Tislelizumab, an Investigational Anti-PD-1 Antibody, Combined With Chemotherapy as First-line Treatment for Lung Cancer in Chinese Patients

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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; 200 mg IV Q3W was established as the RP2D.

Method This phase 2 clinical trial (NCT03432598) assessed tislelizumab (200 mg Q3W) with platinum (plt)-based chemotherapy (Q3W) as first-line treatment for Chinese pts with advanced lung cancer. All pts received tislelizumab + plt doublet (4–6 cycles) until disease progression. Nonsquamous (nsq) NSCLC pts received pemetrexed (PMX) + plt (4 cycles) followed by PMX maintenance; squamous (sq) NSCLC pts received *A*) paclitaxel (PXL) + plt or *B*) gemcitabine + plt; SCLC pts received etoposide + plt. Tumor response (RECIST v1.1) and safety/tolerability were evaluated. PD-L1 expression was retrospectively assessed with the VENTANA PD-L1 (SP263) assay.

Results As of 15 Oct 2018, 54 pts (median age 61 yr; 74% male; 72% current/former smokers; 31% with ≥10% PD-L1 expression on tumor cells) received tislelizumab; 24 pts remain on treatment. Confirmed PR was observed in 36 pts and most occurred within the first 2 assessments. Other efficacy estimates (eg, PFS) are maturing. Grade ≥3 AEs occurring in >15% of pts were decreased neutrophil counts (n=25) and anemia (n=9); immune-related AEs occurring in ≥2 pts were decreased triiodothyronine, hyperthyroidism, hypothyroidism, and pyrexia (n=2 each). One sq-NSCLC pt (*A*) experienced fatal myocarditis/myositis after 1 cycle; other AEs resolved with tislelizumab interruption (n=30), discontinuation (n=4), or other appropriate treatment.

	NSQ (n=16)	SQ (PXL+plt) (n=15)	SQ (Gem+plt) (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 1st assessment, n	0	1	1	1	3
ORR, % (95% CI)	44 (20, 70)	80 (52, 96)	67 (22, 96)	77 (50, 93)	67 (53, 79)

Conclusion Tislelizumab in combination with standard of care plt-based chemotherapy was generally well tolerated and demonstrated antitumor activity.