Randomized, global, phase 3 study of tislelizumab plus chemotherapy versus chemotherapy as first-line treatment for advanced or metastatic esophageal squamous cell carcinoma (RATIONALE-306): China subgroup analysis

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Abstract:

Background: Tislelizumab, an anti-programmed cell death protein 1 (PD-1) antibody, + chemotherapy (chemo) demonstrated a statistically significant and clinically meaningful improvement in overall survival (OS) vs placebo + chemo, with a manageable safety profile, as a first line (1L) treatment for patients (pts) with advanced or metastatic esophageal squamous cell carcinoma (ESCC) at interim analysis of the phase 3 RATIONALE-306 study. We report data from the China subgroup analysis.

Methods: In this randomized, double-blind, global study, adults with unresectable locally advanced or metastatic ESCC, with no prior systemic treatment for advanced disease were enrolled regardless of programmed death-ligand 1 (PD-L1) expression status. Pts were randomized (1:1); stratified by region, prior definitive therapy, and investigator-chosen chemo (platinum + fluoropyrimidine or platinum + paclitaxel). Pts received tislelizumab (T) 200 mg intravenously + chemo (C) (Arm T+C) or placebo (P) + chemo (Arm P+C) once every three weeks; treatment continued until disease progression by investigator per RECIST v1.1, intolerable toxicity, or withdrawal. The primary endpoint was OS in the intent-to-treat (ITT) population. Secondary endpoints included investigator-assessed

progression-free survival (PFS) per RECIST v1.1, objective response rate (ORR), and duration of response (DoR), in addition to safety.

Results: Of 649 pts in the overall population, 370 (57.0%) were enrolled from China. At data cutoff (Feb 28, 2022), the median study follow-up in the China subgroup (ITT population) was 15.8 months (mo) in Arm T+C (n=182) and 10.6 mo in Arm P+C (n=188). Longer OS (median OS 16.6 mo vs 11.2 mo; unstratified hazard ratio [HR] 0.69, 95% confidence interval [CI] 0.54, 0.89) and PFS (median PFS 8.3 mo vs 5.6 mo; unstratified HR 0.58, 95% CI 0.45, 0.75) indicate survival benefit in Arm T+C vs P+C, respectively. Arm T+C had higher response rates and more durable responses than Arm P+C; ORR was 64.8% vs 44.1% (odds ratio 2.33 [95% CI 1.53, 3.55]) respectively, and median DoR was 7.4 mo (95% CI 5.6, 9.5) vs 5.7 mo (95% CI 4.3, 7.5), respectively. Similar proportions of pts in Arm T+C vs P+C had ≥1 treatment-related adverse event (TRAE; 98.8% vs 98.9%) and ≥grade 3 TRAEs (72.9% vs 73.4%). Serious TRAEs occurred in 27.6% vs 21.2% of pts in Arm T+C vs P+C, and TRAEs leading to death occurred in 2.9% vs 1.6% of pts, respectively. Treatment-emergent adverse events leading to discontinuation occurred in 28.2% vs 17.4%, in Arm T+C vs P+C.

Conclusions: In the China subgroup, 1L tislelizumab + chemo demonstrated clinically meaningful improvement in OS, PFS, ORR, and DoR vs placebo + chemo in pts with advanced or metastatic ESCC, with a manageable safety profile, consistent with published results in the overall population.