Cancers of the Pancreas, Small Bowel, and Hepatobiliary Tract

Studies presented in oral sessions with links to abstracts and conclusions cited from abstracts:

First author: Pascal Hammel

Abstract 204: Phase II LAPACT Trial of nab-paclitaxel (nab-P) plus gemcitabine (G) for patients with locally advanced pancreatic cancer (LAPC).

Conclusion:

• Induction treatment with nab-paclitaxel plus gemcitabine was tolerable and QOL was maintained in most patients

• nab-Paclitaxel plus gemcitabine had promising antitumor activity - DCR of 78% and ORR of 33%

• nab-Paclitaxel plus gemcitabine induction allowed conversion of unresectable to resectable tumors in 15% of patients

- Despite all patients being considered unresectable at baseline, 16 of 107 achieved either an R0 or R1 resection following the induction phase

• Median TTF with nab-paclitaxel plus gemcitabine induction followed by IC treatment was 8.8 months (90% CI, 6.67 - 9.82 months) and exceeded the protocol-specified target of 6.6 months

• Patients who participated in the LAPACT trial had a median PFS of 10.8 months and a 1-year estimated OS rate of 72%

A *nab*-P + G induction regimen in LAPC appears tolerable and feasible and is associated with encouraging antitumor activity and promising TTF and PFS. NCT02301143. Clinical trial information: NCT02301143

J Clin Oncol 36, 2018 (suppl 4S; abstr 204)

First author: Chigusa Morizane, MD, PhD

Abstract 205: Randomized phase III study of gemcitabine plus S-1 combination therapy versus gemcitabine plus cisplatin combination therapy in advanced biliary tract cancer: A Japan Clinical Oncology Group study (JCOG1113, FUGA-BT).

Conclusions:

Primary endpoint: Median OS: 13.4/15.1 months

Secondary endpoints: Median PFS: 5.8/6.8 months; RR 32.4/29.8%. AE: Both regimens are tolerable; Clinically significant AE: 35.1/29.9%; SAE: TRD 3/0; % planned dose: GEM: 75.7%/CDDP: 76.7%; GEM: 76.2%/S-1: 75.3%

GS demonstrated non-inferiority to GC in OS with good tolerability and was considered as new convenient option of standard of care without hydration for advanced BTC. Clinical trial information: UMIN000010667.

J Clin Oncol 36, 2018 (suppl 4S; abstr 205)

First author: Masatoshi Kudo, MD, PhD

Abstract 206: Randomized, Open Label, Multicenter, Phase II Trial comparing Transarterial Chemoembolization (TACE) plus Sorafenib with TACE Alone in Patients with Hepatocellular Carcinoma (HCC): TACTICS Trial.

Conclusions: Sorafenib in combination with TACE significantly improved PFS over TACE alone in patients with unresectable HCC. TACE in combination with sorafenib was clinically feasible. Adverse events were consistent with the known safety profile with previous TACE combination trials.

Longer sorafenib treatment duration (38.7 weeks) may be the key of success of this trial as compared with previous failed trials (Post TACE; 17 weeks, SPACE; 21 weeks, TACE 2; 17.1 weeks).

New intrahepatic lesions should not be regarded as progressive disease/stopping rule of the study in TACE combination trial.

The TACTICS trial clearly showed TACE in combination with sorafenib is a treatment option to improve clinical outcome and may be a standard of care in patients with intermediate stage HCC.

Clinical trial information: NCT01217034

J Clin Oncol 36, 2018 (suppl 4S; abstr 206)

First author: Ghassan Abou-Alfa, MD

Abstract 207: Cabozantinib (C) versus placebo (P) in patients (pts) with advanced hepatocellular carcinoma (HCC) who have received prior sorafenib: results from the randomized phase 3 CELESTIAL trial.

Conclusion: C significantly improved OS and PFS vs P in previously treated pts with advanced HCC after prior systematic anticancer therapy. The safety profile is acceptable with a low rate of discontinuation due to treatment-related adverse events were consistent with the known safety profile of C.

Cabozantinib represents a new treatment option for advanced HCC patients after prior systemic anticancer therapy. Clinical trial information: NCT01908426

J Clin Oncol 36, 2018 (suppl 4S; abstr 207)

First author: Ramesh Ramanathan, MD

Abstract 208: A phase IB/II randomized study of mFOLFIRINOX (mFFOX) + pegylated recombinant human hyaluronidase (PEGPH20) versus mFFOX alone in patients with good performance status metastatic pancreatic adenocarcinoma (mPC): SWOG S1313 (NCT #01959139).

Conclusions: OS in the mFFOX control arm (15.1 mo) is longest yet reported. Addition of PEGPH20 to mFFOX is not recommended for further study and appears to be detrimental (HR = 0.48). The impact of

PEGPH20 on OS was unexpected and in contrast to favorable results reported for the combination of gemcitabine/nab-paclitaxel + PEGPH20 especially in the HA high cohort (Hingorani S et al. A 4008, ASCO 2017). PEGPH20 with mFFOX caused increased toxicity (mostly GI and TE events) and decreased treatment duration compared to mFFOX alone. Tumor HA content will be analyzed. Funding: NIH/NCI grants CA180888, CA180819; and in part by Halozyme Inc. Clinical trial information: 01959139.

J Clin Oncol 36, 2018 (suppl 4S; abstr 208)

First author: Andrew Zhu

Abstract 209: KEYNOTE-224: Pembrolizumab in Patients with Advanced Hepatocellular Carcinoma Previously Treated with Sorafenib.

Conclusion: Pembrolizumab treatment resulted in durable responses and favorable PFS and OS in pts with advanced HCC previously treated with sorafenib. Safety was generally comparable to that established for pembrolizumab monotherapy and no viral flares were seen. A phase III randomized trial evaluating pembrolizumab vs placebo as second line therapy in this population is underway (KEYNOTE-240: Clinical trial information:NCT02702401). Clinical trial information: NCT02702414

J Clin Oncol 36, 2018 (suppl 4S; abstr 209)

First author: Sang Min Yoon

Abstract 210: Effect of transarterial chemoembolization plus external beam radiotherapy on survival of patients with hepatocellular carcinoma showing macroscopic vascular invasion compared with sorafenib: A randomized trial.

Conclusions: In patients with advanced HCC showing MVI, first-line treatment with TACE+RT was well-tolerated and provided improved progression-free survival, objective response rate, time to disease progression, and overall survival, compared with sorafenib treatment. Clinical trial information: NCT01901692

J Clin Oncol 36, 2018 (suppl 4S; abstr 210)

First author: Kyaw Aung, MBBS, MRCP, PhD

Abstract 211: Genomics-driven precision medicine for advanced pancreatic ductal carcinoma (PDAC): Early results from the COMPASS trial (NCT02750657).

Conclusions:

Prospective genomic profiling of advanced PDAC is safe and feasible with clinically meaningful turn-around time.

Patients with unstable genomic subtype and those with germline BRCA2 mutations and a "second hit" in tumor may respond better to m-FFX.

Response to chemotherapy differs between tumor RNA subtypes.

GATA6 expression by RNA in-situ hybridization is a robust surrogate marker for RNA subtypes.

NCT02750657

J Clin Oncol 36, 2018 (suppl 4S; abstr 211)