703P Assessment of disease burden in the phase III CELESTIAL trial of cabozantinib (C) versus placebo (P) in advanced hepatocellular carcinoma (HCC)

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Background: Extrahepatic spread (EHS) and macrovascular invasion (MVI) are poor prognostic factors in HCC. In the CELESTIAL trial (NCT01908426), C improved overall survival (OS) and progression-free survival (PFS) vs P in patients (pts) with previously treated advanced HCC. Median OS was 10.2 mo with C vs 8.0 mo with P (HR, 0.76; 95% CI, 0.63–0.92; P = 0.0049). Median PFS was 5.2 mo with C versus 1.9 mo with P (HR, 0.44; 95% CI, 0.36–0.52; P < 0.0001). Here, we analyze OS and PFS based on (i) EHS, (ii) MVI, and (iii) the sum of target lesion diameters (SOD) at baseline.

Methods: A total of 707 pts, stratified by disease etiology, geographic region, and the presence of EHS and/or MVI, were randomized 2:1 to receive C, 60 mg once daily (N = 470) or P (N = 237). Eligible patients had a pathologic diagnosis of HCC, Child-Pugh score A, and ECOG performance status ≤1. Pts received prior sorafenib and ≤2 lines of prior systemic therapy. Tumors were assessed every 8 weeks by investigator.

Results: In the overall population, 78% pts had EHS, 30% had MVI and 85% had EHS and/or MVI. Among pts with EHS, 50% had metastasis to the lung, 40% to lymph nodes and 17% to bones. C improved OS (HR ≤ 0.8) vs P in pts with or without MVI (Table). C also improved OS vs P in pts with EHS or high SOD. PFS was improved with C irrespective of the extent of the disease.

Table: 703P

	No. pts		Median OS, mo		OS HR (95% CI)	Median PFS, mo		PFS HR (95% CI)
	C	P	C	P		C	P	
EHS								
Yes	369	182	9.6	6.9	0.72 (0.58-0.89)	5.0	1.9	0.46 (0.37-0.56)
No	101	55	12.0	12.3	0.96 (0.63-1.46)	5.4	1.9	0.45 (0.31-0.66)
MVI								
Yes	129	81	7.6	5.3	0.75 (0.54-1.03)	3.7	1.8	0.42 (0.31-0.58)
No	339	156	12.4	9.7	0.80 (0.64-1.01)	5.5	1.9	0.48 (0.38-0.59)
SOD								
< median	231	120	12.5	10.5	0.94 (0.71-1.24)	5.5	1.9	0.48 (0.37-0.61)
≥ median	234	117	8.2	5.3	0.58 (0.45-0.76)	4.2	1.9	0.44 (0.34-0.57)

Conclusions: C generally improved OS in pt subgroups defined by extent of disease burden. The presence of MVI, EHS, or high SOD at baseline was associated with shorter OS in both treatment groups.

Clinical trial identification: NCT01908426.

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