Randomized, global, Phase 3 study of tislelizumab (TIS) + chemotherapy (chemo) vs chemo as first-line (1L) therapy for advanced or metastatic esophageal squamous cell carcinoma (ESCC) (RATIONALE-306): Asia subgroup

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Background: TIS, an anti-PD-1 antibody, + chemo as 1L therapy demonstrated statistically significant and clinically meaningful improvement in overall survival (OS) vs placebo (PBO) + chemo in patients (pts) with advanced or metastatic ESCC, with a manageable safety profile, at interim analysis of the Phase 3 RATIONALE-306 study. We report data from the Asia subgroup.

Methods: Adults with unresectable locally advanced or metastatic ESCC, with no prior systemic treatment for advanced disease were enrolled and randomized (1:1; stratified by region, prior definitive therapy, and investigator [INV]-chosen chemo) to receive TIS 200 mg (Arm A) or PBO (Arm B) IV Q3W, 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 (ITT) population. Secondary endpoints included: progression-free survival (PFS), objective response rate (ORR), and duration of response (DoR) per INV; and safety.

Results: Of 649 randomized pts, 486 (74.9%) were from Asia (243 pts per arm). At data cutoff (Feb 28, 2022), the median (m) follow-up in the Asia subgroup was 16.5 months (mo) in Arm A vs 10.6 mo in Arm B. OS (mOS 18.3 vs 11.5 mo; unstratified HR 0.67 [95% CI 0.54, 0.84]) and PFS (mPFS 7.2 vs 5.6 mo; unstratified HR 0.62 [95% CI 0.50, 0.76]) were improved in Arm A vs B, respectively. Arm A had higher ORR (64.2% vs 42.8%, odds ratio 2.40 [95% CI 1.66, 3.45]) and longer mDoR (7.1 mo [95% CI 5.6, 8.4] vs 5.6 mo [95% CI 4.4, 7.1]) than Arm B. Similar proportions of pts in Arm A vs B had ≥1 treatment-related AEs (TRAEs; 97.5% vs 98.8%), ≥Grade 3 TRAEs (70.1% vs 68.3%), and TRAEs leading to death (2.1% vs 1.2%), respectively. Serious TRAEs occurred in 29.9% vs 19.8% of pts, and discontinuation due to treatment-emergent AEs occurred in 28.2% vs 18.1%, in Arm A vs B, respectively.

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