeletal muscle index (SMI) by dividing it by height $(m)^2$. Gender-specific sarcopenia was defined by median value of SMI. The optimal cut for continuous inflammation biomarker was determined by bias-adjusted log-rank test. Overall Survival (OS) was set as primary outcome and Cox proportional hazard model was performed. **Results:** 57 patients were included; 77.2% male, 52.6% Caucasian, 58.5% ECOG PS 0-1, 80.7% Child Pugh A. Treatment was second line and beyond in 71.9%. The median follow-up time was 6 months. Sarcopenia cut-off for males and females was SMI of 43 and 39, respectively. 49.1% of patients had sarcopenia. Median OS was 5 vs. 14.3 months in sarcopenic vs. non-sarcopenic patients (p=0.054). Median OS was 5 and 17.5 months in patients with BMI <25 and BMI ≥ 25 respectively (p=0.034). Median OS was 3.6 and 14.3 months for patients with neutrophil to lymphocyte ratio (NLR) $\geq$ 5.15 vs. NLR $<$ 5.15 ($p<0.001$). In multivariable Cox regression model, higher baseline NLR was associated with worse OS (HR: 4.17, 1.52-11.39, p=0.005). Gender specific sarcopenia showed a trend of worse OS (HR: 1.71, 0.73-4.00, p=0.215) but was not statistically significant. BMI<25 was associated with worse OS (HR: 2.73, 1.15-6.53, p=0.023). In the association with PFS, neither baseline BMI nor gender specific sarcopenia showed statistical significance. **Conclusions:** Baseline BMI and NLR may predict OS after immunotherapy treatment. After controlling for baseline Child Pugh Score and NLR, gender specific sarcopenia was not associated with OS significantly. Research Sponsor: None.

554 Poster Session (Board #D15), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM and Poster Walks, Fri, 4:45 PM-5:30 PM

First-in-human phase I trial of small activating RNA (saRNA) oligonucleotide MTL-CEBPA in combination with sorafenib in patients with advanced hepatocellular carcinoma (HCC).

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Background: MTL-CEBPA is the first saRNA to enter clinical trials and targets the transcription factor C/EBPα, a master regulator of myeloid cell differentiation. We have previously reported a favourable safety profile of MTL-CEBPA given as a single agent QWx3 every 28 days, in patients with HCC (Sarker D et al, ASCO 2018). After discontinuation of MTL-CEBPA, three out of five patients treated with sorafenib off study have had maintained complete radiological response (CR) of 7-18 months duration; 2 patients demonstrated resolution of lung metastases $>$ 1 year. Here we provide updated data on phase 1 patients treated with sorafenib off study as well as subsequent combination cohorts. **Methods:** MTL-CEBPA 130mg/m^2 QWx3 or BIW and sorafenib 400mg bd were administered to patients with HCC using combination or sequential dosing regimens, in cohorts either tyrosine kinase inhibitor naive or resistant. On treatment liver biopsies evaluated changes in M2 macrophages (CD163). Flow cytometry of peripheral blood determined changes in myeloid cell populations. **Results:** 12 patients have been treated with MTL-CEBPA co-administered with sorafenib and 14 patients treated with MTL-CEBPA followed by sorafenib (23M/3F, median age 65.5years, range 44-83, ECOG PS 0/1: 18/8). The most common treatment-related AEs (all grades/grade 3) in this group include facial flushing (4/0), raised AST (3/1) raised ALT (2/1), fatigue (5/0), raised ALP (2/0), and anaemia (2/2), diarrhoea (3/0), rash (2/0) and anorexia (1/0). 1 TKI naïve patient in the co-administration cohort has maintained CR at 7 months and two patients have SD (ongoing at 3 & 4 months both in sequential cohort). IHC in the patient with CR has demonstrated 95% reduction in M2 macrophages with significant decrease in frequency of immature CD10- neutrophils (-85.7%; p = 0.0078), PMN-MDSCs (-49.3%; p = 0.00145) and M-MDSCs (-18.4%; P = 0.0072). All responding patients have underlying HBV or HCV. **Conclusions:** MTL-CEBPA is a novel saRNA targeting myeloid cells which may result in a significantly enhanced oncological response in HCC of viral aetiology. Updated safety and efficacy data will be presented. Clinical trial information: NCT02716012. Research Sponsor: MINA Therpaeutics.

555 Poster Session (Board #D16), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Predictors of immunotherapy (IO) response in hepatocellular carcinoma (HCC).

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Background: Despite advances in understanding the molecular pathways of HCC, therapeutic options are limited and patient survival is dismal. IO is a promising HCC treatment. There are currently no indicators to identify which patients (pts) will have a prolonged response. **Methods:** In this single-institutional retrospective analysis, pts received one of five IO containing regimens with nivolumab, pembrolizumab, atezolizumab plus bevacizumab, durvalumab or cemiplimab until disease progression (PD) or unacceptable toxicity. Relevant factors including: stage, viral etiology, vascular invasion (VI), tumor thrombus (TT), multifocal disease, toxicity grade, steroid use for IO mediated toxicities and derived Neutrophil-to Lymphocyte ratio (dNLR), were correlated to clinical outcome: progression free survival (PFS), overall survival (OS), response rate (RR), using Pearson's chi-square test or student's t-test . Responses were assessed using RECIST v 1.1 criteria for stable disease (SD), partial response (PR) and PD were correlated with best response and PFS. OS was calculated by the Kaplan-Meier method. **Results:** Cohort demographics (n = 76) were: 72% male; 38% African American, 30% Caucasian and 16% Asian; 29% of pts had HBV, 41% had HCV, 1% had both HBV/HCV and 13% had no viral etiology (n = 64). The majority of pts were stage III (43%) or IV (38%). At the start of IO, 32% had VI, 32% had TT and 80% had multifocal or metastatic disease. 65% of pts experienced IO toxicity, with 24.3% at grade 3 or higher, and 34% requiring steroids. Best response to IO was SD in 65.7% of pts, PR in 25.7% and PD in 8.6%. Median OS was 13m (95% CI 7.9-18.1) from the start of IO and median PFS (n = 65) was 14m (95% CI 6.8-21.2). Median OS and PFS were significantly improved in pts with PR compared to PD (45 vs 8m, $p < 0.0005$, PFS 15 vs 3m p = 0.007). Both OS and PFS showed benefits for SD of $\geq$2 months compared to those with PD (11 vs 8m, $p < .0005$, PFS 5 vs 3m p = .007). VI, TT, stage, viral etiology, toxicity grade or dNLR did not correlate with OS, PFS and RR, however need of steroid treatment trended toward worse outcome. **Conclusions:** PR and SD are independent predictors for prolonged PFS and OS in HCC pts receiving IO therapy. Absence of steroid use for toxicity trended toward improved IO response. Research Sponsor: None.

556 Poster Session (Board #D17), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Phase II study of copanlisib in combination with gemcitabine and cisplatin in advanced cholangiocarcinoma.

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Background: First line therapy for advanced cholangiocarcinoma (CCA) is currently gemcitabine and cisplatin. However, survival rarely exceeds one year with this regimen. PI3K/AKT activation has been shown to increase resistance to chemotherapy in CCA; therefore, inhibiting this pathway may improve chemotherapy's efficacy. This phase II study evaluated the safety and efficacy of copanlisib, a potent and reversible pan-class I PI3K inhibitor, with gemcitabine and cisplatin in advanced CCA. **Methods:** Between July 2016 and April 2019, pts with histologically confirmed advanced/unresectable CCA received cisplatin (25 mg/m^2), gemcitabine (1000mg/m^2), and copanlisib 60mg on day 1 and 8, every 21 days as first line treatment. The primary endpoint was PFS at 6 months. Secondary endpoints were RR, median OS and PFS, and safety profile. A single-arm Simon's two-stage minimax design with one-sided 10% type I error and 80% power was used. Based on ABC-01 and ABC-02 studies, PFS6 for gemcitabine and cisplatin were 57.1% and 59.3%, respectively. Therefore, PFS6 of 57% was considered not to warrant further study and ≥72% to warrant further investigation. **Results:** Twenty-four pts received at least one dose of the study drug (62.5% female, median age 64 years), with 70.8% intrahepatic, 16.7% extrahepatic, and 12.5% gallbladder cancer. For all pts, median OS was 13.9 months (95% CI: 6.8-17.9) and median PFS was 6.2 months (95% CI: 1.3-11.1). PFS at 6 and 12 months was 57.0% and 42.2%, and 6 and 12-month OS was 73.9% and 53.2%, respectively. Only 19 pts were considered evaluable for RR. Five pts were either lost to follow up, withdrew consent, or died before a second scan was done. Six pts achieved PR (31.5%) and 11 (57.9%) had SD. Grade 3 or higher adverse events (AE) occurred in 75% of pts. The most common grade 3/4 AEs were decreased neutrophil count (40%) and increased lipase (20%). Treated related AEs led to drug discontinuation for 3 pts (12.5%) and dose modification for 7 pts (29.2%). **Conclusions:** Gemcitabine, cisplatin, and copanlisib in combination did not meet the primary endpoint of 6-month PFS. However, additional correlative work is ongoing to identify a possible biomarker for copanlisib. Clinical trial information: NCT02631590. Research Sponsor: Bayer AG.

557 Poster Session (Board #D18), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Clinical characteristics and outcomes of patients with advanced hepatocellular carcinoma treated with immunotherapy: A real-world retrospective study.

Adel Chergui, Eswar Gadde, Seda Serra Tolu, Ana Acuna-Villaorduna, Rafi Kabarriti, Sanjay Goel, Andreas Kaubisch; Jacobi Medical Center, Bronx, NY; Montefiore Medical Center, Bronx, NY; Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY

Background: Advanced HCC is an aggressive malignancy with dismal prognosis. Newer agents, including immunotherapy (IT), have been granted accelerated approval. Information outside clinical trials is scarce. This study is aimed to describe the clinical characteristics and outcomes of HCC patients treated with IT. **Methods:** Patients with HCC treated with IT were identified using the institutional data-mining software, Clinical Looking Glass. Patient demographics, clinical, and treatment characteristics were collected. Progression-free survival (PFS) was defined as time from treatment initiation to disease progression or death, and overall-survival (OS) as time from diagnosis of advanced disease to death. PFS and OS were plotted using Kaplan-Meier curves. **Results:** A total of 52 patients; median age 64 years; male predominance (38, 73.1%) were identified. There were 24 (54.5%) Hispanics, 9 (20.5%) Non-Hispanic Blacks, 7 (15.9%) Non-Hispanic White and 4 (9.1%) Asians. Cirrhosis was seen in 41 (83.7%), and median MELD score was 8 (IQ: 7-10). Hepatitis B and C infection were encountered in 12 (24.5%) and 22 (44%) patients, respectively. Imaging evidence of intravascular invasion was seen in 16 (34.8%) and extrahepatic metastases in 7 (14.9%) cases. Local treatment was provided to 29 (59.2%) and radiation treatment to 14 (28.6%) patients. Nivolumab was used in all the cases, as first-line treatment in 17 (32.7%) and as ≥ second line in 35(67.3%). The median PFS was 6.2 (3.1-10.6) months and was similar in first-line and ≥ second line treatment (8 vs 5.9 months, p=0.90). The median OS was 24.2 (18-28) months; there was a tendency towards higher survival rates in patients that were treated in ≥ second line (16.8 vs 25.2 months, 0=0.07). **Conclusions:** In this multiethnic cohort, the "real world" experience of the benefit of IT in HCC is encouraging, with a median OS exceeding two years. Expanded data may elucidate the differences if any, between use of IT as front vs. second line therapy, in PFS and OS. Research Sponsor: None.

558 Poster Session (Board #D19), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Intensity-modulated proton therapy using dose-painting pencil beam scanning for high-risk hepatocellular carcinoma.

Stephanie K. Schaub, Stephen R. Bowen, Matthew J. Nyflot, Smith Apisarnthanarax; University of Washington, Seattle, WA; Department of Radiation Oncology, University of Washington, Seattle, WA

Background: High rates of local control are achievable with hypofractionated proton therapy with passive techniques for hepatocellular carcinoma (HCC), but may have limitations when tumors are adjacent to organs-at-risk (OARs), which may result in tumor underdosage and lead to inferior local control. We present the first reported series of HCC patients treated with pencil beam scanning (PBS) intensity-modulated proton therapy (IMPT) using a simultaneous-integrated boost and protection (SIB/SIP) technique to escalate tumor dose while protecting adjacent OARs. **Methods:** Twenty-five HCC patients were treated between 2015-2019 with a 15-fraction regimen using IMPT SIB/SIP. SIB/SIP dose levels generally ranged from 36.0-67.5 GyRBE to minimize dose to OARs at their respective dose-limiting thresholds (e.g. luminal gastrointestinal organs, chest wall). Radiation-induced liver disease (RILD) was defined by a Child-Pugh (CP) score increase of 2 or greater and/or any RTOG grade 3 enzyme elevation. Other toxicities were graded by CTCAEv5.0. Overall survival (OS), progression-free survival (PFS), and local control were calculated using the Kaplan-Meier method. **Results:** Patients most commonly had BCLC stage B or C disease (84%) and CP-A (80%) and ALBI grade 2 (60%) liver function. Median gross tumor volume (GTV) size and volume were 12.3 cm (range 2.17-20.57) and 461 cc (range 4.68-2439), and 32% had gross vascular invasion. Median mean and minimum dose delivered to the gross tumor volume (GTV) was 64.0 GyRBE (EQD2 76.1, BED 91.3, range 54.3-69.6) and 45.1 GyRBE (EQD2 48.9, BED 58.7, range 33.4-67.7), respectively. Median mean dose to liver minus GTV was 15.0 GyRBE (range, 8.2-19.6). 1-year OS, PFS, and local control were 66%, 32%, and 84%, respectively. No isolated local failures occurred. Two patients experienced RILD with no RILD-related deaths. Two grade 3 non-GI toxicities occurred: 1 rib fracture and 1 pneumonitis. No acute or late GI grade $\geq$2 occurred. **Conclusions:** In our series of HCC patients with large tumors near OARs, IMPT SIB/SIP allows for tumor dose escalation while sparing of OARs and results in favorable local control and acceptable toxicities. Research Sponsor: None.

559 Poster Session (Board #D20), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Real-world efficacy and safety of immune checkpoint inhibitors in advanced hepatocellular carcinoma: Experience of a tertiary Asian center.

