Sitravatinib + Tislelizumab in Patients with Metastatic Non-small Cell Lung Cancer (NSCLC)

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Background: Patients (pts) with advanced NSCLC often develop progressive disease, with limited treatments for pts who are heavily pretreated with anti-PD-(L)1 antibodies and/or chemotherapy. 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 increases the ratio of M1/M2 polarized macrophages, potentially augmenting antitumor 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: Pts had confirmed metastatic nonsquamous (NSQ) or squamous (SQ) NSCLC treated with 1–3 lines of prior systemic therapy with/without an anti-PD-(L)1 inhibitor. Pts with *EGFR/ BRAF* mutations or *ALK/ROS1* rearrangements were ineligible. Sitravatinib was given 120 mg orally QD and tislelizumab 200 mg IV Q3W. The primary endpoint was safety/tolerability. Secondary endpoints were objective response rate (ORR), duration of response (DoR), disease control rate (DCR), and progression-free survival (PFS).

Results: On 13 Oct 2020, 75 pts (NSQ, n=46; SQ, n=29) were treated; 47 pts were refractory/resistant (R/R) to PD-(L)1 therapy and 28 pts were PD-(L)1 naïve. Median age was 60 yrs (range: 25–79). Median study follow-up was 10.1 mo (range: 0.4–18.8). All pts had a

treatment-emergent adverse event (TEAE); 73% of pts had a Grade ≥3 TEAE (most common: hypertension [n=12]). Confirmed ORR was 17% (95% CI: 9.1–27.7); DCR was 85% (95% CI: 74.0–92.0). Median DoR was 7.0 mo (95% CI: 2.9–not estimable). Median PFS was 5.5 mo (95% CI: 4.1–7.0). There was a trend toward higher ORR in pts with PD-L1 IC expression ≥10%. In R/R pts confirmed ORR was 14% (95% CI: 5.2–27.4).

Conclusions: Sitravatinib + tislelizumab had a manageable safety profile and demonstrated preliminary antitumor activity in pts with NSQ or SQ NSCLC who were pretreated or naïve to PD-(L)1 treatment. Further investigation in these pts is warranted.