621PD Phase II trial of tepotinib vs sorafenib in Asian patients (pts) with advanced hepatocellular carcinoma (HCC)

B-Y. Ryoo[1], Z. Ren[2], T-Y. Kim[3], H. Pan[4], K-M. Rau[5], H.J. Choi[6], J-W. Park[7], J.H. Kim[8], C-J. Yen[9], B-H. Kim[10], D. Zhou[11], J. Straub[12], C. Zhao[13], S. Qin[14]

[1]Department of Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, [2]Liver Cancer Institute, Department of Hepatic Oncology, Zhongshan Hospital, Fudan University, Shanghai, China, [3]Division of Medical Oncology, Seoul National University Hospital, Seoul, Republic of Korea, [4]School of Medicine, Sir Run Run Shaw Hospital, Zhejiang University, Hangzhou, China, [5]Division of Hematology-Oncology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Taiwan, China, [6]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Republic of Korea, [7]Center for Liver Cancer, National Cancer Center, Goyang-si, Republic of Korea, [8]Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Republic of Korea, [9]Department of Internal Medicine, National Cheng Kung University Hospital, Taiwan, China, [10]Department of Internal Medicine, Kyung Hee University Hospital, Seoul, Republic of Korea, [11]GBEM, Merck Serono Pharmaceutical R&D Co, Beijing, China, [12]Global Early Development, Merck KGaA, Darmstadt, Germany, [13]Global Clinical Development Oncology, EMD Serono Inc, Billerica, MA, USA, [14]Medical Oncology Department, PLA Cancer Center, Nanjing Bayi Hospital, Nanjing, China

Background: MET is a potential therapeutic target in HCC. Tepotinib, a potent and highly selective MET inhibitor, has antitumor activity in pts with MET+ tumors. Phase 1b of the current trial (NCT01988493), confirmed the recommended phase 2 dose (RP2D) of tepotinib in Asian advanced HCC pts; here we describe phase 2 outcomes for tepotinib vs sorafenib.

Methods: Asian adults with MET + (2+ or 3+ by immunohistochemistry) advanced HCC (Barcelona clinic liver cancer Stage B/C; Child-Pugh Class A without encephalopathy; Eastern Cooperative Oncology Group performance status 0–1; no prior systemic advanced HCC therapy) were randomized (1:1) to tepotinib 500 mg once daily (RP2D) or sorafenib 400 mg twice daily in 21-day cycles. Endpoints: time to progression (TTP: primary endpoint), safety, progression-free survival (PFS), overall survival (OS) and tumor response. Efficacy was assessed by independent review committee (IRC) and investigators.

Results: Of 90 pts randomized, 75 were included in the efficacy analysis (tepotinib n = 38, sorafenib n = 37): median age 57 [range 31–78] years; 84.0% <65 years old; 94.7% male). TTP by IRC was statistically significantly longer for tepotinib vs sorafenib (2.8 vs 1.4 months; hazard ratio [HR] (90% confidence interval [CI]): 0.42 (0.26, 0.70); p = 0.0043). Median PFS by IRC was also statistically significantly longer for tepotinib (2.8 vs 1.4 months; HR (90% CI): 0.53 (0.33, 0.84); p = 0.0229). Median OS was similar between arms (tepotinib 9.3 vs sorafenib 8.6 months; HR [90%CI] 0.73 [0.43, 1.12]; p = 0.3039). Objective response rate by IRC was 10.5% (tepotinib) vs 0% (sorafenib) (p = 0.0438). There were 4 partial responses, all in the tepotinib arm. IRC outcomes were supported by investigator read data. In the safety analysis, treatment-related treatment-emergent adverse events (TRTEAEs) occurred in 37/45 (82%) and 43/44 (98%) pts and TRTEAEs grade ≥3 in 13/45 (29%) and 20/44 (46%) pts in the tepotinib and sorafenib arms, respectively. No new safety signals were noted.

Conclusions: Tepotinib provided significantly longer TTP and PFS than sorafenib in Asian pts with MET+ advanced HCC, with fewer reported overall and grade ≥3 TRTEAEs.

Clinical trial identification: NCT01988493.

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