Impact of first-line treatment with tislelizumab on health-related quality of life in Chinese patients with unresectable hepatocellular carcinoma

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ABSTRACT

Background: Analysis of the intent-to-treat (ITT) population of RATIONALE-301 (NCT03412773), a global phase 3 study comparing tislelizumab to sorafenib as first-line treatment in adult patients with unresectable hepatocellular carcinoma (uHCC), found overall survival non-inferiority, numerically higher response rate, a favorable safety profile, and a better health-related quality of life (HRQoL) outcome in patients treated with tislelizumab compared with those treated with sorafenib, particularly in terms of fatigue and physical functioning. This post hoc analysis examined HRQoL in the Chinese subgroup of patients in RATIONALE-301.

Methods: Systemic therapy–naïve adults with histologically confirmed uHCC were randomized 1:1 to receive tislelizumab (200 mg IV once every three weeks, n=342) or sorafenib (400 mg orally twice daily, n=332). HRQoL, one of the key secondary endpoints, was assessed using the EORTC QLQ-C30, QLQ-HCC18, and EQ-5D-5L. At the pre-specified clinical Cycles 4 and 6, a mixed model for repeated measures was performed 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 the index, fatigue, and pain scores of the QLC-HCC18. Time to deterioration was examined with the Kaplan-Meier method using the PRO endpoints.

Results: Analysis was conducted in the subgroup of 425 Chinese patients (tislelizumab, n=215; sorafenib, n=210). For the QLQ-C30 GHS/QoL index score, the difference between the arms in mean change from baseline to Cycle 4 (4.4 [95% CI, 1.7-7.7], *P*=0.0094) and Cycle 6 (6.1 [95% CI, 2.7-9.5], *P*=0.0005) was significantly different. Patients treated with tislelizumab experienced improvement (Cycle 4: 2.1 [95% CI, -1.4 to 5.6]; Cycle 6: 2.4 [95% CI, -1.1 to 6.0]) and patients treated with sorafenib experienced worsening of GHS/QoL (Cycle 4: -2.3 [95% CI, -6.2 to 1.6]; Cycle 6: -3.6 [95% CI, -7.5 to 0.03]). The arms significantly differed in change in fatigue as well as physical functioning at Cycle 4 (fatigue: -5.8 [95% CI, -9.1 to -2.4], *P*=0.0009; physical functioning: 6.0 [95% CI, 3.6-8.5], *P*< 0.0001) and Cycle 6 (fatigue: -8.6 [95% CI, -12.3 to -4.8], *P*<0.0001; physical functioning: 6.3 [95% CI, 3.6-9.0], *P*< 0.0001), with patients treated with tislelizumab maintaining and patients treated with sorafenib worsening. For the HCC18, least-square mean change in the index score and fatigue was also significantly different between the arms at Cycle 4 (index score: -1.9 [95% CI, -3.6 to -0.1], *P*=0.0361; fatigue: -6.9 [95% CI, -10.2 to -3.6], *P*< 0.0001) and

Cycle 6 (index score: -3.8 [95% CI, -5.9 to -1.6], *P*=0.0006; fatigue: -8.4 [95% CI, -12.3 to -4.6], *P*< 0.0001), with patients treated with tislelizumab maintaining and patients treated with sorafenib worsening. There were no differences in the pain score. Patients treated with tislelizumab had a lower risk for deterioration of QLQ-C30 GHS/QoL (hazard ratio [HR]: 0.52 [95% CI, 0.34-0.79]), physical functioning (HR, 0.39 [95% CI, 0.25-0.60]), and fatigue (HR, 0.41 [95% CI, 0.29-0.58]), as well as for deterioration in the HCC18 index (HR, 0.37 [95% CI, 0.20-0.69]) and fatigue (HR, 0.49 [95% CI, 0.34-0.69]). Both arms had a similar risk for deterioration in pain (HR, 0.83 [95% CI, 0.55-1.27]).

Conclusion: In RATIONALE-301, Chinese patients with HCC treated with first-line tislelizumab had better HRQoL outcomes compared with patients treated with sorafenib, particularly in terms of GHS/QoL, fatigue and physical functioning. These results, corroborating the HRQoL findings in the ITT population, along with overall survival non-inferiority, numerically higher response rate, and a favorable safety profile, suggest tislelizumab as a potential first-line treatment option for uHCC.