

First-Line Tislelizumab Plus Chemotherapy in Gastric/Gastroesophageal Junction Cancer: RATIONALE-305 Asian Subgroup

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Conclusions

- In Asian patients in the RATIONALE-305 study
 - Tislelizumab plus chemotherapy showed an improvement in overall survival (OS) versus placebo plus chemotherapy in both the intent-to-treat (ITT) and programmed death-ligand 1 (PD-L1) score ≥5% populations
 - Additionally, tislelizumab plus chemotherapy demonstrated improved progression-free survival (PFS), favorable response rates, and more durable antitumor responses versus placebo plus chemotherapy
 - Tislelizumab plus chemotherapy also showed a manageable safety profile, with no new safety signals identified
- The efficacy and safety results in the Asian patient subgroup were consistent with the results in the overall study population, suggesting this combination can be a first-line treatment option for Asian patients with advanced gastric/gastroesophageal junction cancer (GC/GEJC)¹



Introduction

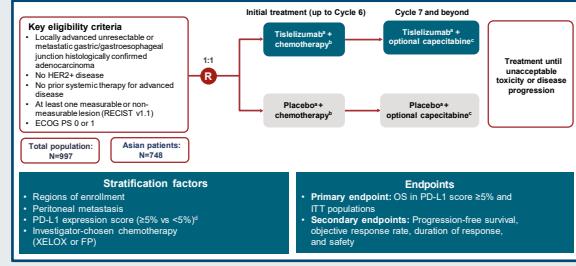
- Gastric cancer is one of the leading causes of cancer-related deaths worldwide; Asia has a notably higher incidence and mortality rate of GC, and the disease is of particular concern in China, South Korea, and Japan²⁻⁵
- Prior to the introduction of immunotherapy, platinum plus fluoropyrimidine chemotherapy was the standard first-line therapy for advanced GC/GEJC, with a median OS of less than 12 months⁶⁻⁸
- The RATIONALE-305 study (NCT03777657) met its primary endpoint, showing significant improvement in OS with tislelizumab plus chemotherapy versus placebo plus chemotherapy in the PD-L1 ≥5% population at interim analysis, and in the ITT population at final analysis, with favorable PFS^{1,9}
- Overall, results of the final analysis supported tislelizumab plus chemotherapy as a potential first-line treatment option for patients with advanced GC/GEJC¹
- Here, we present results from the Asian patient subgroup of the RATIONALE-305 study at final analysis



Methods

- Of 997 randomized patients, 748 (tislelizumab with chemotherapy: n=376; placebo with chemotherapy: n=372) were enrolled from Asia, of whom 403 had a PD-L1 score of ≥5% (Figure 1)
- The Asian subgroup comprised patients from China (including Taiwan), Japan, and South Korea
- As of the data cutoff for the final analysis (February 28, 2023), median study follow-up in the Asian subgroup was 14.5 months (range, 0.1-50.1) and minimum study follow-up in this subgroup was 24.6 months

Figure 1. Study Design and Patient Population

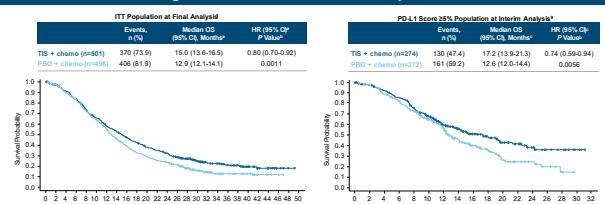


*Tislelizumab 200 mg or placebo (day 1); †Oxaliplatin 100 mg/m²/IV (day 1) and capecitabine 1000 mg/m²/oral (days 1-14 consecutive days from day 1) Q3W (XELOX) or capecitabine 820 mg/m²/day and FP 800 mg/m²/IV (day 1-5) Q3W. ‡Capcitabine as maintenance therapy was optional and only for XELOX-treated patients. §PD-L1 score was determined using the VENTANA PD-L1 SP263 assay by tumor area positivity receptor. ††ITT, intent-to-treat; IV, intravenous; OS, overall survival; PD-L1, programmed death-ligand 1; Q3W, once every 3 weeks; R, randomized; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Results

