186P Phase II trial of tepotinib vs sorafenib for treatment-naïve advanced hepatocellular carcinoma (HCC) in Asian patients

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Background: Met is a therapeutic target in HCC. Tepotinib is a highly-selective Met inhibitor with antitumor activity in pts with MET+ tumors. Here, we report the outcomes of a randomized phase 2 study of tepotinib vs sorafenib in Asian pts with advanced HCC.

Methods: Asian patients with Met overexpression (2+/3+ by immunohistochemistry [IHC; scale 0 to 3+]) advanced HCC (Barcelona clinic liver cancer Stage B/C; Child-Pugh Class A without encephalopathy; ECOG performance status 0–1; no prior systemic therapy for advanced HCC) were randomized (1:1) to tepotinib 500 mg once daily or sorafenib 400 mg twice daily, in 21-day cycles. Primary endpoint was time to progression (TTP; by independent review committee [IRC]); key secondary endpoints included safety, progression-free survival (PFS), overall survival (OS) and objective response rate (ORR). Efficacy was assessed by IRC and by investigators.

Results: Of 90 randomized pts, 75 were included in the efficacy analysis (tepotinib n = 38, sorafenib n = 37): median age was 57 [range 31–78] years; 84% <65 years; 95% male). Median treatment duration (range) was 13 (1–81) weeks for tepotinib vs 12 (<1–62) weeks for sorafenib. Median TTP and PFS by IRC and investigators were significantly longer for tepotinib vs sorafenib (Table). Improved TTP (by IRC) with tepotinib was observed across subgroups. Median OS was similar between arms. ORR by IRC was 10.5% (tepotinib; 4 partial responses) vs 0% (sorafenib) (p = 0.0438). Treatment-related treatment-emergent adverse events (TEAEs) occurred in 82% (grade ≥3: 29%) and 98% (grade ≥3: 45%) of pts with tepotinib and sorafenib, respectively. Hypertension (14%) was the only grade ≥3 treatment-related TEAE occurring in ≥ 10% pts (sorafenib arm). No new safety signals were noted.

Conclusions: In Asian pts with Met-overexpressing advanced HCC, TTP and PFS were significantly longer with tepotinib than with sorafenib and tepotinib treatment was associated with fewer overall and grade ≥3 treatment-related TEAEs.

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Table: 186P

	Tepotinib 500 mg once-daily (n = 38)	Sorafenib 400 mg twice-daily (n = 37)	HR [90% CI]
Median TTP, months			
By IRC	2.9	1.4	0.42 [0.26, 0.70]; p = 0.0043
By investigator	5.6	2.8	0.46 [0.28, 0.73]; p = 0.0059
Median PFS, months			
By IRC	2.8	1.4	0.53 [0.33, 0.84]; p = 0.0229
By investigator	3.2	2.8	0.59 [0.38, 0.92]; p = 0.0496
Median OS, months			
ITT	9.3	8.6	0.73 [0.43, 1.21]; p = 0.3039
Subgroup analyses Median TTP (IRC), months	Tepotinib 500 mg once-daily (n = 38)	Sorafenib 400 mg twice-daily (n = 37)	HR [90% CI]
Age, years (n)			
<65 years	(31) 2.8	(32) 4.4	0.52 [0.31, 0.88]
≥65 years	(7) 4.4	(5) 1.4	0.16 [0.04, 0.73]
Vascular invasion and/or extrahepatic spread (n)[a]			
Present	(12) 2.8	(15) 1.4	0.56 [0.23, 1.35]
Absent	(16) 4.2	(6) 1.4	0.10 [0.03, 0.38]
Gene amplificiation status (n)[a]			
Mean GCN <5	(32) 2.9	(32) 1.4	0.44 [0.26, 0.75]
Mean GCN ≥5	(4) 2.0	(5) 1.4	0.51 [0.12, 2.11]
HBV status (n)[a]			
Negative	(10) 4.2	(6) 1.4	0.33 [0.10, 1.02]
Positive	(24) 2.8	(30) 1.4	0.51 [0.29, 0.89]
AFP elevation (n)			
Yes	(29) 2.8	(32) 1.4	0.55 [0.32, 0.95]
No	(9) 4.2	(5) 1.3	0.19 [0.05, 0.67]
Prior local-regional therapy (n)			
Yes	(20) 2.7	(20) 1.4	0.46 [0.24, 0.87]
No	(18) 4.2	(17) 2.6	0.27 [0.11, 0.67]

[a]Information not available for some patients in the tepotinib and/or sorafenib group AFP, alpha-fetoprotein; CI, confidence interval; GCN, gene copy number; HR, hazard ratio; IHC, immunohistochemistry; IRC, independent review committee; ITT, intent-to-treat; OS, overall survival; PFS, progression-free survival; TTP, time to progression