Kennedy Ng, Lawrence Wen Jun Wong, Su Pin Choo, David Wai-Meng Tai, Sze Huey Tan, Andrea Jing Shi Ang, Joycelyn Jie Xin Lee; National Cancer Centre Singapore, Singapore, Singapore; National University of Singapore, Singapore, Singapore; National Cancer Center Singapore, Curie Oncology, Singapore, Singapore; National Cancer Center Singapore, Singapore, Singapore; Division of Clinical Trials & Epidemiological Sciences, National Cancer Centre Singapore, Singapore, Singapore; Department of Medical Oncology, National Cancer Centre Singapore, Singapore, Singapore

Background: Immune checkpoint inhibitor (ICI) use in advanced hepatocellular carcinoma (HCC) is increasing. Real-world data on efficacy and safety however is lacking, more so when used in patients who fall out of standard clinical trial criteria. **Methods:** We conducted a retrospective review of all patients with advanced HCC seen at our centre who received at least one dose of an ICI between May 2015 - June 2018. Data cutoff was 31 Dec 2018. Responses were evaluated using RECIST v1.1 criteria. **Results:** 114 patients fulfilled inclusion criteria. Median age was 66 years and 88.6% were male. 96.5% had an ECOG PS of 0 – 1. 64.9% received an ICI within a clinical trial setting. 62.3% received monotherapy ICI. 19.6% of patients had Child-Pugh B disease on initiation of ICI, and 69.3% had an ALBI Grade of 2. 50.0% were known to have hepatitis B and 11.4% had hepatitis C. Baseline HBV VL ranged from undetectable to 8210000 IU/mL. 30.7% received prior systemic treatment, most commonly sorafenib (82.9%). Over a median follow-up duration of 5.7 months (0.03 - 42.4), ORR was 18.4%, and disease control rate (DCR) was 51.8%. Median PFS was 2.6 months (1.7 - 3.9), and median OS was 13.9 months (7.0 - 16.2). 5 patients (23.8%) had response duration of more than 18 months. 35.1% received further systemic therapy after ICI. On multivariable analyses, age $\geq$ 65 years, higher albumin level and lower bilirubin level were associated with increased OS. 68.0% of patients experienced adverse events (AEs) of any grade, 12.0% of these being grade 3 - 4. No grade 5 adverse events were observed. Use of antiviral therapy was associated with a lower risk of hepatic AEs (p = 0.04) whilst high baseline HBV VL was not associated with an increased risk of reactivation or hepatic AEs. **Conclusions:** In the real-world setting, responses and adverse event profiles to ICI use are comparable to those observed in clinical trials despite a more heterogenous population base. The expansion of indications for ICI use in advanced HCC beyond current approvals warrants greater study. Research Sponsor: None.

560 Poster Session (Board #D21), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Clinical outcomes of hepatocellular carcinoma patients with Child-Pugh class B treated with stereotactic body radiation therapy.

J Richelcyn Baclay; Stanford University, Stanford, CA

Background: Caution is usually employed in the treatment of patients with hepatocellular carcinoma (HCC) due to the inherent liver radiosensitivity, especially in patients with Child Pugh (CP) B and C classes. This study aims to review the outcomes of patients treated with SBRT for CP class B with HCC. **Methods:** Medical records of all patients with HCC and compromised liver function (CP class B) treated with SBRT between 2003 and 2018 were retrieved after institutional review board approval. Clinical, laboratory, and treatment-related data were collected and analyzed for their correlation to toxicity and survival. Liver function was assessed prior to SBRT and at 1, 3 and 6 months after treatment using the CP score classification. Patients were censored for toxicity after extensive tumor progression in the liver, new liver-directed therapies, or liver transplant. Time-to-events were calculated from date of SBRT. **Results:** A total of 22 patients were identified, but 3 were excluded for incomplete follow-up. Median follow-up time was 33 months (range: 11-95 months). At baseline, 13 (68%) patients had a CP score of 7, and 6 (32%) had a CP score of 8. The median PTV volume was 94 cc (range: 14-710 cc). The median prescribed dose was in 5 fractions (range: 35-45 Gy in 3-5 fractions). After SBRT, 8 (42%) patients presented with worsening in CP score, with a mean increase of 1.5 points (95% CI, 0.6-2.5; p = 0.005) at the first month of follow-up, but followed by recovery in liver function with change in CP score not statistically different from baseline at 3- or 6-month follow-up times (p = 0.35 and p = 0.13, respectively). Eight patients (42%) presented with acute hepatobiliary toxicity, with six of those presenting with ≥grade 2 toxicity. Patients with CP score change ≥2 points (n = 6) showed a significantly higher incidence of acute grade 2 or higher hepatobiliary toxicity (p = 0.001) with a trend toward worse overall survival (33 vs. 51 months, p = 0.45). **Conclusions:** In our cohort, SBRT demonstrated to be safe for patients with Child Pugh Class B liver function. Research Sponsor: None.

561 Poster Session (Board #D22), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Proteomic features of HCC tumors reveal clinically distinct subtypes independent of somatic mutations.

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Background: Recent massive sequencing studies of HCC genomes revealed many new genetic alterations that might be accountable for HCC development and provided comprehensive view of malignant disease. However, genomic profiling of tumors is limited by a loose correlation between genetic alterations and their functional products such as proteins and metabolites. To overcome current limitation, we generated genomic and proteomic data together from HCC tumors and performed integrated analysis of both data sets. **Methods:** We analyzed proteomic data and genomic data such as somatic mutations, mRNA expression, miRNA expression, and copy number alterations from 300 HCC tumors to uncover most correlated genomic alterations with proteins. Clinical significance of identified key protein features were validated in multiple independent cohorts of HCC patients. **Results:** Analysis revealed three subtypes of HCC with substantial difference in proteomic patterns. Based on proteomic characteristics, three subtypes were named to mesenchymal (MES), metabolically active (MA), and kinase-active and genome stable (KAGS) subtypes. When assessed clinical relevance, the overall survival rate of patients in MES subtype was significantly worse than those in MA and KAGS subtype (P = 0.001). Poor clinical outcomes of mesenchymal subtype is validated in multiple independent cohorts (in total of >500 patients). Gene network analysis with integrated genomic and proteomic data further revealed association of subtypes with currently available treatments of HCC such as sorafenib and immunotherapy. In addition, multiple in-depth analysis of integrated data identified potential therapeutic target candidates for each subtype. Functional validation with cell lines demonstrated that some of candidates are essential for survival of HCC cells. **Conclusions:** HCC is classified into three subtypes by integrating genomic and proteomic data. These analyses has identified potential therapeutic targets as well as biomarkers associated with therapeutic targets. Our study demonstrated merit of integrated analysis of proteomic data with genomic data to uncover potential driver genes of HCC development. Research Sponsor: MD Anderson Cancer Center.

562 Poster Session (Board #E1), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Exploring the genomic landscape of hepatobiliary cancers to establish a novel molecular subtype classification.

Anthony Joseph Scholer, Mary Garland-Kledzik, Debopyria Ghosh, Juan Santamaria-Barria, Adam Khader, Javier Orozco, Melanie Goldfarb, Diego M. Marzese; John Wayne Cancer Institute at Providence St. John's Health Center, Santa Monica, CA; Applied Probability and Data Analytics Lab, Rutgers University, Newark, NJ; John Wayne Cancer Institute at Providence Saint John's Health Center, Santa Monica, CA

Background: The current understanding of the genomic landscape of hepatobiliary cancer (HBC) is limited. Recent genomic and epigenomic studies have demonstrated that various cancers of different tissue origins can have similar molecular phenotypes. Therefore, the aim of this study is to evaluate the genomic alterations of HBCs as a first step towards creating a novel molecular subtype classification. **Methods:** A multidimensional analysis of next-generation sequencing for the genomic landscape of HBCs was conducted using mutational data from the AACR-Genomics Evidence Neoplasia Information Exchange database (v. 5.0). From 61 gene mutation platforms, we found 42 genes common to all HBC cases. Associations between histomolecular characteristics of HBCs (hepatocellular (HCC), cholangiocarcinoma (CCA), and gallbladder carcinoma (GBC)) with gene mutations (classified by COSMIC CENSUS) were analyzed using Pearson's $\chi 2$ test. **Results:** A total of 1,017 alterations were identified in 61 genes (516 missense variant, 157 gene amplifications, 101 inactivating mutations, 106 truncating mutations, 84 upstream gene variants, 37 gene homozygous deletions, 16 gene rearrangements) in 329 patients: 115 (35%) CCA, 87 (26.4%) GBC, and 127 (38.6%) HCC. The majority 77.8% (256) of tumors harbored at least two mutations and 38.9% (128) had at least one alteration, with GBC having a higher average number of alterations (3.28) than HCC (3.23) and CCA (2.49) However, HCCs had the higher maximum number of alterations compared to CCA and GBC ($p < 0.05$). The ten genes most frequently altered across all the HBCs were *TP53, TERT, CTNNB1, KRAS, ARID1A, CDKN2A, IDH1, PIK3CA, MYC,* and *SMAD4* with disparities in the distribution of genes altered repeatedly observed ($p < 0.001$). IDH1 mutations were associated with CCA, CTNNB1 and TERT mutations with HCC, and TP53 mutations with both HCC and GBC. **Conclusions:** HBC subtypes appear to have unique mutational landscapes, but also significant overlap of genetic signatures. Therefore, further exploratory genetic and epigenomic research is needed to develop a histomolecular classification algorithm that can be used for prognostic and therapeutic stratification of these cancers. Research Sponsor: None.

563 Poster Session (Board #E2), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Apurinic/apyrimidinic endonuclease-1 and hepatocellular carcinoma.

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Background: The enzyme apurinic/apyrimidinic endonuclease-1 (APE1) is associated with protection against DNA damage and oxidative damage congruent with cancer. The purpose of this study is to investigate hepatic APE1 levels in association with hepatocellular carcinoma (HCC) in order to better stratify patients with underlying liver disease for the development of HCC and identify novel targets for therapy. **Methods:** Hepatic APE1 levels were determined by immunohistochemistry staining and ELISA within liver and tumor samples from patients with HepC±HCC. Hepatic APE1 staining was semi-quantitated using a scale of 0-100. Serum APE1 levels were determined by ELISA. In addition, APE1 staining was quantified in hepatic paraffin embedded sections from $MDR2^{-/-}$ mice with HCC and within $MDR2^{-/+}$ mice controls that do not develop HCC. **Results:** Hepatocyte APE1 staining was lower in livers from patients with HepC and HCC when compared to patients with HepC without HCC. In a similar manner, hepatic APE1 levels were significantly lower in patients with HepC and HCC patients when compared to HepC controls. In contrast, serum APE1 level was greater in patients with HepC and HCC when compared to patients with HepC and no HCC. Moreover, APE1 levels were greater in HCC tumors when compared to non-malignant liver tissue. Hepatocyte APE1 staining in $MDR^{-/-}$ mice with HCC was lower when compared to $MDR2^{-/+}$ mice that do not develop HCC. In addition, cytosolic APE1 staining was increased in HCC tumor of $MDR2^{-/-}$ mice when compared to controls. **Conclusions:** Increased APE1 is a potential biomarker of HCC risk in patients with underlying liver disease and is a novel target for therapy in patients with underlying liver disease whom have a higher risk of developing HCC. Consequently, targeted APE1 inhibition may increase chemotherapy response by reducing tolerance to DNA damage. Additional studies are required to better understand the role of APE1 inhibition in HCC in the face of reduced background hepatic APE1 levels. Research Sponsor: None.

564 Poster Session (Board #E3), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Phase Ib study of regorafenib (REG) plus pembrolizumab (PEMBRO) for first-line treatment of advanced hepatocellular carcinoma (HCC).

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Background: REG is a multikinase inhibitor with immunomodulatory activity and PEMBRO is an anti-PD-1 monoclonal antibody. Both are approved as monotherapy for patients (pts) with HCC previously treated with sorafenib. Based on their potential synergistic effects, we conducted a phase 1b study of REG plus PEMBRO for first-line treatment of advanced HCC. **Methods:** This is an ongoing, open-label, dose-escalation study in pts with advanced HCC who had no prior systemic therapy. In the first cohort, pts received REG 120 mg/day PO for 3 weeks on/1 week off plus PEMBRO 200 mg IV q 3 weeks. In later cohorts, the REG dose could be escalated (160 mg) or reduced (80 mg) based on the modified toxicity probability interval design; the PEMBRO dose is fixed. The primary objective is safety and tolerability. Secondary objectives are to define the maximum tolerated dose (MTD) and recommended phase 2 dose, and to assess antitumor activity. **Results:** As of August 23, 2019, 29 pts have been treated at the REG 120 mg level. Median age is 65 years (range 32–81); 41%/55% of pts are BCLC stage B/C; 100% are Child–Pugh A; ECOG status 0/1 is 72%/28%. Dose-limiting toxicities occurred in 4/18 evaluable pts: grade (Gr) 3 increased ALT/AST with Gr 2 increased bilirubin (n = 2); Gr 3 rash (n = 2). The MTD of REG in the combination was 120 mg. Most common Gr 3 or 4 treatment-emergent adverse events (TEAEs) are shown (n = 29). There were no Gr 5 TEAEs. 59%/31% of pts had REG/PEMRO-related Gr 3 or 4 TEAEs. Dose modifications (reductions or interruptions) of REG/PEMBRO for drug-related TEAEs occurred in 59%/31% of pts. Of 23 evaluable pts, 7 (30%) had a partial response (PR) and 14 (61%) had stable disease (RECIST v1.1); 1 additional pt had PR by mRECIST. **Conclusions:** The combination of REG plus PEMBRO for first-line treatment of advanced HCC showed no unexpected safety signals and encouraging antitumor activity. Accrual is continuing at REG 120 mg dose and an expansion cohort evaluating REG 80 mg plus PEMBRO is planned. Clinical trial information: NCT03347292. Research Sponsor: Bayer.

TEAEs (Gr 3/4 in ≥10% pts), n (%)	Gr 3	Gr 4
AST increased	7 (24)	0
Hypertension	5 (17)	0
ALT increased	3 (10)	1 (3)
Bilirubin increased	4 (14)	0
Lipase increased	4 (14)	1 (3)
Hyperglycemia	3 (10)	0
Hyponatremia	3 (10)	0

MedDRA v22.0; CTCAE v4.03 grade

565 Poster Session (Board #E4), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Association of CXCR2+ granulocytic myeloid derived suppressor cells with the development of cholangiocarcinoma: A possible target for intervention.

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Background: Cholangiocarcinoma (CCA) is the second most common primary liver malignancy, with increasing incidence. Currently, surgical resection offers the only chance for cure, however the prognosis remains poor in part due to high rates of unresectability, recurrence, and poor response to conventional therapy. Thus, new systemic therapies represent an unmet medical need. Few preclinical models exist for identifying and testing new targeted or immune based therapies. Here we present our findings of the immune infiltrate in human CCA tumor microenvironment (TME) and a spontaneous murine model that faithfully recapitulates human disease. **Methods:** Histology and immunohistochemistry (IHC) staining was performed on human CCA and adjacent normal liver. Mice with targeted hepatic Kras activation and loss of p53 (KPPC) spontaneously develop CCA. KPPC hepatic tumors and normal livers from littermate controls underwent histological and gene expression studies. Flow cytometric analysis was performed on bone marrow, spleen, peripheral blood, CCA tumors and normal littermate livers. **Results:** Digital IHC quantification of archival human CCA specimens demonstrated elevated levels of $CD15^{+}CXCR2^{+}$ granulocytic myeloid derived suppressor cells (G-MDSC) compared to adjacent normal liver ($p = < 0.05$). In addition, the CXCR2 ligand, CXCL5, was significantly elevated in CCA tumors compared to adjacent normal liver. In KPPC mice, flow cytometric analysis of hepatic tumors showed an abundance of $CD45^{+}$ leukocytes comprised of immunosuppressive G-MDSC vs normal littermate controls ($p = 0.0007$) which recapitulates human disease. qRT-PCR demonstrated significantly increased expression of *G-csf, Csf1*, *Cxcl1*, *Cxcl2*, and *Cxcl5* ($p = < 0.0001$) in CCA KPPC tumors compared to normal livers. Accordingly, granulocytes in KPPC mice were elevated in both the bone marrow and blood compared to normal littermate controls. **Conclusions:** These data suggest CCA co-opts the ELR+ cytokine/CXCR2 axes to mobilize and recruit immunosuppressive G-MDSC to the TME. Targeted therapy against tumor infiltrating neutrophils can be tested in this pre-clinical model to inform clinical translation. Research Sponsor: URMC Department of Surgery.

