RATIONALE 304: Tislelizumab Plus Chemotherapy Versus Chemotherapy Alone as First-Line Treatment for Nonsquamous Non-Small Cell Lung Cancer in Patients Aged 65-75 Years

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Abstract:

Objectives: Primary results from the phase 3 RATIONALE-304 study (NCT03663205) showed efficacy and a manageable safety/tolerability profile for tislelizumab, an anti-programmed cell death 1 monoclonal antibody, plus chemotherapy, as first-line treatment for nonsquamous non-small cell lung cancer (NSCLC). We report results from patients aged 65-75 years.

Methods: In RATIONALE-304, eligible patients (18-75 years) were treatment-naïve and had locally advanced or metastatic nonsquamous NSCLC. Patients were stratified by disease stage and programmed cell death ligand 1 expression and randomized 2:1 to receive tislelizumab (200 mg intravenously [IV]) plus platinum (carboplatin AUC 5 or cisplatin 75 mg/m^2 IV) plus pemetrexed 500 mg/m^2 every 3 weeks for 4-6 cycles followed by maintenance tislelizumab plus pemetrexed (Arm A), or platinum pemetrexed for 4-6 cycles followed by maintenance pemetrexed (Arm B). Progression-free survival (PFS) by independent review committee (IRC), objective response rate (ORR), and safety were assessed in patients aged 65-75 years.

Results: In total, 97 patients aged 65-75 years were randomized to Arm A (60 patients) or Arm B (37 patients). The median age of patients was 68.0 years, and 76 patients (78.4%) were male. PFS was longer, and ORR higher, in Arm A versus Arm B (**Table**). Overall, 59 patients in Arm A and 37 patients in Arm B experienced ≥1 treatment-emergent adverse event (TEAE). In Arm A, grade ≥3 TEAEs occurred in 43 (72.9%) patients aged 65-75 years versus 150 (67.6%) aged ≥18 years, and in Arm B, 18 (48.6%) patients aged 65-75 years versus 59 (53.6%) patients aged ≥18 years. TEAEs leading to permanent discontinuation of any component of study treatment occurred in 19 (32.2%) patients in Arm A

and five (13.5%) patients in Arm B. Twenty-one (35.6%) patients receiving tislelizumab experienced ≥1 immune-related TEAE.

Conclusions: Observed improvements in PFS and ORR support the treatment benefits of tislelizumab in combination with platinum and pemetrexed chemotherapy in patients aged 65-75 with advanced nonsquamous NSCLC. The safety profile of tislelizumab in patients aged 65-75 years was similar to the safety profile for all patients in the overall study population.

Table

	Arm A (N=60)	**Arm B (N=37)**
PFS		
Events (%)	27 (45.0)	20 (54.1)
Hazard ratio (95% CI)	0.727 (0.407, 1.297)	-
Median, months (95% CI)	9.7 (5.75, 11.53)	7.7 (4.21, 9.76)
ORR, % (95% CI)	53.3 (40.0, 66.3)	40.5 (24.8, 57.9)