RATIONALE 307: 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 + chemotherapy has demonstrated antitumor activity and a manageable tolerability profile as 1L treatment for NSCLC.

Methods In this open-label phase 3 study (NCT03594747), 360 Chinese pts with histologically confirmed stage IIIB/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*-paclitaxel (*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 As of 6 Dec 2019, PFS was significantly improved with tislelizumab + chemotherapy (*Arms A* and *B*) vs chemotherapy (*Arm C*; **Table**). ORR was higher and median DoR was longer in *Arms A* and *B* vs *Arm C*. After a median follow-up of 8.6 mos, median OS was not reached in any arm; median number of treatment cycles were comparable. AEs leading to treatment discontinuation 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 TRAEs were reported in 22.5% (A), 23.7% (B), and 14.5% (C) of pts; 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, tislelizumab + chemotherapy significantly improved PFS and showed higher ORR and longer DoR than chemotherapy. The safety profile aligns with the known profiles of tislelizumab, chemotherapy, and underlying NSCLC.

	Arm A **(n=120)**	***Arm B*** **(n=119)**	***Arm C*** **(n=121)**
Median PFS, mo	7.6	7.6	5.5
Stratified HR	0.52	0.48	NA
P-value	0.0001	<0.0001	
ORR, %	72.5	74.8	49.6
Median DoR, mo	8.2	8.6	4.2