Tislelizumab (TIS) + chemotherapy (chemo) vs placebo (PBO) + chemo as first-line (1L) treatment in gastric/gastroesophageal junction adenocarcinoma (GC/GEJC) 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 + chemo vs. PBO + chemo in GC/GEJC patients with/without peritoneal or liver metastases. The global pivotal study RATIONALE-305 reported survival benefits with TIS + chemo as 1L treatment for GC/GEJC, irrespective of peritoneal or liver metastases.

Background

- Gastric cancer 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 combined with chemotherapy could bring survival benefits to 1L treatment of GC/GEJC patients [1,2].
- Here, we assessed the efficacy of TIS + chemo versus PBO + chemo in patients with/without peritoneal or liver metastases in RATIONALE-305.

Methods

- In RATOINALE-305 study, patients with systemic treatment-naïve GC/GEJC were randomly assigned (1:1) to receive either TIS + chemo or PBO + chemo. Peritoneal metastases is 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 tislelizumab and placebo 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 + chemo, n=501; PBO + chemo, 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 + chemo arm and the PBO + chemo 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 Feb 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 OS in patients without peritoneal metastasis

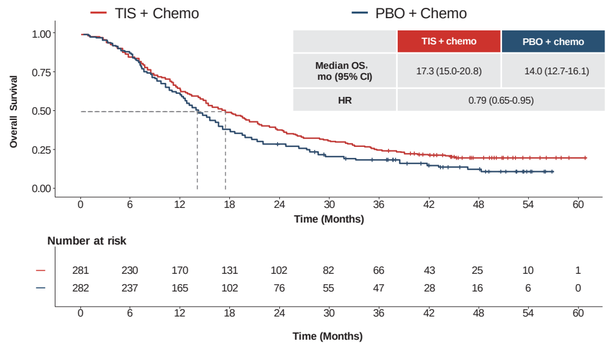


Figure 2 OS in patients with peritoneal metastasis

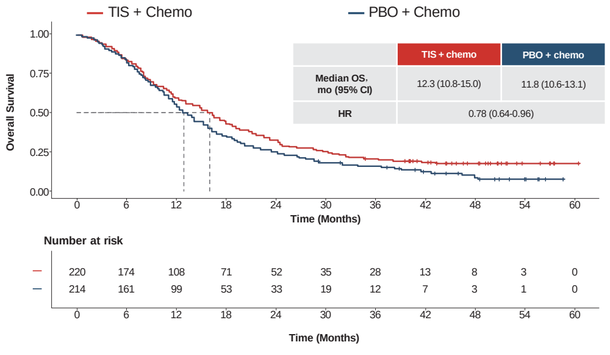


Figure 3 OS in patients without liver metastasis

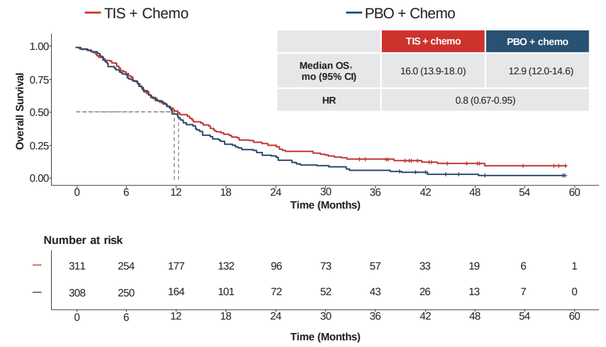
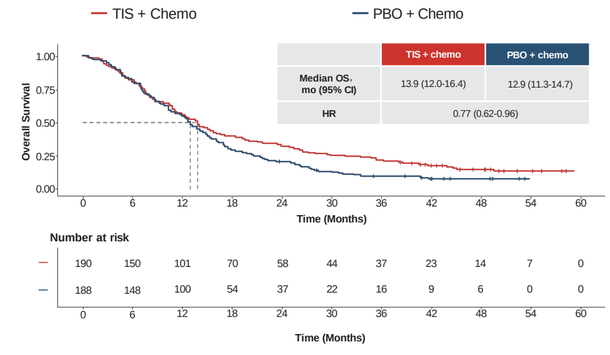


Figure 4 OS in patients with liver metastasis



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