Tislelizumab (TIS) + chemotherapy (CT) vs placebo (PBO) + CT as first-line treatment for locally advanced (LA), unresectable esophageal squamous cell carcinoma (ESCC): PD-L1 Tumor Area Positivity (TAP) score ≥1% subgroup analysis of RATIONALE-306

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ABSTRACT

Background

In RATIONALE-306 (NCT03783442), patients (pts) with LA unresectable or metastatic ESCC who received TIS (intravenously, 200 mg, every 3 weeks) + CT (platinum + fluoropyrimidine or paclitaxel) had longer median overall survival (OS) than pts who received PBO + CT at the interim analysis; improvement was maintained after a ≥3-year follow-up. Post hoc analyses in the PD-L1 TAP ≥1% subgroup showed clinically meaningful improvement with TIS + CT. These data supported the US FDA approval for unresectable or metastatic ESCC. Here we report the subgroup analysis of pts who had LA ESCC with PD-L1 TAP score ≥1%.

Methods

Pts who had LA unresectable ESCC with PD-L1 TAP score ≥1% were included in this post hoc analysis. Efficacy outcomes (OS, progression-free survival [PFS], objective response rate [ORR], duration of response [DoR]) and safety were analyzed.

Results

At data cutoff (Feb 28, 2022), of 649 pts randomized, 63 had LA ESCC with PD-L1 TAP score ≥1% (TIS + CT n=31; PBO + CT n=32; median age 67.0 years; 85.7% male). At median follow-up (TIS + CT 24.4 months; PBO + CT 24.5 months), efficacy with TIS + CT was improved vs PBO + CT (**Table**) and was consistent with the intent-to-treat (ITT) population. Efficacy was maintained after a ≥3-year follow-up (data cutoff: Nov 24, 2023; **Table**).

Tolerability of TIS + CT in this subgroup was consistent with the overall safety analysis set, with no new safety signals. Treatment-related adverse events (TRAEs) with TIS + CT vs PBO + CT were 100.0% vs 96.9% (any grade), 45.2% vs 62.5% (grade ≥3), and 22.6% vs 25.0% (serious). TRAEs led to death in 6.5% vs none, and treatment-emergent AEs led to treatment discontinuation in 38.7% vs 37.5%. Safety results were consistent after a ≥3-year follow-up.

Conclusions

In this post-hoc analysis, the median OS for pts receiving TIS + CT exceeded two years. The regimen was well tolerated. While the findings require validation in future clinical trials, first-line TIS + CT is an encouraging option for pts who have LA unresectable ESCC with PD-L1 TAP score ≥1%.

Table

	Interim Analysis		3-Year Follow-up	
	TIS + CT (n=31)	**PBO + CT (n=32)**	**TIS + CT (n=32)[e]**	**PBO + CT (n=31)[f]**
Median OS, mo (95% CI)	25.6 (15.3, NE)	11.5 (9.0, 21.8)	25.6 (15.3, NE)	12.3 (9.0, 21.8)
HR (95% CI)[a]	0.36 (0.17, 0.77)	–	0.50 (0.26, 0.95)	–
Median PFS,[a] mo (95% CI)	13.2 (6.8, NE)	6.7 (4.2, 9.7)	13.2 (6.8, 27.7)	6.7 (4.2, 9.7)
HR (95% CI)[a]	0.46 (0.22, 0.96)	–	0.47 (0.23, 0.96)	–
ORR,[b,c] n (%)	18 (58.1)	10 (31.3)	19 (59.4)	10 (32.3)
Median DoR,[b,d] mo (95% CI)	Not reached (8.4, NE)	5.7 (1.5, 9.6)	22.1 (6.1, NE)	5.7 (1.5, 9.6)

[a]Stratified. [b]Investigator assessed. [c]Unconfirmed. [d]Based on unconfirmed ORR. [e]One patient's disease status at baseline was changed to LA after interim analysis. [f]One patient's disease status at baseline was changed to metastatic after interim analysis. NE, not estimable.