

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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RATIONALE-301 Study Design

Study Endpoints

Primary endpoint: OS in the ITT population; **key secondary endpoints:** ORR, PFS, and DoR by BIRC per RECIST v1.1, and safety

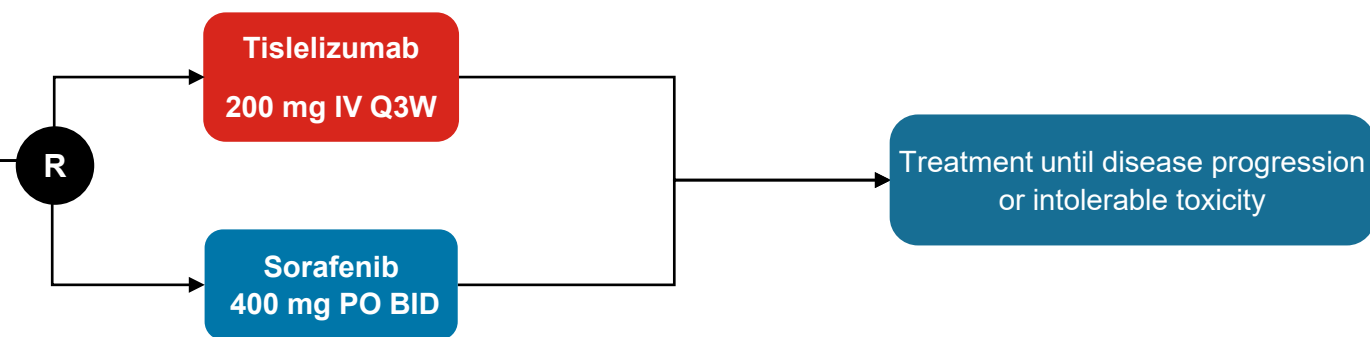
PRO endpoints: Compare HRQoL between tislelizumab and sorafenib

- The EORTC QLQ-C30: GHS/QoL, physical functioning, and fatigue
- The EORTC QLQ-HCC18: index, fatigue, and pain scores

For descriptive purposes the EQ-5D-5L's VAS score was included; stratification factors included macrovascular invasion (present vs absent), extrahepatic spread (present vs absent), ECOG PS (0 vs 1), etiology (HCV vs others including HBV), geography (Asia [excluding Japan], vs Japan vs rest of world)

Key eligibility criteria:

- Histologically confirmed HCC
- Systemic therapy-naïve
- BCLC stage C or B disease not amenable to or progressed after loco-regional therapy
- Child-Pugh class A
- ≥ 1 measurable lesion per RECIST v1.1
- ECOG PS ≤ 1
- No tumor thrombus involving main trunk of portal vein or inferior vena cava

