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.

Authors: Miaozhen Qiu[1], Huiyan Luo[2], Feng-Hua Wang[3], Feng Wang[4], Ming-Ming He[5], Sheng Xu[6], Xiaoxi Pan[7], Rui-Hua Xu[8]

Affiliations: [1]Department of Medical Oncology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University, Guangzhou, China; [2]Sun Yat-sen University Cancer Center, Sun Yat-sen University, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Guangzhou, China; [3]Department of Medical Oncology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Guangzhou, China; [4]Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Guangzhou, China; [5]BeiGene (Shanghai) Co., Ltd., Shanghai, China; [6]BeiGene USA, Inc., Shanghai, China; [7]BeiGene (Beijing) Co., Ltd., Beijing, China; [8]Department of Medical Oncology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Sun Yat-sen University, Guangzhou, China.

ABSTRACT

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 che- motherapy could bring survival benefits to 1L treatment of GC/GEJC patients. Here, we assessed the efficacy of TIS + chemo vs PBO + chemo in patients with/without peritoneal or liver metastases in RATIONALE-305.

Methods: Patients with systemic treatment-na¨ıve GC/GEJC were randomly assigned (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 demon- strated 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.

	With metastases		Without metastases	
	TIS arm	PBO arm	TIS arm	PBO arm
Peritoneum	n=220	n=214	n=281	n=282
Median OS, mo (95% CI)	12.3 (10.6-14.3)	11.8 (10.6-13.0)	17.3 (15.0-20.3)	14.0 (12.6-16.0)
HR (95% CI)	0.78 (0.64-0.96)		0.79 (0.65-0.95)	
Liver	n=190	n=188	n=311	n=308
Median OS, mo (95% CI)	13.9 (11.4-15.6)	12.9 (10.9-14.5)	16.0 (13.6-18.0)	12.9 (11.9-14.4)
HR (95% CI)	0.77 (0.62-0.96)		0.80 (0.67-0.95)	