RANDOMIZED, PHASE 3 STUDY OF SECOND-LINE TISLELIZUMAB VS CHEMOTHERAPY IN ADVANCED OR METASTATIC ESOPHAGEAL SQUAMOUS CELL CARCINOMA (ESCC, RATIONALE 302) IN THE OVERALL POPULATION AND EUROPE/NORTH AMERICA SUBGROUP

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ABSTRACT

Background: The global Phase 3 study RATIONALE 302 (NCT03430843) evaluated efficacy and safety of second-line (2L) tislelizumab (tis), an anti-PD-1 antibody, in patients (pts) with advanced or metastatic ESCC. Here, data are reported from the overall and Europe/North America (EU/NA) populations.

Methods: Eligible adults had disease progression during or after first-line systemic therapy, ≥1 evaluable lesion per RECIST v1.1 and Eastern Cooperative Oncology Group performance score (ECOG PS) of ≤1. Pts were randomized 1:1 to receive tis 200 mg intravenously every 3 weeks or investigator-chosen chemotherapy (ICC; paclitaxel, docetaxel, or irinotecan) and treated until disease progression, intolerable toxicity, or withdrawal. Stratification factors included ICC option, region, and ECOG PS. The primary endpoint was overall survival (OS) in all patients (ITT population). The key secondary endpoint was OS in programmed death ligand 1 positive (PD-L1+; vCPS ≥10%) pts; other secondary endpoints were progression-free survival, overall response rate (ORR), duration of response (DoR), health-related quality of life and safety.

Results: Overall, 512 pts received tis (n=256) or ICC (n=256); 108 (21%) were in the EU/NA subgroup (n=55 tis, n=53 ICC). On 1Dec2020 (data cut-off), median follow-up was 6.9 and 6.8 mo in the overall population and EU/NA subgroup, respectively. Tis improved OS vs ICC in the overall population (median OS 8.6 vs 6.3 mo; HR 0.70, 95% CI 0.57–0.85; *P*=.0001) and in EU/NA pts (median OS 11.2 vs 6.3 mo; HR 0.55; 95% CI 0.35–0.87). Tis was associated with improved ORR (20.3% [95% CI 15.6%–25.8%] vs 9.8% [95% CI 6.4%–14.1%]) and median DoR (7.1 vs 4.0 mo; HR 0.42, 95% CI 0.23–0.75) vs ICC in the overall population and in EU/NA pts (ORR: 20.0% [95% CI 10.4%–33.0%] vs 11.3% [95% CI 4.3%–23.0%]; median DOR: 5.1 vs 2.1 mo; HR 0.42, 95% CI 0.13–1.39). Grade ≥3 treatment-emergent adverse events (TEAEs) in tis vs ICC arms occurred in 46% vs 68% pts (overall) and 56% vs 71% pts (EU/NA). Fewer Grade ≥3 AEs were treatment-related with tis vs ICC (overall: 19% vs 56%; EU/NA: 13% vs 51%). AEs leading to death were similar in the tis vs ICC arms (overall: 14% vs 12%; EU/NA: 6% vs 5%).

Conclusions: 2L tis showed statistically significant and clinically meaningful OS improvement and a favorable safety profile vs ICC in pts with advanced or metastatic ESCC. Efficacy and safety results from the EU/NA subgroup were consistent with those observed in the overall population.