566 Poster Session (Board #E5), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Survival outcomes according to the tumor mutation burden and PD-L1 expression in hepatobiliary tumors.

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Background: Hepatobiliary (HB) tumors are aggressive tumors with emerging evidence for increasing sensitivity to immune checkpoint inhibitors (ICI). Tumor mutation burden (TMB) was found to be a quantitative biomarker associated with production of neoantigens within the tumor and predict the sensitivity to immune therapy. Herein, we explore the TMB, microsatellite instability (MSI) and PD-L1 expression as a potential biomarker of response to immune therapy in HB tumors. **Methods:** We retrospectively assessed all patients with hepatobiliary malignancies who have undergone next generation sequencing (NGS) between October 2009 and June 2019. We then analysed the tumor mutation burden and PD-L1 of these tumors and also identified frequency of patients with no clinically actionable mutations. **Results:** In our total 61 patients with HB tumors predominantly were male (62.3%) with mean age of 63 years. Thirty-four patients had hepatocellular carcinoma, 22 patients had cholangiocarcinoma and 5 patients had gallbladder carcinoma. The most common risk factors were smoking status, cirrhosis, alcohol consumption and hepatitis C virus. The mean TMB reported was 3.2 (1.16 – 7.35). MSI was identified in 13 patients and one was indeterminate. Only 17 patients had PD-L1 positive. At least, 37 patients had one clinically actionable mutation while 24 patients had no clinically actionable mutations. Mean overall survival was 16.6 months, but no statistically significant difference was found by high PD-L1 (3 vs 3.7 months, p=0.3) expression. **Conclusions:** Our data suggests the TMB in HB tumors is low in general irrespective of their underlying risk factors. We also noted more than half had microsatellite stable tumors and PD-L1 expression. Future larger studies are needed to evaluate TMB, MSI and PD-L1 as a potential biomarker in hepatobiliary tumors to help select patients that will benefit from immune therapy. Research Sponsor: None.

567 Poster Session (Board #E6), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Therapeutic targeting of extracellular FGFR2 activating deletions in intrahepatic cholangiocarcinoma.

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Background: Fibroblast growth factor receptor (FGFR) pathway alterations have been identified in approximately 20% of patients (pts) with intrahepatic cholangiocarcinoma (IHCC), most commonly by *FGFR2* fusions. Early phase clinical trials have demonstrated encouraging efficacy of FGFR inhibitors in pts with *FGFR2*-translocated cholangiocarcinoma, but efficacy in pts with other *FGFR2* activating alterations is less clear. **Methods:** Pts with cholangiocarcinoma underwent CLIA-certified next generation DNA sequencing (NGS) to identify actionable alterations. *FGFR2* fusions and other *FGFR2* genomic events were assessed, with genomic characterization performed before and after treatment with FGFR inhibitors in appropriate pts. Novel extracellular domain in-frame deletions (INDELs) of *FGFR2* and apparent resistance mutations were investigated for oncogenic activity and inhibitor resistance *in vitro* and *in vivo*. **Results:** Cholangiocarcinomas from 284 pts (136 male, 148 female; median age, 64 [20-89], including 139 IHCCs, were sequenced. Among the IHCCs, 16 (11.5%) had *FGFR2* fusions, with 9 different gene partners. Surprisingly, 5 (3.6%) IHCCs harbored extracellular domain *FGFR2* INDELs. Two of these IHCCs harbored an exon 5 deletion *FGFR2* p.H167_N173del. Expression of *FGFR2* p.H167_N173del in 3T3 cells resulted in oncogenic transformation. In the clinic, two pts with *FGFR2* p.H167_N173del were treated with Debio1347, an oral FGFR-1/2/3 inhibitor. Both patients achieved a durable partial response (PR) of 11 months, with one of the pts still on active treatment with Debio-1347. The patient who developed acquired resistance underwent repeat biopsy, and NGS identified a secondary mutation (*FGFR2* p. L617F) in the kinase domain. *In vitro* studies demonstrated that this mutation confers resistance to Debio1347. This patient was subsequently treated with another FGFR inhibitor and again experienced a PR lasting 17 months. A third biopsy after disease progression demonstrated a previously undetected L597Q *BRAF* mutation. **Conclusions:** Extracellular domain *FGFR2* in-frame deletions are a novel genomic alteration in IHCC that are transforming and predict clinical sensitivity to FGFR inhibitors. Research Sponsor: Target Cancer Foundation Pharmaceutical/Biotech Company.

568 Poster Session (Board #E7), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Total skeletal, psoas, and rectus abdominis muscle mass as prognostic factors for patients with advanced hepatocellular carcinoma.

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Background: We investigated whether low skeletal muscle mass (LSMM) defined according to different muscle groups on computed tomography (CT) scans could predict prognosis of advanced hepatocellular carcinoma (HCC). **Methods:** We analyzed patients who received first-line sorafenib treatment for advanced HCC in a prospective patient cohort between 2007 and 2012. The muscels areas of total skeletal muscle (TSM), paraspinal muscle (PS), psoas muscle (PM), rectus abdominis (RA), and abdominal wall (AW) were evaluated using a single CT slice at the third lumbar vertebra before treatment. LSMM was determined according to the TSM, PS, PM, RA and AW indices, which was calculated as the parameters divided by the square of the body height. **Results:** We enrolled 137 patients, with a mean age of 57.5 years; 120 were male and 17 were female. Liver disease etiology was hepatitis B virus in 94 (68.6%) patients and hepatitis C virus in 28 (20.4%) patients. All patients had Child-Pugh class A liver reserve. Women had significantly lower TSM index than men did ($p < .001$). Among men, the optimal cut points of the TSM, PM and RA indices for LSMM diagnosis were 39.1, 8.3 and 2.9 cm^2/m^2, respectively. Patients with LSMM exhibited poorer overall survival than patients without LSMM, whether LSMM was defined by TSM index (median 5.1 vs. 8.0 months, $p = 0.007$), PM index (median 5.8 vs. 11.8 months, $p < 0.001$), or RA index (median 7.2 vs. 8.1 months, $p = 0.003$). After adjusting for clinical variables including underweight, age, tumor extent, and performance status, LSMM defined by TSM index (hazard ratio [HR]: 2.123, 95% confidence interval [CI]: 1.124-4.010, p = 0.020), PM index (HR: 1.855, 95% CI: 1.163-2.959, $p = 0.009$), or RA index (HR: 1.650, 95% CI: 1.004-2.710, $p = 0.048$) remained independent predictors for poor OS. **Conclusions:** LSMM defined by TSM, PM and RA indices are independent predictors for poor prognosis of advanced HCC, even after adjusted for body weight. Research Sponsor: Ministry of Science and Technology, Taiwan.

569 Poster Session (Board #E8), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Impact of baseline hepatitis B viremia and management on outcomes in patients (Pts) with advanced hepatocellular carcinoma (HCC) and elevated alpha-fetoprotein (AFP): Outcomes from REACH-2.

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Background: REACH (NCT01140347) and REACH-2 (NCT02435433) were global, randomized, blinded, placebo (PL)-controlled phase 3 trials of ramucirumab (RAM) in pts with advanced HCC following sorafenib. REACH-2 limited enrollment to pts with AFP ≥400 ng/mL, and met its primary OS endpoint, consistent with the prespecified REACH subgroup with baseline AFP ≥400 ng/mL. Analysis of pooled individual pt data from REACH (AFP ≥400 ng/mL) and REACH-2 showed improved OS with RAM vs PL for pts with hepatitis B virus (HBV) etiology (7.7 vs 4.5 mos; HR 0.74, 95% CI 0.55, 0.99). Here we investigate survival and liver function in REACH-2 pts with HBV etiology tested for serum HBV DNA. **Methods:** Pts had advanced HCC, Child-Pugh A, ECOG PS 0/1, AFP ≥400 ng/mL, prior sorafenib treatment, and were randomized (2:1) to receive RAM 8 mg/kg or PL Q2W. Pretreatment serum HBV DNA was quantified by HBV-specific PCR (Roche) by a central lab. HBV DNA > 15 IU/mL were detectable (HBV DNA+), < 15 IU/mL were undetectable (HBV DNA-). OS in pooled treatment arms was evaluated using Kaplan-Meier method and Cox proportional hazards model. Liver function was assessed at baseline and before each cycle with the ALBI linear predictor. Outcomes were assessed by concomitant antiviral therapy. Adverse events (AEs) were graded by NCI-CTCAE v4.0. **Results:** Of 107 REACH-2 pts with HBV etiology, 106 had available PCR samples and were included in a pooled analysis (70 RAM and 36 PL pts). 48 pts were HBV DNA+ and 58 pts were HBV DNA-. HBV DNA+ pts had poorer median OS vs HBV DNA- pts (5.3 vs 10.1 mos, unstratified HR 1.45 95% CI 0.93, 2.28). HBV DNA+ pts taking concomitant antiviral therapy (n = 36) had numerically improved OS compared with those without (n = 12) (5.8 vs 4.0 mos). No difference in OS was noted for HBV DNA- pts by antiviral therapy use (n = 39 antiviral; n = 19 no antiviral) (10.2 vs 9.7 mos for yes vs no antiviral). In pts taking antiviral therapy, regardless of HBV DNA serology, liver function was improved and liver injury/failure related AEs were less frequent. **Conclusions:** Our data reinforce the use of antiviral therapy to improve outcomes in pts with advanced HBV-associated HCC and elevated AFP. Clinical trial information: NCT02435433. Research Sponsor: Eli Lilly and Company.

570 Poster Session (Board #E9), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Oncology precision medicine for hepatobiliary and pancreatic cancer: Insights and updates upon an institutional review.

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Background: Hepatobiliary cancers - hepatocellular carcinoma (HCC), intra or extrahepatic cholangiocarcinoma (I/EC), and gallbladder carcinoma (GB) - and pancreatic adenocarcinoma (PC) do have actionable alterations (AA). The importance of testing early in a patient's (pts) course to identify oncology precision medicine (OPM) options could be paramount for progression free survival (PFS). **Methods:** We identified pts with HCC, IC, EC, GB or PC in our OPM database since the centralization of our system. Pts who underwent molecular panel testing had AA's identified and stratified by cancer type. Treatment course was analyzed using swimmers plots. **Results:** 456pts were diagnosed with HCC, IC, EC, GB or PC. 104/456pts (23%) were ordered for molecular testing and 88/456pts (19.3%) completed testing: 18/88pts (20.4%) I/EC, 2/88pts (2.3%) HCC, 5/88pts (5.7%) GB, and 63/88pts (71.6%) PC. Of the PC pts, 3/63 (4.8%) had a BRCA mutation. These pts did not receive targeted therapy. Overall, 5/88pts (5.7%) had a BRAF mutation (2 PC, 2 I/EC, 1GB). Thus, 8/88 (9.1%) of tested pts became eligible for some form of targeted therapy over their treatment course. Of those with a BRAF mutation, only 2/5 pts had OPM testing sent with initial diagnostic workup, and 2/5 eventually began targeted therapy. One had a progression free survival (PFS) of 2.5months while the other discontinued secondary to toxicity. **Conclusions:** Our data showed that we are testing a minority of pts with pancreas and hepatobiliary cancers. Of those tested, it may have occurred too late in the course of illness to improve outcomes. Given the potential utility of uncovering potential germline alterations like BRCA1/2 as well as pragmatic AAs including somatic BRCA and BRAF, we are moving to a more systematic evaluation of pts to capture and respond to these issues. Research Sponsor: None.

Pts with completed testing and actionable alterations.

Completed Testing	N = Number of Pts
PC Pts	63/88 (71.6%)
GB Pts	5/88 (5.7%)
HCC Pts	2/88 (2.3%)
I/EC Pts	18/88 (20.4%)
BRAF Mutation Pts	5/88 (5.7%)
PC pts BRCA Mutation	3/63 (4.8%)
Actionable Alterations	8/88 (9.1%)

571 Poster Session (Board #E10), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Preoperative serum artemin (ARTN) as a predictive biomarker of recurrence following curative resection for hepatocellular carcinoma (HCC).

Sophie Feng, Hao-Wen Sim, Roxana Bucur, Reenika Aggarwal, Phillipe Abreu, Monali Ray, Michael Herman, Dangxiao Cheng, Zhuo Chen, Wenjiang Zhang, Paul David Greig, Alice Chia-chi Wei, Carol-Anne Moulton, Ian M. McGilvray, Sean P. Cleary, Steven Gallinger, Gonzalo Sapisochin, Jennifer J. Knox, Geoffrey Liu, Eric Xueyu Chen; Princess Margaret Cancer Centre, Toronto, ON, Canada; The Kinghorn Cancer Centre, St Vincent's Hospital Sydney, Sydney, Australia; Princess Margaret-University Health Network, Toronto, ON, Canada; Princess Margaret Cancer Centre Division of Medical Oncology and Hematology, Toronto, ON, Canada; Toronto General Hospital, University Health Network, Toronto, ON, Canada; University of Toronto, Toronto, ON, Canada; Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; Toronto General Hospital, Toronto, ON, Canada; Division of General Surgery, University Health Network, University of Toronto, Toronto, ON, Canada; Mayo Clinic, Rochester, MN

Background: Tumor-induced generation of splenic erythroblast- like cells (Ter-cells) has been shown to promote tumor progression. These Ter-cells produce the glial-line derived neurotropic factor, ARTN. We investigated the association of pre-operative serum ARTN and the risk of recurrence in HCC patients (pts) undergoing curative resection. **Methods:** Blood samples were collected prior to surgery as part of an institutional molecular epidemiologic study. Serum ARTN concentration was measured using an enzyme-linked immunosorbent assay (ELISA). Demographics, pathological variables known to be associated with outcomes and clinical outcomes were collected. Uni- and multivariate analysis were conducted. The optimal cutpoint method was used to define high and low ARTN concentrations. Cox models (hazard ratios, HR) were used to compare progression-free (PFS, primary endpoint), and overall survival (OS) of pts with high vs low serum ARTN. **Results:** Pre-operative blood samples were available for 58 pts. Median age was 63 years (range: 25-85 years); 74% were male and 50% were Asian. Etiology of liver disease was hepatitis B (43%) and hepatitis C (22%); 43% of tumors were $\leq$5cm, and vascular invasion was seen in 62%. A baseline alpha-fetoprotein (AFP) of $>$ 100 mcg/L was observed in 36% pts. Median follow-up was 18.9 months. Median ARTN concentration was 0.322 ng/mL. The optimal ARTN concentration cut-off was 0.206 ng/mL. Median PFS for pts with high ($>$ 0.206 ng/mL) vs low ($\leq$0.206 ng/mL) ARTN was 15.7 vs 55 months (p = 0.04) respectively. Three year PFS was 34% vs 55%, and three year OS 54% vs 91% for high vs low groups. Univariate analysis found that high ARTN concentration (HR 2.44, p = 0.05) and multifocal tumors were associated with a worse PFS. In a multivariate analysis adjusted for AFP $>$ 100mcg/L, vascular invasion, hepatitis status and multifocal tumors, high ARTN remained a negative prognostic factor for PFS, aHR 3.32 (95% CI: 1.22-9.05, p = 0.02). **Conclusions:** A high pre-surgery serum ARTN is associated with earlier recurrence in HCC pts undergoing curative resection. ARTN should be further studied in HCC to determine its value as a prognostic marker. Research Sponsor: None.

