Sitravatinib + Tislelizumab in Patients with Anti-PD-(L)1 Refractory/Resistant Metastatic NSCLC

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Background: Patients with metastatic non-small cell lung cancer (NSCLC) who are refractory/resistant (R/R) to anti-PD-(L)1 therapies have limited treatment options. Sitravatinib is a spectrum-selective tyrosine kinase inhibitor targeting TAM and VEGFR2 receptors, which can reduce the number of myeloid-derived suppressor cells, regulatory T cells, and increase the ratio of M1/M2 polarized macrophages, potentially augmenting antitumor immune responses. Tislelizumab, is an anti-PD-1 antibody engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis, a potential mechanism of resistance. This phase 1b study assessed safety/tolerability and antitumor activity of sitravatinib + tislelizumab in solid tumors (NCT03666143). We report results from NSCLC cohorts.

Methods: Eligible patients had metastatic non-squamous (NSQ) or squamous (SQ) NSCLC with radiographic disease progression on/after anti-PD-(L)1 therapy as their most recent treatment. Patients with *EGFR/BRAF* mutations *or ALK/ROS1* rearrangements were ineligible. Treatment included sitravatinib 120 mg orally QD and tislelizumab 200 mg IV Q3W. The primary endpoint was safety and tolerability. Key secondary endpoints included investigator-assessed objective response rate (ORR), duration of response (DoR), disease control rate (DCR) and progression-free survival (PFS).

Results: As of 13 Oct 2020, 47 patients with NSQ (n=24) and SQ (n=23) NSCLC were enrolled with a median study follow-up of 7.8 months (range: 0.4–18.1). Median age was 60 years (range: 25–79) and 72% of patients had ≥2 lines of prior therapies. All patients had a treatment-emergent adverse event (TEAE); 68% had a Grade ≥3 TEAE (most common: hypertension, 19%). Confirmed ORR was 14% (95% CI: 5.2–27.4) and DCR was 86% (95% CI: 72.7–94.8). Median DoR was 6.9 months (95% CI: 3.1–NE). Median PFS was 5.2 months (95% CI: 4.1–5.9). There was no association between PD-L1 expression and clinical response.

Conclusions: Sitravatinib plus tislelizumab demonstrated a manageable safety profile and promising antitumor activity in patients with PD-(L)1 antibody pretreated NSCLC. Further investigation of this combination in these pts is warranted.