Tislelizumab + Chemotherapy vs Chemotherapy Alone as First-line Treatment for Locally Advanced/Metastatic Nonsquamous NSCLC (nsq-NSCLC)

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

Methods In this open-label phase 3 study (NCT03663205), Chinese pts were randomized 2:1 to receive tislelizumab 200 mg + platinum (carboplatin AUC 5 or cisplatin 75 mg/m^2) + pemetrexed 500 mg/m^2, 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 overall survival (OS), objective response rate (ORR_{IRC}), duration of response (DoR_{IRC}), and safety/tolerability.

Results As of 23 Jan 2020, 334 pts with nsq-NSCLC (*A*, n=223; *B*, n=111) were randomized; median study follow-up was 9.8 mo (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 mo vs 7.6 mo). ORR_{IRC}

was 57% (95% CI: 50.6, 64.0) and 37% (95% CI: 28.0, 46.6) in *Arms A* and *B*, respectively. Median DoR in *Arm A* was 8.5 mo (95% CI: 6.80, 10.58) and 6.0 mo (95% CI: 4.99, NE) in Arm *B*. In *Arm A*, 221 pts (99.5%) had a treatment-related AE (TRAE); 185 pts (83%) had AEs related to tislelizumab. Of 140 pts (63%) with grade ≥3 TRAEs in *Arm A*, 69 (31%) were considered related to tislelizumab by the investigator. In *Arm B*, 107 pts (97%) had a TRAE, of which 50 (46%) were grade ≥3. Across the entire study, four pts (1%) had fatal pneumonitis; 3 of which were considered possibly related to tislelizumab.

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