572 Poster Session (Board #E11), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Circulating levels of soluble urokinase plasminogen activator receptor (suPAR) to predict outcome after resection of biliary tract cancer.

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Background: Surgical resection is the only curatively intended therapy for patients with biliary tract cancer (BTC), but 5-year survival rates after tumor resection have remained below 30%, corroborating the need for better preoperative stratification tools to identify the ideal surgical candidates. The soluble urokinase plasminogen activator receptor (suPAR) represents a mediator of inflammation and has recently been associated with cancer. In this study, we evaluated a potential role of suPAR as a novel biomarker in patients undergoing resection of BTC. **Methods:** Tumor expression of uPAR, the membrane bound source of suPAR, was analyzed by IHC in 108 BTC samples. Serum levels of suPAR were analyzed by ELISA in a training and validation cohort comprising a total of 117 BTC patients and 76 healthy controls. **Results:** A high tumoral uPAR expression was associated with an adverse outcome after BTC resection. In line, circulating levels of suPAR were significantly elevated in BTC patients compared to healthy controls and patients with primary sclerosing cholangitis (PSC). Using a small training set, we established an optimal prognostic suPAR cut-off value of 3.72ng/ml for BTC patients. Importantly, preoperative suPAR serum levels above this cut-off value were associated with significantly impaired overall survival in both the training and validation cohort. Multivariate Cox-regression analysis including clinicopathological parameters such as the tumor stage, markers of systemic inflammation or organ dysfunction and established tumor markers revealed suPAR as an independent prognostic marker following BTC resection. Finally, high preoperative suPAR levels were indicative for acute kidney injury after tumor resection. **Conclusions:** Circulating suPAR represents a previously unrecognized biomarker in patients with resectable BTC, which might be useful to preoperatively identify the ideal candidates for tumor resection. Research Sponsor: German Research Foundation.

573 **Poster Session (Board #E12), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

Role of Wnt5a in suppressing invasiveness of hepatocellular carcinoma via epithelial mesenchymal transition.

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Background: Wnt signaling pathway includes canonical pathway and non-canonical pathway. Wnt/β-Catenin pathway as canonical pathway is associated with the development of hepatocellular carcinoma (HCC). On the other hand, the association between aberrant activation of non-canonical pathway activated by Wnt5a and tumor progression of HCC is not well-known. We investigated the significance of the expression of Wnt5a in HCC. **Methods:** Immunohistochemical staining of Wnt5a was performed on the specimen of 243 patients who underwent hepatic resection for HCC. We investigated whether the expression of Wnt5a correlated with the clinicopathological factors, survival, and recurrence in HCC patients. The expression of Wnt5a in human HCC cell lines HLE, HLF, HepG2 and Huh7 was investigated by western blotting. The effects of overexpression or knockdown of Wnt5a on cell lines were evaluated by proliferation assay and invasion assay and changes in epithelial mesenchymal transition (EMT) related molecules were studied by western blotting. **Results:** The Wnt5a expression was positive in 63 patients (25.9%) and negative in 180 patients (74.1%). The Wnt5a negative was significantly associated with poorly differentiation (P = 0.003) and vascular invasion positive (P = 0.046). By univariate analysis, Wnt5a negative (P = 0.020) was identified as a significant prognostic factor of OS. Multivariate analysis of OS showed that Wnt5a negative (HR 1.895, 95% CI 1.053-3.409, P = 0.033) was identified as an independent prognostic factor. In the HCC cell lines, the Wnt5a expression was lower in HLE and HLF than in HepG2 and Huh7. Knockdown of Wnt5a by shRNA increased the proliferation and invasiveness in Huh7 with high expression of Wnt5a. As a result, the expression of E-cadherin decreased. In HLF with low expression of Wnt5a, overexpression of Wnt5a inhibited the invasiveness and the expression of vimentin decreased. **Conclusions:** Wnt5a negative was associated with poorly differentiation and vascular invasion, and was independent poor prognostic factor in HCC patients. Wnt5a may be a tumor suppressor involved in EMT mediated changes of invasiveness. Research Sponsor: None.

574 Poster Session (Board #E13), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

NTRK gene fusions in biliary tract cancers.

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Background: Gene fusions involving one of the 3 neurotrophic tyrosine receptor kinases (*NTRK*) have been identified in approximately 1% of solid tumors and inhibitors of TRK (e.g. larotrectinib) have been shown to have anti-tumor activity regardless of tumor type. *NTRK* gene fusions have been previously reported in bilio-pancreatic cancers. It is of interest therefore to determine the incidence and molecular characteristics of *NTRK* gene fusions in patients with bilio-pancreatic cancers. **Methods:** Formalin-fixed paraffin-embedded archival blocks from surgical resections, biopsies or cytological samples of biliary tract tumors including intra-hepatic cholangiocarcinoma (IH), extra-hepatic cholangiocarcinoma (EH), perihilar cholangiocarcinoma (PH) and gallbladder tumors (G) were selected/retrieved from the tumor bank of the CUB Hôpital Erasme between January 2010 and July 2019. A two-step diagnostic method incorporating *immunohistochemistry (IHC) screening* followed by NGS analysis was used. Pan-TRK IHC (monoclonal antibody clone EPR17341 [AbCam, Cambridge, MA]) was used for the screening method. *Staining* intensity (negative, *weak*, moderate or strong) and localization (cytoplasmic or nuclear) were evaluated. The presence of at least weak staining tumor cells led to testing by a RNA-based NGS panel (Oncomine Focus Assay, ThermoFisher scientific). **Results:** 145 archival tumors samples (81 surgical resections, 48 biopsies and 16 cytology) have been selected, including 61 IH, 32 PH, 26 EH and 26 G (67 female and 78 male). 134 samples were suitable to perform IHC. 17 samples were IHC positive. Intensity of staining was weak in 16 samples and moderate in one. Staining location was cytoplasmic (14/17), nuclear (2/17), and nuclear+cytoplasmic (1/17). NGS testing of the 17 IHC positive samples revealed a single *NTRK*3 gene fusion (*ETV6*(4)-*NTRK3*(14)). In this case (female patient with a poorly differentiated PH, deceased), IHC had a weak focal cytoplasmic and nuclear staining. Overall in the patients screened by IHC and confirmed by NGS, the percentage of *NTRK* fusions was 0.75%. **Conclusions:** *NTRK* gene fusions are rare in biliary cancers but testing is of high interest due to the emergence of possible treatment with specific TRK inhibitors. Research Sponsor: Bayer Healthcare.

575 Poster Session (Board #E14), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Genomic characterization of HBV-infected hepatocellular carcinoma patients using circulating tumor DNA.

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Background: Hepatocellular carcinoma (HCC) is a leading cause of mortality, with Hepatitis B virus (HBV) infection as a dominant etiology. Surgery or ablation may be curative for early-stage HCC. Thus, effective detection strategies are needed. We investigated genomic aberrations in circulating tumor DNA (ctDNA) as a potential diagnostic marker of HCC in HBV-infected patients. **Methods:** We identified early stage (BCLC 0-A) HCC cases (n = 21) and cancer-free controls (n = 15) from a cohort of Asian patients with HBV, undergoing surveillance at Thomas Jefferson University Hospital between 2013-2017. Blood samples were collected. Circulating cell-free DNA was isolated from plasma and assayed by capture-based next-generation sequencing of a targeted panel of 23 genes implicated in HCC pathogenesis. Sequencing data analysis and somatic mutation identification were conducted using a computational pipeline. Using area under the curve (AUC) in receiver operating characteristic analysis, we evaluated gene alterations and clinical factors (age, gender, cirrhosis) in an exploratory early detection HCC model. **Results:** Mutant *ARID1A*, *ATM*, *CDKN2A*, *CTNNB1*, *ERBB2*, *TP53* genes were increased in HCC cases relative to non-cancer patients (85.7% *vs* 53.3%, *P* = 0.058; 42.9% *vs* 6.7%, *P* = 0.025; 38.1% *vs* 6.7%, *P* = 0.051; 42.9% *vs* 0%, *P* = 0.005; 52.4% *vs* 13.3%, *P* = 0.016; 100% *vs* 66.7%, *P* = 0.008, respectively). HCC patients had higher prevalence of cirrhosis than controls (90.5% vs. 60%, P = 0.046). Using the 6 mutant genes alone, the AUC for discriminating HCC from non-cancer patients was 0.827 (95% confidence interval [CI]: 0.701-0.953), which was greater than the AUC for discriminating cirrhosis from non-cirrhosis (0.531). When the 6 mutant genes were combined with clinical factors, the AUC of the exploratory HCC detection model increased to 0.914 (*P*= 0.045). **Conclusions:** We identified 6 genomic aberrations in ctDNA that were more prevalent in HCC patients compared with non-cancer patients. Combining these alterations with clinical factors may identify HCC in HBV-infected patients at an early stage. These findings warrant further validation in future studies. Research Sponsor: American Cancer Society Institutional Research Grant.

577 Poster Session (Board #E16), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Gamma-synuclein as a potential novel prognostic marker promoting tumor cell migration in biliary tract carcinoma.

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Background: Biliary tract carcinoma (BTC) is a highly malignant tumor, but the detailed pathological mechanism of its development and progression remain ill-defined. Gamma-synuclein (SNCG) promotes invasive behavior in pancreatic cancer and a range of other cancers, and SNCG expression is reportedly a prognostic factor. However, the role of SNCG in BTC remains unknown. Consequently, we investigated the clinicopathological significance and function of SNCG in BTC. **Methods:** Using surgically resected BTC specimens from 149 patients with adenocarcinoma [extrahepatic cholangiocarcinoma (ECC) (n =98); intrahepatic cholangiocarcinoma (ICC) (n =51)], we immunohistochemically evaluated SNCG positivity and checked for correlations with clinicopathological factors and outcomes. Furthermore, cell lines with high expressions of SNCG were selected from 17 BTC cell lines by using immunohistochemistry and qPCR. Cell proliferation and migration assays were then performed in the presence and absence of SNCG (silenced using). **Results:** SNCG expression was found in 32 of 149 (21.4%) BTC patients. SNCG expression was significantly correlated with poorly differentiated tumor (P = 0.001) and lymph node metastases (P = 0.001). SNCG positivity was also correlated with poorly differentiated tumor in both ECC and ICC (P = 0.008 and P = 0.03, respectively), but was correlated with lymph node metastases only in ECC (P = 0.003). Multivariate analyses identified SNCG expression as an independent prognostic factor of poor overall survival (P = 0.008) and poor recurrence-free survival (RFS) (P = 0.006). SNCG expression in both ECC and ICC was significantly associated with poor prognosis in univariate analysis, and multivariate analysis identified SNCG as an independent prognostic factor of poor RFS for ECC (P = 0.03). High SNCG expression was found in 3 BTC cell lines (NCC-BD1, NCC-BD3, and NCC-CC6-1). Functional analysis revealed that SNCG silencing by siRNA suppressed cell migration significantly in NCC-BD1 and NCC-CC6-1 and downregulated cell proliferation in NCC-CC6-1. **Conclusions:** Our results suggest that SNCG may promote tumor cell activity and is potentially a novel prognostic marker in BTC. Research Sponsor: JSPS KAKENHI grant No. 16K10609.

578 Poster Session (Board #E17), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Primary versus metastatic intrahepatic cholangiocarcinoma: A comparative comprehensive genomic profiling (CGP) study.

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Background: Genomic alterations (GA) characteristic of IHCC are well known. We queried whether the GA of IHCC from primary tumor biopsies (p-bx) would differ from IHCC metastasis biopsies (m-bx). **Methods:** CGP was performed on 1,268 cases of advanced stage IHCC using p-bx in 1,048 cases and m-bx from 220 cases. Tumor mutational burden (TMB) was determined on 0.8-1.1 Mbp of sequenced DNA and microsatellite instability (MSI) was determined on 114 loci. PD-L1 expression in tumor cells (Dako 22C3) was measured by IHC. **Results:** M-bx sites included: lymph nodes (63), soft tissues (47), peritoneum (34), lung/pleura (27), omentum (15), bone (10), GYN tract (5), brain (2), Upper GI (2), colon (2), bladder (1), abdomen (1) and adrenal (1). The GA per sample were similar as were biomarkers of immuno-oncology (IO) drug response. The *KRAS* mutation frequency was doubled in the m-bx compared to the p-bx ($p < 0.001$), and enrichment of the potentially targetable *KRAS* G12C was also observed. Frequencies of untargetable GA were similar overall. *IDH1* ($p < 0.001$) and *FGFR2* GA known to be enriched in IHCC were less frequent in the m-bx cohort. GA in *STK11* were more frequently identified in m-bx. **Conclusions:** GA found in p-bx vs m-bx in IHCC are significantly different; the m-bx cohort featuring greater *KRAS* and lower *IDH1* and *FGFR2* GA. This suggests that the m-bx group may contain a significant number of non-IHCC cases whose metastatic lesions were actually derived from other primary sites incorrectly assigned the diagnosis of IHCC. Research Sponsor: Foundation Medicine Inc.

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

579 Poster Session (Board #E18), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Circulating free DNA (cfDNA) and tissue next-generation sequencing analysis in a phase II study of infigratinib (BGJ398) for cholangiocarcinoma with *FGFR2* fusions.

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Background: Fibroblast growth factor receptor 2 (FGFR2) alterations occur in 11% of cholangiocarcinomas, 85% of which are fusions. A multicenter, open-label, phase II study is currently evaluating the efficacy of infigratinib, a selective FGFR1–3 tyrosine kinase inhibitor, in patients with previously treated advanced cholangiocarcinoma containing *FGFR2* fusions. We report detailed biomarker analyses from this study. **Methods:** Patients with advanced or metastatic cholangiocarcinoma containing *FGFR2* fusions whose disease had progressed following cisplatin- or gemcitabine-based therapy were eligible. Patients received oral infigratinib 125 mg once daily on days 1–21 every 28 days. Comprehensive genomic profiling (CGP) was performed on tumor tissue and cfDNA collected prior to the start of therapy. The primary endpoint was investigator-assessed overall response rate (ORR) [RECIST version 1.1]. Data cut-off (prespecified): August 8, 2018. Trial registration: NCT02150967. **Results:** At data cut-off, 71 patients with *FGFR2* fusions were included (62% women; median age 53 years; 55% received ≥2 prior lines of therapy). Median duration of treatment was 5.5 months. ORR (confirmed and unconfirmed) was 31.0% (95% CI 20.5–43.1%) and confirmed ORR was 26.9% (95% CI 16.8–39.1%). 33 unique *FGFR2* fusion genes were identified in 71 enrolled patients. The most common fusion gene partner was *BICC1* (32%; 23/71). Pathogenic variants in 9 other druggable genes were identified in 32% of patients (13/37) who underwent CGP. *FGFR2* fusions were concordant in 67% (8/12) of patients with tumor tissue and cfDNA at screening. **Conclusions:** The large assortment of *FGFR2* fusion genes identified in this study underscores the diversity of *FGFR2* rearrangements that may drive cholangiocarcinoma. Although cfDNA analysis was performed in a minority, these preliminary data suggest that cfDNA analysis may be valuable for the identification of *FGFR2* fusions and to study intratumoral heterogeneity. Clinical trial information: NCT02150967. Research Sponsor: QED Therapeutics.

