Tislelizumab Combined With Chemotherapy as First-Line Treatment in Chinese Patients With Advanced Lung Cancer

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Background

Immune checkpoint inhibitors have shown efficacy in patients with NSCLC as monotherapy and in combination with chemotherapy. Tislelizumab is a humanized IgG4 monoclonal antibody to PD-1 specifically engineered to minimize F_cYR binding on macrophages, possibly minimizing negative interactions with other immune cells. In a phase 1 study, tislelizumab was generally well tolerated and showed antitumor activity; 200mg IV Q3W was established as the recommended dose.

Method

This multi-arm phase 2 study, consisting of safety run-in and dose-extension phases, assessed tislelizumab in combination with platinum-based chemotherapy (by tumor histology) as a potential first-line treatment for Chinese patients with lung cancer. All patients received tislelizumab at 200mg Q3W in combination with 4–6 cycles of platinum-doublet until disease progression. Nonsquamous (nsq) NSCLC patients received pemetrexed + platinum Q3W for 4 cycles followed by pemetrexed maintenance, while squamous (sq) NSCLC patients received paclitaxel + platinum (A) or gemcitabine + platinum (B) Q3W, and small-cell lung cancer (SCLC) patients received etoposide + platinum Q3W. Tumor response (RECIST v1.1) and safety/tolerability were evaluated.

Result

As of 21 Feb 2018, 48 patients (median age, 62 years [range: 36–75], 71% male, 71% current/former smokers) received tislelizumab treatment (median, 3 cycles [range: 1–7]); 44 patients remain on the study. Across the four cohorts, confirmed and unconfirmed partial responses were observed in 13 and 9 patients, respectively (**Table**). The most frequent AEs were chemotherapy-related hematologic toxicities. The most commonly reported grade ≥3 treatment-related AEs were neutropenia (20.8%) and anemia (12.5%); the most common grade 3 immune-related AEs were pyrexia (6.3%) and rash (6.3%). One sq-NSCLC patient experienced a fatal myocarditis/myositis following one cycle of paclitaxel/cisplatin; all other treatment-related AEs were managed/resolved by study-drug interruption (n=15) or discontinuation (n=4) and appropriate treatment.

Best Overall Response (Patients With ≥1 Post-Baseline Tumor Assessment)					
	nsq-NSCLC (n=9)	**sq-NSCLC [A] (n=12)**	**sq-NSCLC [B] (n=5)**	**SCLC (n=8)**	**Total (N=34)**
PR	**4 (44.4)**	**9 (75)**	**4 (80)**	**5 (62.5)**	**22 (64.7)**
Confirmed PR	1 (11.1)	4 (33.3)	4 (80)	4 (50)	13 (38.2)
Unconfirmed PR	3 (33.3)	5 (41.7)	0 (0)	1 (12.5)	9 (26.5)
SD	**3 (33.3)**	**2 (16.7)**	**1 (20)**	**2 (25)**	**8 (23.5)**
PD	**1 (11.1)**	**0 (0)**	**0 (0)**	**1 (12.5)**	**2 (5.9)**
NE	**1 (11.1)**	**1 (8.3)**	**0 (0)**	**0 (0)**	**2 (5.9)**

Data presented as n (%).

Abbreviations: nsq-NSCLC, non-squamous non-small cell lung cancer; NE, not evaluable; PD, progressive disease; PR, partial response; SCLC, small cell lung cancer; SD, stable disease; sq-NSCLC, squamous non-small cell lung cancer.

Conclusion

Tislelizumab, in combination with platinum doublets, demonstrated preliminary antitumor activity and was generally well tolerated in patients with advanced lung cancer.