Tislelizumab + chemotherapy (CT) vs placebo + CT in patients with locally advanced esophageal squamous cell carcinoma: RATIONALE-306 subgroup analysis

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ABSTRACT

Introduction: In RATIONALE-306 (NCT03783442), participants (pts) with metastatic/locally advanced (LA) esophageal squamous cell carcinoma (ESCC) were randomized to IV tislelizumab (TIS) 200 mg or placebo (PBO) every 3 weeks plus investigator-chosen chemotherapy (CT; platinum+fluoropyrimidine/paclitaxel) until disease progression, unacceptable toxicity, death, or withdrawal of consent, whichever occurred first. There was improvement in overall survival (OS) in the intent-to-treat (ITT) population (primary endpoint) and a subgroup of pts with PD-L1 Tumor Area Positivity (TAP) score ≥10% (secondary endpoint). At the 3-yr follow-up, improvement was sustained in TIS+CT (HR, 0.70; 95% CI: 0.59, 0.83) vs PBO +CT in the ITT population.

Aim: We report a post hoc analysis of RATIONALE-306 in pts with LA ESCC.

Methods: Pts with LA ESCC, with non-metastatic disease and deemed unfit for surgery or definitive chemoradiation, were retrospectively selected and included in this analysis. Efficacy outcomes (OS, progression-free survival [PFS], objective response rate [ORR]) and safety were analyzed.

Results: At data cutoff (August 22, 2024), of 649 pts randomized (TIS+CT n=326; PBO +CT n=323), 88 had LA ESCC (TIS+CT n=49; PBO+CT n=39; median age 66.0 yrs; 85.2% male). At a minimum 45-month follow-up, efficacy was improved in pts with LA ESCC compared to the ITT population. The median OS for TIS+CT was 25.6 months (95% CI: 19.4, 36.3) vs 12.3 months (95% CI: 9.0, 21.7) for PBO+CT (HR, 0.49; 95% CI: 0.29, 0.84). Median PFS for TIS+CT was 9.7 months (95% CI: 6.9, 19.6) compared to 6.9 months (95% CI: 4.2, 9.7) for PBO +CT (HR, 0.56; 95% CI: 0.31, 1.01). The ORR was 61.2% (30 of 49 pts) for TIS+CT compared to 38.5% (15 of 39 pts) for PBO+CT.

Tolerability in the LA ESCC subgroup was consistent with the ITT population, with no new safety signals. Treatment-related adverse events with TIS+CT vs PBO+CT were 100.0% vs 92.3% (any grade), 59.2% vs 59.0% (grade ≥3), and 28.6% vs 20.5% (serious), respectively.

Conclusions: In this subgroup analysis of pts with LA ESCC, first-line TIS+CT showed substantial and clinically meaningful improvements in efficacy, with tolerable safety.