Impact of baseline liver function on overall survival (OS) and safety in patients (pts) with unresectable hepatocellular carcinoma (HCC) treated with first-line (1L) tislelizumab (TIS): Results from the RATIONALE-301 study

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Background and aims: TIS is a monoclonal antibody with high binding affinity to programmed cell death protein 1. The phase 3 RATIONALE-301 study (NCT03412773) demonstrated non-inferior OS with TIS versus sorafenib (SOR) (median [m] OS 15.9 vs 14.1 months [mo], respectively; HR: 0.85 [95 % CI: 0.71, 1.02]) in 1L treatment of pts with unresectable HCC; OS superiority versus SOR was not met. As liver function is a known predictor of survival in pts with HCC, we evaluated baseline liver function and its impact on OS and safety in pts enrolled in RATIONALE-301.

Methods: Systemic therapy-naïve adults with histologically confirmed HCC were randomized (1:1) to receive TIS (200 mg intravenously every 3 weeks) or SOR (400 mg orally twice daily) until disease progression, intolerable toxicity, or withdrawal. The primary endpoint was OS. In this exploratory analysis, OS and safety were assessed by Child-Pugh score (CPS; 5 vs 6) and albumin-bilirubin (ALBI) grade (1 vs 2).

Results: In pts randomized to TIS (n = 342), at baseline, 76.9 % and 22.5 % had a CPS of 5 and 6, respectively, and 74.9 % and 23.7 % had an ALBI grade of 1 and 2, respectively. In pts randomized to SOR (n = 332), 74.7 % and 25.3 % had a CPS of 5 and 6, respectively, and 68.1 % and 29.5 % had an ALBI grade 1 and 2, respectively. At data cutoff (July 11, 2022; minimum study follow-up 33 mo), mOS was similar in pts treated with TIS and SOR, and numerically longer

in pts with CPS 5 vs 6, and ALBI grade 1 vs 2, regardless of treatment arm (Table). Incidence of any grade and grade ≥ 3 treatment-emergent adverse events (TEAEs) and treatment-related adverse events (TRAEs) were lower in pts treated with TIS versus SOR across CPS and ALBI grades (Table).

Conclusions: Survival was similar between arms, and TIS showed a favorable safety profile compared with SOR, regardless of CPS or ALBI grade, supporting the primary analysis. Pts with CPS 6 and ALBI grade 2 had poorer mOS than those with CPS 5 and ALBI grade 1, regardless of treatment arm, affirming that pts with better liver function have improved outcomes.

Table

	CPS 5		CPS 6		ALBI grade 1		ALBI grade 2	
Efficacy*	**TIS (n = 263)**	**SOR (n = 248)**	**TIS (n = 77)**	**SOR (n = 84)**	**TIS (n = 256)**	**SOR (n = 226)**	**TIS (n = 81)**	**SOR (n = 98)**
Median OS, mo (95 % CI)	19.5 (15.4, 23.5)	18.4 (14.5, 20.9)	8.7 (6.2, 12.3)	8.3 (5.6, 10.0)	19.9 (15.9, 24.2)	16.9 (13.7, 19.8)	9.5 (7.3, 10.8)	9.1 (6.2, 13.1)
Unstratified HR (95 % CI)	0.88 (0.71, 1.08)		0.73 (0.52, 1.03)		0.85 (0.69, 1.06)		0.83 (0.60, 1.14)	
Safety, n (%)†	**TIS (n = 261)**	**SOR (n = 243)**	**TIS (n = 75)**	**SOR (n = 81)**	**TIS (n = 256)**	**SOR (n = 226)**	**TIS (n = 81)**	**SOR (n = 98)**
TEAE any grade	251 (96.2)	243 (100)	72 (96.0)	81 (100)	244 (95.3)	226 (100)	80 (98.8)	98 (100)
TEAE grade ≥ 3	120 (46.0)	155 (63.8)	42 (56.0)	57 (70.4)	113 (44.1)	145 (64.2)	49 (60.5)	67 (68.4)
TRAE any grade	194 (74.3)	238 (97.9)	63 (84.0)	73 (90.1)	194 (75.8)	218 (96.5)	65 (80.2)	93 (94.9)
TRAE grade ≥ 3	56 (21.5)	131 (53.9)	18 (24.0)	42 (51.9)	46 (18.0)	121 (53.5)	29 (35.8)	52 (53.1)

*Efficacy analysis set; †Safety analysis set.