

Recurrent patient-reported outcome (PRO)-based deterioration predicts overall survival (OS) in patients with advanced gastric adenocarcinoma with PD-L1 score of $\geq 5\%$: Results from the RATIONALE-305 trial

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Background: The RATIONALE-305 trial (NCT03777657) demonstrated that adding tislelizumab to chemotherapy (T+C) improved OS compared to placebo plus chemotherapy (P+C) in all patients with gastric cancer (GC), including those with PD-L1 score of $\geq 5\%$. PROs as secondary endpoints indicated better HRQoL in the T+C arm. Here, we developed a joint model framework to evaluate if PRO data provide prognostic insights into OS in patients with PD-L1 expression $\geq 5\%$.

Methods: Longitudinal PRO data from 238 T+C and 237 P+C patients in the PD-L1 $\geq 5\%$ subgroup were analyzed. A linear mixed model (LMM) assessed adjusted change from baseline in PRO scores for T+C. Associations between longitudinal PRO changes and risk of future recurrent PRO-based symptomatic deterioration (RS-D) events were assessed using a recurrent event Cox model. A terminal event Cox model estimated the treatment effect on the risk of death.

Results: In the LMM, significant T+C improvement was observed for QLQ-C30 GHS/QoL ($P=0.0055$), STO22 upper GI symptoms ($P=0.0119$), and dietary restrictions ($P=0.0195$) compared to P+C. In the recurrent event Cox model, significant RS-D longitudinal associations were observed for all symptomatic domains except GHS/QoL, with hazard ratios (HRs) ranging from 1.01 to 1.06, indicating a 1.2%-5.8% increased risk of future RS-D events per 1-point worsening in PRO scores. In the terminal event Cox model, T+C significantly reduced risk of death in all PRO domains compared to P+C (HRs: 0.647-0.731), reflecting a 27%-35% lower likelihood of death.

Conclusions: Compared to P+C, T+C was associated with significant improvements in GHS/QoL, upper GI symptoms, and dietary restrictions, while also showing a significant reduction in risk of death. These findings reinforce the prognostic value of PRO data for OS in patients with GC with PD-L1 score of $\geq 5\%$, highlighting their role in optimizing patient-centered treatment strategies.

Disclosure Statement: The authors declare that there are conflicts of interest.