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

Sub-category: Multidisciplinary Treatment

Category: Cancers of the Pancreas, Small Bowel, and Hepatobiliary Tract

Meeting: 2018 Gastrointestinal Cancers Symposium

Abstract No: 207

Poster Board Number: Poster Session B (Board #A4)

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

Author(s): Ghassan K. Abou-Alfa, Tim Meyer, Ann-Lii Cheng, Anthony B. El-Khoueiry, Lorenza Rimassa, Baek-Yeol Ryoo, Irfan Cicin, Philippe Merle, Joong-Won Park, Jean-Frédéric Blanc, Luigi Bolondi, Heinz Josef Klämpen, Stephen Lam Chan, Vincenzo Dadduzio, Colin Hessel, Anne E. Borgman-Hagey, Gisela Schwab, Robin Kate Kelley; Memorial Sloan Kettering Cancer Center, New York, NY; University College London, London, United Kingdom; National Taiwan University Hospital, Taipei, Taiwan; Norris Comprehensive Cancer Center, USC Keck School of Medicine, Los Angeles, CA; Humanitas Clinical and Research Center, Rozzano, Italy; Asan Medical Center, University of Ulsan, Seoul, Korea, Republic of (South); Trakya University School of Medicine, Edirne, Turkey; Groupement Hospitalier Lyon Nord, Lyon, France; National Cancer Center, Goyang, Korea, Republic of (South); Hôpital Saint-André, Bourdeaux, France; Istituto Oncologico Veneto, IRCCS, Padova, Italy; Academic Medical Center, Amsterdam, Netherlands; Sir YK Pao Center for Cancer, State Key Laboratory in Oncology in South China, Hong Kong, Hong Kong; Universitat Oberta de Catalunya/ Istituto Oncologico Veneto, IRCCS, Padova, Italy; Exelixis, Inc., South San Francisco, CA; UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA

**Abstract Disclosures**

Abstract:

**Background:** C, an inhibitor of MET, VEGFR, and AXL, has previously shown clinical activity in pts with advanced HCC. This phase 3 trial (NCT01908426) evaluated C vs P in previously treated pts with advanced HCC. **Methods:** In this double-blind, global, phase 3 trial, pts were randomized 2:1 to receive C (60 mg qd) or matched P stratified by disease etiology (HBV, HCV, other), geographic region (Asia, other), and presence of extrahepatic spread and/or macrovascular invasion (EHS/MVI). Eligible pts had pathologic diagnosis of HCC, Child-Pugh score A, ECOG PS
≤1, and must have received prior sorafenib. Pts received up to two lines of prior systemic therapy for HCC and must have progressed following at least one. The primary endpoint was overall survival (OS). Secondary endpoints were investigator-assessed progression-free survival (PFS) and objective response rate (ORR) per RECIST 1.1. The study was designed to detect a hazard ratio (HR) for OS of 0.76 (90% power, 2-sided α = 0.05) at the final analysis with two prespecified interim analyses at 50% and 75% of the planned 621 events.

Results: As of 1 Jun 2017, 707 pts were randomized, and 484 deaths had occurred (317 out of 470 for C; 167 out of 237 for P). Baseline characteristics were balanced between the two arms: median age was 64 years, 82% were male, 38% had HBV, 24% had HCV, 25% enrolled in Asia, 78% had EHS, 30% had MVI, 85% had EHS/MVI, and 27% had received two prior systemic therapy regimens for advanced HCC. The study met the primary endpoint at the second planned interim analysis with median OS 10.2 mo for C vs 8.0 mo for P (HR 0.76, 95% CI 0.63-0.92; p = 0.0049). Median PFS was 5.2 mo for C vs 1.9 mo for P (HR 0.44, 95% CI 0.36-0.52; p < 0.001), and ORR was 4% vs 0.4% (p = 0.0086). The most common grade 3/4 adverse events (predominantly grade 3) with higher incidence in the C vs P arm included hand-foot skin reaction (17% vs 0%), hypertension (16% vs 2%), increased aspartate aminotransferase (12% vs 7%), fatigue (10% vs 4%), and diarrhea (10% vs 2%).

Conclusion: C significantly improved OS and PFS vs P in previously treated pts with advanced HCC. Adverse events were consistent with the known safety profile of C.

Clinical trial information: NCT01908426