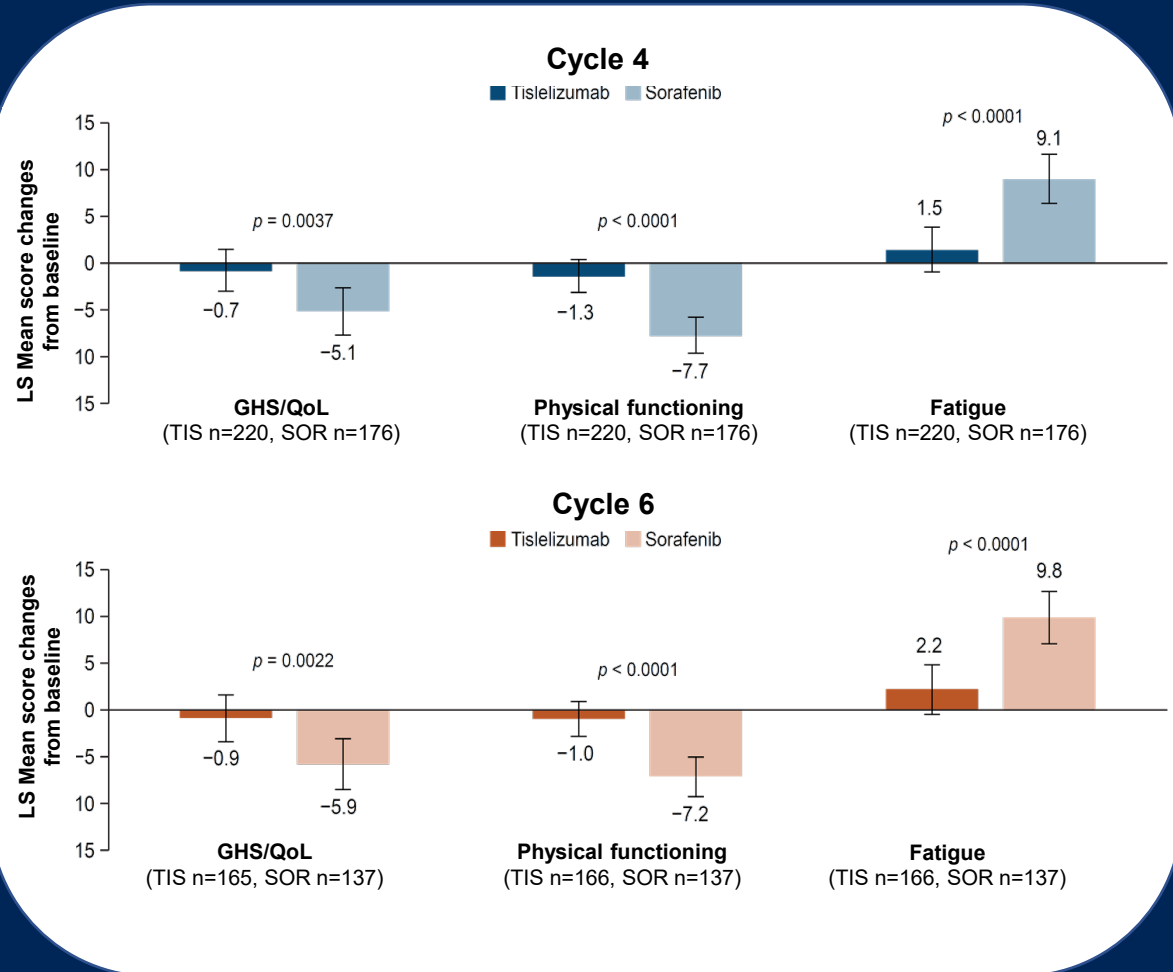


The demographics and clinical characteristics were generally balanced across the two treatment arms and were representative of the target patient population

