Tislelizumab + Chemotherapy vs Placebo + Chemotherapy as First-Line Treatment in Gastric/Gastroesophageal Junction Adenocarcinoma Patients With/Without Peritoneal or Liver Metastases: A Post Hoc Analysis of RATIONALE-305 Study

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CONCLUSIONS

- This post hoc analysis demonstrated that peritoneal or liver metastases are poor prognostic factors. Notably, an OS improvement was observed with TIS + CT versus PBO + CT in GC/GEJC patients with/without peritoneal or liver metastases
- The pivotal global RATIONALE-305 study reported survival benefits with TIS + CT as 1L treatment for GC/GEJC, irrespective of peritoneal or liver metastases

INTRODUCTION

- Gastric cancer (GC) patients with peritoneal or liver metastases had poor prognosis, and the efficacy of immunotherapy in these patients remains unclear. The global phase 3 RATIONALE-305 study (NCT03777657) demonstrated that tislelizumab (TIS) combined with chemotherapy (CT) could bring survival benefits to first-line (1L) treatment of GC/gastroesophageal junction adenocarcinoma (GEJC) patients[1,2]
- Here, we assessed the efficacy of TIS + CT versus placebo (PBO) + CT in patients with/without peritoneal or liver metastases in RATIONALE-305

METHODS

- In the RATIONALE-305 study, patients with systemic treatment-naïve GC/GEJC were randomly assigned (1:1) to receive either TIS + CT or PBO + CT. Peritoneal metastases was a stratification factor
- In this post hoc analysis, regression analyses were conducted to explore the associations between peritoneal or liver metastases and overall survival (OS). Relative treatment effect between TIS and PBO was assessed in each subgroup. The Kaplan-Meier method was used to estimate the median OS, and hazard ratios (HRs) for OS were estimated using Cox proportional hazards models

RESULTS

Patient Disposition and Regression Analysis

- In RATIONALE-305, among the 997 randomized patients (TIS + CT, n=501; PBO + CT, n=496), 434 (43.5%) had peritoneal metastases (220 in TIS arm; 214 in PBO arm) and 378 (37.9%) had liver metastases (190 in TIS arm; 188 in PBO arm) at baseline
- Regression analyses demonstrated that peritoneal metastasis (HR, 1.54 [95% CI 1.34-1.77]) or liver metastasis (HR, 1.18 [95% CI 1.02-1.36]) were significantly associated with shorter OS

Baseline Characteristics

- The baseline characteristics of the patients in the TIS + CT arm and the PBO + CT arm were balanced within each subgroup of patients with/without peritoneal metastasis and the patients with/without liver metastasis, including PD-L1 expression levels

Overall Survival

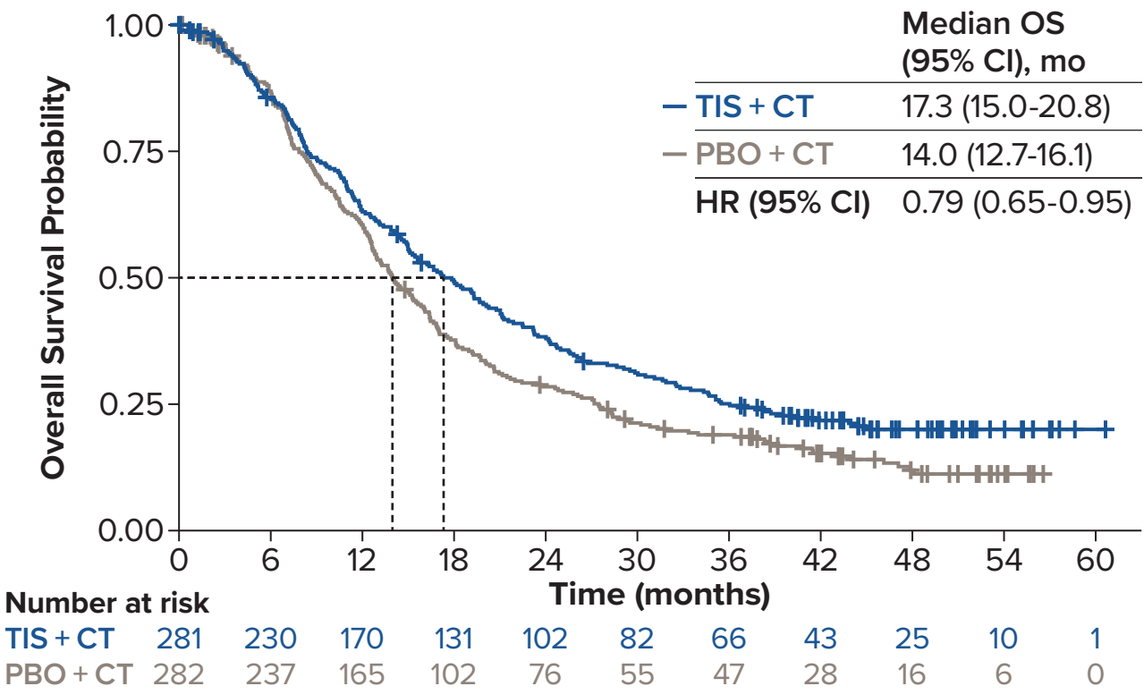
Patients With/Without Peritoneal Metastasis

