Tislelizumab versus sorafenib in first-line treatment of unresectable hepatocellular carcinoma: Impact on health-related quality of life in RATIONALE-301 population

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Introduction: RATIONALE-301 (NCT03412773), a global Phase 3 study, comparing tislelizumab (TIS) to sorafenib (SOR) as 1L treatment in adult patients (pts) with unresectable HCC (uHCC), met its primary endpoint of OS non-inferiority. This analysis examined the HRQoL outcomes in pts in both arms.

Methods: Systemic therapy-naïve adults with histologically confirmed uHCC were randomized 1:1 to receive TIS (200 mg IV Q3W, n=342) or SOR (400 mg PO BID, n=332). HRQoL was assessed using EORTC QLQ-C30, QLQ-HCC18 and EQ5D-5L. A mixed model for repeated measures using key pre-specified PRO endpoints of global health status/quality of life (GHS/QoL), physical functioning and fatigue scales of the QLQ-C30, and HCC18 index score,

fatigue and pain scores at the key pre-specified clinical cycles 4 and 6 were performed. Time to deterioration was examined with the Kaplan-Meier method using the PRO endpoints.

Results: At both cycles, TIS had better HRQoL outcomes than SOR, as indicated by LS mean differences in GHS/QoL, physical functioning, fatigue and HCC symptom index, but not for pain. TIS had a lower risk for deterioration of QLQ-C30 GHS/QoL (hazard ratio [HR] 0.68 [95% CI, 0.49-0.94]), physical functioning (0.53 [0.39-0.73]) and fatigue (0.48 [0.37, 0.63]) as well as for deterioration in the HCC18 index (0.53 [0.34-0.81]) and fatigue (0.60 [0.46-0.80]). Both arms had a similar risk for deterioration in pain (HR 0.78 [0.56-1.09]). TIS maintained while SOR declined EQ-5D-5L VAS (general health status) scores at cycle 4 (mean change from baseline =-0.4 [SD = 14.52] vs -4.3 [12.92]) and cycle 6 (-0.2 [17.03] vs -5.4 [13.09]).

Conclusion: Pts with HCC treated with 1L TIS had better HRQoL outcomes compared with pts treated with SOR, particularly in terms of fatigue and physical functioning. These results, along with effects an overall survival, response rate, and a favorable safety profile, support the benefit of TIS as a potential 1L treatment option for uHCC.

	Cycle 4 **TIS** **n=220** **Mean (95% CI)**	**Cycle 4** **SOR** **n=176** **Mean (95% CI)**	**Cycle 4** **Est Mean treatment Diff (95% CI)**	**Cycle 6** **TIS** **n=166** **Mean (95% CI)**	**Cycle 6** **SOR** **n=137** **Mean (95% CI)**	**Cycle 6** **Est Mean treatment Diff (95% CI)**
QLQ-C30						
GHS/QoL	-0.7 (-3.0, 1.6)	-5.1 (-7.6, -2.6)	4.3 (1.4, 7.3)*	-0.9 (-3.4, 1.6)	-5.9 (-8.6, -3.2)	5.0 (1.8, 8.2)*
Physical functioning	-1.3 (-3.1, 0.5)	-7.7 (-9.6, -5.8)	6.4 (4.2, 8.6)*	-1.0 (-3.0, 0.9)	-7.2 (-9.3, -5.1)	6.2 (3.7, 8.6)*
Fatigue	1.5 (-0.9, 3.9)	9.1 (6.5, 11.7)	-7.6 (-10.6, -4.7)*	2.2 (-0.4, 4.8)	9.8 (7.0, 12.6)	-7.6 (-10.8, -4.3)*

QLQ-HCC18						
Index Score	1.6 (0.4, 2.9)	3.9 (2.6, 5.2)	-2.3 (-3.8, -0.8)*	2.2 (0.6, 3.7)	4.9 (3.2, 6.5)	-2.7 (-4.7, -0.7)*
Fatigue	1.9 (-0.4, 4.2)	8.1 (5.6, 10.6)	-6.2 (-9.0, -3.4)*	1.8 (-0.9, 4.5)	7.8 (4.9, 10.7)	-6.0 (-9.4, -2.5)*
Pain	1.9 (-0.3, 4.0)	2.5 (0.2, 4.8)	-0.6 (-3.3, 2.1)	2.4 (-0.1, 4.9)	2.8 (0.1, 5.4)	-0.4 (-3.6, 2.9)

*p≤0.01 (nominal p)