

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

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ABSTRACT

Introduction: Gastric cancer patients with peritoneal or liver metastases have poor prognosis, and the efficacy of immunotherapy in these patients remains unclear. The global phase 3 RATIONALE-305 trial (NCT03777657) demonstrated that tislelizumab (TIS) combined with chemotherapy (chemo) could bring survival benefits to first-line (1L) treatment of patients with gastric/gastroesophageal junction adenocarcinoma (GC/GEJC).

Aim: Here, we assessed the efficacy of TIS+chemo vs placebo (PBO)+chemo in patients with/without peritoneal or liver metastases in RATIONALE-305.

Methods: Patients with systemic treatment-naïve GC/GEJC were randomized (1:1) to receive either TIS+chemo or PBO+chemo. Regression analyses were conducted to explore the associations between peritoneal or liver metastases and 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: 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 showed peritoneal and liver metastases were significantly associated with shorter OS. Baseline characteristics were balanced between TIS and chemo arms within each subgroup, including PD-L1 expression levels. As of data cut-off on Feb 28, 2024, OS was longer in the TIS arm compared with the PBO arm in patients with peritoneal metastases (HR= 0.78, 95% CI 0.64-0.96) or without (HR = 0.79, 95% CI 0.65-0.95). OS improvement was also observed in patients with liver metastases (HR = 0.77, 95% CI 0.62-0.96) or without (HR = 0.80, 95% CI 0.67-0.95).

Conclusions: This post hoc analysis demonstrated OS improvement with TIS+chemo vs PBO+chemo in GC/GEJC patients with/without peritoneal or liver metastases. To our knowledge, RATIONALE-305 is the first global pivotal study reporting survival benefits with TIS+chemo as 1L treatment for GC/GEJC, irrespective of peritoneal or liver metastases.