- The data cut-off date of this analysis was February 28, 2024
- In patients without peritoneal metastasis, OS was longer in the TIS arm compared with the PBO arm (median OS: 17.3 vs 14.0 months; HR, 0.79 [95% CI 0.65-0.95]) (**Figure 1**)
- In patients with peritoneal metastasis, OS was longer in the TIS arm compared with the PBO arm (median OS: 12.3 vs 11.8 months; HR, 0.78 [95% CI 0.64-0.96]) (**Figure 2**)

Patients With/Without Liver Metastasis

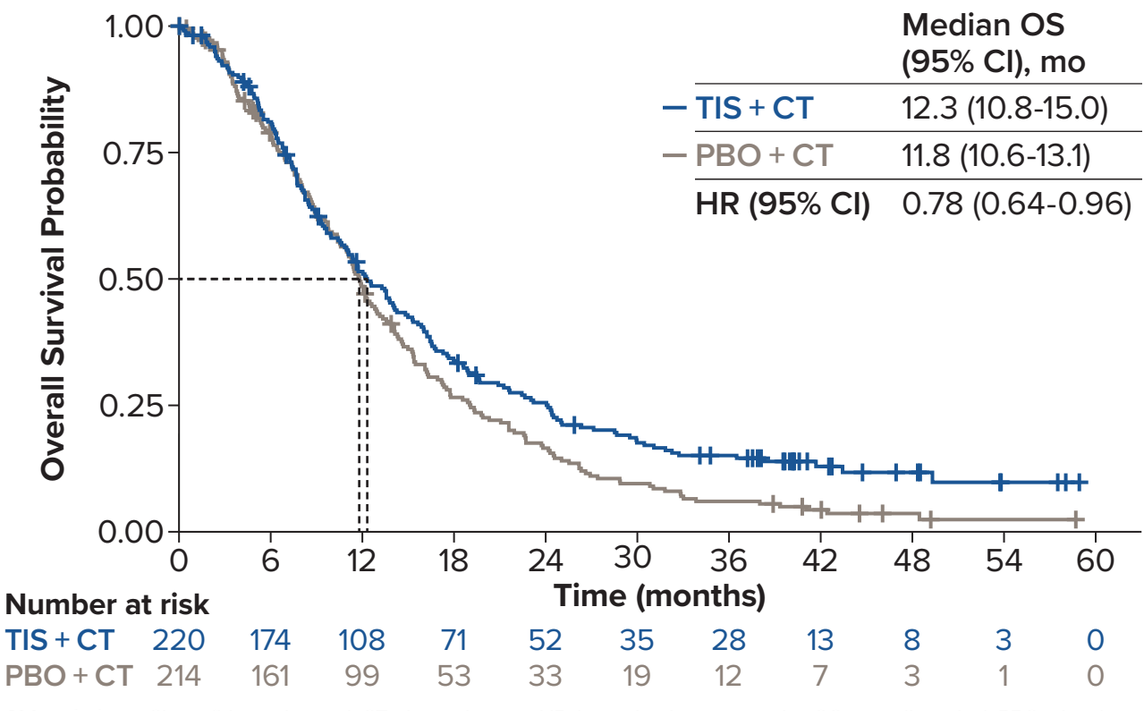
- In patients without liver metastasis, OS was longer in the TIS arm compared with the PBO arm (median OS: 16.0 vs 12.9 months; HR, 0.8 [95% CI 0.67-0.95]) (**Figure 3**)
- In patients with liver metastasis, OS was still longer in the TIS arm compared with the PBO arm (median OS: 13.9 vs 12.9 months; HR, 0.77 [95% CI 0.62-0.96]) (**Figure 4**)