580 Poster Session (Board #E19), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Comparison of the clinical features, treatment patterns, and tumor mutations of patients with intrahepatic (ICC) and extrahepatic (ECC) cholangiocarcinoma.

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Background: Though studies indicate that the genomic profiles of ICC and ECC are distinct, the clinical features that differentiate them still remain to be well characterized. The purpose of this study was to further analyze these differences and patient treatment patterns in a multi-center cohort. **Methods:** A retrospective chart review was performed at 8 institutions on patients (pts) with ICC or ECC diagnosed after June 2009. Data on demographics, risk factors, treatments, pathology and overall survival (OS) were collected. Tumor genotyping results from CLIA-certified tissue assays were analyzed. Fisher's exact, Wilcoxon rank sum and log-rank tests were used to compare sub-groups. **Results:** In a database of 737 pts with cholangiocarcinoma, 538(73%) had ICC and 199(27%) had ECC. Pts with ICC more often presented in later stages, had tumors $>$ 5cm at resection ($p < 0.0001$) and had metastases to the liver, lymph nodes, lung and/or bone ($p < 0.01$). Pts with ICC more often received liver directed therapy, targeted therapy and multiple lines of systemic therapy and they more often enrolled in a clinical trial (all $p < 0.01$). Pts with ECC were more likely to be male, undergo surgery, receive adjuvant chemotherapy and/or chemoradiation (all $p < 0.05$). Mutation profiling performed in 381 (52%) pts (ICC/ECC = 301/80) showed that pts with ICC were more likely to have IDH1 mutations and FGFR2 fusions, whereas pts with ECC were more likely to have KRAS, APC, SMAD4, WNT, TGFb and TP53 mutations (all $<$ 0.05). Factors that did not differ significantly between pts with ICC and ECC include race, rates of primary sclerosing cholangitis, median diagnosis CA19-9 levels and R1 resection rate. Median OS from diagnosis was 18.9 months in ICC and 17.3 months in ECC ($p = 0.8471$). **Conclusions:** While pts with ICC and ECC have some similarities in their clinical features, differences in metastases patterns and molecular profiling significantly impact their management such that pts with ICC receive more liver-directed therapy, targeted therapy and more lines of systemic therapy. Further prospective studies are needed as referral patterns to tertiary care centers may have impacted these results. Research Sponsor: None.

581 Poster Session (Board #E20), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Patient-derived organoids for personalized drug screening in intrahepatic cholangiocarcinoma.

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Background: Despite standard treatment with gemcitabine and cisplatin, median survival for unresectable Intrahepatic Cholangiocarcinoma (ICC) is < 1 year. Clearly, novel therapeutic strategies are urgently needed. The paucity of targetable mutations in ICC and the as yet unproven benefit of genetically targeted drugs led us to ask whether a reliable clinical benefit may be revealed by patient-specific therapeutic testing in novel models of ICC. Here we describe our ability to establish patient-derived three-dimensional organoid cultures (PDO) that enable individualized identification of active single agents or drug combinations in surrogate models of ICC. **Methods:** To model patient-specific drug responses, we used the freshly resected ICCs from small samples of single patient tumors to generate PDXs and PDOs, small spheroidal clusters of tumor cells grown *in vitro*. We have employed a high-throughput drug screening platform using AI-enhanced robotics (Yamaha Motor Corporation) to identify and distribute single, uniformly sized PDOs into 384-well ultra-low adherent plates. This is coupled with a TECAN D300e drug dispenser that rapidly delivers nanoliter volumes of a 34-drug panel, thereby facilitating rapid, reliable drug response analyses. **Results:** Our data show that PDOs retain characteristic genomic and histological features of the patients' tumors. Drug responses were specific to each patient tumor, but PDOs from all patients responded to a greater or lesser degree to mTOR inhibition, suggesting that this pathway is important in ICC. The responses of PDO to the mTOR inhibitor Sapanisertib (INK128), was recapitulated in the same patient's PDX. Further, INK128 was synergistic with gemcitabine in patient 970 PDOs as well as *in vivo* in PDX also from patient 970. **Conclusions:** As it is believed that PDX can predict patient responses to drugs, our results suggest that PDO may also predict patient drug responses. The establishment of PDO may allow economical patient-specific, high throughput drug screens that could ultimately inform clinical practice. Research Sponsor: Littlefield FoundationPharmaceutical/Biotech Company.

Patient	INK128 IC_{50} (mM)	Gemcitabine IC_{50} (mM)	Highest Single Agent Synergy Score
970	0.025	0.89	10.4
981	0.41	0.0003	0.90
922	0.066	0.79	-6.3
896	0.009	194.9	-1.2

582 Poster Session (Board #E21), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Hepatocyte-derived intrahepatic cholangiocarcinoma requires Yap and Sox9: A clinical and preclinical analysis.

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Background: Intrahepatic cholangiocarcinoma (ICC) is a liver tumor of increasing incidence and devastating prognosis. WGS and WES have identified numerous molecular pathways and fusions in ICC. Recent studies have also suggested hepatocyte as a cell source in a subset of ICCs, especially those associated with chronic liver insult such as non-alcoholic steatohepatitis (NASH) or primary sclerosing cholangitis (PSC). **Methods:** Since co-expression of myristoylated AKT (myrAKT) & Notch intracellular domain (NICD) in hepatocytes using sleeping beauty transposon/transposase-based hydrodynamic tail vein injection (SB-HTVI) lead to ICC, we initiated a comprehensive analysis of mechanism of ICC development in patients and in this preclinical model. **Results:** Over 90% of CC samples exhibited high levels of nuclear SOX9 & YAP, in addition to a significant positivity for pAKT in ICCs as compared to extrahepatic CC. We also identified upregulation of p-AKT, SOX9 & YAP in hepatocytes of patients with PSC and NASH. This was also seen in many murine models of cholestatic injury and NASH. While co-expression of myrAKT+NICD led to hepatocyte-derived ICC, conditional deletion of either Yap or Sox9 significantly delayed and almost completely abrogated ICC development. While Yap deletion impaired the initial HC-to-BEC fate conversion, Sox9 elimination had no such effect on reprograming. Interestingly, following deletion of either Yap or Sox9 we observed a few AKT/NICD-driven ICC tumors expressing either Sox9 or Yap but not both. This also occurred in a small subset of human CC tumors which may be Sox9+Yap- (4%) or Sox9-Yap+ (3.7%), showing that deletion of Yap or Sox9 is not sufficient to completely abrogate ICC development. We finally demonstrated that conditional deletion of both Yap & Sox9 completely blocked development of ICC tumors in the myrAKT+NICD model. **Conclusions:** Thus, we show that cholestatic injury or NASH in humans and mice induces hepatocyte-to-cholangiocyte reprograming to increase the risk of ICC development. We also provide evidence for critical but distinct roles of Yap and Sox9 in ICC development and demonstrate the therapeutic potential of targeting these factors for treatment of subsets of ICC. Research Sponsor: U.S. National Institutes of Health Intramural Endowed Chair.

583 Poster Session (Board #E22), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Beta-catenin mutations in hepatocellular cancer, tumor cell metabolism, and the response of these tumors to mTOR inhibition.

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Background: Hepatocellular cancer (HCC) continues to grow in incidence despite approval of many new therapies including immune checkpoint inhibitors (ICIs) and TKIs. Genomic landscape of HCC is becoming increasing apparent through WGS and WES. One major driver of HCC is the Wnt/b-catenin pathway. Mutations in CTNNB1, which encodes for b-catenin, are evident in 26-37% of all human HCCs. However, expression of mutant-b-catenin in liver in mice is insufficient for HCC development. Indeed, analysis of HCC cases has revealed CTNNB1 mutations to significantly co-exist with other aberrations including activation/overexpression of Met and Myc and mutations in TERT promoter or mutations in NFE2L2/KEAP1, APOB and ARID2. **Methods:** Using sleeping beauty transposon/transposase and hydrodynamic tail vein injection, we co-expressed mutant-CTNNB1 (S45Y, S33Y or T41A) and one other clinically relevant co-occurrence to study significance and biology of HCC. Any novel findings in the preclinical model were validated in HCC patient cohorts. **Results:** Co-expression of mutant-CTNNB1 and one relevant co-occurrence led to development of HCC in mice in 6-10 weeks. All HCC in these models showed a dramatic increase in glutamine synthetase (GS), encoded by Glul, a known target of the Wnt/b-catenin signaling pathway in the liver. This led to an increase in glutamine levels in the tumor-bearing livers. Increased glutamine in the tumors in turn led to increased levels of phospho-mTOR-S2448, a marker of mTORC1 activation. In fact, examination of ~400 patient HCCs showed a significant correlation between positive GS and p-mTOR-S2448 staining. Treatment of Met-b-catenin model with Rapamycin led to notable and significant decrease in HCC burden. **Conclusions:** Our studydemonstrates b-catenin-mutated HCC to be positive for both GS and in turn mTORC1 active. This provides a novel opportunity for personalized medicine in HCC and CTNNB1-mutated HCCs may be vulnerable to therapeutic targeting by mTOR and more specially, mTORC1 inhibitors. Research Sponsor: U.S. National Institutes of Health Intramural Endowed Chair.

584 **Poster Session (Board #F1), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

Novel therapeutic avenues for cholangiocarcinoma treatment: A meta-analysis.

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Background: Cholangiocarcinoma (CCA) is a rare cancer of the bile ducts but has been increasing in incidence. The mainstay of treatment of CCA is resection or chemoradiation for more advanced disease, with immunotherapy being an evolving field in treatment. A better understanding of CCA pathogenesis will pave new avenues for treatment. **Methods:** We employed our STARGEO platform to conduct a meta-analysis of public data from NCBI's Gene Expression Omnibus. We performed meta-analysis with 259 CCA tumor samples against 16 normal intrahepatic duct samples as a control. We then analyzed the signature in Ingenuity Pathway Analysis. **Results:** Our analysis revealed FXR/RXR and LXR/RXR activation as top canonical pathways. Top upstream regulators identified included HNF1A (with predicted inhibition) and ERBB2 (with predicted activation). The most upregulated genes included several extracellular matrix proteins implicated in cancer including COL1A1, LAMC2 (correlated with poor prognosis in CCA), KRT17 (a keratin implicated in various malignancies but not well described in CCA), and LAMB3 (exerts tumorigenesis through PI3k/Akt signaling). Additionally, we found stark upregulation of the immunophillin FKPBP1A, which is involved in mTOR activation. We also noted upregulation of ubiquitin-associated gene UBASH3B, which inhibits endocytosis in EGFR and has been described in breast cancer but not CCA. From our investigation of immune checkpoint inhibitors, we found upregulation of classically described inhibitors such as CTLA4, TIGIT, and BTLA. In addition, we found upregulation of SIGLEC7, which has been recently shown to suppress immune function by binding to terminal sialic acid on glycans on the surface of immune cells. **Conclusions:** Our analysis highlights the possible role of ERBB2 and several extracellular genes in the pathogenesis of CCA. We also identify the role of genes not previously described in CCA such as FKBP1A and UBASH3B. Lastly, our results promote the promise of immunotherapy in CCA treatment. Research Sponsor: None.

585 Poster Session (Board #F2), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

The world-wide incidence of biliary tract cancer (BTC).

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Background: Existing epidemiologic research for BTC is limited to certain subtypes, eg gallbladder cancer (GBC), or combines BTC with liver cancer, and only reports regional statistics. Main sources for global BTC epidemiology (particularly anatomic sites) are literature reviews, which can be subject to limitations like inconsistent classification of subtypes, and varying standard population adjustment and comparison timeframes. Given the increasing incidence of BTC, it is critical to monitor global epidemiology to provide insight to public health management and clinical program development. **Methods:** We evaluated BTC incidence in 15 countries using the Cancer Incidence in Five Continents database Volume XI (CI5 XI) from the International Agency for Research on Cancer. Most CI5 XI registries cover data from 2008-12 with some variations. Incidence was examined by country, region, and anatomic site (extrahepatic cholangiocarcinoma, ECC; intrahepatic cholangiocarcinoma, ICC; GBC; ampulla of Vater cancer, AVC; and unspecified BTCs). Incidence was adjusted to standard world population and reported as age-standardized rate (ASR; per 100,000 person-years) with standard error (SE). **Results:** The highest incidence of total BTC was in South Korea (SK; ASR = 3.00, SE = 0.02) and lowest in the UK (ASR = 0.66, SE = 0.01). Overall, BTC incidence was higher in Asian countries than Western, and in Asian-Americans than the general US population (ASR = 1.00, SE = 0.02 and 0.77, SE $>$ 0.01, respectively). In Thailand, BTC incidence was higher in the North than South (ASR = 1.93, SE = 0.05 and 1.05, SE = 0.03, respectively). GBC and ECC are the top common subtypes in most countries reported. SK had the highest incidence of all subtypes, with ASR $>$ 2 in GBC, ECC, and ICC. Outside of SK, GBC and ECC were most common in Japan (ASR = 1.93, SE = 0.02 and 2.66, SE = 0.03, respectively); ICC was most common in Thailand (ASR = 1.73, SE = 0.05) and high in France (ASR = 1.01, SE = 0.03). **Conclusions:** These registry data support past reports of higher BTC incidence in Asian vs Western countries as well as regional variation within countries. Data also suggests that high BTC rates in Asian populations may not be entirely geographical as Asian-Americans suffer a higher BTC incidence than the overall US population. Research Sponsor: AstraZeneca.

586 Poster Session (Board #F3), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Association of objective response by mRECIST with better overall survival (OS) in patients with advanced hepatocellular carcinoma (HCC) treated with systemic therapies: A systematic review and meta-analysis of randomized controlled trials.

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Background: EASL guidelines for management of HCC recommends assessing tumor response according to mRECIST at all stages of the disease (EASL guidelines, J Hep 2018). Several studies have reported that objective response by mRECIST predicted overall survival (OS) but definitive data are still lacking. **Methods:** The PubMed database and ASCO meeting library were searched for full reports of randomized trials in patients with advanced HCC treated by systemic therapy up to August 31, 2018. We search strategy used the following terms: HCC, mRECIST, OS and objective response rate (ORR). We assess the association between ORR and OS in a meta-analysis of pooled data by using random effects model comparing patients achieving objective response (complete or partial response) versus non responders (stable disease, progressive disease) and displayed the results as per hazard ratio (HR, 95% CI). **Results:** Among 14 articles assessing response by mRECIST to systemic therapies in randomized studies in advanced HCC, 4 studies (5 trials) including 1,463 patients were considered eligible. Systemic therapies tested included lenvatinib, sorafenib, brivanib and nintedanib. Overall, ORR as per mRECIST ranged from 11.5% to 18.8%, being the median OS for responders of 18.5 to 27.2 mo (as opposed 8.9 to 11.4 for non-responders). As per random effects model, the HR for overall survival (responders versus non responders) was 0.47 (95% confidence interval 0.34–0.66, $p<0.001$). **Conclusions:** Objective response by mRECIST to systemic therapies in patients with advanced HCC is significantly and strongly associated to OS. Patients achieving an objective response can expect a significantly longer OS. Research Sponsor: None.

