

## Tislelizumab (TIS) plus chemotherapy (CT) vs placebo (PBO) plus CT as first-line (1L) treatment of advanced gastric or gastroesophageal junction adenocarcinoma (GC/GEJC): final analysis (FA) results of the RATIONALE-305 study

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### ABSTRACT

**Background:** TIS (anti-PD-1 antibody) + CT demonstrated significant overall survival (OS) benefit vs PBO+CT 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  $\geq 5\%$ ) population in the global, phase 3 RATIONALE-305 study (NCT03777657). Here, we present primary analysis results in the ITT population at the pre-specified final analysis.

**Material (Patients) and 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 CT (5-FU + cisplatin or capecitabine + oxaliplatin). The primary endpoints were OS in PD-L1-positive and ITT populations. Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), and duration of response (DoR) by INV per RECIST v1.1, and safety.

**Results:** At data cutoff (February 28, 2023), 997 pts were randomized (n=501, TIS+CT; n=496, PBO+CT). Minimum study follow-up was 24.6 months (mo). OS was significantly improved in the TIS arm vs 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  $\geq 3$  treatment-related adverse events (TRAEs) occurred in 268 (53.8%) vs 246 (49.8%) pts; TRAEs led

to treatment discontinuation in 16.1% vs 8.1% pts, and death in 1.2% vs 0.4% pts, in TIS vs PBO arms, respectively.

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

<b>Endpoint</b>	<b>TIS + CT (n=501)</b>	<b>PBO + CT (n=496)</b>
<b>OS</b>		
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)	
1-sided <i>P</i> -value	0.0011	
<b>PFS</b>		
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)	
<b>ORR, % (95% CI)</b>	47.3 (42.9-51.8)	40.5 (36.2-45.0)
<b>Median DoR, mo (95% CI)</b>	8.6 (7.9-11.1)	7.2 (6.0-8.5)