

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

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Background: In the phase 3 RATIONALE-301 study (NCT03412773), TIS, a PD-1 inhibitor, showed non-inferior overall survival (OS) vs SOR (hazard ratio [HR] 0.85, 95% confidence interval [CI]: 0.71, 1.02), and a favorable safety profile, in the 1L treatment of patients (pts) with unresectable HCC. Here, efficacy and safety of TIS vs SOR in Japanese pts are presented.

Method: Systemic therapy-naïve adults with histologically confirmed Barcelona Clinic Liver Cancer Stage B or C HCC were enrolled. Pts were randomized (1:1) to receive TIS (200 mg IV Q3W) or SOR (400 mg PO BID) until disease progression, intolerable toxicity, or withdrawal of consent. The primary endpoint was OS; secondary endpoints included objective response rate (ORR), progression-free survival (PFS), and duration of response (DoR) by blinded independent review committee per RECIST v1.1, and safety.

Results: Of 674 randomized pts, 77 were from Japan (TIS n=38, SOR n=39). In the Japanese subgroup, the median (m) OS for TIS vs SOR (25.0 vs 23.9 months [mo]; unstratified HR 0.78, 95% CI: 0.44, 1.38) was numerically longer than the overall population (15.9 vs 14.1 mo; stratified HR 0.85, 95% CI: 0.71, 1.02). Japanese pts had a higher confirmed ORR for TIS vs SOR (13.2% vs 7.7%; odds ratio 1.87 [95% CI: 0.40, 8.71]), similar mPFS (4.0 vs 4.2 mo; unstratified HR 1.15, 95% CI: 0.65, 2.02), with mDoR not reached. TIS-treated pts had fewer \geq grade 3 treatment-emergent adverse events (TEAEs; 35.1% vs 62.2%) and \geq grade 3 treatment-related TEAEs (TRAEs; 18.9% vs 54.1%) vs SOR,

similar to the overall population (48.2% vs 65.4%; 22.2% vs 53.4%, respectively). Fewer pts discontinued TIS vs SOR due to TRAEs (10.8% vs 16.2%).

Conclusions: In the Japanese subgroup, TIS demonstrated a higher mOS and ORR, and a favorable safety profile vs SOR, consistent with the overall population, with a numerically longer mOS than the overall population, representing a potential 1L treatment option for Japanese pts with unresectable HCC.