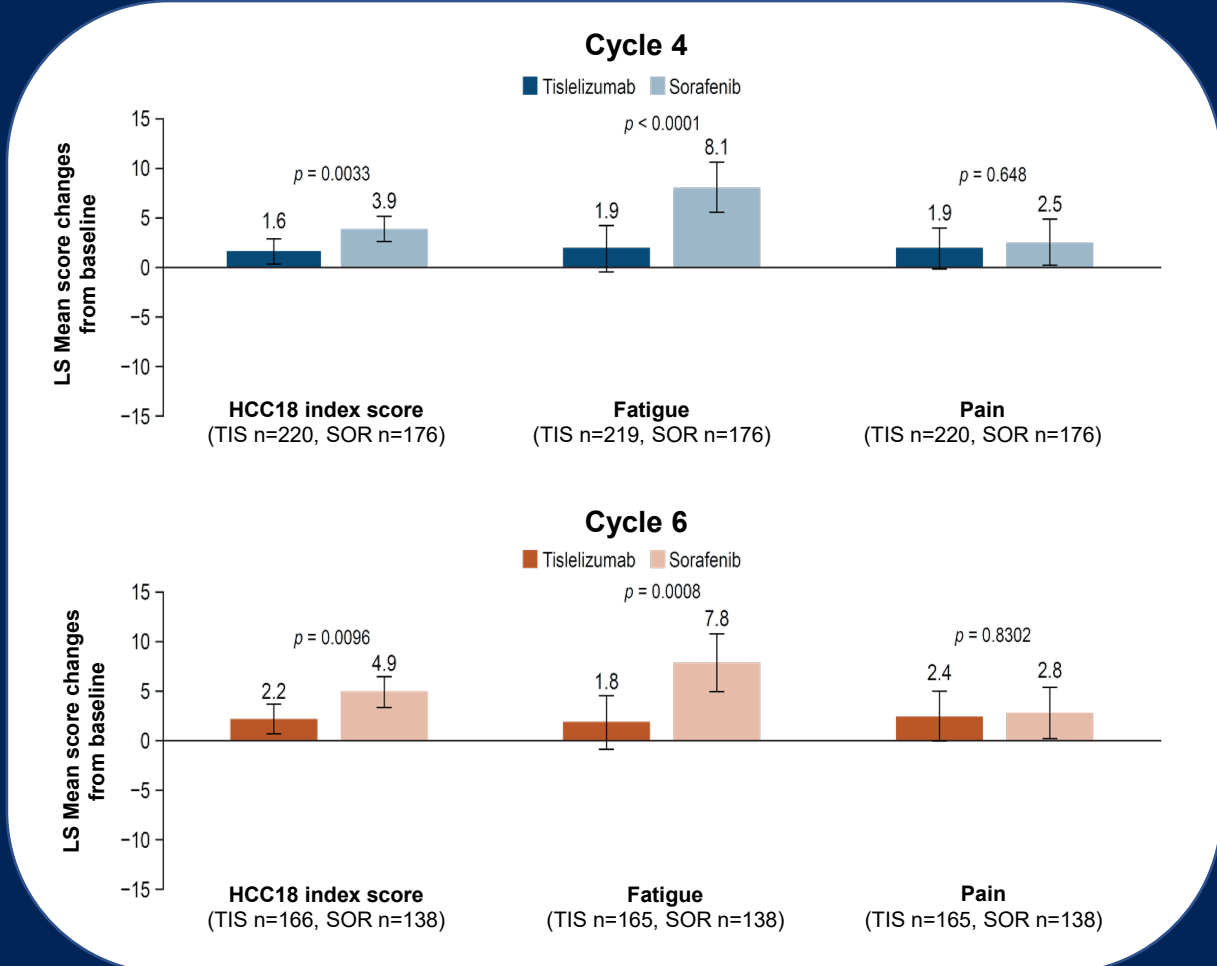
BCLC, Barcelona Clinic Liver Cancer; BID, Twice daily; BIRC, blinded independent review committee; DoR, duration of response; ECOG PS, European Cooperative Oncology Group performance status; EORTC, European Organisation for Research and Treatment of Cancer; EQ-5D-5L, EuroQoL Five-Dimensions Five-Levels; GHS/QoL, global health status/quality of life; HBV, hepatitis B virus; HCV, hepatitis C virus; HCC, hepatocellular carcinoma; HRQoL, health-related quality of life; ITT, intent-to-treat; IV, intravenous; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, oral; PRO, patient-reported outcome; Q3W, Once every 3 weeks; QLQ-C30, Quality of Life Questionnaire Core 30 items; QLQ-HCC18, Quality of Life Questionnaire Hepatocellular Carcinoma 18 Questions; R, randomized; VAS, visual analog scale; RECIST, Response Evaluation Criteria In Solid Tumors.

Change from Baseline in HRQoL Scores

Change from Baseline for EORTC QLQ-C30



Change from Baseline for EORTC at Cycle 4 and Cycle 6 QLQ-HCC18



Reported p values are nominal. EORTC, European Organisation for Research and Treatment of Cancer; GHS/QoL, global health status/quality of life; HRQoL, health-related quality of life; LS, least square; n, patients with baseline and at least one post-baseline measurement; QLQ-C30, Quality of Life Questionnaire Core 30; QLQ-HCC18, Quality of Life Questionnaire Hepatocellular Carcinoma 18 Questions; SOR, sorafenib; TIS, tislelizumab.

