Updated Analysis of Tislelizumab Plus Chemotherapy vs Chemotherapy Alone as First-line Treatment of Advanced Squamous Non-Small Cell Lung Cancer (SQ NSCLC)

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Background: Tislelizumab, a monoclonal anti-PD-1 antibody, + chemotherapy was generally well tolerated and had antitumor activity in patients (pts) with advanced NSCLC.

Methods: In this open-label phase 3 study (NCT03594747), 360 Chinese pts with SQ NSCLC (randomized 1:1:1) received IV Q3W: tislelizumab 200 mg (D1) + paclitaxel 175 mg/m^2 (D1) and carboplatin AUC 5 (D1) in *Arm A*; tislelizumab + *nab*-paclitaxel 100 mg/m^2 (D1, 8, and 15) and carboplatin in *Arm B*; or paclitaxel and carboplatin in *Arm C*. Patients were stratified by disease stage (IIIB vs IV) and tumor cell PD-L1 expression (<1% vs 1-49% vs ≥50%) via VENTANA PD-L1 (SP263) Assay. The primary endpoint was PFS (RECIST v1.1) by Independent Review Committee; secondary endpoints included ORR, DoR, OS, and safety/tolerability. Association of blood tumor mutational burden (bTMB) with efficacy was explored.

Results: Combination therapy (*Arms A* and *B*) had significantly improved PFS and higher ORR/DoR vs chemotherapy (*C*). There was no association between PD-L1 expression and PFS or ORR (**Table**). With an optimized bTMB cutoff of 6 mut/Mb (selected by ROC), combination therapy improved PFS over chemotherapy in pts with high- (HR, 0.31; 95% CI: 0.14, 0.67) and low-bTMB (HR, 0.66; 95% CI: 0.27, 1.59). Median OS was not reached in any arm. Discontinuation of any treatment due to AEs was reported in 12.5%, 29.7%, and 15.4% of pts in *Arms A*, *B*, and *C*, respectively. The most common grade ≥3 AE was decreased neutrophil count, in line with known hematological toxicities of chemotherapy. Six

treatment-related AEs led to death (n=1 [*A*]; n=2 [*B*]; n=3 [*C*]); none were solely attributed to tislelizumab.

Conclusions: In pts with SQ NSCLC, combination therapy significantly improved clinical outcomes vs chemotherapy, regardless of PD-L1 expression and bTMB. The safety profile was similar to those of tislelizumab, chemotherapy, and underlying NSCLC, with no new safety signals.

ITT Population N=360	***Arm A* n=120**	***Arm B* n=119**	***Arm C* n=121**
Median PFS, mo	**7.6**	**7.6**	**5.5**
HR[a]	0.52	0.48	
P-value[b]	0.0001	<0.0001	
ORR, %	**72.5**	**74.8**	**49.6**
Median DoR	**8.2**	**8.6**	**4.2**
PD-L1 ≥50% N=125	***Arm A* n=42**	***Arm B* n=42**	***Arm C* n=41**
Median PFS, mo	**7.6**	**7.6**	**5.5**
HR[c]	0.50	0.43	
ORR, %	**78.6**	**88.1**	**53.7**
PD-L1 1-49% N=91	***Arm A* n=30**	***Arm B* n=30**	***Arm C* n=31**
Median PFS, mo	**7.6**	**NE**	**4.2**
HR[c]	0.44	0.31	
ORR, %	**70.0**	**66.7**	**41.9**
PD-L1 <1% N=144	***Arm A* n=48**	***Arm B* n=47**	***Arm C* n=49**
Median PFS, mo	**7.6**	**7.4**	**5.5**
HR[c]	0.64	0.69	
ORR, %	**68.8**	**68.1**	**51.0**

Abbreviations: DoR, duration of response; HR, hazard ratio; ITT, intention-to-treat; mo, months; NE, not evaluable; ORR, objective response rate; PFS, progression-free survival.
[a]Stratified; [b]One-sided log-rank test; [c]Non-stratified.