Tislelizumab (TIS) plus chemotherapy (CT) vs placebo (PBO) plus CT as first-line (1L) treatment for recurrent or metastatic nasopharyngeal cancer (NPC): 3-year follow-up from the RATIONALE-309 study

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ABSTRACT

Background: The RATIONALE-309 study met its primary endpoint at interim analysis, with 1L TIS + CT demonstrating statistically and clinically superior progression-free survival (PFS) compared to PBO + CT for patients (pts) with recurrent or metastatic NPC. Here we report longer follow-up results.

Methods: Treatment-naïve pts with recurrent or metastatic NPC were randomly assigned 1:1 to receive TIS 200 mg intravenously or PBO with gemcitabine + cisplatin every 3 weeks (Q3W) for 4-6 cycles, followed by TIS or PBO Q3W until disease progression (PD), unacceptable toxicity or withdrawal. After independent review committee (IRC)-confirmed PD, pts in the PBO arm could cross over to receive TIS alone. The primary endpoint was IRC-assessed PFS (PFS_{IRC}). Secondary endpoints included overall survival (OS), investigator-assessed PFS, time to second PD or death (PFS2) and safety. Efficacy analyses were done in the intent-to-treat population.

Results: 263 pts were randomized (TIS + CT, n=131; PBO + CT, n=132). At data cutoff (Dec 8, 2023; median follow-up: 27.5 mo), sustained PFS_{IRC} improvement for TIS + CT was shown, with stratified HR (95% CI) of 0.53 (0.39, 0.71). Median PFS_{IRC} (95% CI) was 9.6 (7.6, 11.6) mo for TIS + CT and 7.4 (5.6, 7.6) mo for PBO + CT. TIS + CT demonstrated clinically meaningful OS improvement, with stratified HR of 0.73 (0.51, 1.05). Median OS (95% CI) was 45.3 (33.4, not estimable [NE]) mo for TIS + CT and 31.8 (25.0, NE) mo for PBO + CT. The impact of high in-study crossover (52.3%) on OS was assessed: stratified HR with the Rank-Preserving Structural Failure Time Model was 0.56 (0.27, 1.19) and with the two-stage method was 0.62 (0.40, 0.97) for TIS + CT vs PBO + CT. Median PFS2 (95% CI) was 45.3 (31.5, NE) mo for TIS + CT and 20.5 (13.9, 27.2) mo for PBO + CT; unstratified HR, 0.51 (0.34, 0.75). No unexpected safety signals were identified.

Conclusions: At 3-year follow-up in RATIONALE-309, TIS + CT continues to demonstrate sustained PFS benefit and clinically meaningful improvement in OS and PFS2 vs PBO + CT despite a high rate of crossover, with an acceptable safety profile, providing evidence for TIS as an effective 1L treatment option for pts with recurrent or metastatic NPC.