Safety and Efficacy of Sitravatinib + Tislelizumab in Patients With PD-L1+, Locally Advanced/Metastatic, Squamous NSCLC

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Abstract:

Aims: Sitravatinib, an investigational selective tyrosine kinase inhibitor, reduces the number of myeloid-derived suppressor cells, which promotes expansion of antitumor cytotoxic T cells and increases the ratio of M1/M2-polarized macrophages. Tislelizumab, a clinical-stage anti-PD-1 antibody engineered to minimize binding to FcγR on macrophages, has shown clinical activity in patients with advanced solid tumors.

Methods: In SAFFRON-103 Cohort I (NCT03666143), patients with PD-L1+, locally advanced/metastatic squamous NSCLC without prior systemic treatment in the metastatic setting were enrolled; PD-L1+ was defined as PD-L1 staining on ≥1% of tumor cells (VENTANA SP263 immunohistochemistry assay). Patients with documented *EGFR* mutation, *ALK/ROS1* rearrangement, or *BRAF* mutation were not eligible. Patients received sitravatinib 120mg orally QD plus tislelizumab 200mg intravenously Q3W until unacceptable toxicity, withdrawal, or death. Primary endpoint was safety/tolerability; other endpoints included investigator-assessed ORR, DCR, PFS, and OS.

Results: Between 12/05/2020 and 10/02/2021, 24 patients were enrolled (median age 65.0 years [range: 56-71]; 91.7% male). Median study follow-up was 9.4 months (range: 0.4-16.2). At the data cut-off (08/11/2021), AEs were reported in 100% (any grade) and 66.7% (grade ≥3) of patients. Treatment-related AEs (TRAEs) of any grade or grade ≥3 were observed in 95.8% and 58.3% of patients, respectively; hypertension was the most common grade ≥3 TRAE (16.7%). Serious AEs were observed in 50.0% of patients; AEs led to death in two patients (death, n=1; pneumonia, n=1), neither AE was considered treatment related. Confirmed ORR was 30.4% (95% CI: 13.2, 52.9), with all seven patients achieving partial response; DCR was 78.3% (95% CI: 56.3, 92.5). Median PFS was 5.4 months (95% CI: 2.8, 8.6), while median OS was not reached (95% CI: 6.7, not estimable).

Conclusions: Sitravatinib plus tislelizumab demonstrated a manageable safety/tolerability profile and antitumor activity in systemic therapy-naïve patients with PD-L1+, locally advanced/metastatic squamous NSCLC.

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