Tislelizumab (TIS) plus chemotherapy (chemo) vs placebo (PBO) plus chemo as first-line treatment of advanced gastric or gastroesophageal junction adenocarcinoma (GC/GEJC): Health-related quality of life outcomes in the RATIONALE-305 study

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ABSTRACT

Introduction: RATIONALE-305 (NCT03777657) demonstrated statistically significant and clinically meaningful improvements in overall survival (OS) with TIS+chemo (n=501) over PBO+chemo (n=496) as first-line treatment in patients with advanced GC/GEJC. We examined health-related quality of life (HRQoL) outcomes in the RATIONALE-305 study at the final analysis.

Methods: Adults with previously untreated, unresectable, or metastatic GC/GEJC were randomized (1:1) to TIS 200 mg or PBO IV once every 3 weeks plus investigator-choice of chemo. HRQoL was assessed using EORTC QLQ-C30 and the QLQ-STO22. A mixed model for repeated measures of patient-reported outcomes (PRO) endpoints at clinical Cycles 4 and 6 was performed. Time to deterioration was examined.

Results: TIS+chemo had improved outcomes (least-square mean change from baseline) vs PBO+chemo (Table) as indicated by the estimated mean treatment difference at Cycle 6 for QLQ-C30 GHS/QoL (2.52 [95% CI, 0.29-4.74]), physical functioning (2.46 [0.49-4.43]), fatigue (-3.01 [-5.78 to -0.24]), and STO22 index score (-1.62 [-3.12 to -0.12]), and maintaining upper gastrointestinal symptoms (-1.74 [95% CI, -3.55 to 0.06)] and pain (-1.88 [-4.03 to 0.27]). Patients receiving TIS+chemo had lower risk of deterioration of GHS/QoL (HR, 0.77 [95% CI, 0.60-0.98]), physical functioning (0.72 [0.57-0.92]), STO22 index score (0.64 [0.45-0.92]), pain/discomfort (0.74 [0.58-0.96]), and upper gastrointestinal symptoms (0.73 [0.56-0.95]).

Conclusions: Patients treated with TIS+chemo had better HRQoL outcomes vs those treated with PBO+chemo, particularly for GHS/QoL, physical functioning, fatigue, GC/GEJC symptoms, pain/discomfort, and upper GI symptoms. These results, along with prolonging of OS and other

secondary efficacy endpoints, as well as a tolerable safety profile, support the benefit of TIS+chemo as a potential first-line treatment option for GC/GEJC.

	Cycle 4 TIS+chemo n=501 Mean (95% CI)	**Cycle 4 PBO+chemo n=496 Mean (95% CI)**	**Cycle 6 TIS+chemo n=501 Mean (95% CI)**	**Cycle 6 PBO+chemo n=496 Mean (95% CI)**
QLQ-C30 GHS/QoL	1.35 (-0.24, 2.94)	-0.45 (-2.04, 1.13)	0.93 (-0.71, 2.57)	-1.58 (-3.24, 0.07)
Physical functioning	-2.47 (-3.77, -1.18)	-3.92 (-5.21, -2.62)	-2.76 (-4.22, -1.30)	-5.22 (-6.69, -3.75)
Fatigue	1.75 (-0.09, 3.60)	3.07 (1.23, 4.91)	1.71 (-0.32, 3.75)	4.73 (2.68, 6.77)
QLQ- STO22 Index score	-1.71 (-2.77, -0.66)	-0.61 (-1.66, 0.45)	-1.84 (-2.95, -0.74)	-0.22 (-1.34, 0.89)
Dysphagia	-2.78 (-3.99, -1.57)	-1.27 (-2.48, -0.06)	-2.79 (-3.93, -1.64)	-2.01 (-3.17, -0.86)
Pain/discomfort	-6.88 (-8.39, -5.36)	-4.64 (-6.16, -3.13)	-5.97 (-7.56, -4.38)	-4.09 (-5.69, -2.49)
Dietary restrictions	-0.31 (-1.75, 1.12)	0.61 (-0.82, 2.05)	-0.25 (-1.79, 1.30)	1.08 (-0.48, 2.63)
Upper gastrointestinal symptoms	-3.14 (-4.40, -1.87)	-1.54 (-2.80, -0.28)	-3.24 (-4.58, -1.90)	-1.49 (-2.84, -0.14)