RATIONALE 304: Tislelizumab + Chemotherapy vs Chemotherapy Alone as First-line Treatment for Locally Advanced/Metastatic Nonsquamous Non-Small Cell Lung Cancer (nsq-NSCLC)

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Background: Tislelizumab + chemotherapy has shown antitumor activity with a favorable tolerability profile in patients with histologically confirmed nsq-NSCLC.

Methods: In this open-label phase 3 study (NCT03663205), Chinese patients were randomized 2:1 to receive tislelizumab 200 mg + platinum (carboplatin AUC 5 or cisplatin 75 mg/m²) + pemetrexed 500 mg/m², followed by maintenance tislelizumab + pemetrexed (Arm A) or platinum + pemetrexed and maintenance pemetrexed (Arm B). Patients with known EGFR mutations or ALK rearrangement were ineligible. Patients were stratified by disease stage (IIIB vs IV) and tumor cell PD-L1 expression (<1% vs 1-49% vs ≥50%) assessed using the VENTANA PD-L1 (SP263) Assay. Platinum was administered for 4-6 cycles at investigator’s discretion; crossover to tislelizumab was allowed. Treatment beyond progression was allowed for tislelizumab. The primary endpoint, progression-free survival per RECIST v1.1, was assessed by Independent Review Committee (PFSIRC); key secondary endpoints included objective response rate (ORRIRC) and safety/tolerability.

Results: As of 23 Jan 2020, 334 patients with nsq-NSCLC (A, n=223; B, n=111) were randomized; median study follow-up was 9.8 months (95% CI: 9.23, 10.38). PFSIRC was significantly longer with tislelizumab combination therapy than chemotherapy alone (P=0.0044; HR=0.645 [95% CI: 0.462, 0.902]; median PFSIRC: 9.7 months vs 7.6 months). ORRIRC was 57% (95% CI: 50.6, 64.0) and 37% (95% CI: 28.0, 46.6) in Arms A and B,

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respectively. In Arm A, 221 patients (99.5%) had a treatment-related adverse event (TRAE); 185 patients (83%) had adverse events (AEs) related to tislelizumab. Of 140 patients (63%) with grade ≥3 TRAEs in Arm A, 69 (31%) were considered related to tislelizumab by the investigator. In Arm B, 107 patients (97%) had a TRAE, 50 of which (46%) were grade ≥3. Discontinuation from all study drugs due to an AE occurred in 7.6% (Arm A) and 7.2% (Arm B) of patients.

**Conclusion:** Tislelizumab + chemotherapy was generally well tolerated and demonstrated antitumor activity in patients with nsq-NSCLC.