A phase 1b study to assess safety, tolerability, pharmacokinetics, and preliminary antitumor activity of sitravatinib in combination with tislelizumab in patients (pts) with advanced solid tumors

Jun Guo,[1] Qing Zhou,[2] Dingzhi Huang,[3] Xinmin Yu,[4] Jun Zhao,[1] Qian Chu,[5] Zhiyong Ma,[6] Michael Millward,[7] Bo Gao,[8] Jeffrey Goh,[9] Ben Markman,[10] Mark Voskoboynik,[11] Hui Gan,[12] Jermaine Coward,[9] Cheng Chen,[13] Xiao Xiang,[14] Jingjun Qiu,[14] Yingying Xu,[13] Liu Yang,[13] Yi-Long Wu[2]

[1]Beijing Cancer Hospital, Beijing, China; [2]Guangdong General Hospital, Guangzhou, Guangdong, China; [3]Tianjin Medical University Cancer Institute & Hospital, Tianjin, China; [4]Zhejiang Cancer Hospital, Hangzhou, China; [5]Tongji Hospital, Tongji Medical College Huazhong University of Science, Wuhan, China; [6]Henan Cancer Hospital, Zhengzhou, China; [7]University of Western Australia, Crawley, and Linear Clinical Research, Perth, WA, Australia; [8]Blacktown Cancer and Haematology Centre, Blacktown, NSW, Australia; [9]ICON Cancer Foundation, South Brisbane, and University of Queensland, St Lucia, QLD, Australia; [10]Monash Health, Melbourne, VIC, Australia; [11]Nucleus Network, Melbourne, VIC, Australia; [12]Austin Hospital, Heidelberg, VIC, Australia; [13]BeiGene (Shanghai) Co., Ltd., Shanghai, China; [14]BeiGene (Beijing) Co., Ltd., Beijing, China

Background: Sitravatinib is an investigative, orally bioavailable, spectrum-selective receptor tyrosine kinase (RTK) inhibitor with immune modulatory and potential antitumor activity that has been shown to potently inhibit split kinase receptors (eg, VEGFR2, KIT) and TAM receptors (eg, AXL, MER). Tislelizumab is an investigational, humanized IgG4 monoclonal antibody that has been shown to have high affinity and binding specificity for programmed cell death receptor-1 (PD-1). Tislelizumab was engineered to minimize binding to FcγR on macrophages to abrogate antibody-dependent phagocytosis. The primary objective is to examine the safety and tolerability of sitravatinib combined with tislelizumab in pts with advanced solid tumors.

Methods: Adult pts with histologically or cytologically confirmed, locally advanced or metastatic solid tumors are enrolling in the open-label, multicenter, nonrandomized, phase 1b clinical trial. Entry criteria include Eastern Cooperative Oncology Group Performance Status ≤1 and adequate end-organ function. All pts will receive sitravatinib 120 mg PO QD and tislelizumab 200 mg IV Q3W. Pts are to be enrolled in 5 cohorts (n≈20 pts/cohort): Cohort A: anti-PD-(L)1 antibody-refractory/-resistant, metastatic, nonsquamous non-small cell lung cancer (NSCLC); Cohort B: anti-PD-1(L)1 antibody-naive, metastatic, nonsquamous NSCLC; Cohort C: anti-PD-(L)1 antibody-refractory/-resistant, metastatic, clear cell renal cell carcinoma (RCC); Cohort D

(China only): metastatic or advanced RCC without prior therapy; Cohort E: anti-PD-(L)1 antibody-naive, recurrent, platinum-resistant, epithelial ovarian cancer. The primary endpoint is to assess safety and tolerability by monitoring adverse events (AEs) and serious AEs. Secondary endpoints include overall response rate, duration of response, disease control rate, progression-free survival assessed by RECIST version 1.1, and plasma concentrations and derived pharmacokinetic parameters of single- and repeated-dose sitravatinib. Forty pts have enrolled as of 5 June 2019 at the sites in Australia and China.

Clinical trial registry number: NCT03666143