Randomized, global, phase 3 study of tislelizumab (TIS) + chemotherapy (chemo) versus placebo (PBO) + chemo as first-line (1L) treatment for advanced or metastatic oesophageal squamous cell carcinoma (ESCC) (RATIONALE-306): non-Asia subgroup.

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Background: TIS, an anti-programmed cell death protein 1 (PD-1) antibody, + chemo as 1L therapy demonstrated statistically significant and clinically meaningful improvement in overall survival (OS) vs PBO + chemo in patients with advanced or metastatic ESCC (hazard ratio [HR] 0.66 [95% confidence interval (CI) 0.54, 0.80]; *P*<0.0001), with a manageable safety profile, at interim analysis of the phase 3, double-blind RATIONALE-306 study (NCT03783442). Here, we report data from the non-Asia subgroup (Europe, Northern America, and Oceania).

Methods: Adults with advanced or metastatic ESCC, with no prior systemic treatment for advanced disease were randomized 1:1, (stratified by region, prior definitive therapy, and investigator [INV]-chosen chemo) to receive TIS 200 mg intravenously (IV) once every 3 weeks (Q3W) (Arm A) or PBO IV Q3W (Arm B), with platinum + fluoropyrimidine, or platinum + paclitaxel until disease progression by INV per RECIST v1.1, intolerable toxicity, or withdrawal. The primary endpoint was OS in the intent-to-treat population. Secondary endpoints included: progression-free survival (PFS), objective response rate (ORR), and duration of response (DoR) by INV per RECIST v1.1; OS in the programmed death-ligand 1 score ≥10%; and safety.

Results: Of 649 randomized patients, 163 (25.1%) were from the non-Asia subgroup (Arm A, n=83; Arm B, n=80). At data cutoff (Feb 28, 2022), the median study follow-up time in the non-Asia subgroup was 16.0 months (mo) in Arm A vs 8.4 mo in Arm B. OS (median 16.3 vs 9.0 mo; unstratified HR 0.66 [95% CI 0.45, 0.96]) and PFS (median 7.7 vs 5.5 mo; unstratified HR 0.59 [95% CI 0.41, 0.83]) were improved in Arm A vs Arm B, respectively. Arm A had higher ORR (61.4% vs 41.3%, odds ratio 2.27 [95% CI 1.21, 4.25]) and longer median DoR (7.1 mo [95% CI 5.6, 9.6] vs 5.7 mo [95% CI 3.8, 8.3]) than Arm B. More patients in Arm A vs Arm B experienced ≥1 treatment-related adverse event (TRAE; 94.0% vs 88.5%), serious TRAEs (25.3% vs 17.9%), and discontinuation due to treatment-emergent AEs (42.2% vs 35.9%, respectively). Similar proportions of patients in Arm A vs Arm B had ≥grade 3 TRAEs (56.6% vs 52.6%), and TRAEs leading to death (1.2% vs 1.3%), respectively.

Conclusions: In the non-Asia subgroup, 1L TIS + chemo showed a clinically meaningful improvement in OS vs PBO + chemo in patients with advanced or metastatic ESCC, with a manageable safety profile, consistent with published results in the overall population.