HRQoL Scores

Change from Baseline for EQ-5D-5L VAS Scores at Cycle 4 and Cycle 6

| | Tislelizumab (N=342) | | Sorafenib (N=332) | |
|----------|-----------------------|--------------------------------|-----------------------|--------------------------------|
| | Observed Mean (SD), n | Change from Baseline Mean (SD) | Observed Mean (SD), n | Change from Baseline Mean (SD) |
| Baseline | 80.8 (16.16) 327 | -- | 82.8 (14.37) 321 | -- |
| Cycle 4 | 81.8 (14.82) 213 | -0.4 (14.52) | 79.4 (15.10) 171 | -4.3 (12.92) |
| Cycle 6 | 82.8 (15.42) 160 | -0.2 (17.03) | 78.7 (15.35) 133 | -5.4 (13.09) |

At Cycles 4 and 6, VAS scores were maintained for the tislelizumab arm while scores worsened in the sorafenib arm

Time to Deterioration for EORTC QLQ-C30 and QLQ-HCC18

| | Tislelizumab (N=342) | Sorafenib (N=332) |
|--|--------------------------|-------------------|
| QLQ-C30 | | |
| GHS/QoL scale, n (%) | 68 (19.9) | 85 (25.6) |
| Stratified ^a HR (95% CI) | 0.68 (0.49, 0.94) | |
| Physical functioning scale, n (%) | 57 (16.67) | 94 (28.3) |
| Stratified ^a HR (95% CI) | 0.46 (0.33, 0.64) | |
| Fatigue, n (%) | 96 (28.1) | 150 (45.2) |
| Stratified ^a HR (95% CI) | 0.48 (0.37, 0.63) | |
| QLQ-HCC18 | | |
| Index score, n (%) | 41 (12.0) | 53 (16.0) |
| Stratified ^a HR (95% CI) | 0.53 (0.34, 0.81) | |
| Pain, n (%) | 70 (20.5) | 75 (22.6) |
| Stratified ^a HR (95% CI) | 0.78 (0.56, 1.09) | |
| Fatigue, n (%) | 91 (26.6) | 121 (36.4) |
| Stratified ^a HR (95% CI) | 0.60 (0.46, 0.80) | |

Risk for deterioration of GHS/QoL, physical functioning, and fatigue were lower in the tislelizumab arm

^aStratification factors included Eastern Cooperative Oncology Group performance status (0 versus 1) and investigator-chosen chemotherapy option (paclitaxel versus docetaxel versus irinotecan cells). CI, confidence interval; EORTC, European Organisation for Research and Treatment of Cancer; EQ-5D-5L, EuroQoL Five-Dimensions Five-Levels; GHS/QoL, global health status/quality of life; HR, hazard ratio; HRQoL, health-related quality of life; QLQ-C30, Quality of Life Questionnaire Core 30 QLQ-HCC18, Quality of Life Questionnaire Hepatocellular Carcinoma 18 Questions; SD, standard deviation; VAS, visual analogue scale.

Conclusions

- RATIONALE 301 met its primary endpoint of OS and key secondary endpoints of ORR and safety
- Tislelizumab monotherapy as a first-line treatment for patients with uHCC was associated with more favorable HRQoL outcomes than sorafenib
- Compared with patients receiving sorafenib, tislelizumab-treated patients had less worsening in general health status, physical functioning, fatigue, and HCC symptom index

These results, along with effects on OS, ORR, and a favorable safety profile, support the benefit of tislelizumab as a potential first-line treatment option for uHCC

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HCC, hepatocellular carcinoma; HRQoL, health-related quality of life; ORR, objective response rate; OS, overall survival; uHCC, unresectable hepatocellular carcinoma.