Tislelizumab + chemotherapy (CT) vs placebo + CT as first-line treatment for locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma: RATIONALE-305 European/North American patient subgroup

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ABSTRACT

Background: Tislelizumab (TIS), an anti-programmed cell death protein-1 monoclonal antibody, plus CT, demonstrated significant overall survival (OS) benefit vs placebo (PBO) + CT as first-line therapy in patients (pts) with advanced gastric or gastroesophageal junction adenocarcinoma (GC/GEJC) in the randomized, double-blind, global, phase 3 RATIONALE-305 study (NCT03777657). Here we present results from the European/North American (Eu/NA) pts subgroup analysis.

Material (patients) and methods: Adults with previously untreated, HER2-negative, locally advanced unresectable, or metastatic GC/GEJC, regardless of programmed death-ligand 1 (PD-L1) expression status were enrolled. Eligible pts were randomized (1:1) to receive TIS 200 mg or PBO intravenously once every 3 weeks plus CT (5-fluorouracil + cisplatin or capecitabine + oxaliplatin). The primary endpoint was OS in the PD-L1+ (tumor area positivity score ≥5%) and intent-to-treat (ITT) analysis sets. Secondary endpoints included progression-free survival (PFS), objective response rate (ORR), duration of response (DoR), and safety.

Results: Of 997 pts enrolled, 249 (25.0%) were from Eu/NA (TIS+CT, n=125; PBO+CT, n=124). After a minimum follow-up of 26.6 months (mo), TIS+CT resulted in OS improvements vs PBO+CT in the PD-L1+ (hazard ratio [HR]=0.75, [95% CI, 0.52-1.07]; 24 mo rate 27.6% vs 12.5%) and ITT analysis sets (HR=0.71, [95% CI, 0.54-0.94]; 24 mo rate 27.6% vs 13.6%). TIS+CT resulted in favorable PFS vs PBO+CT (HR=0.84, 95% CI, 0.63-1.11), numerically higher ORR (36.0% vs 31.5%), and longer DoR (median 7.5 mo [95% CI, 4.4-12.0] vs 5.0 mo [95% CI, 3.9-6.7]). Sixty (48.8%) pts in the TIS+CT arm and 61 (49.2%) pts in the PBO+CT arm experienced grade ≥3 treatment-related adverse events (TRAEs). Sixteen (13.0%) and seven (5.6%) pts discontinued treatment due to TRAEs in the TIS+CT and PBO+CT arms, respectively. Deaths due to TRAEs occurred in two (1.6%) pts in the TIS+CT arm and one (0.8%) pt in the PBO+CT arm.

Conclusions: TIS+CT showed OS benefit vs PBO+CT and a manageable safety profile in pts in the Eu/NA subgroup with previously untreated, HER2-negative, locally advanced unresectable, or metastatic GC/GEJC. These findings are consistent with the published results in the overall study population.