Tislelizumab (TIS) Plus Chemotherapy (Chemo) vs Placebo (PBO) Plus Chemo as First-Line (1L) Treatment of Advanced Gastric or Gastroesophageal Junction Adenocarcinoma (GC/GEJC): Final Analysis Results of the RATIONALE-305 Study

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Background: TIS (anti-PD-1 antibody) plus (+) chemo demonstrated significant overall survival (OS) benefit vs PBO + chemo as 1L treatment in patients (pts) with advanced GC/GEJC at a pre-specified interim analysis of the PD-L1-positive (tumor area positivity score ≥5%) population in the global, phase 3 RATIONALE-305 study (NCT03777657). Here, we present primary analysis results in the intent-to-treat (ITT) population at the pre-specified final analysis.

Methods: Adults with previously untreated, HER2-negative, locally advanced, unresectable, or metastatic GC/GEJC, regardless of PD-L1 expression status, were randomized (1:1) to receive TIS 200 mg or PBO IV once every 3 weeks

plus investigator (INV)-choice of chemo (5-FU + cisplatin or capecitabine + oxaliplatin). The primary endpoints were OS in the PD-L1-positive and ITT populations. Secondary endpoints included progression-free survival, objective response rate, and duration of response by INV per RECIST v1.1, and safety.

Results: At data cutoff, 997 pts were randomized (501 pts to TIS + chemo; 496 pts to PBO + chemo). Minimum study follow-up was 24.6 mo . OS in the TIS arm was significantly improved compared with the PBO arm in the ITT population (median OS: 15.0 mo vs 12.9 mo, respectively; HR=0.80 [95% CI: 0.70, 0.92]; 1-sided *P*=0.0011). Additional main efficacy results are presented in the **Table**. Grade ≥3 treatment-related adverse events (TRAEs) occurred in 268 (53.8%) pts in the TIS arm and 246 (49.8%) pts in the PBO arm; TRAEs led to treatment discontinuation in 16.1% vs 8.1% of pts, respectively, and death in 1.2% vs 0.4%, respectively.

Conclusions: In the ITT population, TIS + chemo showed statistically significant and clinically meaningful improvement in OS vs PBO + chemo, and was well tolerated. These data support the TIS + chemo combination as a potential 1L treatment option for pts with advanced GC/GEJC.

Table

Endpoint	TIS + Chemo (n=501)	PBO + Chemo (n=496)
OS		
Median, mo (95% CI)	15.0 (13.6, 16.5)	12.9 (12.1, 14.1)
HR (95% CI)	0.80 (0.70, 0.92)	
P-value	0.0011	
PFS		
Median, mo (95% CI)	6.9 (5.7, 7.2)	6.2 (5.6, 6.9)
HR (95% CI)	0.78 (0.67, 0.90)	
ORR, % (95% CI)	47.3 (42.9, 51.8)	40.5 (36.2, 45.0)
mDoR, mo (95% CI)	8.6 (7.9, 11.1)	7.2 (6.0, 8.5)

ITT population.

Data cutoff: 28 February 2023.

Chemo, chemotherapy; CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; mDoR, median duration of response; mo, months; ORR, objective response rate; OS, overall survival; PBO, placebo; PFS, progression-free survival; TIS, tislelizumab.