- Improved OS differences of 2.1 and 4.6 months in favor of tislelizumab plus chemotherapy versus placebo plus chemotherapy were observed in the overall ITT and PD-L1 score ≥5% populations at final and interim analysis, respectively (Figure 2)¹⁰

Figure 2. Overall Survival: Overall Population



*Cox regression model was stratified by regions (east Asia vs rest of the world), PD-L1 expression, and presence of peritoneal metastasis. †p-values are one-sided and based on the stratified log-rank test. *Cox regression model was stratified by regions (east Asia vs rest of the world) and presence of peritoneal metastasis. Chemotherapy, HR, hazard ratio; ITT, intent-to-treat; OS, overall survival; PBO, placebo; PD-L1, programmed death-ligand 1; TIS, tislelizumab.

- Demographics and baseline characteristics of patients in the Asian subgroup were similar to those of the overall ITT population (Table 1)

Table 1. Demographics and Baseline Disease Characteristics

	Asian Subgroup ITT Population	Overall ITT Population
Tislelizumab + Chemotherapy (n=376)	61.0 (23.0-86.0)	60.0 (23.0-86.0)
Placebo + Chemotherapy (n=372)	61.0 (20.5-83.0)	61.0 (25.0-86.0)
Tislelizumab + Chemotherapy (n=501)	346 (69.8)	346 (69.8)
Placebo + Chemotherapy (n=496)	346 (69.8)	346 (69.8)
Age, median (range), years	59.0 (23.0-86.0)	59.0 (23.0-86.0)
Sex, male, n (%)	258 (68.6)	261 (70.2)
ECOG PS, n (%)	0 120 (31.9) 256 (68.1)	102 (27.4) 270 (72.6)
Primary tumor location, n (%)*	Stomach 329 (87.5) GEJ 47 (12.5)	319 (85.8) 52 (14.0)
PDL1-TAP score, n (%)	≥5% 202 (53.7) <5% 174 (46.3)	201 (54.0) 171 (46.0)
Metastatic disease, n (%)	373 (99.2)	369 (99.2)
Peritoneal metastasis, n (%)	165 (43.9)	160 (43.0)
Investigator-chosen, chemo, n (%)	Oxaliplatin/capecitabine 370 (98.4) Capecitabine/5-fluorouracil 6 (1.6)	367 (98.7) 51 (1.3)

Data cutoff: February 28, 2023. *The diagnosis of 1 patient was updated from gastric adenocarcinoma to pancreatic cancer after randomization and the patient remained in the ITT population. Chemotherapy, HR, hazard ratio; ECOG PS, Eastern Cooperative Oncology Group Performance Status; GEJ, gastroesophageal junction; ITT, intent-to-treat; PBO, placebo; PD-L1, programmed death-ligand 1; TAP, tumor area positivity; TIS, tislelizumab.

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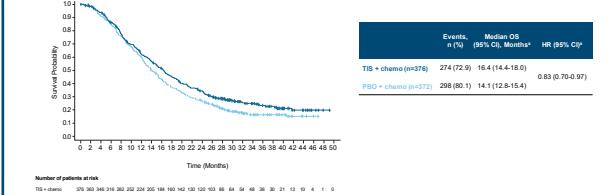
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- An improvement in OS was observed with tislelizumab plus chemotherapy versus placebo plus chemotherapy in the ITT population (Figure 3)

Figure 3. Overall Survival: Asian Subgroup (ITT Population)

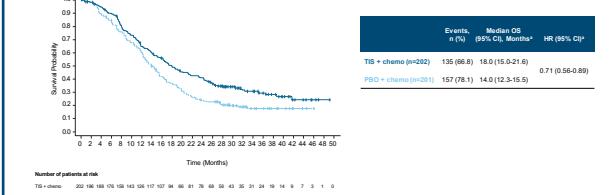


Data cutoff: February 28, 2023.