587 Poster Session (Board #F4), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Nationwide survey of pancreaticobiliary maljunction focusing on biliary cancer incidence in Japan.

Mitsuo Shimada, Hiroki Ishibashi, Yuji Morine, Masayuki Kubota, Hideki Fujii, Japanese Study Group on Pancreaticobiliary Maljunction; Tokushima University, Tokushima, Japan; Niigata University, Niigata, Japan; Kofu Municipal Hospital, Kofu-City, Japan

Background: Pancreaticobiliary maljunction (PBM) is known to be a unique entity closely related to biliary carcinogenesis. We herein report update analysis of PBM focusing on biliary cancer as third report of Japan-nationwide survey. **Methods:** From 1990 to 2015, 3,419 patients with PBM were registered at 141 medical institutions in Japan. 3,289 (1,344 pediatric and 1,945 adult patients) out of 3,419 patients were fully investigated, according to presence of bile duct dilatation (BDD), age (pediatric or adult), etc. **Results:** In pediatric patients, only 3 cases with BDD (0.124%) had bile duct cancers. On the other hand, in adults, biliary cancer incidence was 21.1% in patients with BDD and 43.5% in patients without BDD. The rates were extremely high in comparison with 0.0174% of Japanese prevalence of biliary cancer 2013. The cancer incidences of bile duct, gallbladder and both in adults with BDD/without BDD were 6.7%/4.1%, 13.0%/37.3%, and 1.4%/2.1%, respectively. In patients without associated biliary cancers, extrahepatic bile duct resection (EHBDRx) combined with cholecystectomy was performed in 89.5% of adults with BDD, while, in only 31.2% adults without BDD. Regarding the new biliary cancer occurrence of patients having follow-up data, the rate was 0.3% in 354 patients with BDD who underwent EHBDRx, while that was 4.0% in 75 patients without BDD who underwent simple cholecystectomy. In patients without BDD, cancer incidence (6.7%) in the late period (2010 to 2015) was higher than those (3.3% and 3.5%) in early and middle period (1990 to 1999, and 2000 to 2009). **Conclusions:** This updated nationwide survey of PBM revealed characteristics of associated and newly occurred biliary cancers, and could be widely used as a reference data for diagnosis and treatment of PBM. Research Sponsor: None.

588 Poster Session (Board #F5), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Progression-free survival in patients with cholangiocarcinoma with *FGFR2* fusions or rearrangements: An exploration of response to systemic therapy.

Kristen Bibeau, Luis Féliz, Scott Barrett, Ling Na, Christine Francis Lihou, Ekatherine Asatiani; Incyte Corporation, Wilmington, DE

Background: Most cholangiocarcinoma (CCA) patients (pts) are diagnosed with advanced disease and are ineligible for surgery. *FGFR2* fusions or rearrangements are present in 10–16% of pts with intrahepatic CCA (iCCA) and are reported to be oncogenic drivers. However, little data are available on the role of *FGFR2* genetic alterations in the response to systemic cancer therapy. FIGHT-202 is a phase 2 study of pemigatinib (a selective, potent, oral FGFR1–3 inhibitor) in pts with previously treated advanced/metastatic CCA (NCT02924376); primary results were reported at ESMO 2019. FIGHT-202 enrolled pts who progressed on ≥1 prior therapy, allowing the examination of the role of *FGFR2* alterations on the response to prior therapy. The objective of this post hoc analysis was to evaluate progression free survival (PFS) on standard systemic therapy received prior to study enrollment among pts with CCA harboring *FGFR2* fusions or rearrangements (*FGFR2*+). **Methods:** Case report forms were reviewed to determine disease history and exposure to prior lines of systemic cancer therapies (LOSCT) in the advanced setting before receiving pemigatinib. Only pts with sufficient data on prior LOSCT were included in this analysis. Median PFS was calculated using the Kaplan-Meier method. **Results:** 102 pts were included in this analysis (median age 54.5, 61.8% female). Median PFS on first-line therapy was 5.5 (95% CI: 4.0, 8.0) months. Among the 38 pts (37.3%) with ≥2 prior LOSCT, median PFS on second-line therapy was 4.4 (95% CI: 3.0, 5.3) months. **Conclusions:** This analysis provides data about PFS on standard systemic therapies for pts with *FGFR2*+ CCA. Median PFS on first-line therapy was lower than historical published data, and median PFS on second-line therapy was slightly longer than previously reported, in unselected CCA populations. Limitations of this analysis include retrospective examination of investigator reported data, and that clinical trial participants may not truly reflect a general CCA patient population. The short PFS on standard therapies in pts with *FGFR2*+ CCA highlights the need for development of other options including targeted therapies to improve outcomes. Research Sponsor: Incyte Corporation.

589 Poster Session (Board #F6), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Increased frequency of PD-1+CD57+Siglec-7- dysfunctional NK cells in patients with nonalcoholic fatty liver disease.

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Background: The proportion of non-alcoholic fatty liver disease (NAFLD) has been increasing as a cause of hepatocellular carcinoma (HCC) worldwide. Natural killer (NK) cells are involved in the first line of immune defense against cancer. NK cell function is regulated by activating and inhibitory NK cell receptors. However, the role of NK cells in the pathogenesis of NAFLD and NAFLD-HCC is still largely unknown. In this study, we aimed to clarify the phenotypic and functional features of NK cells in NAFLD and NAFLD-HCC patients. **Methods:** We performed mass cytometry (CyTOF) and flow cytometry analysis of NK cells in 33 NAFLD patients (22 chronic hepatitis (CH), 8 liver cirrhosis (LC), 3 with HCC (HCC)) and 9 healthy donors (HDs). We compared surface markers on NK cells in cancerous and non-cancerous intrahepatic lymphocytes (IHLs). We also measured NK cell function in the presence of IL-12 and IL-18. **Results:** The frequency of NK cells was lower in NAFLD patients compared to HDs. PD-1, CD57, ILT2 were highly expressed, and Siglec-7, NKp30, NKp46 were downregulated on NK cells from NAFLD patients, compared with those of HDs. In NAFLD patients, Siglec-7 levels on NK cells were negatively correlated with PD-1 and CD57, and positively correlated with NKp30 and NKp46. The other inhibitory markers (NKG2A, KIR3DL1 and KIRDL2/L3), activating markers (CD69 and NKG2D) and checkpoint markers (Tim-3 and TIGIT) were comparable between NAFLD patients and HDs. PD-1 and CD57 expression levels on NK cells were also significantly upregulated in NAFLD-HCC patients than those in HDs. CD57 was rarely expressed on NK cells in non-cancerous IHLs, on the other hand, highly expressed in cancerous IHLs. The IFNγ production and CD107a expression on NK cells were also decreased in NAFLD patients. PD-1^{+}CD57^{+}Siglec-7^{-} NK cells were observed in NAFLD patients, rarely in HDs. PD-1^{+}CD57^{+}Siglec-7^{-} NK cells were functionally impaired compared to other NK subsets. **Conclusions:** In patients with NAFLD, NK cells are reduced and functionally impaired, the reason of which may be the increased proportion of dysfunctional PD-1^{+}CD57^{+}Siglec-7^{-} NK subset, and dysfunctional NK cells might be related to impairment of surveillance for HCC. Research Sponsor: None.

590 Poster Session (Board #F7), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Significance of frailty in prognosis after hepatectomy in older patients with hepatocellular carcinoma.

Shinichiro Yamada, Mitsuo Shimada, Yuji Morine, Satoru Imura, Tetsuya Ikemoto, Yusuke Arakawa, Yu Saito, Masato Yoshikawa, Katsuki Miyazaki; Tokushima University, Tokushima, Japan; Department of Surgery, Tokushima University, Tokushima, Japan

Background: An aging society has come, and "Frailty" is becoming increasingly important in surgery. Recently, clinical frail scale (CFS), which is simple criteria for frailty, has been reported to be useful for prognostic prediction of non-cardiac surgery (Ann Surg. 2018). Herein we report a new knowledge about frailty for patients with hepatocellular carcinoma (HCC) undergoing hepatectomy. **Methods:** Eighty-one patients over 75 years who underwent hepatectomy for HCC between 2007 and 2018 were enrolled in this study. Frailty was diagnosed as CFS$\geq$4, and patient were divided into 2 groups, frailty (n = 17) and no frailty (n = 64). Clinicopathological factors were compared between 2 groups. **Results:** Patients' background, such as age, gender, preoperative comorbidity, and liver function showed no significant difference between 2 groups. Regarding tumor factors, frailty group showed significant larger tumor diameter, more advanced stage ($p < 0.05$) and tendency of high PIVKA-II ($p = 0.15$) compared with no frailty group. Frailty group showed significant high CRP level ($p < 0.01$), high modified Glasgow prognostic score (mGPS, $p = 0.04$) and tendency of high neutrophil-lymphocyte ratio (NLR, $p = 0.14$). Frailty group also showed tendency of higher rate of postoperative complication ($p = 0.11$) and longer postoperative hospital stay ($p = 0.09$). Overall and disease-free survival rate were significantly worse in frailty group ($p = 0.03$). In univariate analysis for overall survival, AFP$\geq$10, PIVKA-II$\geq$400, frailty and mGPS high (1, 2) were prognostic factor. Multivariate analysis revealed that frailty was independent prognostic factor. In univariate analysis of disease-free survival, only frailty was detected as prognostic factor. **Conclusions:** Frailty is an independent prognostic factor for HCC patients who underwent hepatectomy. Research Sponsor: None.

TPS591 **Trials in Progress Poster Session (Board #P4), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

Phase II trial of the PARP inhibitor, niraparib, in BAP1 and other DNA damage response (DDR) pathway deficient neoplasms including cholangiocarcinoma.

Thomas J. George, David L. DeRemer, Hiral D. Parekh, Ji-Hyun Lee, Merry Jennifer Markham, Karen Colleen Daily, Frederic J. Kaye, Stephen Staal, Dennie V. Jones, Bruce K. Stechmiller, Carmen Joseph Allegra, Robert A. Hromas; University of Florida Health Cancer Center, Gainesville, FL; University of Florida/UF Health Cancer Center, Gainesville, FL; UF Health Cancer Center, Gainesville, FL; Univ of Florida, Gainesville, FL; University of Texas Health Science Center at San Antonio, San Antonio, TX

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

DNA damage response genes with mutations eligible for Cohort B.

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

TPS592 **Trials in Progress Poster Session (Board #P5), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

FIGHT-302: Phase III study of first-line (1L) pemigatinib (PEM) versus gemcitabine (GEM) plus cisplatin (CIS) for cholangiocarcinoma (CCA) with *FGFR2* fusions or rearrangements.

Tanios S. Bekaii-Saab, Juan W. Valle, Eric Van Cutsem, Lorenza Rimassa, Junji Furuse, Tatsuya Ioka, Davide Melisi, Teresa Macarulla, John A. Bridgewater, Harpreet Singh Wasan, Mitesh J. Borad, Christine F. Lihou, Huiling Zhen, Luis Féliz, Ekatherine Asatiani, Ping Jiang, Arndt Vogel; Mayo Clinic, Phoenix, AZ; The Christie NHS Foundation Trust, Manchester, United Kingdom; University Hospitals Gasthuisberg Leuven and KU Leuven, Leuven, Belgium; Humanitas Clinical and Research Center-IRCCS, Humanitas University, Rozzano, Milan, Italy; Kyorin University, Tokyo, Japan; Osaka International Cancer Institute, Osaka, Japan; University of Verona, Verona, Italy; Vall d'Hebrón University Hospital and Vall d'Hebrón Institute of Oncology, Barcelona, Spain; University College London Cancer Institute, London, United Kingdom; Hammersmith Hospital, Imperial College Health Care Trust, London, United Kingdom; Incyte Corporation, Wilmington, DE; Hannover Medical School, Hannover, Germany

Background: For advanced CCA, standard of care 1L systemic treatment is GEM + CIS. Genetic alterations in intrahepatic CCA provide potential therapeutic targets. Fibroblast growth factor receptor (FGFR) 2 gene rearrangements driving CCA tumorigenesis were identified almost exclusively in intrahepatic CCA patients (pts) (incidence, 10–16%). In phase 2, PEM (INCB054828), a selective, potent, oral FGFR1–3 inhibitor elicited an objective response rate (ORR) of 35.5% and median progression-free survival (PFS) of 6.9 months (mo) in previously treated, locally advanced or metastatic CCA with *FGFR2* rearrangements (NCT02924376). FIGHT-302, a randomized, open-label, phase 3 study will evaluate efficacy and safety of 1L PEM vs GEM + CIS in unresectable/metastatic CCA with *FGFR2* fusions or rearrangements (NCT03656536). **Methods:** Eligible pts are adults with confirmed unresectable/metastatic CCA; no prior systemic therapy for advanced disease $<$ 6 mo before enrollment; radiographically measurable/evaluable disease (per RECIST v1.1); ECOG PS $\leq$1; documented *FGFR2* fusions or rearrangements. Exclusions include clinically significant corneal or retinal disorder; history of calcium and phosphate homeostasis disorder or systemic mineral imbalance with ectopic soft tissue calcification; untreated CNS metastases or history of uncontrolled seizures. Pts will be randomized (1:1; stratified by region and tumor burden) to PEM 13.5 mg QD on a 21-day (d) cycle or GEM (1000 mg/m^2) + CIS (25 mg/m^2) on D1 and D8 of 21-d cycles (max 8). Crossover to PEM allowed after confirmed progression. PEM titration to 18 mg from cycle 2 allowed for pts without hyperphosphatemia (serum phosphate $>$ 5.5 mg/dL) and Grade $\geq$2 treatment-related adverse events during cycle 1. Hyperphosphatemia will be managed with diet modifications, phosphate binders, diuretics, or dose adjustments. Treatment will continue until progression or unacceptable toxicity. Primary endpoint is PFS (by independent review). Secondary endpoints are ORR, overall survival, duration of response, disease control rate, safety, and quality of life. Four pts (target N = 432) are enrolled as of Sep 25, 2019. Clinical trial information: NCT03656536. Research Sponsor: Incyte Corporation.

TPS593 **Trials in Progress Poster Session (Board #P6), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

Phase II study of fluorouracil (FU), leucovorin (LV), and nanoliposomal irinotecan (nal-IRI) in previously treated advanced biliary tract cancer (NAPOLI-2).

