Tislelizumab (TIS) combined with chemotherapy (CT) as first-line (1L) therapy for locally advanced or metastatic non-squamous non-small cell lung cancer (LA/M nsq-NSCLC): programmed death-ligand 1 (PD-L1) expression ≥50% subgroup analysis of the randomized, phase 3 RATIONALE-304 trial

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ABSTRACT

Background: The open-label phase 3 RATIONALE-304 study (NCT03663205) compared the efficacy and safety of 1L TIS (a programmed cell death protein-1 inhibitor) plus CT (TIS+CT) vs CT in LA/M nsq-NSCLC. This analysis focused on patients (pts) from RATIONALE-304 with PD-L1 expression ≥50%.

Methods: Pts with histologically confirmed stage IIIB/IV nsq-NSCLC were randomized (2:1) to 4-6 cycles of TIS + platinum-based CT and pemetrexed every 3 weeks (Q3W), followed by maintenance TIS and pemetrexed, or platinum-based CT and pemetrexed Q3W followed by maintenance pemetrexed. Progression-free survival (PFS) assessed by independent review committee (IRC) was the primary endpoint; secondary endpoints included overall survival (OS), objective response rate (ORR), duration of response (DoR), and safety.

Results: The PD-L1 ≥50% population included 110 pts (TIS+CT, n=74; CT, n=36). At 16.5 months of median study follow-up (range 0.0-26.9 months), TIS+CT improved PFS compared with CT alone (stratified hazard ratio [HR]=0.31; 95% confidence interval [CI]: 0.18, 0.55), with median PFS (95% CI) of 14.6 months (11.5 months, not estimable [NE]) vs 4.6 months (3.5, 9.7 months), respectively. Median OS was NE for TIS+CT vs 13.1 months (HR=0.39; 95% CI: 0.22, 0.71) for CT. An ad hoc analysis at 23.4 months of median follow-up indicated median (95% CI) OS for TIS+CT of 43.4 months (24.2 months, NE) vs 13.1 months (5.6, 19.4 months) for CT (stratified HR=0.34; 95% CI: 0.21, 0.57). The confirmed ORR_{IRC} was 70.3% (95% CI: 58.5%, 80.3%) for TIS+CT and 30.6% (95% CI: 16.3%, 48.1%) for CT. Long-term exposure analysis (≥35 cycles) revealed a 4-year OS rate of 90.5% (95% CI: 67.0%, 97.5%), an ORR_{IRC} of 100%, and median DoR not reached (95% CI: 29.6 months, NE) for TIS+CT. The safety profile of TIS+CT was manageable and consistent with previous analyses.

Conclusion: In pts with LA/M nsq-NSCLC and PD-L1 expression ≥50%, 1L TIS+CT demonstrated clinically meaningful improvement in PFS, OS, ORR, and DoR, and a manageable safety profile compared with CT.