Phase 3 Study of Tislelizumab Plus Chemotherapy vs Chemotherapy Alone as First-line (1L) Treatment for Advanced Squamous Non-Small Cell Lung Cancer (sq NSCLC)

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Background Tislelizumab is an anti-PD-1 antibody engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis. Tislelizumab in combination with chemotherapy has demonstrated a manageable tolerability profile and preliminary efficacy as 1L treatment for NSCLC.

Methods In this open-label phase 3 study (NCT03594747), Chinese pts with histologically confirmed stage IIIB or IV sq NSCLC were randomized (1:1:1) to receive IV Q3W: tislelizumab (200 mg, D1) + paclitaxel (P; 175 mg/m^2, D1) and carboplatin (carb; AUC 5, D1) (*Arm A*); tislelizumab + *nab*-P (100 mg/m^2; D1, 8, and 15) and carb (AUC 5, D1) (*Arm B*); or P (175 mg/m^2, D1) and carb (AUC 5, D1) (*Arm C*). Chemotherapy was administered for 4-6 cycles followed by tislelizumab. Patients were stratified by tumor stage and PD-L1 expression. The primary endpoint, PFS per RECIST v1.1, was assessed by Independent Review Committee; key secondary endpoints included OS, ORR, DoR, and safety/tolerability.

Results Across 360 pts, median PFS was significantly improved with tislelizumab plus chemotherapy (*Arms A* and *B*) compared with chemotherapy alone (*Arm C*) (**Table**). As of 6 Dec 2019, ORRs were higher and median DoRs were longer in *Arms A* and *B* vs *Arm C*. Across all arms, median OS was not reached and median number of treatment cycles were comparable. Adverse events (AEs) leading to discontinuation of any treatment were reported in 12.5%, 29.7%, and 15.4% of pts in *Arms A*, *B*, and *C*, respectively. The most commonly reported grade ≥3 AEs were hematologic in nature (eg, neutropenia) and consistent with known chemotherapy AEs. Serious treatment-related AEs (TRAEs) were reported in 72 pts (37.5% [*A*]; 38.9% [*B*]; 23.6% [*C*]); TRAEs leading to death were reported in 6 pts (n=1 [*A*]; n=2 [*B*]; n=3 [*C*]), none of which were solely attributed to tislelizumab.

Conclusions As 1L treatment for advanced sq NSCLC, addition of tislelizumab to P/carb or *nab*-P/carb chemotherapy significantly improved PFS and showed higher ORR and longer DoR than chemotherapy alone. The safety profile is in line with the known profiles of tislelizumab, chemotherapy, and underlying NSCLC; no new safety signals were identified with addition of tislelizumab to chemotherapy.

	Arm A **(n=120)**	***Arm B*** **(n=119)**	***Arm C*** **(n=121)**
Median PFS, mo (95% CI)	7.6 (6.0-9.8)	7.6 (5.8-11.0)	5.5 (4.2-5.7)
Stratified HR (95% CI)	0.52 (0.4-0.7)	0.48 (0.3-0.7)	NA
P-value	0.0001	<0.0001	
ORR, % (95% CI)	72.5 (63.6, 80.3)	74.8 (66.0, 82.3)	49.6 (40.4, 58.8)
Median DoR, (95% CI)	8.2 (5.0, NE)	8.6 (6.3, NE)	4.2 (2.8, 4.9)