Benjamin Adam Weinberg, Hongkun Wang, Katrina Pedersen, Amikar Sehdev, Max W. Sung, Jimmy J. Hwang; Ruesch Center for the Cure of Gastrointestinal Cancers, Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC; Mayo School of Graduate Medical Education, Rochester, MN; Indiana University, Indianapolis, IN; Tisch Cancer Institute at Mount Sinai, New York, NY; Levine Cancer Institute, Atrium Health, Charlotte, NC

Background: Biliary tract cancers (BTCs) are rare and aggressive malignancies. The current standard of care for advanced BTC is gemcitabine (GEM) plus cisplatin . Although there is no established second-line treatment, regimens such as FOLFOX, XELOX, FOLFIRI, XELIRI, GEM, and capecitabine have activity. Nal-IRI contains IRI free base encapsulated in liposome nanoparticles which shelter IRI from conversion to its active metabolite (SN-38) and increase intratumoral levels of SN-38 compared with IRI. FU/LV/nal-IRI has shown overall survival benefit and acceptable toxicity in patients (pts) with metastatic pancreatic adenocarcinoma following GEM-based therapy in the NAPOLI-1 trial. **Methods:** This is a single arm, open label, multicenter phase II study of pts with advanced BTC previously treated with gemcitabine plus platinum chemotherapy. Pts will receive nal-IRI 70 mg/m^2 IV over 90 minutes, LV 400 mg/m^2 IV over 30 minutes, and FU 2400 mg/m^2 over 46 hours, every 14 days. The primary objective is to determine progression-free survival (PFS) rate at 4 months (4mo) using RECIST v. 1.1 criteria and central radiology review. Response assessments will occur using imaging every 8 weeks. All pts who receive at least 1 dose of the study treatment will be eligible for the primary analysis. We will substitute pts who screen fail or do not begin treatment. Median PFS reported for pts receiving second-line 5-FU doublet chemotherapy is 3 months with a PFS_{4mo} of 30%. FU/LV/nal-IRI would be of interest if it could increase the PFS_{4mo} to 50% or higher. We will use a 2-stage Simon Minimax design. Using a one-sided α of 0.05 and 80% power, 39 pts will be required to detect a difference in PFS_{4mo} between 30% and 50%. Assuming a dropout rate of 10%, 44 pts will be enrolled across the 5 study sites. Enrollment began in Q2 2019. Clinical trial information: NCT04005339. Research Sponsor: Ipsen.

TPS594 **Trials in Progress Poster Session (Board #P7), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

Phase II trial of trifluridine/tipiracil and irinotecan for the treatment of advanced refractory biliary tract cancer.

Hao Xie, Mitesh J. Borad, Daniel H. Ahn, Tanios S. Bekaii-Saab, Nguyen H. Tran, Zhaohui Jin, Henry C. Pitot, Lucas J. Huebner, Qian Shi, Jaclynn Wessling, Lori M. Durgin, Minetta C. Liu, Tara L. Hogenson, William J Phillips, Martin Fernandez-Zapico, Steven R Alberts, Amit Mahipal; Mayo Clinic, Rochester, MN; Mayo Clinic Cancer Center, Scottsdale, AZ; Mayo Clinic, Phoenix, AZ

Background: Effective treatment options are very limited for patients with advanced refractory biliary tract cancer (BTC). Fluoropyrimidine-based chemotherapy regimen such as 5-fluorouracil and irinotecan are frequently utilized for these patients after first-line therapy despite lack of FDA approval. Trifluridine/tipiracil (FTD/TPI) is a novel oral nucleoside with antitumor activity in both fluoropyrimidine sensitive and resistant tumors due to its unique mechanisms of action. Given early toxicity and efficacy data from our previous study on single-agent trifluridine/tipiracil (FTD/TPI) in advanced BTC, the clinical evaluation of its combination with irinotecan represents a rational approach for the treatment of advanced refractory BTC. **Methods:** This is a single-arm phase II trial with a two-stage design to assess the efficacy of trifluridine/tipiracil (FTD/TPI) and irinotecan in advanced refractory BTC. Key eligibility criteria include histologically confirmed advanced, unresectable BTC who have progressed on at least one line of systemic therapy and have measurable disease per RECIST v1.1. Target accrual is 25. Treatment includes trifluridine/tipiracil (FTD/TPI) 25 mg/m^2 on days 1-5 and irinotecan 180 mg/m^2 on day 1 in 14-day cycles. Patients will be evaluated for response every 4 cycles and in the absence of disease progression, therapy may be given up to 2 years. The primary end point is the progression-free survival rate at 16 weeks. Secondary endpoints include overall response rate, disease control rate, progression-free survival, overall survival, and incidence of adverse events. Correlative biomarker studies include evaluations of circulating tumor DNA and circulating tumor cells at baseline, after 4 cycles and at progression; and development of patient-derived tumor organoids from pre-treatment biopsies for parallel treatments. This study was approved and funded in part by the National Comprehensive Cancer Network (NCCN) Oncology Research Program from general research support provided by Taiho Oncology, Inc. Clinical trial information: NCT 04072445. Research Sponsor: Taiho Oncology, Inc National Comprehensive Cancer Network (NCCN).

TPS595 **Trials in Progress Poster Session (Board #P8), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

Phase I study of a new concept cancer vaccine composed artificial intelligence (AI)-designed shared-antigen peptides plus combined synergistically activating antigen-specific CTL reaction (CYT001) in patients with advanced hepatocellular carcinoma (CRESCENT 1).

Sadahisa Ogasawara, Hiroaki Kanzaki, Keisuke Koroki, Kengo Kanayama, Susumu Maruta, Kazufumi Kobayashi, Souichiro Kiyono, Masato Nakamura, Naoya Kanogawa, Takayuki Kondo, Eiichiro Suzuki, Yoshihiko Ooka, Shingo Nakamoto, Akinobu Tawada, Tetsuhiro Chiba, Makoto Arai, Hiroyuki Nakada, Nobuko Yamaguchi, Hideki Hanaoka, Naoya Kato; Department of Gastroenterology, Graduate School of Medicine, Chiba University, Chiba, Japan; Department of Gastroenterology, Graduate School of Medicine, Chiba, Chiba, Japan; Department of Gastroenterology, Graduate School of Medicine, Chiba, Chiba, Chiba, Japan; Translational Research and Development Center, Chiba University Hospital, Chiba, Japan; Clinical Research Centre, Chiba University Hospital, Chiba, Japan; Department of Gastroenterology, Graduate School of Medicine, Chiba University Hospital, Chiba, Japan

Background: CYT001 (CYTLIMIC Inc.) is a novel cancer vaccine involving artificial intelligence (AI)-designed shared-antigen peptides and optimal combined adjuvants that boost the cancer-immunity cycle. The two multi-HLA reactive peptides heat shock protein 70 (HSP70) and glypican 3 (GPC3) were screened by an AI-based prediction system according to the proteome, mRNA, and histopathology data fromhuman samples. These immunogenic peptides were confirmed to show cross-reactivity to HLA-A 24:02, 02:01, and 02:06. Poly-ICLC (Oncovir Inc.) binds to Toll-like receptor 3 (TLR3) and melanoma differentiation antigen 5 (MDA5) on antigen-presenting cells (APCs)and activates APCs. LAG-3Ig (Immutep Inc.) binds to the major histocompatibility complex (MHC) class II molecules of APCs and activates APCs. Both poly-ICLC and LAG-3Ig synergistically activate antigen-specific CTL reactions as effective combination adjuvants. The present study aims to evaluate the safety and tolerability of CYT001 (mixture of HSP70 peptide [2.0 mg], GPC3 peptide [2.0 mg], poly-ICLC [1.0 mg], and LAG-3Ig [1.4 mg]) in patients with advanced hepatocellular carcinoma (HCC). **Methods:** This is a single-center, phase 1, open-label, single-arm, investigator-initiated clinical trial of CYT001 for advanced HCC patients with no eligible standard systemic therapy, Child–Pugh A liver disease, and HLA-A 24:02, 02:01, or 02:06. Enrolled patients will receive CYT001 as a subcutaneous injection on days 1, 8, 15, and 21 in the 1st and 2nd cycles, days 1 and 15 in the 3rd and 4th cycles, and day 1 in the 5th cycle or later of 28-day cycles. The primary endpoint is dose-limiting toxicity, and the secondary endpoints are safety and the response rate. The transition of the CTL reactions of both the HSP70 and GPC3 peptides will be evaluated using blood samples of the subjects. Exploratory analyses include investigation of candidate biomarkers for treatment efficacy using liver tumor biopsy samples (baseline and after the 1st cycle) and blood samples (baseline and every days of administration). Clinical trial information: jRCT2031190072. Research Sponsor: CYTLIMIC Inc.

TPS596 Trials in Progress Poster Session (Board #P9), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

Phase Ib/II study of sorafenib (SOR) and pembrolizumab (PEM) in advanced hepatocellular cancer (HCC).

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Background: SOR has been the backbone of advanced HCC therapy with poor outcome. Anti-PD-1 therapy is approved as a second-line treatment option in HCC due to its promising efficacy and safety. Our preclinical work showed that SOR is immunomodulatory and may be synergistic when combined with anti-PD-1 therapy. Guided by this data, we initiated this multicenter study of SOR and PEM in advanced HCC patients (pts). **Methods:** Pts who have Child-Pugh Class A, ECOG PS of 0/1, biopsy-proven measurable HCC that is unresectable or metastatic, are included. Pts must not receive either SOR or anti-PD-1 therapy before. A total of 27 pts will be enrolled from 2 sites. Pts must have the following lab values: ANC $\geq$ 1,500/ mc; Hgb $\geq$ 8.5 g/dL; Plts $\geq$75,000/ mcL; serum total bilirubin $\leq$ 2.0 mg/dL; AST/ALT $\leq$ 5 X ULN; serum creatinine $\leq$ 1.5 X ULN. Pts with active hep B must be on antiviral therapy. Pts would be on a 4-week run-in of SOR alone at 400mg BID to ensure tolerability and stable dose (minimum 200 BID) before beginning PEM 200mg IV q3 weeks. Both drugs would be administered until progression or unacceptable toxicity with response assessment q6 weeks by RECIST 1.1 criteria. Primary endpoint: response rate. Secondary endpoints: safety, overall survival, and progression-free survival. Correlative Endpoints: Pre-treatment levels of immunosuppressive cells and the functional activity of effector T cells would be compared to post-treatment blood and tumor samples. The first 6 pts who completed 4 weeks of SOR-only treatment and began the combination therapy (addition of PEM at a fixed dose of 200 mg Q3W) would comprise the safety lead-in. Pts who withdrew before initiation of combination therapy (for reasons other than DLT) would be replaced. Dose-Limiting toxicity was defined as any $\geq$ grade 3 clinically significant toxicity, which is deemed possibly treatment-related and occurs within the first cycle of combination therapy. Toxicity would be assessed by NCI CTCAEV4.0. Status: First patient enrollment on 12/19/2017. On 11/28/2018, our 6th patient completed the SOR lead-in phase and began combination treatment with SOR and PEM. As of Sept 12, 2019, thirteen pts have enrolled, and 9 pts have received combination treatment. Support: Merck. Clinical trial information: NCT03211416. Research Sponsor: Merck.

TPS597 **Trials in Progress Poster Session (Board #P10), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

FIDES-01, a phase II study of derazantinib in patients with unresectable intrahepatic cholangiocarcinoma (iCCA) and FGFR2 fusions and mutations or amplifications (M/A).

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Background: Deregulation of the FGFR signaling pathway is implicated in various cancers. In iCCA, FGFR genetic aberrations include FGFR2 fusions and, less commonly, FGFR2 M/A. iCCA prognosis is poor, and chemotherapeutic and targeted treatment options are limited. While FGFR2 fusions are acknowledged oncogenic drivers, the oncogenic potential of FGFR2 M/A is less well defined. Derazantinib (DZB) is an investigational, oral small-molecule kinase inhibitor with activity against FGFR1, 2 and 3, which demonstrated antitumor activity in patients with unresectable iCCA with FGFR2 fusions. Based on preliminary efficacy data demonstrating durable responses of $>$ 6 months and a clinically meaningful progression-free survival in a subset of iCCA patients harboring FGFR2 M/A (NCT01752920), the multicenter, multicohort open-label phase 2 study FIDES-01 is evaluating the effect of DZB in separate cohorts of iCCA patients with FGFR2 fusions or FGFR2 M/A. **Methods:** The new cohort evaluates 300 mg once daily dosing of DZB in patients with unresectable iCCA with FGFR2 M/A per liquid or tissue biopsy-based next generation sequencing and at least one previous systemic therapy. Treatment will continue until progressive disease, intolerance, withdrawal of informed consent, or death. Using a Simon's two-stage design, the primary endpoint to assess the antitumor activity of DZB is the proportion of patients with PFS at 3 months (PFS3; per RECIST 1.1 central review). Secondary objectives are evaluation of median PFS, objective response rate, duration of response, safety profile, quality of life (incl., QLQ-C30, QLQ-BIL21, EQ-5D), and symptom response from baseline. Current status: The study was initiated in July 2019 with planned enrollment of 43 patients with confirmed FGFR2 M/A. Clinical trial information: NCT03230318. Research Sponsor: Basilea Pharmaceutica International Ltd. Pharmaceutical/Biotech Company.

TPS598 **Trials in Progress Poster Session (Board #P11), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

A phase II, randomized, controlled trial of nivolumab in combination with BMS-986253 or cabiralizumab in advanced hepatocellular carcinoma (HCC) patients.

Theodore Welling, Nina Beri, Despina Siolas, Deirdre Jill Cohen, Daniel Jacob Becker, Hua Zhong, Jennifer J. Wu, Paul Eliezer Oberstein, Thomas Benjamin Karasic; Laura and Isaac Perlmutter Cancer Center, NYU Langone Health, New York, NY; Perlmutter Cancer Center, NYU Langone Health, New York, NY; New York University, Mattituck, NY; Laura and Isaac Perlmutter Cancer Center, NYU Langone Health, and ECOG-ACRIN, New York, NY; Department of Medical Oncology, NYU Langone Medical Center, New York, NY; NYU Langone Health, New York, NY; University of Pennsylvania Abramson Cancer Center, Philadelphia, PA

Background: Tyrosine kinase inhibitors can prolong survival in advanced HCC patients, but response rates have been minimal. Recently, immune checkpoint inhibition with nivolumab (nivo) demonstrated objective response rates (ORR) of 15% (escalation phase) and 20% (expansion phase) in the Checkmate 040 study. Pre-clinical and translational studies have demonstrated that IL-8 and tumor associated macrophages (TAMs) contribute to HCC progression and recurrence following treatment. Therefore, rationale exists to evaluate combinatorial approaches to target TAM function combined with checkpoint inhibitory therapy. This phase II, randomized study will evaluate the safety and efficacy of combined anti-CSF1R (Cabiralizumab) or anti-IL-8 (BMS-986253) in combination with Nivo in advanced HCC. **Methods:** Advanced HCC patients without prior systemic treatment and disease measurable by RECISTv1.1 with Childs A liver function are eligible. Patients will be enrolled (n=25 per arm) to Nivo 240 mg IV Q2 weeks monotherapy, Nivo 240 mg IV + BMS-986253 1200 mg IV Q2 weeks, or Nivo 240 mg IV + Cabiralizumab 4 mg/kg IV Q2 weeks. Primary endpoints include safety and ORR determined by RECISTv1.1. Secondary endpoints include time to response, duration of response, progression free survival, and overall survival. Exploratory endpoints include analysis of tumor microenvironment immune and tumor cell profiling of pre- and on-treatment tumor tissue. Clinical trial information: NCT04050462. Research Sponsor: Bristol-Myers Squibb.

