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

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Abstract:

Aims: Sitravatinib, an investigational and 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 is a clinical-stage anti-PD-1 antibody engineered to minimize binding to FcγR on macrophages that has shown clinical activity in patients with advanced solid tumors.

Methods: In SAFFRON-103 Cohort H (NCT03666143), patients with PD-L1+, locally advanced/metastatic nonsquamous 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. The primary endpoint was safety/tolerability; other endpoints included investigator-assessed ORR, DCR, PFS, and OS.

Results: Between 07/11/2019 and 23/12/2020, 22 patients were enrolled (median age 60.5 years [range: 41-78]; 68.2% male). Median study follow-up was 11.8 months (range: 0.9-17.9). At the data cut-off (08/11/2021), AEs were reported in 100.0% (any grade) and 59.1% (grade ≥3) of patients. Treatment-related AEs (TRAEs) of any grade or grade ≥3 were observed in 95.5% and 50.0% of patients, respectively; the most common grade ≥3 TRAE was hypertension (13.6%). Serious AEs were reported in 45.5% of patients; two patients experienced TRAEs leading to death (death, n=1; pneumonitis, n=1). Confirmed ORR was 57.1% (95% CI: 34.0, 78.2), with all 12 patients achieving partial response; DCR was 85.7% (95% CI: 63.7, 97.0). Median PFS was 11.1 months (95% CI: 5.5, not estimable [NE]) and median OS was 17.4 months (95% CI: 11.8, NE).

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