Tislelizumab Plus Chemotherapy (Chemo) Versus Placebo Plus Chemo 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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Background:

Tislelizumab (TIS), an anti-programmed cell death protein 1 monoclonal antibody, plus chemo, demonstrated significant overall survival (OS) benefit vs placebo (PBO) plus chemo (15.0 vs 12.9 months [mo], hazard ratio [HR]=0.80, 95% confidence interval [CI]: 0.70, 0.92, *P*=0.0011) 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.

Methods:

This double-blind, global, phase 3 study evaluated adult pts with previously untreated, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced unresectable, or metastatic GC/GEJC, regardless of programmed death-ligand 1 (PD-L1) expression status. Eligible pts were randomized (1:1) to receive TIS 200 mg or PBO intravenously once every 3 weeks plus investigator chosen chemo (5-fluorouracil + cisplatin or capecitabine + oxaliplatin). The primary endpoint was OS in the PD-L1+ (patients with 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 plus chemo arm, n=125; PBO plus chemo arm, n=124). In the Eu/NA pts subgroup, after a minimum follow-up of 26.6 mo at final analysis, TIS plus chemo resulted in OS improvements vs PBO plus chemo in the PD-L1+ (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 plus chemo resulted in favorable PFS vs PBO plus chemo (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 plus chemo arm and 61 (49.2%) pts in the PBO plus chemo arm experienced grade ≥3 treatment-related treatment-emergent adverse events (TRAEs). Sixteen (13.0%) and seven (5.6%) pts discontinued treatment due to TRAEs in the TIS plus chemo and PBO plus chemo arms, respectively. Deaths due to TRAEs occurred in two (1.6%) pts in the TIS plus chemo arm and one (0.8%) pt in the PBO plus chemo arm.

Conclusions:

TIS plus chemo showed OS benefit compared with PBO plus chemo 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.