Randomized Phase 3 Study of Tislelizumab Plus Chemotherapy Versus Chemotherapy Alone as First-Line Treatment for Advanced Non-Squamous Non-Small Cell Lung Cancer (nsq-NSCLC): RATIONALE-304 Updated Analysis

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Background: Interim analysis of the open-label phase 3 RATIONALE-304 study (NCT03663205) demonstrated clinical benefit of tislelizumab (TIS) plus chemotherapy (chemo) as first-line (1L) therapy in patients with advanced nsq-NSCLC vs chemo alone, with significantly improved progression-free survival (PFS) and a manageable safety profile. Here, we report the updated results.

Methods: Adults with treatment-naive, stage IIIB (not amenable to curative surgery/radiotherapy)/IV nsq-NSCLC were randomized (2:1) to receive platinum (carboplatin or cisplatin) and pemetrexed (PEM) every 3 weeks either with TIS (Arm A) or without (Arm B), followed by maintenance TIS + PEM (Arm A) or PEM (Arm B). The primary endpoint was PFS in Arm A vs Arm B, per independent review committee (IRC). Secondary endpoints included overall survival, objective response rate (ORR), duration of response (DoR), and safety.

Results: As of 15 July 2022, the median PFS per IRC was 9.8 (95% confidence interval [CI]: 8.9, 11.7) vs 7.6 (95% CI: 5.4, 8.0) months (mo) in Arm A vs Arm B, respectively (stratified hazard ratio 0.61 [95% CI: 0.46, 0.82]). ORR was greater in Arm A (51.6% [95% CI: 44.8, 58.3]) vs Arm B (27.9% [95% CI: 19.8, 37.2]) and median DoR was longer (14.5 [95% CI: 10.1, 24.4] vs 8.4 [95% CI: 6.0, 15.5] mo, respectively). TIS plus chemo was tolerable with no new safety signals identified after longer follow-up. The incidences of ≥grade 3 treatment-emergent adverse events (TEAEs) and of TEAEs leading to death (including disease progression-related AEs) in Arm A and Arm B were 69.4% and 56.4%, and 4.1% and 1.8%, respectively.

Conclusions: In RATIONALE-304, the addition of TIS to platinum plus PEM continued to demonstrate favorable efficacy and was generally well tolerated as 1L treatment of advanced nsq-NSCLC vs chemo alone, with no new safety signals identified.