

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 (PFS_{IRC}); key secondary endpoints included objective response rate (ORR_{IRC}) 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). PFS_{IRC} was significantly longer with tislelizumab combination therapy than chemotherapy alone ($P=0.0044$; HR=0.645 [95% CI: 0.462, 0.902]; median PFS_{IRC}: 9.7 months vs 7.6 months). ORR_{IRC} was 57% (95% CI: 50.6, 64.0) and 37% (95% CI: 28.0, 46.6) in *Arms A* and *B*,

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.