Quality-Adjusted Survival Comparison for Tislelizumab (TIS) + Chemotherapy (CT) Versus Placebo (PBO) + CT as First-Line (1L) Treatment in Gastric/Gastroesophageal Junction Adenocarcinoma (GC/GEJC) Patients With Peritoneal Metastasis (PM): Long-Term Follow-Up From RATIONALE-305

BACKGROUND:
There is an unmet need for better treatment among patients (pts) with PM. A post hoc analysis of the phase 3 RATIONALE-305 (NCT03777657) trial showed that TIS + CT as 1L treatment for GC/GEJC pts with PM improved survival compared to PBO + CT (Qiu et al, 2025). The current study evaluated whether this survival benefit translated into quality of life (QoL) adjusted survival gains.

METHODS:
This post hoc analysis used long-term follow-up data from the RATIONALE-305 trial (minimum follow-up 3 years; data cutoff February 28, 2024). The analysis focused on the intent-to-treat (ITT) population and subgroups defined by programmed death ligand-1 (PD-L1) ≥1% as well as ≥5% by Tumor Area Positivity (TAP) score. The well-established Quality-adjusted Time Without Symptoms or Toxicity (Q-TWiST) methodology was used. QoL adjusted survival was calculated as the average time spent in three distinct health states during the trial follow-up: survival time with grade 3/4 toxicity, survival without progression/toxicity, and survival post progression, each weighted by QoL utility parameters specific to that state. A sensitivity analysis (SA) using trial-derived, treatment-specific EQ-5D utility values was also conducted. QoL adjusted relative survival gains ≥15% were considered "clearly clinically important," in line with commonly accepted Q-TWiST benchmarks (DOI 10.1007/s11136-005-1579-7).

RESULTS:
At the maximum follow-up of 57 months in all randomized pts in RATIONALE-305, TIS + CT (n=501) pts experienced greater mean QoL adjusted survival than PBO + CT (n=496) (16.3 vs 13.1 months). Among pts with PM, TIS + CT (n=220) showed higher mean QoL adjusted overall survival than PBO + CT (n=214) (13.4 vs 10.8 months; 17.7% relative Q-TWiST gain) that was clearly clinically important. QoL adjusted survival benefit was also clearly clinically important in TIS + CT pts with PM with PD-L1 TAP score ≥1% (16.8% gain) and PD-L1 score ≥5% (33.0% gain) compared with PBO + CT. SA results further favored TIS + CT (Table).

CONCLUSIONS:
Treatment with TIS + CT resulted in clinically meaningful improvement in long-term quality-adjusted survival for GC/GEJC pts with PM versus those receiving CT alone.

Table. TIS + CT vs PBO + CT Treatment Difference

	Mean Q-TWiST, months (95% CI)	Relative Q-TWiST Gain
Pts with PM[a]		
ITT pts (n=434)	2.6 (0.1 to 5.0), *P*=0.04	17.7%
PD-L1 TAP ≥1% (n=386)	2.5 (0.1 to 5.1), *P*<0.05	16.8%
PD-L1 TAP ≥5% (n=217)	4.7 (1.1 to 8.6), *P*=0.02	33.0%
Pts with PM (SA using EQ-5D scores)[b]		
ITT pts (n=434)	3.1 (0.8 to 5.5), *P*<0.01	21.3%
PD-L1 TAP ≥1% (n=386)	3.1 (0.5 to 5.6), *P*=0.02	20.8%
PD-L1 TAP ≥5% (n=217)	4.8 (1.3 to 8.2), *P*<0.01	33.9%

[a] Using standardized base case Q-TWiST utility weights.
[b] Using US mapping algorithm weights.

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