Tislelizumab Plus Chemotherapy as First-line Treatment for Chinese Patients With Lung Cancer

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Background Tislelizumab, an investigational anti-PD-1 antibody, was engineered to minimize binding to FcγR on macrophages in order to abrogate antibody-dependent phagocytosis, a mechanism of T-cell clearance and potential resistance to anti-PD-1 therapy. Previous reports showed tislelizumab was generally well tolerated and had antitumor activity in patients (pts) with advanced solid tumors.

Method This phase 2 study (NCT03432598) assessed tislelizumab (200 mg Q3W) with platinum (plat)-based chemotherapy (Q3W) as first-line treatment for pts with advanced lung cancer. All pts received tislelizumab + plat for 4-6 cycles (at the investigator's discretion) until disease progression. Nonsquamous (nsq) NSCLC pts received plat + pemetrexed (PMX) for 4 cycles followed by PMX maintenance. Squamous (sq) NSCLC pts received *A*) plat + paclitaxel (PXL) or *B*) plat + gemcitabine; SCLC pts received plat + etoposide. Tumor response (RECIST v1.1) and safety/tolerability were evaluated.

Results As of 25 Feb 2019, 54 pts (median age 61 yr; 74% male; 72% current/former smokers) received tislelizumab; 14 pts remained on treatment. Median follow-up ranged from 12.1 (SCLC) to 15.2 (sq NSCLC [*B*]) mo. Overall, 36 pts achieved a confirmed PR (**Table**); median time to response was 6 wks. Despite long follow-up, neither DoR nor PFS were mature. The most common AEs were anemia (n=44) and decreased neutrophil and white blood cell counts (n=40 each); the most common grade ≥3 AEs were decreased neutrophil count (n=26) and anemia (n=10). Immune-related AEs were reported in 15 pts—the most common were grade ≤2 thyroid disorders (n=9). After one tislelizumab dose, a sq NSCLC pt (*A*) experienced dyspnea, myocarditis, and rhabdomyolysis with a fatal outcome. Other AEs resolved with tislelizumab interruption (n=32), discontinuation (n=5), or other appropriate treatment.

	NSQ (n=16)	SQ (A) (n=15)	SQ (B) (n=6)	SCLC (n=17)	**Total (N=54)**
PR, n	7	12	4	13	36
SD, n	8	2	1	2	13
PD, n	1	0	0	1	2
Missing, n	0	1	1	1	3
ORR, % (95% CI)	**44 (20, 70)**	**80 (52, 96)**	**67 (22, 96)**	**77 (50, 93)**	**67 (53, 79)**
DCR, % (95% CI)	**94 (70, 100)**	**93 (68, 100)**	**83 (36, 100)**	**88 (64, 99)**	**91 (80, 97)**

Conclusion Tislelizumab plus standard of care plat-based chemotherapy was generally well tolerated and demonstrated antitumor activity.