Tislelizumab (TIS) versus sorafenib (SOR) in first-line (1L) treatment of unresectable hepatocellular carcinoma (HCC): the RATIONALE-301 Chinese subpopulation analysis

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Background: TIS is a humanized monoclonal antibody with high affinity and binding specificity to programmed cell death protein 1 receptor. In the phase 3 trial RATIONALE-301 (NCT03412773), TIS showed non-inferior overall survival (OS) vs SOR (hazard ratio 0.85, 95% confidence interval [CI]: 0.71, 1.02), and was well tolerated in 1L treatment of patients (pts) with unresectable HCC. This analysis assessed and compared efficacy and safety of TIS in the Chinese subgroup with the overall population of RATIONALE-301.

Methods: This open-label trial enrolled systemic therapy-naïve adults with histologically confirmed Barcelona Clinic Liver Cancer Stage C or B HCC. Pts were randomized (1:1) to receive TIS (200 mg IV every 3 weeks [TIS Arm]) or SOR (400 mg orally twice daily [SOR Arm]) until disease progression, intolerable toxicity, or treatment discontinuation due to other reasons. The primary endpoint was OS. Secondary endpoints included objective response rate (ORR), duration of response (DoR), and progression-free survival, all by blinded independent review committee, and safety.

Results: Of 674 randomized pts, 425 were from China. In the Chinese subgroup, median follow-up was 13.8 months (mo, 95%CI: 0.1, 50.8) in TIS arm vs 13.1 mo (95%CI: 0.1, 49.4) in SOR arm, similar to the overall population. Efficacy data in the Chinese subgroup were similar to the overall population and characterised by higher ORR and longer DoR in the TIS arm vs the SOR arm (Table). In the Chinese subgroup, 53 pts (24.9%) had grade ≥3 treatment-related adverse events in TIS arm vs 112 pts (54.6%) in SOR arm, similar to the overall population (22.2% and 53.4%, respectively).

	Chinese Subgroup		**Overall Population**	
	TIS (n=215)	**SOR (n=210)**	**TIS (N=342)**	**SOR (N=332)**
mOS, mo (95%CI)	14.2 (11.6, 18.1)	13.4 (11.4, 15.4)	15.9 (13.2, 19.7)	14.1 (12.6, 17.4)
ORR, % (95%CI)	12.6 (8.4, 17.7)	6.2 (3.3, 10.4)	14.3 (10.8, 18.5)	5.4 (3.2, 8.4)
mDoR, mo (95%CI)	42.9 (9.7, NE)	11.0 (6.2, 19.6)	36.1 (16.8, NE)	11.0 (6.2, 14.7)
mPFS, mo (95%CI)	2.1 (2.1, 2.1)	2.4 (2.1, 4.1)	2.1 (2.1, 3.5)	3.4 (2.2, 4.1)

ITT Analysis Set; Data cutoff: Jul 11, 2022.
CI, confidence interval; ITT, intent-to-treat; mo, months; m, median; DoR, duration of response; NE, not evaluable;
ORR, confirmed objective response rate; OS, overall survival; PFS, progression-free survival; SOR, sorafenib; TIS, tislelizumab.

Conclusions: TIS demonstrated a numerically longer OS, higher ORR, more durable responses, and a favourable safety profile vs SOR in the Chinese subgroup, consistent with the overall population representing a potential 1L treatment option for Chinese pts with unresectable HCC.