TPS599 **Trials in Progress Poster Session (Board #P12), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

A phase II clinical trial of the phosphatidylserine targeting antibody, bavituximab, in combination with pembrolizumab in patients with advanced hepatocellular carcinoma.

Muhammad Shaalan Beg, Hao Zhu, David Hsieh, Syed Mohammad Ali Kazmi, Aravind Sanjeevaiah, Amit G. Singal, Radhika Kainthla, Leticia Khosama, Kimberli Crane, Rolf A. Brekken, Adam Charles Yopp; The University of Texas Southwestern Medical Center, Dallas, TX; San Juan Onc Assoc, Farmington, NM; Alaska Native Medical Center, Anchorage, AK; University of Texas Southwestern Medical Center, Dallas, TX; Division of Surgical Oncology Department of Surgery, Hamon Center for Therapeutic Oncology Research, Dallas, TX; Department of Surgery, University of Texas Southwestern Medical Center, Dallas, TX

Background: Phosphatidylserine (PS) is an immunosuppressive lipid segregated to the inner leaflet of the plasma membrane of normal cells. PS is externalized to the outer leaflet of the plasma membrane on cells that line tumor blood vessels, tumor cells and exosomes in the tumor microenvironment creating a specific target for anticancer treatments. Bavituximab is a PS targeting antibody that binds to PS via β2 glycoprotein-1 (β2GP1), an abundant serum glycoprotein. Bavituximab can modulate the tumor immune microenvironment to promote anti-tumor immune activity. This clinical trial is evaluating the effect of combining bavituxumab and the checkpoint inhibitor pembrolizumab in patients with advanced hepatocellular carcinoma (HCC). **Methods:** This is a single arm phase 2 clinical trial for patients with histologically confirmed HCC which is not eligible for curative and/or loco-regional therapy. No prior systemic therapy for HCC is allowed. Patients should be $>$ 18 years, have Child-Pugh Score A, ECOG 0-1 and meet the following laboratory criteria: total bilirubin $\leq$ 2.0, INR $\leq$ 1.7; Hgb $\geq$ 8.5 g/dl; AST, ALT $\leq$5 times ULN; platelet $\geq$ 50,000/mm3; and albumin $\geq$ 2.5 g/dl. Major exclusion criteria include thromboembolic event within the last 6 months, clinically evident ascites, GI bleeding within 2 months, uncontrolled hypertension, HIV and autoimmune disease (except DM1, childhood allergies and thyroid abnormalities if adequately controlled. Dosing is as follows: Bavituximab: 3 mg/kg IV weekly, pembrolizumab: 200 mg IV every 3 weeks. The primary objective is to determine the overall response rate (ORR) of therapy. Secondary objectives are to determine the safety, tolerability and other measures of clinical efficacy (overall survival, 6 month PFS, and duration of response). Tumor and blood samples are being collected to assess for pharmacodynamic biomarkers. A minimax two-stage method will be used to analyze ORR after the first 15 patients are accrued. If 3 or more of the first 15 patients have either a complete or partial response, 13 additional patients will be enrolled. ORR will be analyzed by RECIST 1.1 criteria. Clinical trial information: NCT03519997. Research Sponsor: Merck, Oncologie.

TPS600 **Trials in Progress Poster Session (Board #P13), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

A phase III study of futibatinib (TAS-120) versus gemcitabine-cisplatin (gem-cis) chemotherapy as first-line (1L) treatment for patients (pts) with advanced (adv) cholangiocarcinoma (CCA) harboring fibroblast growth factor receptor 2 (*FGFR2*) gene rearrangements (FOENIX-CCA3).

Mitesh J. Borad, John A. Bridgewater, Chigusa Morizane, Rachna T. Shroff, Do-Youn Oh, Markus H. Moehler, Junji Furuse, Karim A. Benhadji, Helen He, Juan W. Valle; Mayo Clinic Cancer Center, Scottsdale, AZ; University College London Cancer Institute, London, United Kingdom; National Cancer Center Hospital, Tokyo, Japan; University of Arizona Cancer Center, Tucson, AZ; Seoul National University Hospital, Seoul, South Korea; Johannes Gutenberg-University Clinic, Mainz, Germany; Kyorin University, Tokyo, Japan; Taiho Oncology, Princeton, NJ; The Christie NHS Foundation Trust, Manchester, United Kingdom

Background: Pts with adv CCA have poor survival outcomes, and chemotherapy offers limited survival benefit (5-year survival rates, 5–10%; median overall survival [OS], 8–12 months). *FGFR2* gene rearrangements are known to be early drivers of oncogenesis in ~15% of pts with intrahepatic (i) CCA. Futibatinib, an oral, highly selective, irreversible FGFR1-4 inhibitor has shown antitumor activity against a broad spectrum of FGFR-deregulated tumors in preclinical studies. In a previous study, futibatinib demonstrated clinical activity and tolerability in heavily pretreated pts with adv CCA harboring *FGFR2* gene rearrangements. This phase 3 trial (FOENIX-CCA3) is designed to evaluate futibatinib vs gem-cis as 1L therapy for pts with adv iCCA harboring *FGFR2* rearrangements. **Methods:** FOENIX-CCA3 is a multicenter, open-label, randomized phase 3 study that will be conducted in pts with metastatic or unresectable iCCA harboring *FGFR2* rearrangements (assessed at screening by a central laboratory). Pts must have an ECOG performance status of 0 or 1 and should not have received previous systemic anticancer therapy for adv disease (adjuvant/neoadjuvant therapy ≥6 mo prior to randomization is permissible). Pts with clinically-significant alterations in calcium-phosphorus homeostasis or ectopic mineralization/calcification will be excluded. Approximately 216 pts will be randomized (1:1 ratio) to receive 20 mg futibatinib once daily until disease progression or other discontinuation criteria are met or gem-cis (on days 1 and 8 of a 21-day cycle) for 8 cycles or until disease progression, whichever occurs first. Pts will be stratified by prior surgical excision (yes vs no), geographic region, and locally adv vs metastatic disease. The primary endpoint is progression-free survival (PFS) assessed by independent central review (ICR). Secondary endpoints include objective response rate and disease control rate based on ICR, OS, PFS per investigator assessment, and safety. The anticipated start date is in April, 2020. Research Sponsor: Taiho Oncology.

TPS601 Trials in Progress Poster Session (Board #P14), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM

A phase II randomized placebo-controlled study investigating the combination of yiv-906 and sorafenib (SORA) in HBV (+) patients (Pts) with advanced hepatocellular carcinoma (HCC).

James J. Harding, Ghassan K. Abou-Alfa, Yuankai Shi, Jacqueline Whang-Peng, Man Fung Yuen, Wasif M. Saif, Aiping Tian, Shanzhi Gu, Wing Lam, Shwu-Huey Liu, Yung-Chi Cheng, Edward Chu, Yun Yen; Memorial Sloan Kettering Cancer Center, New York, NY; National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing Key Laboratory of Clinical Study on Anticancer Molecular Targeted Drugs, Beijing, China; Taipei Medical University, Taipei, Taiwan; Queen Mary Hospital, The University of Hong Kong, Hong Kong, China; Northwell Health Cancer Institute, Lake Success, NY; Cancer Institute and Hospital, Chinese Academy of Medical Sciences, Beijing, China; Department of Interventional Radiology,Hunan Cancer Hospital, Changsha, China; Yale School of Medicine, Yale University, New Haven, CT; Yiviva Inc., New York, NY; University of Pittsburgh Medical Center, Pittsburgh, PA; TMU Research Center of Cancer Translational Medicine, Taipei Medical University, Taipei, Taiwan

Background: First-line systemic treatment options for advanced HCC pts are limited to the multi-targeted tyrosine kinase inhibitors, SORA and lenvatinib. Both agents improve outcomes for pts with advanced disease, but are associated with increased rate of grade $\geq$ 3 treatment-related adverse events. YIV-906 (PHY906, KD018) is derived from Huang-Qin-Tang, a traditional Chinese medicine documented 1800 years ago to treat gastrointestinal ailments. Preclinical data indicate YIV-906 increases inflammation in the tumor microenvironment by M1 macrophages activation/proliferation resulting in HCC tumor rejection *in vivo* and reduces SORA associated toxicity. Clinical experience with YIV-906 plus SORA suggests safety and potential clinical benefit to HCC pts with chronic HBV infection. **Methods:** This is a proof-of-concept, international, multicenter, double-blind, placebo-controlled, randomized phase 2 study designed to compare the efficacy of YIV-906 and SORA to SORA alone in advanced HCC pts (NCT04000737). Key eligibility criteria include age $\geq$ 18 years, HBV-associated HCC, $\geq$ 1 measurable untreated lesion, Child-Pugh A liver function, and no prior systemic therapy. An estimated 125 pts will be randomized 2:1 to receive the investigational (YIV-906 plus SORA) or control (placebo plus SORA) arm until disease progression or unacceptable toxicity. Pts will be stratified by metastatic status (extrahepatic/vascular invasion vs none) and ECOG performance status (0 vs. 1). The primary endpoint is progression-free survival (PFS). Secondary endpoints include objective response rate and disease control rate by mRECIST, time to progression, overall survival, quality of life, and safety by CTCAE version 4.0. Translational correlatives include pharmacokinetics, effects on oral/gut microbiota, and exploratory soluble biomarkers analysis. For the primary endpoint, sample size of 41 pts in control arm and 84 pts in the investigational arm achieves 90% power at a 0.05% significance level to detect a hazard ratio of 0.5 assuming the median PFS of the control SORA arm is 3.6 months and that of the combination arm is 7.3 months. Clinical trial information: NCT04000737. Research Sponsor: Yiviva Inc.

TPS602 Trials in Progress Poster Session (Board #P15), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM and Poster Walks, Fri, 4:45 PM-5:30 PM

NUC-1031 in combination with cisplatin for first-line treatment of patients with advanced biliary tract cancer (NuTide:121).

Jennifer J. Knox, Mairead Geraldine McNamara, Lipika Goyal, Mark Doherty, Christoph Springfeld, Joon Oh Park, Aimery De Gramont, Helena Verdaguer, John Raymond Zalcberg, Daniel H. Palmer, T.R. Jeffry Evans, Paul J. Ross, Juan W. Valle; Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; Princess Margaret Cancer Centre, Toronto, ON, Canada; Massachusetts General Hospital, Boston, MA; Department of Medical Oncology, University College Hospital Galway, Galway, Ireland; Heidelberg University Hospital, Medical Oncology, National Center for Tumor Diseases, Heidelberg, Germany; Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; Franco-British Institute, Levallois-Perret, France; Vall d'Hebron Institute of Oncology, Barcelona, Spain; Peter MacCallum Cancer Centre, Melbourne, Australia; University of Liverpool, Liverpool, United Kingdom; University of Glasgow, Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom; Guy's Hospital, London, United Kingdom; The Christie NHS Foundation Trust, Manchester, United Kingdom

Background: Biliary tract cancer (BTC) carries a poor prognosis and has no approved treatments. Although gemcitabine + cisplatin (GemCis) is accepted as the global standard of care (SoC) for 1st-line treatment, the reported unconfirmed ORR and OS from randomized studies of this combination are low at 18.5-26.1% and 11.2-11.7 months, respectively. NUC-1031, a phosphoramidate transformation of gemcitabine, is designed to overcome key cancer resistance mechanisms associated with gemcitabine. Promising signs of efficacy have been observed with single-agent NUC-1031 in a Phase I study in advanced solid tumors (Blagden et al 2018) and in the Phase Ib ABC-08 study of NUC-1031 + cisplatin 25 mg/m^2 on days 1 and 8 of a 21-day cycle for the 1st-line treatment of advanced BTC. Of 14 patients (pts) enrolled in 2 cohorts (NUC-1031: 625 mg/m^2 and 725 mg/m^2), 1 pt achieved a CR and 6 pts achieved PR, giving an unconfirmed ORR of 50% and representing an approximate doubling of ORR over SoC. The combination was well-tolerated with no unexpected adverse events or dose-limiting toxicities. The RP2D of NUC-1031 in combination with cisplatin is 725 mg/m^2. The tolerability profile together with robust efficacy signals suggested NUC-1031 + cisplatin may represent a more effective therapy than GemCis for BTC and led to initiation of a global Phase III study. **Methods:** A Phase III, open-label, randomized head-to-head study of NUC-1031 + cisplatin versus GemCis for 1st-line treatment of advanced BTC will include pts ≥18 years with histologically- or cytologically-proven BTC (including cholangiocarcinoma, gallbladder, or ampullary cancer), 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. 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: NCT04163900. Research Sponsor: NuCana.

TPS603 **Trials in Progress Poster Session (Board #P16), Fri, 12:00 PM-1:30 PM and 4:30 PM-5:30 PM**

Phase II HEPANOVA trial of tumor treating fields concomitant with sorafenib for advanced hepatocellular carcinoma.

Anca Grosu, Eleni Gkika, Thomas B. Brunner, Robert Thimme; German Cancer Consortium (DKTK) Core Center Heidelberg and DKTK Partner Site Freiburg, Freiburg, Germany; German Cancer Research Center (DKFZ), Heidelberg, Germany and German Cancer Consortium (DKTK) partner site Essen, Essen, Germany; Department of Radiation Oncology, University Hospitals Freiburg, Freiburg Im Breisgau, Germany; University of Freiburg, Freiburg, Germany

Background: Tumor Treating Fields (TTFields) are a non-invasive, regional antimitotic treatment modality, which has been approved for the treatment of glioblastoma and malignant pleural mesothelioma by the FDA. TTFields predominantly act by disrupting the formation of the mitotic spindle during metaphase. TTFields were effective in multiple preclinical models of hepatocellular carcinoma (HCC), leading to a significant increase in cell death. The Phase 2 HEPANOVA [NCT03606590] study is the first trial testing TTFields in HCC patients, and is designed to test the safety and efficacy of adding TTFields to sorafenib in advanced HCC. **Methods:** (N = 25) with unresectable HCC who are not amenable to any local treatment will be enrolled in this prospective, single-arm study. The study enrolls patients with ECOG score of 0-2 and Barcelona clinic liver cancer (BCLC) stage 0-C. Patients must have a measurable disease per RECIST Criteria. Having implanted electronic devices in the torso is exclusionary. Sorafenib will be administered at standard dose (400 mg twice daily). TTFields (150 kHz) will be delivered for 18 hours/day until local disease progression per RECIST Criteria. Clinical follow up will be performed q4w, and a CT/MRI scan q12w. Following disease progression in the liver, patients will discontinue TTFields and be followed monthly for survival. Overall response rate will be the primary endpoint and in-field control rate, progression-free survival rate at 12 month (PFS12), OS rate at 1 year and toxicity will all be secondary endpoints. Sample size was calculated using an Exact test for proportions considering the weighted average of ORR of patients who had either complete or partial response per RECIST criteria in historical studies with sorafenib is 4.5%. A sample size of 25 patients was required to achieve a power of approximately 80% at a one-sided alpha level of 0.05 using a single sample Exact test for proportions. Clinical trial information: NCT03606590. Research Sponsor: Novocure.