Randomized Phase 3 Study of Tislelizumab Plus Chemotherapy Versus Chemotherapy Alone as First-Line Treatment for Advanced Squamous Non-Small Cell Lung Cancer (sq-NSCLC): RATIONALE-307 Updated Analysis

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Background: Interim analysis of the open-label phase 3 RATIONALE-307 study (NCT03594747) demonstrated clinical benefit, including significantly improved progression-free survival (PFS) with a manageable safety profile, of tislelizumab (TIS) plus chemotherapy (chemo) as first-line (1L) therapy in patients (pts) with advanced sq-NSCLC vs chemo alone. Here, we report updated results.

Methods: Adults with previously untreated stage IIIB (not amenable to curative surgery/radiotherapy)/IV sq-NSCLC were randomized (1:1:1) to intravenous TIS (200mg, 21-day cycles) + paclitaxel + carboplatin (Arm A); TIS + nab-paclitaxel + carboplatin (Arm B); or paclitaxel + carboplatin (Arm C). The primary endpoint was PFS in Arms A and B vs Arm C, per independent review committee (IRC). Secondary endpoints included overall survival, objective response rate (ORR), duration of response (DoR), and safety.

Results: As of 30 September 2020 (median follow-up 16.7 months), of 360 randomized pts, 355 received treatment. The updated median (95% confidence interval [CI]) PFS benefit was maintained for Arms A (7.7 [95%CI: 6.7, 10.4] months [mo], stratified hazard ratio [HR] 0.45 [95%CI: 0.33, 0.62]) and B (9.6 mo [95%CI: 7.4, 10.8], HR 0.43 [95%CI: 0.31, 0.60]) vs C (5.5 mo [95%CI: 4.2, 5.6]). Consistent improvements in ORR in Arms A (74.2% [95%CI: 65.4, 81.7]) and B (73.9% [95%CI: 65.1, 81.6]) vs C (47.9% [95%CI: 38.8, 57.2]) were observed. Median DoR in Arms A and B was 8.4 (95%CI: 5.0, 15.8) mo and 8.6 (95%CI: 7.1, 12.5) mo, respectively vs 4.3 (95%CI: 2.9, 5.4) mo in Arm C. The incidences of any grade (Arm A 100%; Arm B 99.2%; Arm C 100%) or ≥grade 3 (Arm A 89.2%; Arm B 87.3%; Arm C

84.6%) treatment-emergent adverse events (TEAE) were similar between arms. The rate of treatment discontinuation due to TEAE was similar between Arms A (17.5%) and C (15.4%), and lower than in Arm B (32.2%). No new safety signal was identified.

Conclusions: In RATIONALE-307, the addition of TIS to chemo continued to demonstrate clinical benefit as 1L treatment of advanced sq-NSCLC vs chemo alone after a longer follow-up, with a manageable safety profile.