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

Authors: [1]Qing Zhou, [2]Xinmin Yu, [3]Bo Gao, [4]Zhiyong Ma; [5]Qian Chu, [6]Dingzhi Huang, [7]Jun Zhao, [8]Daphne Day, [8]Amy Louise Body, [9]Hongming Pan, [10]Jiuwei Cui, [11]Cheng Chen, [11]Xiao Xiang, [11]Cong Fei, [11]Liu Yang, [12]Yi-Long Wu

Affiliations: [1]Guangdong Lung Cancer Institute, Guangdong General Hospital, and Guangdong Academy of Medical Sciences, Guangzhou, China; [2]Department of Medical Oncology, Cancer Hospital of University of Chinese Academy of Sciences & Zhejiang Cancer Hospital; [3]Blacktown Cancer and Hematology Centre, Blacktown, NSW, Australia; [4]The Affiliated Cancer Hospital of Zhengzhou University/Henan Cancer Hospital, Zhengzhou, China; [5]Department of Oncology, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology; [6]Tianjin Medical University Cancer Institute and Hospital, Tianjin Key Laboratory of Cancer Prevention and Therapy, National Clinical Research Center for Cancer; [7]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education, Beijing), Department of Thoracic Medical Oncology, Peking University Cancer Hospital & Institute, Beijing, China; [8]Monash Health and Monash University, Melbourne, Australia; [9]Sir Run Run Shaw Hospital, Zhejiang University, Hangzhou, China; [10]The First Hospital of Jilin University, Changchun, China; [11]BeiGene (Beijing) Co., Ltd., Beijing, China; [12]Guangdong Provincial Key Laboratory of Translational Medicine in Lung Cancer, School of Medicine, Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital and Guangdong Academy of Medical Sciences, South China University of Technology, Guangzhou 510080, China.

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.