Tislelizumab + chemotherapy vs placebo + chemotherapy in HER2-negative advanced or metastatic gastric or gastro-oesophageal junction adenocarcinoma (GC/GEJC): RATIONALE-305 study minimum 3-year survival follow-up

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ABSTRACT

Background: Tislelizumab (TIS; an anti–programmed cell death protein 1 antibody) + chemotherapy (CT) demonstrated significant overall survival (OS) benefit versus (vs) placebo (PBO) + CT as first-line (1L) therapy for advanced gastric or gastro-oesophageal junction adenocarcinoma (GC/GEJC) in all randomized patients (pts; hazard ratio [HR], 0.80) and pts with programmed death-ligand 1 (PD-L1) Tumour Area Positivity (TAP) score ≥5% (HR, 0.71) in the phase 3 RATIONALE-305 study (NCT03777657). 2-year OS rates for TIS + CT vs PBO + CT were 32.7% vs 23.4%, respectively. We report efficacy and safety after a minimum 3-year follow up.

Methods: Adults with locally advanced, nonresectable or metastatic, human epidermal growth factor receptor 2 negative (HER2-negative), untreated GC/GEJC were randomized (1:1) to intravenous TIS 200 mg or PBO every 3 weeks + investigator-chosen CT (oxaliplatin + capecitabine or cisplatin + 5-fluorouracil). TAP score was evaluated in tumour tissue using the VENTANA PD-L1 (SP263) assay. Primary endpoint was OS in all randomized pts and pts with PD-L1 TAP ≥5%. Secondary endpoints included investigator-assessed progression-free survival (PFS), objective

response rate, duration of response (DoR) per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, and safety.

Results: A total of 997 pts were randomized (TIS + CT, n=501; PBO + CT, n=496). At 3-year follow up (min: 36.6 months), improvements in OS, PFS, and DoR in TIS + CT vs PBO + CT were maintained (Table). Grade ≥3 treatment-related adverse events (TRAEs) were similar in both arms, occurring in 269/498 pts (54.0%) with TIS + CT and 246/494 pt (49.8%) with PBO + CT; TRAEs led to any treatment discontinuation in 16.7% vs 8.1% and led to death in 1.2% vs 0.4% pts, respectively.

Conclusions: After a minimum 3-year follow up, TIS + CT as 1L treatment for GC/GEJC continued to demonstrate clinically meaningful improvements in OS, PFS, and DoR compared with PBO + CT, with no new safety signals. These long-term data further support TIS + CT as a new 1L treatment option for advanced HER2-negative GC/GEJC.

Table

	TIS + CT (n=501)		PBO + CT (n=496)
Median OS, mo (95% CI)	15.0 (13.6, 16.5)		12.9 (12.1, 14.1)
HR (95% CI)[a]		0.79 (0.69, 0.90)	
OS rate at 36 mo, % (95% CI)	20.7 (17.1, 24.4)		13.4 (10.5, 16.6)
Median PFS, mo (95% CI)[b]	6.9 (5.7, 7.2)		6.2 (5.6, 6.9)
HR (95% CI)[a]		0.79 (0.68, 0.91)	
PFS at 36 mo (95% CI)	15.0 (11.6, 18.8)		7.5 (5.1, 10.5)
Objective response rate, % (95% CI)[b]	47.3 (42.9, 51.8)		40.5 (36.2, 45.0)
Median DoR, mo (95% CI)[a]	8.6 (7.9, 11.1)		7.2 (6.0, 8.5)
Remaining in response at 36 mo, % (95% CI)	24.5 (18.8, 30.6)		14.4 (9.3, 20.5)

[a]Stratified.

[b]Investigator evaluated.