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

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ABSTRACT

Background: In RATIONALE-306 (NCT03783442), pts with metastatic/locally advanced ESCC were randomized to IV TIS 200 mg or PBO every 3 weeks + investigator-chosen CT (platinum + fluoropyrimidine/paclitaxel) until disease progression or intolerable toxicity. The primary endpoint of improvement in overall survival (OS) was met in all pts and in pts with PD-L1 Tumor Area Positivity (TAP) score ≥10%. At 3-year follow-up, improvement was sustained in TIS + CT (HR=0.70, 95% CI: 0.59, 0.83), and (HR=0.70, 95% CI: 0.52, 0.95), respectively, vs PBO +CT. We report a post hoc subgroup analysis 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, PFS, objective response rate [ORR]) and safety were analysed.

Results: At data cutoff (Aug 22, 2024), of 649 pts randomized (TIS + CT n=326; PBO + CT n=323; median age 66.0 years; 85.2% male), 88 had LA ESCC (TIS + CT n=49; PBO + CT n=39). At median follow-up (TIS + CT 49.8 mo; PBO +CT 51.2 mo), efficacy with TIS + CT was improved in pts with LA ESCC (Table) compared to the intent-to-treat (ITT) population. Tolerability in the LA ESCC subgroup was consistent with the ITT population, with no new safety signals. Treatment (tx)-related adverse events (TRAEs) 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). TIS vs PBO TRAEs led to death in 2.0% vs 0.0%, and tx-emergent adverse events led to tx discontinuation in 40.8% vs 35.9%. In total, 46.6% of pts (TIS + CT 42.9%; PBO + CT 51.3%) had subsequent anticancer therapy and 23.9% (TIS + CT 18.4%; PBO + CT 30.8%) had subsequent radiation therapy, similar to the ITT population.

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.

	TIS + CT (n=49)	PBO + CT (n=39)
Median OS, mo (95% CI)	25.6 (19.4, 36.3)	12.3 (9.0, 21.7)
HR (95% CI)	0.49 (0.29, 0.84)	-
Median PFS[a], mo (95% CI)	9.7 (6.9, 19.6)	6.9 (4.2, 9.7)
HR (95% CI)	0.56 (0.31, 1.01)	-
ORR[a], n (%)	30 (61.2)	15 (38.5)
Time to response[a], mo (range)	1.4 (1.2-23.3)	2.6 (1.2-4.2)

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