

**Tislelizumab (TIS) + chemotherapy (CT) vs placebo (PBO) + CT in HER2-negative advanced or metastatic gastric or gastroesophageal junction adenocarcinoma (GC/GEJC): RATIONALE-305 study minimum 3-year survival follow-up**

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**Background:** TIS (an anti-programmed cell death protein 1 antibody) plus CT demonstrated significant overall survival (OS) benefit vs PBO+CT as first-line (1L) therapy for advanced GC/GEJC in all randomized patients (pts; hazard ratio [HR], 0.80) and pts with PD-L1 Tumor Area Positivity (TAP) score  $\geq 5\%$  (HR, 0.71) in the phase 3 RATIONALE-305 study (NCT03777657). Two-yr OS rates for TIS+CT vs PBO+CT were 32.7% vs 23.4%, respectively. We report on efficiency and safety/tolerability after a minimum 3-yr follow-up.

**Methods:** Adults with locally advanced, nonresectable or metastatic, HER2-negative, untreated GC/GEJC were randomized (1:1) to intravenous TIS 200 mg or PBO every 3 wks plus investigator-chosen CT (oxaliplatin+capecitabine or cisplatin+5-fluorouracil). TAP score was evaluated in tumor tissue using the VENTANA PD-L1 (SP263) assay. The primary endpoint was OS in all randomized pts and pts with PD-L1 TAP  $\geq 5\%$ . Secondary endpoints included investigator-assessed progression-free survival (PFS), objective response rate (ORR), duration of response (DoR), and safety.

**Results:** A total of 997 pts were randomized (TIS+CT, n=501; PBO+CT, n=496). At the 3-yr follow-up (minimum: 36.6 mos), the median OS was 15.0 mos (95% CI: 13.6, 16.5) for the TIS+CT arm, compared to 12.9 mos (95% CI: 12.1, 14.1) for the PBO+CT arm (HR, 0.79; 95% CI: 0.69, 0.90). The median PFS was 6.9 mos (95% CI: 5.7, 7.2) in the TIS+CT group and 6.2 mos (95% CI: 5.6, 6.9) in the PBO+CT group (HR, 0.79; 95% CI: 0.68, 0.91). The ORR was 47.3% (95% CI: 42.9, 51.8) in the TIS+CT group and 40.5% (36.2, 45.0) in the PBO+CT arm. DoR Improvement in TIS+CT vs PBO+CT was maintained. Grade  $\geq 3$  treatment-related adverse events were similar in both arms.

**Conclusions:** After a minimum 3-yr follow-up, TIS+CT as 1L treatment for GC/GEJC continued to demonstrate clinically meaningful improvements in OS, PFS, and DoR compared with PBO+CT, with no new safety signals. These long-term data further support TIS+CT as a new 1L treatment option for advanced HER2-negative GC/GEJC

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