RATIONALE-306 subgroup analysis of patients (pts) with advanced/metastatic esophageal squamous cell cancer (ESCC) and Tumor Area Positivity (TAP) score ≥5%

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ABSTRACT

Background: In RATIONALE-306 (NCT03783442), first-line (1L) tislelizumab (TIS) + chemotherapy (CT) had significant OS benefit vs placebo (PBO) + CT in advanced ESCC at primary analysis and 3-yr follow- up in all pts (HR=0.70, 95% CI: 0.59, 0.83) and pts with a tumor PD-L1 TAP score ≥10% (HR=0.70, 95% CI: 0.52, 0.95). Reflecting the EMA approval of 1L TIS + CT in pts with advanced/metastatic ESCC and a tumor PD-L1 TAP score ≥5%, this abstract reports the clinical outcomes in this subgroup.

Methods: RATIONALE-306 has been previously described. Briefly, pts with advanced ESCC were randomized 1:1 to IV TIS 200 mg or PBO every 3 weeks + investigator-chosen CT (platinum + fluoropyrimidine or paclitaxel) until disease progression or intolerable toxicity. Primary endpoint was OS; secondary endpoints were PFS, ORR, DoR, and safety/tolerability. PD-L1 was assessed by TAP score via VENTANA (SP263) Assay, then by combined positive score (CPS).

Results: Of 649 pts randomized (TIS + CT n=326; PBO + CT n=323), 358 (55.2%) had a tumor PD-L1 TAP score ≥5% (TIS + CT n=172; PBO + CT n=186). At 45.2 mo follow-up (database lock: Aug 22, 2024), this subgroup had continued improvement in efficacy outcomes with TIS + CT vs PBO + CT (**Table**). TAP score 5% and CPS 5 cutoffs had 84.9% overall percentage agreement, showing substantial concordance. The tolerability profile in this subgroup had no new safety signals. Treatment (tx)-related adverse events (TRAEs) with TIS + CT vs PBO + CT were 97.7% vs 98.4% for any grade, 70.2% vs 66.5% for grade ≥3, and 29.2% vs 20.5% for serious TRAEs. TRAEs led to death in 2.9% vs 1.6%; tx-emergent adverse events led to discontinuation in 34.5% vs 23.2% in the TAP ≥5% subgroup, similar to the overall population.

Conclusions: In RATIONALE-306, efficacy and safety outcomes of 1L TIS + CT in pts with ESCC and a tumor TAP score ≥5% remained consistent with primary analysis and 3-yr follow-up results, demonstrating clinically meaningful and sustained improvement.

	TIS + CT PD-L1 TAP score ≥5% (n=172)	PBO + CT PD-L1 TAP score ≥5% (n=186)
Median OS, mo **(95% CI)**	19.1 (16.1, 24.1)	10.0 (8.6, 11.9)
HR (95% CI)	0.61 (0.48, 0.78)	-
Median PFS[a], mo **(95% CI)**	8.2 (7.0, 9.8)	5.5 (4.3, 6.4)
HR (95% CI)	0.50 (0.39, 0.65)	-
ORR[a], n (%)	123 (71.5)	77 (41.4)
Median DoR[a], mo **(95% CI)**	7.1 (5.8, 9.7)	5.4 (4.1, 5.8)

[a]Investigator assessed. DoR, duration of response; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.