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 \( \geq 3 \) 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

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

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.