Figure 1. Overall Survival in Patients Without Peritoneal Metastasis



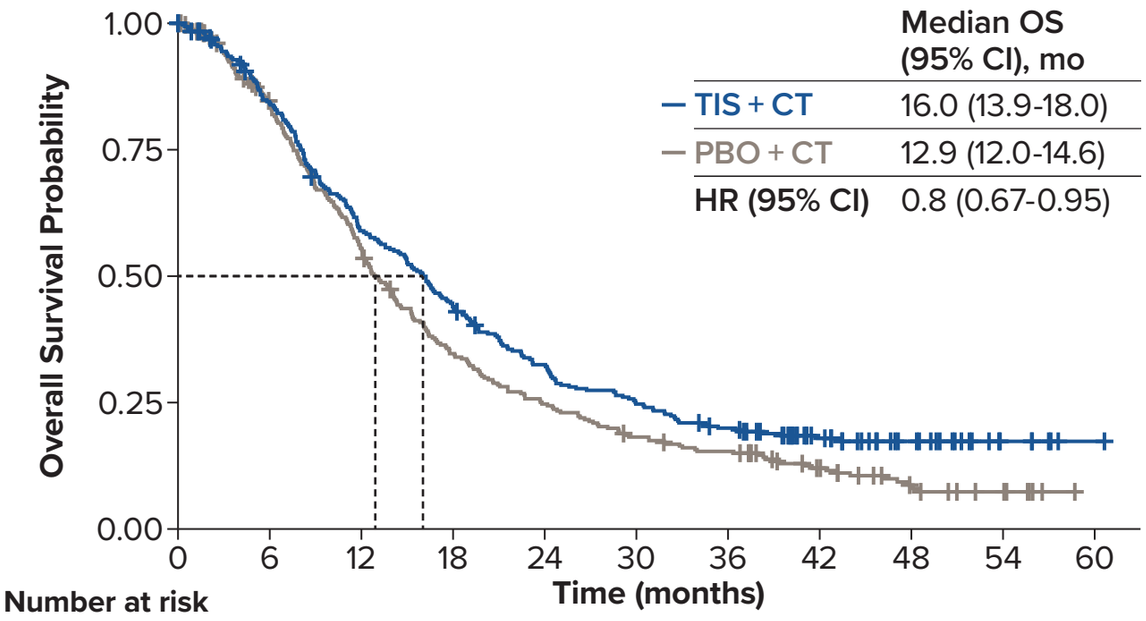
Abbreviations: CI, confidence interval; CT, chemotherapy; HR, hazard ratio; mo, months; OS, overall survival; PBO, placebo; TIS, tislelizumab.

Figure 2. Overall Survival in Patients With Peritoneal Metastasis



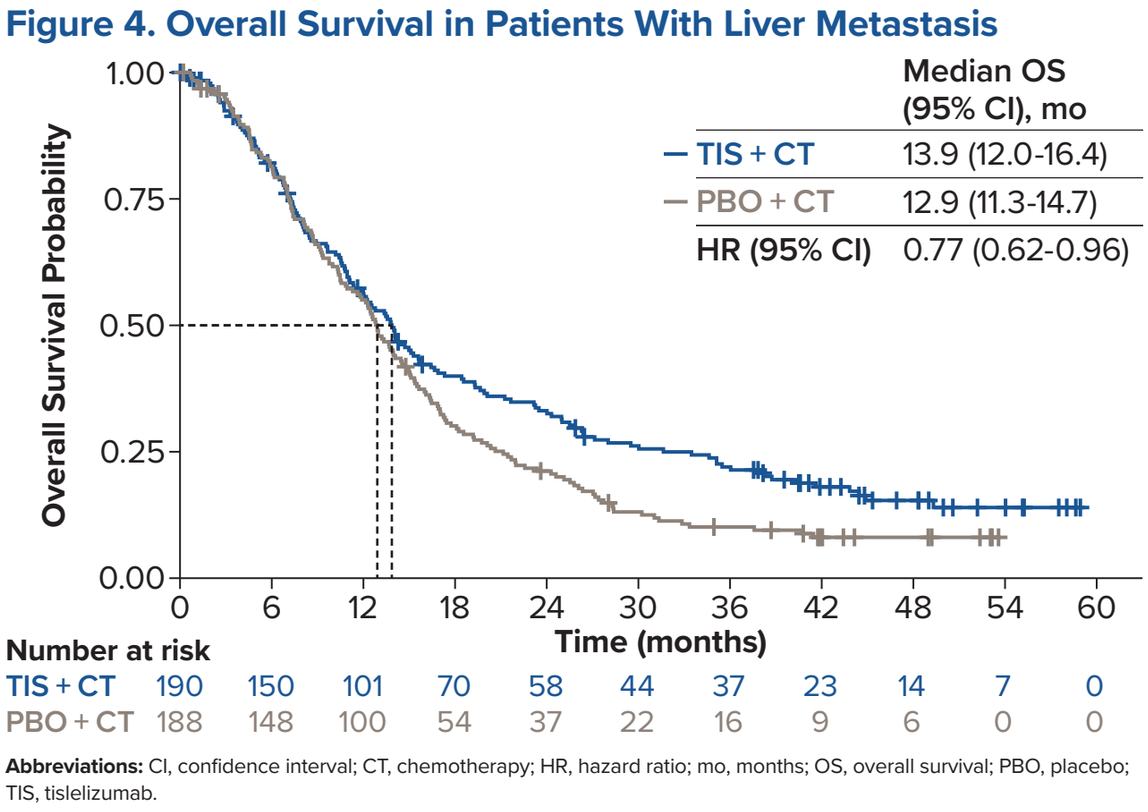
Abbreviations: CI, confidence interval; CT, chemotherapy; HR, hazard ratio; mo, months; OS, overall survival; PBO, placebo; TIS, tislelizumab.

Figure 3. Overall Survival in Patients Without Liver Metastasis



Abbreviations: CI, confidence interval; CT, chemotherapy; HR, hazard ratio; mo, months; OS, overall survival; PBO, placebo; TIS, tislelizumab.

Figure 4. Overall Survival in Patients With Liver Metastasis



Abbreviations: CI, confidence interval; CT, chemotherapy; HR, hazard ratio; mo, months; OS, overall survival; PBO, placebo; TIS, tislelizumab.

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DISCLOSURES

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