*HR and 95% CIs were estimated from an unstratified Cox regression model including treatment as a covariate. Chemotherapy, HR, hazard ratio; ITT, intent-to-treat; OS, overall survival; PBO, placebo; TIS, tislelizumab.

- An improvement in OS was also observed with tislelizumab plus chemotherapy versus placebo plus chemotherapy in the PD-L1 score ≥5% population (Figure 4)

Figure 4. Overall Survival: Asian Subgroup (PD-L1 Score ≥5% Population)

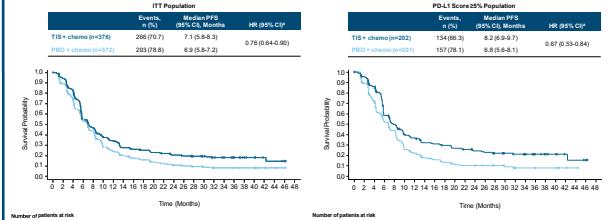


Data cutoff: February 28, 2023.

*HR and 95% CIs were estimated from an unstratified Cox regression model including treatment as a covariate. Chemotherapy, CI, confidence interval; HR, hazard ratio; OS, overall survival; PBO, placebo; PD-L1, programmed death-ligand 1; TIS, tislelizumab.

- Improved PFS was observed with tislelizumab plus chemotherapy versus placebo plus chemotherapy in the ITT and PD-L1 score ≥5% populations (Figure 5)

Figure 5. Progression-Free Survival: Asian Subgroup



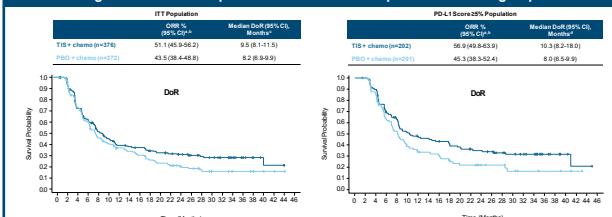
Data cutoff: February 28, 2023.

*HR was calculated on an unstratified Cox regression model.

Chemotherapy, HR, hazard ratio; ITT, intent-to-treat; PFS, progression-free survival; TIS, tislelizumab.

- Tislelizumab plus chemotherapy showed a favorable objective response rate and duration of response compared with placebo plus chemotherapy in the ITT and PD-L1 score ≥5% populations (Figure 6)

Figure 6. Disease Response and Duration of Response: Asian Subgroup



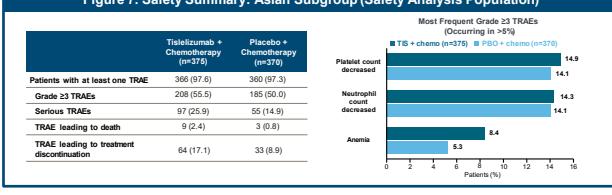
Data cutoff: February 28, 2023.

*HR was calculated using the unstratified Cochran-Mantel-Haenszel method. †ORR was defined as the proportion of patients with a confirmed complete response or partial response. ‡DoR analysis was performed on 191 patients in the TIS + chemo arm and 162 patients in the PBO + chemo arm.

Chemotherapy, DoR, duration of response; PBO, placebo; PD-L1, programmed death-ligand 1; TIS, tislelizumab.

- No new safety signals with tislelizumab plus chemotherapy were identified in the Asian subgroup (Figure 7)

Figure 7. Safety Summary: Asian Subgroup (Safety Analysis Population)



Data cutoff: February 28, 2023. Data are n (%)

Chemotherapy, PBO, placebo; TIS, tislelizumab; TRAE, treatment-related adverse event.

Presenter Disclosures

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